HIV/SIV Vaccine Trials Database 2007

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http://www.hiv.lanl.gov/content/vaccine/home.html

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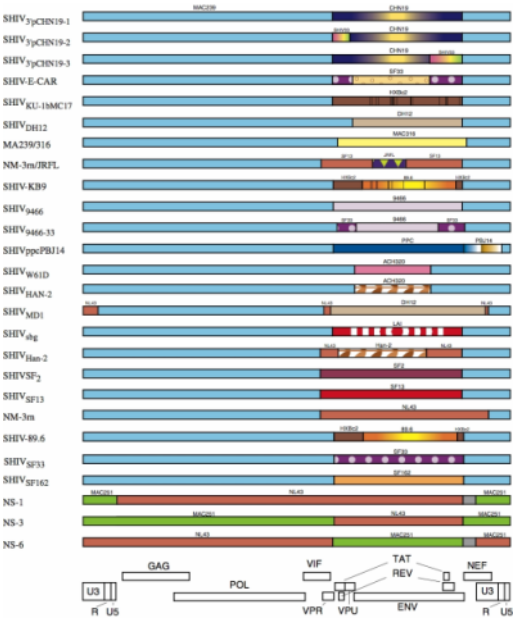
The Cover Image



This figure gives an overview of SHIV strains that are presently in use in the vaccine field, and indicates which section of the genomes are derived from HIV-1 (and which strain of HIV-1), and which from a SIV strain. All isolates have a separate color code, so that identifying the structure and composition of the genome of the strains can be done at a glance. For further information, see Reagents for HIV/SIV Vaccine Studies by Rama Thakallapalli and Carla Kuiken, in the 2001 HIV sequence compendium.

Citing this publication

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I. INTRODUCTION AND HISTORICAL OVERVIEW

The development of an effective vaccine against HIV is urgently needed given the continual increase in the number of people infected with HIV, estimated to be about 40 million, in addition to 25 million people who have already died due to HIV since the beginning of the epidemic two decades ago. A general consensus is that the development of an effective vaccine is the best way to tackle this epidemic. Unfortunately, the effort to develop a good and reliable vaccine against HIV has proven to be difficult. HIV is the most studied infectious agent in medical history. The vaccine research is increasingly becoming an important focus as a large number of data continue to emerge from different laboratories. As of October 2006, a quick search using a string argument containing "HIV OR SIV AND vaccine" yielded 8946 references. Using the search string "((HIV OR SIV) AND vaccine) AND macaque", 990 references were retrieved from PUBMED.

Since traditional approaches for vaccine development have proven ineffective for HIV, it is important to encourage new methodologies and to increase the numbers of studies in order to speed up the process required to develop an effective vaccine against HIV. Consequently, a large number of studies on HIV and SIV-related vaccines are being generated. In addition, studies vary considerably in the way the vaccine trials are being conducted, the design and formulation of vaccines, the doses, the animals used, the challenge viruses, etc. This makes it difficult to adequately compare the studies. It is important to continue to monitor the data generated by researchers working to understand the complexity of HIV pathogenicity and to follow up the ongoing preclinical research in animal models and phase I-III human trials.

To begin to address this problem, we have constructed a relational database named Nonhuman Primate HIV/SIV Vaccine Trials Database to serve the scientific community, particularly those engaged in vaccine development as well as policy makers.

The published data pertaining to HIV vaccine development in nonhuman primate models have been curated and compiled in such a way that users can interactively search and retrieve them online through the internet. For a study to qualify for entry in the database, the trial must meet the following criteria: 1) SIV, SHIV or HIV-based vaccine or passive immunization have been used in nonhuman primates; 2) an assessment for immunogenicity or immunotherapeutic property of the immunogen has been performed. A challenge virus may or may not have also have been injected to the immunized and control animals to assess the efficacy of the vaccine.

Historically, prior to the development of this database, Dr. Jon Warren at the EMMES Corporation had maintained a similar database, though organized differently, and with different data fields and somewhat different nomenclature. The studies in that database include those published through 1999. We have made that database accessible through the internet, and integrated it into the search interface of the Los Alamos National Laboratory vaccine database. This will be available to the public until we have integrated all of those studies into the Los Alamos database.

The Los Alamos Nonhuman Primate HIV/SIV Vaccine Trials Database home page can be accessible at following web page, http://www.hiv.lanl.gov/content/vaccine/home.html, and is depicted in Figure 1.

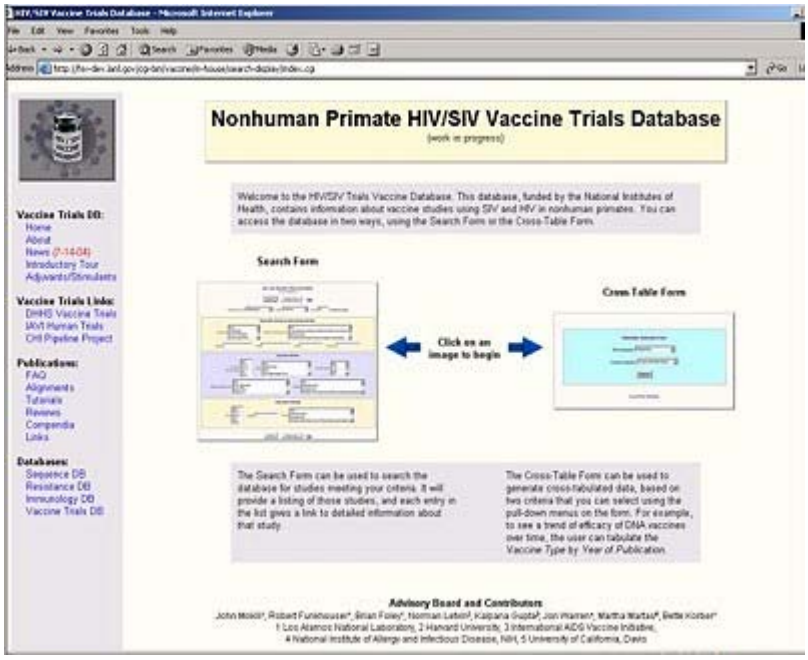

Figure 1: Home page of the Vaccine Trials database

The data in the database can be accessed in two ways, using the Search Form or the Cross-Table Form which are displayed on the home page. The Search Form allows users to retrieve technical information pertaining to vaccine studies using multiple choice menus to construct logical arguments for searching the database. The search argument is a combination of items chosen from the menus which include the study Objectives, the Species or experimental animal model, the Reference, the Vaccine and Challenge virus (Figure 2).

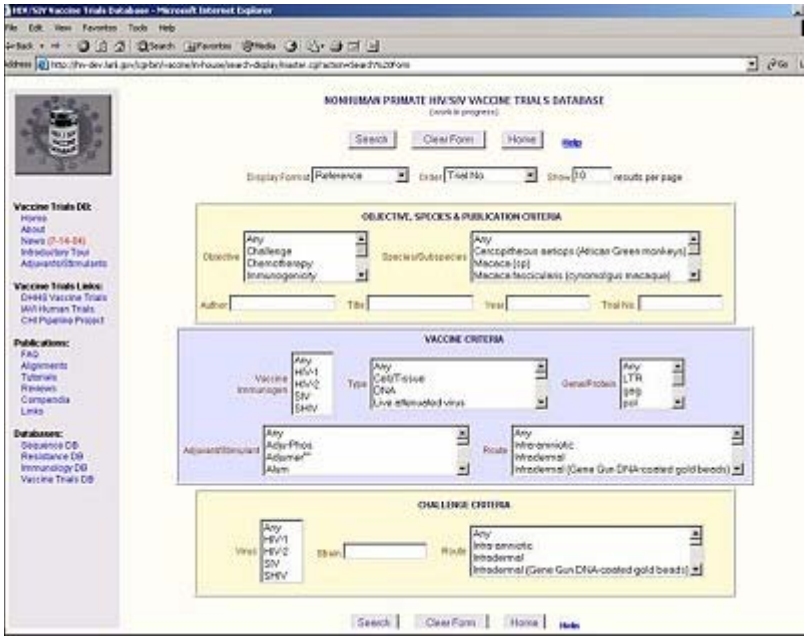

Figure 2: Search Form

The data entered in the database can also be retrieved using the Cross-Table Search Form. This tool was designed to allow users to retrieve data in a cross-tabulated format. For example, as depicted on Figure 3, a tabulation of the origin of vaccine immunogens (HIV-1, HIV-2, SIV or SHIV) by the subtype shows that the great majority of vaccines trials used so far are based on subtype B.

In the example shown in figure 3, the number in each bifurcation box refers to the number of studies in the database and the ratio of animals protected from infection with the challenge virus over the total number of animals immunized and challenged.

	HIV-1 subtype										
Immunogen Origin	**A**	**B**	**C**	**CRF02_AE**	**D**	**F**	**G**	**H**	**J**	**K**	**L**
HIV-1	1	66 [85/321]	1	1	1	0	0	0	0	0	0
HIV-2	0	0	0	0	0	0	0	0	0	0	0
SHIV	0	10 [2/42]	0	0	0	0	0	0	0	0	0
SIV	0	21 [22/142]	0	0	0	0	0	0	0	0	0

Figure 3. Example of an output using the Cross-Table Form. In this specific case, the HIV subtype (across) and the Virus (down) from which the immunogen was based.

Organization and Contents of the Compendium

This vaccine trials compendium is divided in 5 sections:

- Trial Summaries
- Vaccines
- Challenges
- Adjuvants and Stimulants
- References

An introduction is provided at the beginning of each section.

II. TRIAL SUMMARIES

This section contains a listing of studies compiled in the database. There are currently 516 trials in the relational database created at LANL and 218 trials carried over from Jon Warren's database. This listing is a printed version of the results of searching our database with the default settings (find any or all) and the Trial Summary display format. Each summary contains data from the following fields unless they are empty in the database:

1. Trial number
2. Title
3. Authors
4. Citation and PubMed ID number
5. Objectives
6. Species/subspecies
7. Vaccine name, type, formulation and route of inoculation
8. A short description of the vaccine
9. Challenge virus name and route
10. A summary of the main findings

The database itself contains much more detailed information for each trial, including information about each group of animals.

NHP.1 (11726972) **Mucosal AIDS vaccine reduces disease and viral load in gut reservoir and blood after mucosal infection of macaques.**

Authors: Belyakov IM, Hel Z, Kelsall B, Kuznetsov VA, Ahlers JD, Nacsa J, Watkins DI, Allen TM, Sette A, Altman J, Woodward R, Markham PD, Clements JD, Franchini G, Strober W, Berzofsky JA

Journal: Nat Med 2001 Dec;7(12):1320-6.

Objectives: Challenge, Immunogenicity. To compare whether a mucosal vaccine could induce mucosal CTLs and protect rhesus macaques against mucosal infection with SHIV more effectively than the same vaccine given subcutaneously.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: PCLUS3-CL10/PCLUS6.1-CL10/PCLUS3_POL_143/PCLUS3_GAG_372 *Type:* Synthetic Protein/Peptide *Routes:* Intrarectal, Subcutaneous *Formulation:* PCLUS3-CL10/PCLUS6.1-CL10/PCLUS3_POL_143/PCLUS3_GAG_372 + MONTANIDE ISA 51, LT-R192G + Saline, PBS

Challenge: SHIV-KU2 *Route:* Intrarectal

Main Findings:

- Mucosal SIV specific CTL can be induced by intrarectal immunization of macaques with synthetic-peptide vaccine coupled with LT(R192G) adjuvant
- CTL response correlates with helper response
- CD4+ T cells preserved better in animal mucosally immunized than in animals immunized by subcutaneous route and control
- In contrast with subcutaneous immunization, intrarectal immunization reduced viral load to undetectable level

NHP.2 (11282197) **Vaccination with DNA containing tat coding sequences and unmethylated CpG motifs protects cynomolgus monkeys upon infection with simian/human immunodeficiency virus (SHIV89.6P).**

Authors: Cafaro A, Titti F, Fracasso C, Maggiorella MT, Baroncelli S, Caputo A, Goletti D, Borsetti A, Pace M, Fanales-Belasio E, Ridolfi B, Negri DR, Sernicola L, Belli R, Corrias F, Macchia I, Leone P, Michelini Z, ten Haaft P, Butto S, Verani P, Ensoli B

Journal: Vaccine 2001 Apr 6;19(20-22):2862-77.

Objectives: Challenge, Immunogenicity. To test the immunogenicity and protective value of a tat-expressing vector containing defined unmethylated CpG sequences (pCV-tat) in cynomolgus monkeys challenged with SHIV.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: HIV BH10-tat protein *Type:* Recombinant Subunit Protein *Routes:* Intradermal, Intramuscular *Formulation:* HIV BH10-tat protein + PBS

Vaccine Name: pCV-tat *Type:* DNA *Routes:* Intradermal, Intramuscular *Formulation:* pCV-tat + Saline, PBS

Challenge: SHIV89.6P *Route:* Intravenous

Main Findings:

- Intramuscular inoculation of the pCV-tat contained primary infection with HIV89.6P virus
- Control of CD4 T cell decline in all the vaccinated monkeys
- Correlation between undetectable virus replication and negative virus isolation in all cases with anti-tat CTLs
- CD8-mediated non-cytolytic antiviral activity not present in all protected animals
- CpG-rich tat DNA vaccine, potential for cross-clade application in human as a therapeutic and preventive vaccine

NHP.3 (11514732) **Induction of simian immunodeficiency virus (SIV)-specific CTL in rhesus macaques by vaccination with modified vaccinia virus Ankara expressing SIV transgenes: influence of pre-existing anti-vector immunity.**

Authors: Sharpe S, Polyanskaya N, Dennis M, Sutter G, Hanke T, Erfle V, Hirsch V, Cranage M

Journal: J Gen Virol 2001 Sep;82(Pt 9):2215-23.

Objectives: Immunogenicity. To assess the immunogenicity of an MVA vaccine expressing structural and regulatory genes of SIV, and the influence of pre-existing immunity to vector in immunized Mamu A*01 MHC class 1 rhesus monkeys.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: MVA-SIVmacJ5 (gag-pol) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* MVA-SIVmacJ5 (gag-pol) + PBS

Vaccine Name: MVAmacJ5-nef *Type:* Recombinant Vector (virus/bacteria) *Route:* Intraocular *Formulation:* MVAmacJ5-nef + PBS

Vaccine Name: MVA SIVsmH4 gag-pol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intraocular *Formulation:* MVA SIVsmH4 gag-pol + PBS

Main Findings:

- MVA SIVmacJ5 gag-pol construct was poorly immunogenic
- Nab weak and transient
- SIV-specific CTL detected in all animals immunized with MVA-SIV vaccines, 4-8 weeks post immunization (not in control animals). One immunization is enough and boosting does not increase the magnitude of immune response
- MVA-SIVnef produced the strongest response compared to MVA-SIVtat and MVA-SIVrev

NHP.4 (11413371) **Cross-protection against mucosal simian immunodeficiency virus (SIVsm) challenge in human immunodeficiency virus type 2-vaccinated cynomolgus monkeys.**

Authors: Walther-Jallow L, Nilsson C, Soderlund J, ten Haaft P, Makitalo B, Biberfeld P, Bottiger P, Heeney J, Biberfeld G, Thorstensson R

Journal: J Gen Virol 2001 Jul;82(Pt 7):1601-12.

Objectives: Challenge, Immunogenicity. To compare the efficacy of a live attenuated HIV-2 vaccine alone versus boosting with live non-pathogenic HIV-2 following priming with ALVAC HIV-2 (recombinant canarypox virus expressing HIV-2 env, gag and pol).

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: HIV-2 SBL6669 *Type:* Live Virus *Route:* Intravenous

Vaccine Name: ALVAC-HIV-2 (gag,pol,gp125) *Type:* Recombinant Vector (virus/bacteria) *Route:* ND

Vaccine Name: HIV-2 native gp125 *Type:* Purified Viral Products *Route:* ND

Challenge: SIVsm *Route:* Intrarectal

Main Findings:

- Vaccination with an ALVAC HIV-2 vaccine followed by exposure to live HIV-2 could induce cross-protection against mucosal infection with SIVsm and seemed to be more efficient than immunization with a live HIV-2 vaccine only.

NHP.5 (11429125) **A conformational C4 peptide polymer vaccine coupled with live recombinant vector priming is immunogenic but does not protect against rectal SIV challenge.**

Authors: Patterson LJ, Robey F, Muck A, Van Remoortere K, Aldrich K, Richardson E, Alvord WG, Markham PD, Cranage M, Robert-Guroff M

Journal: AIDS Res Hum Retroviruses 2001 Jun 10;17(9):837-49.

Objectives: Challenge, Immunogenicity. To compare SIV peptomer and native gp120 subunit boosts following two adenovirus type 5 host range (Ad5hr)-SIVenv recombinant priming immunizations.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Peptomer SIVmac251 (gp120: 435-452) *Type:* Synthetic Protein/Peptide *Routes:* Subcutaneous, Intramuscular

Vaccine Name: Ad5hr-SIVenv *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Oral, Intranasal *Formulation:* Ad5hr-SIVenv + Water

Vaccine Name: Native SIV gp120 *Type:* Purified Viral Products *Route:* Intramuscular

Challenge: SIVmac251(32H) *Route:* Intrarectal

Main Findings:
- Peptomer immunization elicited peptomer and SIV gp120-specific binding antibodies
- Only native gp120 boosting elicited SIV neutralizing antibodies
- Upon intrarectal challenge with SIVmac32H, all nine macaques became infected
- The solely envelope-based vaccine conferred no protection

NHP.6 (11483779) **Antibody protects macaques against vaginal challenge with a pathogenic R5 simian/human immunodeficiency virus at serum levels giving complete neutralization in vitro.**

Authors: Parren PW, Marx PA, Hessell AJ, Luckay A, Harouse J, Cheng-Mayer C, Moore JP, Burton DR

Journal: J Virol 2001 Sep;75(17):8340-7.

Objectives: Challenge, Immunogenicity. To evaluate the role of passive intravenous transfer of the human neutralizing monoclonal antibody b12 to provide dose-dependent protection to macaques vaginally challenged with the R5 virus SHIV162P4

Species/Subspecies: Macaca (sp)

Vaccine Name: IgG1 b12 *Type:* Passive Antibody *Route:* Intravenous

Challenge: SHIV162P4 *Route:* Vaginal or perivaginal

Main Findings:
- Passive immunization with b12 antibody protects monkeys from challenge with SHIV
- The immunization with b12 antibodies induced sterile protection in vaccinees.

NHP.7 (11287566) **Vaccine-elicited V3 loop-specific antibodies in rhesus monkeys and control of a simian-human immunodeficiency virus expressing a primary patient human immunodeficiency virus type 1 isolate envelope (a)**

Authors: Letvin NL, Robinson S, Rohne D, Axthelm MK, Fanton JW, Bilska M, Palker TJ, Liao HX, Haynes BF, Montefiori DC

Journal: J Virol 2001 May;75(9):4165-75.

Objectives: Challenge, Immunogenicity. To evaluate the role of vaccine elicited antibodies in the protection against SHIV containing the envelope of a primary isolate of HIV.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: C4/89.6-V3 *Type:* Synthetic Protein/Peptide *Route:* Intramuscular

Vaccine Name: C4/89.6P-V3 *Type:* Synthetic Protein/Peptide *Route:* Intramuscular

Challenge: SHIV89.6, SHIV89.6P *Route:* Intravenous

Main Findings:
- SHIV-89.6 not suitable to assess viral set point between vaccinees and controls
- Both peptides (vaccine and mock) were immunogenic- the mock C4/scrbl-V3 was immunogenic due to the presence of C4 fragment in the peptide
- Immunization with the C4/89.6-V3 peptide generated 10-fold-higher titre of V3-specific antibodies than infection with SHIV-89.6
- Neutralization of immunogens (C4/89.6-V3, C4/89.6P) induced Ab were virus specific (SHIV-89.6 and SHIV-89.6P, respectively)

NHP.8 (10655111) **Protection of macaques against vaginal transmission of a pathogenic HIV-1/SIV chimeric virus by passive infusion of neutralizing antibodies.**

Authors: Mascola JR, Stiegler G, VanCott TC, Katinger H, Carpenter CB, Hanson CE, Beary H, Hayes D, Frankel SS, Birx DL, Lewis MG

Journal: Nat Med 2000 Feb;6(2):207-10.

Objectives: Challenge, Passive Immunization. To evaluate the protective effect of HIV-1 specific antibodies using the SHIV-macaque vaginal challenge model.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Monoclonal antibody 2G12 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name: Monoclonal antibody 2F5 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name: HIVIG *Type:* Passive Antibody *Route:* Intravenous

Challenge: SHIV89.6PD *Route:* Vaginal or perivaginal

Main Findings:

- 14 antibody-treated macaques were either completely protected against infection or against pathogenic manifestations of SHIV-infection.
- Some types of antibody response could play a role in protection against mucosal transmission of HIV-1.
- 5/5 control animals were viremic upon SHIV challenge and had decline CD4+ T cells.

NHP.9.1 (11017146) **Viremia control following antiretroviral treatment and therapeutic immunization during primary SIV251 infection of macaques**

Authors: Hel Z, Venzon D, Poudyal M, Tsai WP, Giuliani L, Woodward R, Chougnet C, Shearer G, Altman JD, Watkins D, Bischofberger N, Abimiku A, Markham P, Tartaglia J, Franchini G

Journal: Nat Med 2000 Oct;6(10):1140-6.

Objectives: Challenge, Immunogenicity, Immunotherapy. To explore the effect of therapeutic immunization in the context of ART during primary infection using the simian immunodeficiency virus (SIV251) macaque model.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: NYVAC-SIV-gag-pol-env (NYVAC-SIV-gpe) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Challenge: SIVmac251 *Route:* Intravenous

Main Findings:

- Vaccination of Rhesus macaques with the highly attenuated poxvirus-based NYVAC-SIV vaccine expressing structural genes elicited vigorous virus-specific CD4 + and CD8+ T cell responses in macaques that responded effectively to ART
- Following discontinuation of a six-month ART regimen, viral rebound occurred in most animals, but was transient in six of eight vaccinated animals
- Viral rebound was also transient in four of seven mock-vaccinated control animals

NHP.9.2 (12890631) **Prior DNA immunization enhances immune response to dominant and subdominant viral epitopes induced by a fowlpox-based SIVmac vaccine in long-term slow-progressor macaques infected with SIVmac251.**

Authors: Radaelli A, Nacsa J, Tsai WP, Edghill-Smith Y, Zanotto C, Elli V, Venzon D, Tryniszewska E, Markham P, Mazzara GP, Panicali D, De Giuli Morghen C, Franchini G

Journal: Virology 2003 Jul 20;312(1):181-95.

Objectives: Immunogenicity, Immunotherapy, Chemotherapy. To investigate whether a combination of DNA and recombinant poxvirus vaccine can induce high level of virus-specific CD4+ T-cell response and broadens the cytolytic activity in SIVmac251-infected macaques.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: FP-SIV-gp (FP74) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name: SIV-pcDNA3gag/pol *Type:* DNA *Routes:* Intradermal, Intramuscular

Main Findings:

- The combination of a DNA expressing the gag and pol genes (DNA-SIV-gp) of SIVmac239 followed by a recombinant fowlpox expressing the same SIVmac genes (FP-SIV-gp) was significantly more immunogenic than two immunizations of FP-SIV-gp in SIVmac251-infectedmacaques treated with ART
- The DNA/FP combination significantly expanded and broadened Gag-specific T-cell responses
- The combination of these vaccine modalities also induced a sizeable expansion in most

macaques of Gag-specific CD8-(CD4+) T-cells able to produce TNF-alpha

NHP.10 (11257382) **Expansion of HBV-specific memory CTL primed by dual HIV/HBV genetic immunization during SHIV primary infection in rhesus macaques.**

Authors: Borgne SL, Michel ML, Camugli S, Corre B, Le Grand R, Riviere Y

Journal: Vaccine 2001 Mar 21;19(17-19):2485-95.

Objectives: Challenge, Immunogenicity. To evaluate the humoral and cellular immune response to immunization with HIV/HBV vaccine and the protection against SHIV challenge

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pCMV-V3.S (HBV-HIV vaccine) *Type:* DNA *Route:* Intradermal

Challenge: SHIVsbg0.1 *Route:* Intravenous

Main Findings:

- DNA-immunized primates and control challenged with SHIV were all infected
- Peak viremia correlates with HBV envelop specific CTL precursor detected in primary infection
- HBV or SHIV specific cytotoxicity corresponded in part to CD8 T cells presenting a memory phenotype

NHP.11 (11160726) **Polyvalent envelope glycoprotein vaccine elicits a broader neutralizing antibody response but is unable to provide sterilizing protection against heterologous Simian/human immunodeficiency virus infection in pigtailed macaques.**

Authors: Cho MW, Kim YB, Lee MK, Gupta KC, Ross W, Plishka R, Buckler-White A, Igarashi T, Theodore T, Byrum R, Kemp C, Montefiori DC, Martin MA

Journal: J Virol 2001 Mar;75(5):2224-34.

Objectives: Challenge, Immunogenicity. To compare the breadth of NAb and protective immune response following vaccination of pigtailed macaques with envelope protein(s) derived from either single or multiple viral isolates against the challenge with SHIVDH12

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Vaccine Name: Recombinant vaccinia virus-HIVgp160 (cocktail) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intradermal

Vaccine Name: Poly-gp120H *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* Poly-gp120H + QS-21

Vaccine Name: Poly-gp120H (-DH12) *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* Poly-gp120H (-DH12) + QS-21

Vaccine Name: Mono-gp120H (89.6) *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* Mono-gp120H (89.6) + QS-21

Vaccine Name: Mono-gp120H (DH12) *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* Mono-gp120H (DH12) + QS-21

Challenge: SHIV.DH12 (MD1) *Route:* Intravenous

Main Findings:

- Mixtures of HIV-1 envelope glycoproteins elicit broader immune responses than individual Env immunogens
- 5/8 animals immunized with polyvalent vaccines made NAbs against three or more viral strains
- NAb activity almost entirely homologous to strains used in the vaccine
- No sterilizing protection against heterologous SHIV challenge
- Protection of animals against SIV or HIV-1 infection correlates with the presence of NAbs, not gp120 binding activity

NHP.12 (11145897) **DNA vaccination of macaques with several different Nef sequences induces multispecific T cell responses.**

Authors: Couillin I, Letourneur F, Lefebvre P, Guillet JG, Martinon F

Journal: Virology 2001 Jan 5;279(1):136-45.

Objectives: Immunogenicity. To study the ability of DNA vaccine to induce a wide spectrum of TCL responses to recognize several epitopes and multiple isolates.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pCI-Nef plasmid *Type:* DNA *Route:* Intradermal

Main Findings:

- DNA immunization with several sequences elicits multispecific T cell responses that recognize several epitopes expressed in the different Nef immunogens
- DNA immunization with Nef sequences induced interferon-gamma (IFN-gamma) secreting cell responses directed against several regions of Nef
- CD8+ T cells were predominantly involved in anti-Nef IFN-gamma secreting cell responses

NHP.13 (11462016) **Protection against simian immunodeficiency virus vaginal challenge by using Sabin poliovirus vectors.**

Authors: Crotty S, Miller CJ, Lohman BL, Neagu MR, Compton L, Lu D, Lu FX, Fritts L, Lifson JD, Andino R

Journal: J Virol 2001 Aug;75(16):7435-52.

Objectives: Challenge, Immunogenicity. To assess the immunogenicity and protection of a vector-based vaccine (polio Sabin 1 and 2) coupled with SIV genes against vaginal challenge with highly pathogenic SIVmac251

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: pSabRV1-SIV *Type:* DNA *Route:* Intranasal

Vaccine Name: pSabRV2-SIV *Type:* DNA *Route:* Intranasal

Challenge: SIVmac251 *Route:* Vaginal or perivaginal

Main Findings:

- 4/7 vaccinated animals exhibited substantial protection against the vaginal SIV challenge
- All 12 control monkeys became SIV positive (infection)
- No virological evidence of infection following challenge in 2/7 SabRV-SIV-vaccinated monkeys, indicating complete protection
- Two additional SabRV-SIV-vaccinated monkeys exhibited a pronounced reduction in postacute viremia to $<10^3$ copies/ml, suggesting that the vaccine elicited an effective cellular immune response
- 3/6 control animals developed clinical AIDS by 48 weeks postchallenge. In contrast, all seven vaccinated monkeys remained healthy as judged by all clinical parameters

NHP.14 (11134278) **Immunogenicity and protective efficacy of oligomeric human immunodeficiency virus type 1 gp140.**

Authors: Earl PL, Sugiura W, Montefiori DC, Broder CC, Lee SA, Wild C, Lifson J, Moss B

Journal: J Virol 2001 Jan;75(2):645-53.

Objectives: Challenge, Immunogenicity. To test the immunogenicity and protective efficacy of oligomeric gp140 in the rhesus macaque model, against homologous challenge with SHIV-HXB2

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: HIV-1 IIIB gp140 *Type:* Purified Viral Products *Route:* Intramuscular *Formulation:* HIV-1 IIIB gp140 + QS-21

Challenge: SHIV-IIIB/HXB2 *Route:* Intravenous

Main Findings:
- Strong neutralizing antibodies against a homologous virus and modest neutralization of heterologous laboratory-adapted isolates were elicited
- No neutralization of primary isolates
- 3/4 vaccinated macaques exhibited no evidence of virus replication
- Infected animals demonstrated high, sustained neutralizing antibody titers to the challenge strain, while those that were protected exhibited waning titers

NHP.15 (11462019) **Postnatal passive immunization of neonatal macaques with a triple combination of human monoclonal antibodies against oral simian-human immunodeficiency virus challenge.**

Authors: Hofmann-Lehmann R, Vlasak J, Rasmussen RA, Smith BA, Baba TW, Liska V, Ferrantelli F, Montefiori DC, McClure HM, Anderson DC, Bernacky BJ, Rizvi TA, Schmidt R, Hill LR, Keeling ME, Katinger H, Stiegler G, Cavacini LA, Posner MR, Chou TC, Andersen J, Ruprecht RM

Journal: J Virol 2001 Aug;75(16):7470-80.

Objectives: Challenge, Passive Immunization. To develop prophylaxis against mother-to-child of SIV by postnatal passive immunization of neonatal macaques with a triple combination of human monoclonal antibodies

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Monoclonal antibody 2G12 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name: Monoclonal antibody 2F5 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name: IgG1 b12 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name: Monoclonal antibody F105 *Type:* Passive Antibody *Route:* Intravenous

Challenge: SHIV89.6, SHIV-vpu+ *Route:* Oral

Main Findings:
- Two neonates macaques passively immunized with monoclonal antibodies (F105, 2G12, and 2F5), were protected from oral SHIV-vpu+ challenge, while four untreated control animals became persistently infected
- Among SHIV89.6P-challenged animals, the MAb combination was partially successful in preventing infection
- Half of the treated infants were protected from the acute, severe T-cell depletion

NHP.16.1 (11257383) **Modulation of antigen-specific cellular immune responses to DNA vaccination in rhesus macaques through the use of IL-2, IFN-gamma, or IL-4 gene adjuvants.**

Authors: Kim JJ, Yang JS, Manson KH, Weiner DB

Journal: Vaccine 2001 Mar 21;19(17-19):2496-505.

Objectives: Challenge, Immunogenicity. To examine the effects of cytokine gene adjuvants to enhance the level of cell-mediated immune responses generated by a multicomponent DNA vaccine in the rhesus macaque primate model

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: HIV env_{MN}/rev(pCEnv) *Type:* DNA *Route:* Intramuscular *Formulation:* HIV env_{MN}/rev(pCEnv) + Bupivacaine, IL-2 in pCDNA3 + PBS

Vaccine Name: pCSGag/Pol.SIV *Type:* DNA *Route:* Intramuscular *Formulation:* pCSGag/Pol.SIV + Bupivacaine, IL-2 in pCDNA3 + PBS

Challenge: SHIV-IIIB/HXB2 *Route:* Intravenous

Main Findings:
- Coadministration of Il-2 and IFN-gamma cDNA enhances antigen-specific T cell-mediated immune response
- Antibody-specific responses can be driven to a higher level through the use of cytokine genetic adjuvants in rhesus macaques
- Overall, low CTL response
- The stimulated T cells from vaccinated rhesus macaques produced higher levels of IFN-

gamma than the control animals
- 3/8 immunized and challenged animals were protected from SHIV challenge
- Protection to SHIV challenge was associated with CTL.

NHP.16.2 (11437655) **Protection from immunodeficiency virus challenges in rhesus macaques by multicomponent DNA immunization.**

Authors: Kim JJ, Yang JS, Nottingham LK, Lee DJ, Lee M, Manson KH, Wyand MS, Boyer JD, Ugen KE, Weiner DB

Journal: Virology 2001 Jul 5;285(2):204-17.

Objectives: Challenge, Immunogenicity. To test the ability of rhesus macaques immunized with DNA vaccines enconding HIV env/rev and SIV gag/pol to control infection with SIVmac239

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: HIV env MN *Type:* DNA *Route:*

Vaccine Name: HIV env_{MN}/rev(pCEnv) *Type:* DNA *Route:* Intramuscular *Formulation:* HIV env_{MN}/rev(pCEnv) + Bupivacaine, IL-2 in pCDNA3 + PBS

Vaccine Name: pCSGag/Pol.SIV *Type:* DNA *Route:* Intramuscular *Formulation:* pCSGag/Pol.SIV + Bupivacaine, IL-2 in pCDNA3 + PBS

Challenge: SIVmac239, SHIV89.6P, SHIV-IIIB/HXB2 *Route:* Intravenous

Main Findings:
- Following the pathogenic challenges, all three vaccinated animals were negative for viral coculture and antigenemia and were negative by PCR
- The control animals exhibited antigenemia by 2 weeks postchallenge and exhibited greater than 10 logs of virus/10^6 cells in limiting dilution coculture

NHP.17 (11145906) **Sequential immunization of macaques with two differentially attenuated vaccines induced long-term virus-specific immune responses and conferred protection against AIDS caused by heterologous simian human immunodeficiency Virus (SHIV(89.6)P).**

Authors: Kumar A, Lifson JD, Li Z, Jia F, Mukherjee S, Adany I, Liu Z, Piatak M, Sheffer D, McClure HM, Narayan O

Journal: Virology 2001 Jan 5;279(1):241-56.

Objectives: Challenge, Immunogenicity. To investigate the immunological response and protection in rhesus macaques sequentially immunized with live vaccines ΔvpuΔnefSHIV-4 (vaccine-I) and Δvpu SHIVPPC (vaccine-II)

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SHIV-4 (Deltavpu-Deltanef)-I *Type:* Live Attenuated Virus *Route:* Subcutaneous

Vaccine Name: SHIV-PPC (Deltavpu) *Type:* Live Attenuated Virus *Route:* Oral

Challenge: SHIV89.6P *Route:* Intravenous

Main Findings:
- The vaccine viruses did not replicate productively in the PBMCs of the vaccinated animals
- 4/4 vaccinees developed binding antibodies against both vaccine envelope glycoproteins but neutralizing antibodies were elicited by only one vaccine; and virus-specific CTLs that recognized homologous as well as heterologous pathogenic SHIVs
- 3 naive control animals were infected with the challenged strain and 2/3 controls were immunocompromised and succumbed to AIDS 6mpc
- 4/4 vaccinees became infected with challenge virus but virus in these animals replicated approximately 200- to 60,000-fold less efficiently than in control animals and eventually, plasma viral RNA became undetectable in three of the four vaccinates.

NHP.18 (11581387) **Role of CD8(+) lymphocytes in control of simian immunodeficiency virus infection and resistance to rechallenge after transient early antiretroviral treatment.**

Authors: Lifson JD, Rossio JL, Piatak M Jr, Parks T, Li L, Kiser R, Coalter V, Fisher B, Flynn BM, Czajak S, Hirsch VM, Reimann KA, Schmitz JE, Ghrayeb J, Bischofberger N, Nowak MA, Desrosiers RC, Wodarz D

Journal: J Virol 2001 Nov;75(21):10187-99.

Objectives: Challenge, Immunogenicity, Immunotherapy. To study the role of CD8+ in the control of SIV infection and rechallenge after tansient early antiretroviral theratpy

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVsmE660 *Type:* Live Virus *Route:* Intravenous

Challenge: SIVsmE660, SIVmac239 *Route:* Intravenous

Main Findings:

- Animals that controlled plasma viremia following transient postinoculation treatment showed substantial resistance to subsequent intravenous rechallenge with homologous (SIVsmE660) and highly heterologous (SIVmac239) SIV isolates, up to more than 1 year later, despite the absence of measurable neutralizing antibody

NHP.19 (11393868) **Control of a mucosal challenge and prevention of AIDS by a multiprotein DNA/MVA vaccine.**

Authors: Amara RR, Villinger F, Altman JD, Lydy SL, O

Journal: Science 2001 Apr 6;292(5514):69-74.

Objectives: Challenge, Immunogenicity. To assess the protective value of an immunization scheme consisting of DNA priming followed by a recombinant modified vaccinia Ankara (rMVA) booster

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIV-HIV89.6 DNA vaccine *Type:* DNA *Routes:* Intradermal, Intramuscular *Formulation:* SIV-HIV89.6 DNA vaccine + PBS

Vaccine Name: rMVA 89.6 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular *Formulation:* rMVA 89.6 + PBS

Challenge: SHIV89.6P *Route:* Intrarectal

Main Findings:

- Two DNA inoculations at 0 and 8 weeks and a single rMVA booster at 24 weeks effectively controlled an intrarectal challenge administered 7 months after the booster.

NHP.20 (11507204) **Evidence for early local viral replication and local production of antiviral immunity upon mucosal simian-human immunodeficiency virus SHIV(89.6) infection in Macaca nemestrina.**

Authors: Ambrose Z, Larsen K, Thompson J, Stevens Y, Finn E, Hu SL, Bosch ML

Journal: J Virol 2001 Sep;75(18):8589-96.

Objectives: Immunogenicity, Immunotherapy. To study the differences in viremia, CD4 T-cell percentages, and mucosal and systemic anti-SHIV humoral and cellular immune responses during primary infection of animals infected either intravenously or intravaginally.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Challenge: SHIV89.6v *Route:* Intravenous, Vaginal or perivaginal

Main Findings:

- SHIV Positive viral cocultures, peripheral blood mononuclear cell viral load peaks, and CD4 cell declines were delayed by 1 week in the intravaginally inoculated animals compared to the animals infected intravenously, demonstrating delayed viral spreading to the periphery
- Mucosal anti-SHIV antibody levels were greater in magnitude and arose more rapidly and mucosal CD8(+) T-cell responses were enhanced in the intravaginally inoculated animals

NHP.21 (11424009) **Protection from secondary human immunodeficiency virus type 1 infection in chimpanzees suggests the importance of antigenic boosting and a possible role for cytotoxic T cells.**

Authors: Balla-Jhagjhoorsingh SS, Mooij P, ten Haaft PJ, Bogers WM, Teeuwsen VJ, Koopman G, Heeney JL

Journal: J Infect Dis 2001 Jul 15;184(2):136-43.

Objectives: Challenge, Immunogenicity. To investigate correlates of protection against secondary and subsequent HIV infection

Species/Subspecies: Pan troglodytes verus (chimpanzee), Macaca (sp)

Vaccine Name: HIV-1 W6.1D gp120 *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* HIV-1 W6.1D gp120 + AS-2 adjuvant

Challenge: HIV-1 Han2 *Route:* Intravenous

Main Findings:

- After exposure to an infectious dose of heterologous primary isolate, 4/8 HIV-1 seropositive chimpanzees resisted secondary infection, whereas 2 naive controls became readily infected
- Only animals who were immunologically boosted were protected
- Protection from heterologous secondary exposure appeared to be related to the repertoire of the cytolytic CD8+ T cell responses to HIV-1

NHP.22 (11356960) **The ability of an oligomeric human immunodeficiency virus type 1 (HIV-1) envelope antigen to elicit neutralizing antibodies against primary HIV-1 isolates is improved following partial deletion of the second hypervariable region**

Authors: Barnett SW, Lu S, Srivastava I, Cherpelis S, Gettie A, Blanchard J, Wang S, Mboudjeka I, Leung L, Lian Y, Fong A, Buckner C, Ly A, Hilt S, Ulmer J, Wild CT, Mascola JR, Stamatatos L

Journal: J Virol 2001 Jun;75(12):5526-40.

Objectives: Immunogenicity. To investigate whether the modified, SF162V2-derived envelope may elicit higher titers of cross-reactive neutralizing antibodies than the unmodified SF162-derived envelope

Species/Subspecies: Macaca mulatta (Rhesus macaque), Macaca (sp)

Vaccine Name: Delta-V2 gp140 oligomeric *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* Delta-V2 gp140 oligomeric + MF59

Vaccine Name: DNA (pCMVKm2) gp140 *Type:* DNA *Routes:* Intradermal, Intramuscular *Formulation:* DNA (pCMVKm2) gp140 + MF59

Vaccine Name: pCMVKm2-Delta-V2 gp140 *Type:* DNA *Routes:* Intradermal, Intramuscular *Formulation:* pCMVKm2-Delta-V2 gp140 + MF59

Vaccine Name: gp140 oligomeric *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* gp140 oligomeric + MF59

Main Findings:

- Modified immunogen was more effective in eliciting potent binding and neutralizing antibodies, against homologous and several heterologous primary HIV-1 isolates

NHP.23 (11595290) **Vaccine-elicited immune responses prevent clinical AIDS in SHIV(89.6P)-infected rhesus monkeys.**

Authors: Barouch DH, Fu TM, Montefiori DC, Lewis MG, Shiver JW, Letvin NL

Journal: Immunol Lett 2001 Nov 1;79(1-2):57-61.

Objectives: Challenge, Immunogenicity. To study the role of adjuvant IL-2/Ig, a fusion protein consisting of IL-2 and the Fc portion of IgG, in DNA vaccines encoding SIVmac239 Gag and HIV-189.6P Env.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: DNA-gag,env *Type:* DNA *Route:* Intramuscular *Formulation:* DNA-gag,env + MF59, IL-2/lg plasmid

Challenge: SHIV89.6P *Route:* Intravenous

Main Findings:

- Animals immunized with DNA vaccines plus IL-2/Ig plasmid or protein developed significantly higher levels of p11C- and p41A-specific CTLs
- No prevention of infection in vaccinees upon intravenous challenge with SHIV89.6

- Control of viremia to nearly undetectable levels in vaccinees
- Control monkeys developed high levels of viremia and exhibited a rapid loss of CD4+ T cells, significant clinical disease progression, and death in half of the animals by day 140 following challenge

NHP.24.1 (11160750) **Elicitation of high-frequency cytotoxic T-lymphocyte responses against both dominant and subdominant simian-human immunodeficiency virus epitopes by DNA vaccination of rhesus monkeys.**

Authors: Barouch DH, Craiu A, Santra S, Egan MA, Schmitz JE, Kuroda MJ, Fu TM, Nam JH, Wyatt LS, Lifton MA, Krivulka GR, Nickerson CE, Lord CI, Moss B, Lewis MG, Hirsch VM, Shiver JW, Letvin NL

Journal: J Virol 2001 Mar;75(5):2462-7.

Objectives: Immunogenicity. To compare the CTL response to vaccination with plasmid DNA, live recombinant vector and infection with simian-human immunodeficiency virus (SHIV).

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: rMVASIV239gagpol.HIV89.6env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name: SHIV89.6 *Type:* Live Virus *Route:* Intravenous

Vaccine Name: SHIV89.6P *Type:* Live Virus *Route:* Intravenous

Vaccine Name: SHIVIIIBc2 *Type:* Live Virus *Route:* Intravenous

Vaccine Name: pV1P-SIVmac239 gag *Type:* DNA *Route:* Intramuscular *Formulation:* pV1P-SIVmac239 gag + IL-2/lg protein

Vaccine Name: pV1P-HIV-1.89.6P env *Type:* DNA *Route:* Intramuscular *Formulation:* pV1P-HIV-1.89.6P env + IL-2/lg protein

Main Findings:

- The p11C-specific CTL response was high frequency and dominant and the p41A-specific CTL response was low frequency and subdominant in both SHIV-infected monkeys and in monkeys vaccinated with recombinant modified vaccinia virus Ankara vectors expressing these viral antigens
- Vaccination with plasmid DNA, but not vaccination with a live recombinant vector or infection with SHIV, elicits potent CTL responses against both dominant and subdominant epitopes in rhesus monkeys
- Plasmid DNA vaccination leads to high-frequency CTL responses specific for both of env p41A and Gag p11C epitopes

NHP.24.2 (11333896) **Reduction of simian-human immunodeficiency virus 89.6P viremia in rhesus monkeys by recombinant modified vaccinia virus Ankara vaccination.**

Authors: Barouch DH, Santra S, Kuroda MJ, Schmitz JE, Plishka R, Buckler-White A, Gaitan AE, Zin R, Nam JH, Wyatt LS, Lifton MA, Nickerson CE, Moss B, Montefiori DC, Hirsch VM, Letvin NL

Journal: J Virol 2001 Jun;75(11):5151-8.

Objectives: Challenge, Immunogenicity. To study the immune responses elicited in rhesus monkeys by a recombinant poxvirus vaccine and the degree of protection afforded against a pathogenic simian-human immunodeficiency virus SHIV-89.6P challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: MVA-SIV gag-pol and HIV-1 89.6 env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Challenge: SHIV89.6P *Route:* Intravenous

Main Findings:

- Immunization with MVA vectors expressing SIVmac239 gag-pol and HIV-1 89.6 env elicited potent Gag-specific CTL responses but no detectable SHIV-specific NAb

responses
- MVA-vaccinated monkeys had high-frequency secondary CTL responses, high-titer secondary SHIV-89.6-specific NAb responses, rapid SHIV-89.6P-specific NAb responses, partial preservation of CD4+ T lymphocytes, reduced setpoint viral RNA levels, and no clinical disease or mortality by day 168 postchallenge (in contrast to control animals)

NHP.27 (10590126) **Vaccination of macaques against pathogenic simian immunodeficiency virus with Venezuelan equine encephalitis virus replicon particles.**

Authors: Davis NL, Caley IJ, Brown KW, Betts MR, Irlbeck DM, McGrath KM, Connell MJ, Montefiori DC, Frelinger JA, Swanstrom R, Johnson PR, Johnston RE

Journal: J Virol 2000 Jan;74(1):371-8.

Objectives: Challenge, Immunogenicity. To evaluate the immunogeneicity and protective value of an SIV vaccine in VEE vector against SIV challenge

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: VEE-SIVsm (SIV MA/CA-VRP and gp160-VRP) *Type:* DNA *Routes:* Intravenous, Subcutaneous

Challenge: SIVsmE660 *Route:* Intravenous

Main Findings:
- 4/4 vaccinees were protected against disease for at least 16 mpc (intravenous) with a pathogenic SIV swarm, while two of four controls required euthanasia at 10 and 11 weeks
- Vaccination reduced the mean peak viral load 100-fold

NHP.28 (10600597) **Protection of macaques against a SHIV with a homologous HIV-1 Env and a pathogenic SHIV-89.6P with a heterologous Env by vaccination with multiple gene-deleted SHIVs.**

Authors: Ui M, Kuwata T, Igarashi T, Ibuki K, Miyazaki Y, Kozyrev IL, Enose Y, Shimada T, Uesaka H, Yamamoto H, Miura T, Hayami M

Journal: Virology 1999 Dec 20;265(2):252-63.

Objectives: Challenge, Immunogenicity. To evaluate the potential of SHIVs as anti-HIV-1 live attenuated virus vaccines

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SHIV-drn *Type:* Live Attenuated Virus *Route:* Intravenous

Vaccine Name: SHIV-dxrn *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge: SHIV-NM-3rN, SHIV89.6P *Route:* Intravenous

Main Findings:
- In 4 macaques that had been vaccinated with SHIV-drn and challenged with SHIV-NM-3rN, no challenge virus was detected by DNA PCR in, or recovered from, two of the macaques. In the other two, challenge virus was detected once and twice, respectively
- Plasma viral loads were much lower than those in unvaccinated controls
- Another four macaques vaccinated with SHIV-dxrn, control of infection was evident but less than that of SHIV-drn-vaccinated macaques
- When the two SHIV-drn-vaccinated macaques were challenged with pathogenic SHIV-89.6P, which has an HIV-1 Env that is antigenically different from that of SHIV-drn, replication of the challenge virus was restricted
- Protection involved not only neutralizing antibodies and killer cell activity, but also other unknown specific and nonspecific immunity elicited by the infection.

NHP.29.1 (12584336) **Simian-Human Immunodeficiency Virus SHIV89.6-Induced Protection against Intravaginal Challenge with Pathogenic SIVmac239 Is Independent of the Route of Immunization and Is Associated with a Combination of Cytotoxic T-Lymphocyte and Alpha Interferon Responses**

Authors: Abel K, Compton L, Rourke T, Montefiori D, Lu D, Rothaeusler K, Fritts L, Bost K, Miller CJ

Journal: J Virol 2003 Mar 1;77(5):3099-3118

Objectives: Challenge, Immunogenicity. To compare the the mucosal (intranasal, intravaginal) vs. intravenous immunization with live nonpathogenic SHIV89.6 in rhesus macaques subsequently challenged intravaginally with SIVmac239

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SHIV89.6 *Type:* Live Virus *Routes:* Intravenous, Vaginal or perivaginal, Intranasal

Main Findings:

- The route of immunization did not affect mucosal challenge outcome after a prolonged period of systemic infection with the nonpathogenic vaccine virus
- Protection from the SIV challenge was associated with the induction of multiple host immune effector mechanisms: vaccinated-protected animals had higher frequencies of SIV Gag-specific cytotoxic T lymphocytes and gamma interferon-secreting cells during the acute phase postchallenge than the vaccinated unprotected ones
- Vaccinated-protected animals had a more pronounced increase in peripheral blood mononuclear cell IFN-gamma mRNA levels than did the vaccinated-unprotected animals in the first few weeks after challenge

NHP.29.2 (14694116) **Gamma interferon-mediated inflammation is associated with lack of protection from intravaginal simian immunodeficiency virus SIVmac239 challenge in simian-human immunodeficiency virus 89.6-immunized rhesus macaques.**

Authors: Abel K, La Franco-Scheuch L, Rourke T, Ma ZM, De Silva V, Fallert B, Beckett L, Reinhart TA, Miller CJ

Journal: J Virol 2004 Jan;78(2):841-54.

Objectives: Challenge, Immunogenicity. To determine the relationship between IFN-Γ-related host immune responses and challenge virus replication in lymphoid tissues of SHIV89.6-vaccinated and unvaccinated rhesus macaques after challenge with SIVmac239

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- Vaccinated-protected monkeys had low tissue viral RNA (vRNA) levels
- Vaccinated-unprotected animals had moderate tissue vRNA levels
- Unvaccinated animals had high tissue vRNA levels
- Vaccinated-protected monkeys had slightly increased tissue IFN-Γ mRNA levels and a high frequency of IFN-Γ secreting T cells responding to in vitro SIVgag peptide stimulation

NHP.30 (11739694) **ALVAC-SIV-gag-pol-env-based vaccination and macaque major histocompatibility complex class I (A*01) delay simian immunodeficiency virus SIVmac-induced immunodeficiency.**

Authors: Pal R, Venzon D, Letvin NL, Santra S, Montefiori DC, Miller NR, Tryniszewska E, Lewis MG, VanCott TC, Hirsch V, Woodward R, Gibson A, Grace M, Dobratz E, Markham PD, Hel Z, Nacsa J, Klein M, Tartaglia J, Franchini G

Journal: J Virol 2002 Jan;76(1):292-302.

Objectives: Challenge, Immunogenicity. To assess whether immunization with an ALVAC-based vaccine expressing the SIVmac251 Gag, Pol, and Env and subsequent boosting with subunit gp120 could confer immunity and prevent or contain SIVmac251 replication following a mucosal exposure to SIVmac251

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: ALVAC-SIV-gpe (vcp180) *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intrarectal, Intramuscular, Intranasal

Vaccine Name: SIVmac251-gp120 *Type:* Purified Viral Products *Routes:* Intrarectal, Intramuscular, Intranasal

Challenge: SIVmac251 (561) *Route:* Intrarectal

Main Findings:

- MHC-I Mamu-A*01 genotype and vaccination of rhesus macaques with ALVAC-SIV-gag-pol-env (ALVAC-SIV-gpe) restrict SIVmac251 replication, preserve CD4+ T cells, and delay disease progression following intrarectal challenge exposure of the animals to SIVmac251
- ALVAC-SIV-gpe immunization induced CTL responses cumulatively in 67% of the immunized animals
- Significant delay in CD4+ T-cell loss was observed in Mamu-A*01-positive macaques
- Neither boosting the ALVAC-SIV-gpe with gp120 immunizations nor administering the vaccine by the combination of mucosal and systemic immunization routes increased significantly the protective effect of the ALVAC-SIV-gpe vaccine
- In the case of intravenous or intrarectal challenge with the chimeric SIV/HIV strains SHIV(89.6P) or SHIV(KU2), respectively, MHC-I Mamu-A*01-positive macaques did not significantly restrict primary viremia

NHP.31 (11017793) **DNA vaccination of macaques by a full genome HIV-1 plasmid which produces noninfectious virus particles.**

Authors: Akahata W, Ido E, Shimada T, Katsuyama K, Yamamoto H, Uesaka H, Ui M, Kuwata T, Takahashi H, Hayami M

Journal: Virology 2000 Sep 15;275(1):116-24.

Objectives: Challenge, Immunogenicity. To evaluate the humoral and cell-mediated immune response to a DNA vaccine containing full genome of HIV-1

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: DNA Vaccine pNL432-ZF1* *Type:* DNA *Route:* Intramuscular

Challenge: SHIV-NM-3rN *Route:* Intravenous

Main Findings:

- Immunological responses against HIV-1 were elicited in all of the vaccinated monkeys: stable anti-HIV-1 Env antibodies were raised in two monkeys and CTL activities were induced in the other monkeys. After holomogous challenge of the macaques intravenously 54 weeks with 100 TCID50 of SHIV-NM-3rN, in all of the vaccinated macaques, the peak plasma viral loads were two to three orders of magnitude lower than those of the naive controls.

NHP.32 (10233957) **Highly attenuated vaccine strains of simian immunodeficiency virus protect against vaginal challenge: inverse relationship of degree of protection with level of attenuation.**

Authors: Johnson RP, Lifson JD, Czajak SC, Cole KS, Manson KH, Glickman R, Yang J, Montefiori DC, Montelaro R, Wyand MS, Desrosiers RC

Journal: J Virol 1999 Jun;73(6):4952-61.

Objectives: Challenge, Immunogenicity. To compare 3 levels of attenuation of SIV-based vaccine and their ability to protect against mucosal challenge with pathogenic SIV

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac239Δ3 *Type:* Live Attenuated Virus *Route:* Intravenous

Vaccine Name: SIVmac239Δ3x *Type:* Live Attenuated Virus *Route:* Intravenous

Vaccine Name: SIVmac239Δ4 *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge: SIVmac251 *Route:* Intravenous, Vaginal or perivaginal

Main Findings:

- All three vaccines elicited strong protective effect up to 1 year from immunization to challenge
- Degree of protection correlated inversely with the level of attenuation
- Protection against vaginal challenge was easier to achieve than protection against intravenous challenge

- Protection associated with high antibody avidity indices
- Protection in absence of detectable serum Nab was associated with CTL response in immunized animals. No vaccine virus recovered in 11 of 12 vaccinees

NHP.33 (11085585) **Enhanced safety and efficacy of live attenuated SIV vaccines by prevaccination with recombinant vaccines.**

Authors: Jones L, Ahmad S, Chan K, Verardi P, Morton WR, Grant R, Yilma T

Journal: J Med Primatol 2000 Aug;29(3-4):231-9.

Objectives: Challenge, Immunogenicity. To evaluate the safety of a live attenuated vaccine (delta nef) in macaques pre-immunized with a recombinant DNA vaccine.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac239-Δnef *Type:* Live Attenuated Virus *Route:* Intravenous

Vaccine Name: vSIVgp120 *Type:* Recombinant Vector (virus/bacteria) *Route:* Intradermal

Vaccine Name: CHO-SIVgp120 *Type:* DNA *Route:* Intramuscular

Vaccine Name: vSIVgp160 *Type:* DNA *Route:* Intradermal

Vaccine Name: bSIVgp120 *Type:* DNA *Route:* Intramuscular

Challenge: SIVmac251 *Route:* Intravenous

Main Findings:

- Preimmunized macaques advanced to disease SLOWER than controls after challenge with virulent SIV
- 5 animals survived for 3 years without disease and only the vaccine virus (SIVΔnef) could be isolated at this time
- In another experiment, preimmunized animals had lower virus loads and no disease compared to controls

NHP.34 (9882330) **Limited protection from a pathogenic chimeric simian-human immunodeficiency virus challenge following immunization with attenuated simian immunodeficiency virus.**

Authors: Lewis MG, Yalley-Ogunro J, Greenhouse JJ, Brennan TP, Jiang JB, VanCott TC, Lu Y, Eddy GA, Birx DL

Journal: J Virol 1999 Feb;73(2):1262-70.

Objectives: Challenge, Immunogenicity. To test the ability of two live attenuated SIV constructs with single deletion to stimulate protective immunity in macaques

Species/Subspecies: Macaca mulatta (Rhesus macaque), Macaca nemestrina (pigtailed macaque)

Vaccine Name: SIVmac239-Δnef *Type:* Live Attenuated Virus *Route:* Intravenous

Vaccine Name: SIV-PBJ6.6Δnef *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge: SHIV89.6PD *Route:* Intravenous

Main Findings:

- Each construct generated high levels of specific immunity in all of the immunized animals
- SIV239Δnef grew to high levels in all immunized animals. The SIVPBj6.6Δnef was effectively controlled by all of the immunized animals
- Challenge strain: SIV89.6PD
- Vaccination with attenuated SIV can protect macaques from disease and in some cases from infection by a highly pathogenic SHIV. Inability to control the immunizing virus may result in rapid disease progression

NHP.35 (10593491) **Protective immunity of gene-deleted SHIVs having an HIV-1 Env against challenge infection with a gene-intact SHIV.**

Authors: Ui M, Kuwata T, Igarashi T, Miyazaki Y, Tamaru K, Shimada T, Nakamura M, Uesaka H, Yamamoto H, Hayami M

Journal: J Med Primatol 1999 Aug-Oct;28(4-5):242-8.

Objectives: Challenge, Immunogenicity. To assess the level of immunogenicity and protection of a SHIV-deleted live attenuated vaccine virus against a gene-intact SHIV challenge virus

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SHIV-dn *Type:* Live Attenuated Virus *Route:* Intravenous

Vaccine Name: SHIV-drn *Type:* Live Attenuated Virus *Route:* Intravenous

Vaccine Name: SHIV-dxrn *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge: SHIV-NM-3rN *Route:* Intravenous

Main Findings:

- Protective immunity of live attenuated SHIV vaccine is inversely dependent upon the level of attenuation of the virus
- Most immunized macaques had HIV-1 env and/or SIV gag-specific CTL responses
- 10/12 vaccinated macaques had NK cell activities higher than those of normal macaques (<10%): NK cells may be involved in protection against challenge

NHP.36 (11112494) **Induction of long-term protective effects against heterologous challenge in SIVhu-infected macaques.**

Authors: Villinger F, Switzer WM, Parekh BS, Otten RA, Adams D, Shanmugam V, Bostik P, Mayne AE, Chikkala NF, McClure HM, Novembre F, Yao Q, Heneine W, Folks TM, Ansari AA

Journal: Virology 2000 Dec 5;278(1):194-206.

Objectives: Challenge, Immunogenicity. To measure the immunogenicity and protective effect of a live attenuated vaccine SIVhu (isolated from a human accidentally exposed) against challenge with SHIV89.6P

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVhu *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge: SIVsmB670, SHIV89.6P *Route:* Intravenous

Main Findings:

- SIVhu which accidentally infected human had a truncated nef which failed to repair itself and added additional stop codons post-infection
- Infection with SIVhu was associated with minimal acute viral replication, followed by undetectable plasma viral loads and only intermittent PCR detection up to 5 ypi
- 3/3 animals infected with SIVhu remained healthy and with stable CD4(+) lymphocyte levels and undetectable plasma viral loads at >20 months post-SHIV89.6p challenge

NHP.37 (10482586) **Protection by live, attenuated simian immunodeficiency virus against heterologous challenge.**

Authors: Wyand MS, Manson K, Montefiori DC, Lifson JD, Johnson RP, Desrosiers RC

Journal: J Virol 1999 Oct;73(10):8356-63.

Objectives: Challenge, Immunogenicity. To examine the ability of a live, attenuated deletion mutant (SIVmac2393), which is missing nef and vpr genes, to protect against challenge by heterologous strains SHIV89.6p and SIVsmE660.

Species/Subspecies: Macaca mulatta (Rhesus macaque), Macaca (sp)

Vaccine Name: SIVmac239Δ3 *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge: SIVsmE660, SHIV89.6P *Route:* Intravenous

Main Findings:

- By the criteria of CD4+ cell counts and disease, strong protection against the SHIV89.6p challenge was observed in 4/4 vaccinated monkeys (group 1)

NHP.38 (11152522) **Persistence of pathogenic challenge virus in macaques protected by simian immunodeficiency virus SIVmacDeltanef.**

Authors: Khatissian E, Monceaux V, Cumont MC, Kieny MP, Aubertin AM, Hurtrel B

Journal: J Virol 2001 Feb;75(3):1507-15.

Objectives: Challenge, Immunogenicity. To investigate virological and immunological characteristics of five rhesus macaques immunized with a nef-inactivated SIVmac251 molecular clone (SIVmac251nef) and challenged 15 months later with the pathogenic SIVmac251 isolate.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac251ΔNef *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge: SIVmac251 *Route:* Intravenous

Main Findings:

- No total protection against homologous virus challenge but control of infection with challenge virus in the absence of a secondary immune response
- Challenge and vaccine viruses may persist in a replication-competent form for long periods after the challenge, possibly resulting in recombination between the two viruses

NHP.39 (11287551) **Quintuple deglycosylation mutant of simian immunodeficiency virus SIVmac239 in rhesus macaques: robust primary replication, tightly contained chronic infection, and elicitation of potent immunity against the parental wild-type strain.**

Authors: Mori K, Yasutomi Y, Ohgimoto S, Nakasone T, Takamura S, Shioda T, Nagai Y

Journal: J Virol 2001 May;75(9):4023-8.

Objectives: Challenge, Immunogenicity. To assess the immunogenicity and protection effect of a deglycosylated SIVmac239 mutant vaccine.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac239Delta5G *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge: SIVmac239 *Route:* Intravenous

Main Findings:

- Monkeys infected with the mutant tolerated a challenge infection with wild-type SIV very well
- Analyses of host responses following challenge revealed no neutralizing antibodies against the challenge virus but strong secondary responses of cytotoxic T lymphocytes against multiple antigens, including Gag-Pol, Nef, and Env
- Quintuple deglycosylation mutant appeared to represent a novel class of SIV live attenuated vaccine

NHP.40 (10191194) **Long-lasting protection by live attenuated simian immunodeficiency virus in cynomolgus monkeys: no detection of reactivation after stimulation with a recall antigen.**

Authors: Sernicola L, Corrias F, Koanga-Mogtomo ML, Baroncelli S, Di Fabio S, Maggiorella MT, Belli R, Michelini Z, Macchia I, Cesolini A, Cioe L, Verani P, Titti F

Journal: Virology 1999 Apr 10;256(2):291-302.

Objectives: Challenge, Immunogenicity. To determine the breadth of the protection after repeated challenges of monkeys with SIV.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: SIVmac251, 32H, (C8) *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge: SIVmac251BK28, SIVmac251,32H.spl *Route:* Intravenous

Main Findings:

- Monkeys immunized with live attenuated C8 vaccine were protected from consecutive challenge with SIVmac251, SIVmac32H
- The C8 virus remained genotypically stable, and depletion of CD4+ cells was not observed during ~3 years of follow-up

NHP.41 (10998338) **Replication of simian immunodeficiency virus (SIV) in ex vivo lymph nodes as a means to assess**

susceptibility of macaques in vivo.

Authors: Margolis L, Glushakova S, Chougnet C, Shearer G, Markham P, Robert-Guroff M, Benveniste R, Miller CJ, Cranage M, Hirsch V, Franchini G

Journal: Virology 2000 Sep 30;275(2):391-7.

Objectives: Challenge, Immunogenicity. To investigate whether infectability of ex vivo lymph nodes could predict resistance and/or susceptibility to SIV infection.

Species/Subspecies: Macaca (sp)

Vaccine Name: SIVmac251 *Type:* Live Virus *Route:* Mucosal

Vaccine Name: SIVsmE660 *Type:* Live Virus *Routes:* Intravenous, Mucosal

Challenge: SIVmne clone A2-clone 5, SIVmac251(32H) *Route:* Mucosal

Main Findings:

- Six macaques, apparently uninfected, following low-dose exposure to the pathogenic SIV(mac251) and SIV(SME660) by the mucosal route, were re-exposed to a less pathogenic SIV(MNE): 4/6 macaques resisted viral infection
- PBMC and lymph-node resistance or susceptibility to infection ex vivo correlate with in vivo infectivity

NHP.42 (10593484) **Antigen-specific cytokine responses in vaccinated Macaca nemestrina.**

Authors: Mulvania T, Lynch JB, Robertson MN, Greenberg PD, Morton WR, Mullins JI

Journal: J Med Primatol 1999 Aug-Oct;28(4-5):181-9.

Objectives: Challenge, Immunogenicity. Macaca nemestrina vaccinated with a minimally pathogenic HIV-2 strain KR. Group 1 was then inoculated with a non-infectious stock of a pathogenic strain, HIV-2287.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Main Findings:

- Both groups 1 and 2 were subsequently challenged with an infectious stock of HIV-2287
- 5/6 group 1 animals were protected against CD4 decline
- 3/6 animals in group 2 were protected
- Analysis of CTL responses demonstrated strong activity against HIV-2(KR)-Gag in group 1
- Strong correlation between CTL responses and antigen-specific T-helper (Th) type 1 responses

NHP.43 (10593486) **An anti-HIV strategy combining chemotherapy and therapeutic vaccination.**

Authors: Rosenwirth B, Bogers WM, Nieuwenhuis IG, Haaft PT, Niphuis H, Kuhn EM, Bischofberger N, Erfle V, Sutter G, Berglund P, Liljestrom P, Uberla K, Heeney JL

Journal: J Med Primatol 1999 Aug-Oct;28(4-5):195-205.

Objectives: Challenge, Immunogenicity, Immunotherapy.

Main Findings:

- Chemotherapy/therapeutic vaccination regimen induced a significant reduction in the steady-state level of viremia in one out of two chronically infected rhesus macaques
- Chemotherapeutic treatment alone did not achieve reduction of viremia in two chronically infected animals. The nature of the immune responses assumed to have been induced by vaccination in one out of the two monkeys remains to be elucidated

NHP.44 (10684264) **Immunization with a modified vaccinia virus expressing simian immunodeficiency virus (SIV) Gag-Pol primes for an anamnestic Gag-specific cytotoxic T-lymphocyte response and is associated with reduction of viremia after SIV challenge.**

Authors: Seth A, Ourmanov I, Schmitz JE, Kuroda MJ, Lifton MA, Nickerson CE, Wyatt L, Carroll M, Moss B, Venzon D, Letvin NL, Hirsch VM

Journal: J Virol 2000 Mar;74(6):2502-9.

Objectives: Challenge, Immunogenicity. To explore the immunogenicity and protective efficacy of rMVA expressing the SIV gag-pol proteins in rhesus monkeys expressing the MHC class I allele, MamuA*01.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: MVAgagpol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intravenous

Challenge: SIVsmE660 *Route:* Intravenous

Main Findings:

- MVA-gag-pol-immunized macaques exhibited a rapid and substantial anamnestic CTL response specific for the p11C, C-M Gag epitopes
- The level at which CTL stabilized after resolution of primary viremia correlated inversely with plasma viral load set point (P = 0.03)
- The magnitude of reduction in viremia in the vaccinees was predicted by the magnitude of the vaccine-elicited CTL response prior to SIV challenge

NHP.45 (10684290) **Comparative efficacy of recombinant modified vaccinia virus Ankara expressing simian immunodeficiency virus (SIV) Gag-Pol and/or Env in macaques challenged with pathogenic SIV.**

Authors: Ourmanov I, Brown CR, Moss B, Carroll M, Wyatt L, Pletneva L, Goldstein S, Venzon D, Hirsch VM

Journal: J Virol 2000 Mar;74(6):2740-51.

Objectives: Challenge, Immunogenicity. To evaluate the protective effects of prior immunization with MVA-SIV recombinant vaccines as a sole immunogen without boosting with Env protein and to optimize expression of Gag-Pol.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: MVA-SIVsmH-4 -env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name: MVA(SIVsmH-4)gag-pol-env *Type:* Purified Viral Products *Route:* Intramuscular

Vaccine Name: MVA SIVsmH4 gag-pol *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intramuscular, Intraocular *Formulation:* MVA SIVsmH4 gag-pol + PBS

Challenge: SIVsmE660 *Route:* Intravenous

Main Findings:

- Although all animals became infected post challenge, plasma viremia was significantly reduced in animals that received the MVA-SIV recombinant vaccines as compared with animals that received nonrecombinant MVA (P = 0.0011 by repeated-measures of analysis of variance)
- Immunization significantly modifies viral load following SIV challenge
- Recombinant MVA has considerable potential as a vaccine vector for human AIDS

NHP.46 (9707609) **Recombinant modified vaccinia virus Ankara-simian immunodeficiency virus gag pol elicits cytotoxic T lymphocytes in rhesus monkeys detected by a major histocompatibility complex class I/peptide tetramer.**

Authors: Seth A, Ourmanov I, Kuroda MJ, Schmitz JE, Carroll MW, Wyatt LS, Moss B, Forman MA, Hirsch VM, Letvin NL

Journal: Proc Natl Acad Sci U S A 1998 Aug 18;95(17):10112-6.

Objectives: Immunogenicity. To explore the utility of MVA as a vector for eliciting AIDS virus-specific CTL in the SIV/rhesus monkey model.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: MVA SIVsmH4 gag-pol *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intramuscular, Intraocular *Formulation:* MVA SIVsmH4 gag-pol + PBS

Main Findings:

- Intramuscular immunization with recombinant MVA-SIVSM gag pol elicited a Gag epitope-specific CTL response readily detected in peripheral blood lymphocytes by using a

functional killing assay. Moreover, those immunizations also elicited a population of CD8+ T lymphocytes in the peripheral blood that bound a specific major histocompatibility complex class I/peptide tetramer
- Tetramer staining may be a useful technology for monitoring CTL generation in vaccine trials in nonhuman primates and in humans

NHP.47 (11101054) **Cross-protection in NYVAC-HIV-1-immunized/HIV-2-challenged but not in NYVAC-HIV-2-immunized/SHIV-challenged rhesus macaques.**

Authors: Patterson LJ, Peng B, Abimiku AG, Aldrich K, Murty L, Markham PD, Kalyanaraman VS, Alvord WG, Tartaglia J, Franchini G, Robert-Guroff M

Journal: AIDS 2000 Nov 10;14(16):2445-55.

Objectives: Challenge, Immunogenicity. To evaluate the immunization with attenuated poxvirus-HIV-1 recombinants followed by protein boosting in rhesus monkeys model.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: vP991, NYVAC HIV-1IIIB gp120.gag-pol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name: vP1047, NYVAC HIV-2.SBL-ISY gp160.gag-pol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name: HIV-1 gp160 *Type:* Purified Viral Products *Route:* Intramuscular *Formulation:* HIV-1 gp160 + Rehydragel HPA

Vaccine Name: HIV-2 gp160 *Type:* Purified Viral Products *Route:* Intramuscular *Formulation:* HIV-2 gp160 + Rehydragel HPA

Challenge: HIV-2.SBL6669, SHIV-IIIB/HXB2 *Route:* Intravenous

Main Findings:
- Both immunization groups developed homologous binding antibodies
- Homologous Nab only observed in NYVAC-HIV-2-immunized macaques
- No cross-reactive neutralizing antibodies detected
- Immunization groups displayed cross-reactive CTL
- Significant CD8AA observed for only one NYVAC-HIV-2-immunized macaque
- Both immunizations significantly reduced viral burdens and partially protected against HIV-2 challenge
- Humoral antibody and/or CTL and CD8AA associated with protection against homologous HIV-2 challenge
- No significant protection observed in the SHIV-challenged macaques, although NYVAC-HIV-1 immunization resulted in significantly lower viral burdens compared with controls

NHP.48 (10717345) **A recombinant avipoxvirus HIV-1 vaccine expressing interferon-gamma is safe and immunogenic in macaques.**

Authors: Kent SJ, Zhao A, Dale CJ, Land S, Boyle DB, Ramshaw IA

Journal: Vaccine 2000 Apr 28;18(21):2250-6.

Objectives: Immunogenicity, Immunotherapy. To construct and assess FPVgag/pol-IFNgamma as a therapeutic vaccine for safety and immunogenicity in Macaca nemestrina previously infected with HIV-1.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Vaccine Name: FPV.HIV-1.gag/pol-IFNgamma *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name: FPV.HIV-1.gag/pol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Challenge: HIV-1.LAI *Route:* Intravenous

Main Findings:
- FPVgag/pol-IFNgamma vaccinations were safe and enhanced T cell proliferative responses to Gag antigens (but not control tetanus antigens)
- Enhanced CTL responses to gag/pol antigens were also observed following IFNgamma

expressing vaccinations
- Since cellular immunity may be critical to controlling or preventing HIV-1 infection, these observations suggest that avipox vectors co-expressing IFNgamma should be further evaluated as therapeutic or preventive HIV-1 vaccines.

NHP.49 (10418922) **Vaccination with Rev and Tat against AIDS.**

Authors: Osterhaus AD, van Baalen CA, Gruters RA, Schutten M, Siebelink CH, Hulskotte EG, Tijhaar EJ, Randall RE, van Amerongen G, Fleuchaus A, Erfle V, Sutter G

Journal: Vaccine 1999 Jun 4;17(20-21):2713-4.

Objectives: Challenge, Immunogenicity. A pilot study to investigate the role of cytotoxic T cell in the containment of primatate lentivirus infection.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: rSFV-SIVmac32H.rev.tat *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name: rMVA.SIVmac32H.tat.rev *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Challenge: SIVmac251(32H) *Route:* Intravenous

NHP.51 (11555138) **Effect of vaccination with recombinant modified vaccinia virus Ankara expressing structural and regulatory genes of SIV(macJ5) on the kinetics of SIV replication in cynomolgus monkeys.**

Authors: Negri DR, Baroncelli S, Michelini Z, Macchia I, Belli R, Catone S, Incitti F, ten Haaft P, Corrias F, Cranage MP, Polyanskaya N, Norley S, Heeney J, Verani P, Titti F

Journal: J Med Primatol 2001 Aug;30(4):197-206.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: MVA-mac(J5) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Challenge: SIVmac251 *Route:* Intravenous

Main Findings:
- Vaccination with rMVA-J5 performed at week 0, 12, and 24 induced a moderate proliferative response to whole SIV, a detectable humoral response to all but Nef SIV antigens, and failed to induce neutralizing antibodies
- All control monkeys were infected by week two and seroconverted by weeks four to eight
- In contrast a sharp increase of both humoral and proliferative responses at two weeks post-challenge was observed in vaccinated monkeys compared to control monkeys
- Although all vaccinated monkeys were infected, vaccination with rMVA-J5 appeared to partially control viral replication during the acute and late phase of infection as judged by cell- and plasma-associated viral load

NHP.52 (12072518) **Immunization of rhesus macaques with a DNA prime/modified vaccinia virus Ankara boost regimen induces broad simian immunodeficiency virus (SIV)-specific T-cell responses and reduces initial viral replication but does not prevent disease progression following challenge with pathogenic SIVmac239.**

Authors: Horton H, Vogel TU, Carter DK, Vielhuber K, Fuller DH, Shipley T, Fuller JT, Kunstman KJ, Sutter G, Montefiori DC, Erfle V, Desrosiers RC, Wilson N, Picker LJ, Wolinsky SM, Wang C, Allison DB, Watkins DI

Journal: J Virol 2002 Jul;76(14):7187-202.

Objectives: Challenge, Immunogenicity. To test the immunogenicity and protective value of a DNA prime/modified vaccinia virus Ankara boost regimen immunization in rhesus macaques against intrarectal challenge with simian immunodeficiency virus (SIV) mac239.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pC-SIVrev *Type:* DNA *Route:* Intradermal

Vaccine Name: rMVA-SIVmac251 32H *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intrarectal, Intradermal

Vaccine Name: pC-SIV17E-Fred (gagpolenv) *Type:* DNA *Route:* Intradermal

Vaccine Name: SIVmac17E-Fr Nef *Type:* DNA *Route:* Intradermal

Challenge: SIVmac239/nef-open *Route:* Intrarectal

Main Findings:

- Immunization resulted in induction of virus-specific CD8+ and CD4+ responses in all vaccinees
- Anamnestic nab responses against laboratory-adapted SIVmac251 developed after the challenge
- No neutralizing antibodies against SIVmac239
- Vaccinated animals had significantly reduced peak viremia compared with controls ($P<0.01$)
- Most animals had gradual CD4 depletion and progressed to disease despite the induction of virus-specific CTL responses and reduced peak viral loads

NHP.53 (12192089) **Crosslinked HIV-1 envelope-CD4 receptor complexes elicit broadly cross-reactive neutralizing antibodies in rhesus macaques.**

Authors: Fouts T, Godfrey K, Bobb K, Montefiori D, Hanson CV, Kalyanaraman VS, DeVico A, Pal R.

Journal: Proc Natl Acad Sci U S A. 2002 Aug 21

Objectives: Immunogenicity. To evaluate the immunogenicity of crosslinked gp120-CD4 complexes in rhesus monkeys.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Crosslinked gp120-CD4 *Type:* Other *Route:* Intramuscular *Formulation:* Crosslinked gp120-CD4 + QS-21

Vaccine Name: Crosslinked gp140-CD4 *Type:* Other *Route:* Intramuscular *Formulation:* Crosslinked gp140-CD4 + QS-21

Vaccine Name: HIV-1 IIIB gp120 *Type:* Purified Viral Products *Route:* Intramuscular *Formulation:* HIV-1 IIIB gp120 + QS-21

Vaccine Name: HIV-1 IIIB gp140 *Type:* Purified Viral Products *Route:* Intramuscular *Formulation:* HIV-1 IIIB gp140 + QS-21

Main Findings:

- The animals immunized with anti-env-CD4 exhibited a broad pattern of neutralization of primary viruses regardless of coreceptor usage and genetic subtype
- anti-env-CD4 neutralization more biased toward primary isolates than laboratory adapted strains, unlike anti-env which neutralized only laboratory adapted strains
- anti-Env-CD4 antisera failed to neutralize SHIV89.6, SHIV89.6P, and SHIVKU2 in the human PBMC-based assays and SIVmac239 in assays with either human or macaque PBMCs

NHP.54 (10933680) **Vaccine protection against simian immunodeficiency virus by recombinant strains of herpes simplex virus.**

Authors: Murphy CG, Lucas WT, Means RE, Czajak S, Hale CL, Lifson JD, Kaur A, Johnson RP, Knipe DM, Desrosiers RC

Journal: J Virol 2000 Sep;74(17):7745-54.

Objectives: Challenge, Immunogenicity. To develop and use replication-competent and replication-defective strains of recombinant herpes simplex virus (HSV) that express envelope and Nef antigens of SIV.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: K81 *Type:* DNA *Routes:* Subcutaneous, Intramuscular

Vaccine Name: d81 *Type:* DNA *Routes:* Intradermal, Intramuscular

Challenge: SIVmac239 *Route:* Intrarectal

Main Findings:

- The HSV recombinants induced antienvelope antibody responses that persisted at relatively stable levels for months after the last administration
- 2/7 rhesus vaccinated monkeys were solidly protected, and another showed a sustained reduction in viral load following rectal challenge with pathogenic SIVmac239 at 22 weeks following the last vaccine administration

NHP.55 (11551502) **An effective AIDS vaccine based on live attenuated vesicular stomatitis virus recombinants.**

Authors: Rose NF, Marx PA, Luckay A, Nixon DF, Moretto WJ, Donahoe SM, Montefiori D, Roberts A, Buonocore L, Rose JK

Journal: Cell 2001 Sep 7;106(5):539-49.

Objectives: Challenge, Immunogenicity. To test live attenuated vesicular stomititis virus vectors expressing SIV ?env and gag genes in rhesus monkeys.

Species/Subspecies: Macaca mulatta (Rhesus macaque), Macaca (sp)

Vaccine Name: VSV-(GI)-Env *Type:* Recombinant Vector (virus/bacteria) *Routes:* Oral, Intramuscular

Vaccine Name: VSV(GCh)-Env+Gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Oral, Intramuscular

Vaccine Name: VSV(GNJ)-Env+Gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Oral, Intramuscular

Challenge: SHIV89.6P *Route:* Intravenous

Main Findings:

- Vectors with glycoproteins from different VSV serotypes boosted response
- 7/8 controls progressed to AIDS at about 148 dpc with severe loss of CD4+ T cells, high viral loads
- 7/8 vaccinees infected with SHIV89.6P remained healthy up to 14 mpc (low or undetectable viral loads)

NHP.56 (10229229) **Neutralizing antibody-independent containment of immunodeficiency virus challenges by DNA priming and recombinant pox virus booster immunizations.**

Authors: Robinson HL, Montefiori DC, Johnson RP, Manson KH, Kalish ML, Lifson JD, Rizvi TA, Lu S, Hu SL, Mazzara GP, Panicali DL, Herndon JG, Glickman R, Candido MA, Lydy SL, Wyand MS, McClure HM

Journal: Nat Med 1999 May;5(5):526-34.

Objectives: Challenge, Immunogenicity. To compare 8 different protocols for their ability to protect against immunodeficiency virus challenges in rhesus macaques.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pRS102 -SIVmac239 gag-pol proteins *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal *Formulation:* pRS102 -SIVmac239 gag-pol proteins + Saline

Vaccine Name: pCMV/nef *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal *Formulation:* pCMV/nef + Saline

Vaccine Name: pJW4303/HXB-2.dpol *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal *Formulation:* pJW4303/HXB-2.dpol + Saline

Vaccine Name: pJW4303/HXB-2.gp140 *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal *Formulation:* pJW4303/HXB-2.gp140 + Saline

Vaccine Name: pJW4303/HXB-2.gp120 *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal *Formulation:* pJW4303/HXB-2.gp120 + Saline

Vaccine Name: Prt-env gp160 *Type:* Purified Viral Products *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal

Vaccine Name: rFPV *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal, Intramuscular

Challenge: SHIV89.6P, SHIV-IIIB/HXB2 *Route:* Intravenous

Main Findings:
- Intradermal DNA priming followed by recombinant fowl pox virus booster immunizations was a more efficient protocol in inducing immune response and containment of challenge infection than the gene gun inoculation method

NHP.57 (10438842) **Effective induction of simian immunodeficiency virus-specific cytotoxic T lymphocytes in macaques by using a multiepitope gene and DNA prime-modified vaccinia virus Ankara boost vaccination regimen.**

Authors: Hanke T, Samuel RV, Blanchard TJ, Neumann VC, Allen TM, Boyson JE, Sharpe SA, Cook N, Smith GL, Watkins DI, Cranage MP, McMichael AJ

Journal: J Virol 1999 Sep;73(9):7524-32.

Objectives: Challenge, Immunogenicity. To test multi-CTL epitope gene and a DNA prime-MVA boost vaccination regimen in rhesus macaques.

Species/Subspecies: Macaca mulatta (Rhesus macaque), Macaca (sp)

Vaccine Name: pTH.HW DNA *Type:* DNA *Route:* Intradermal (Gene Gun DNA-coated gold beads)

Vaccine Name: MVA.HW *Type:* Recombinant Vector (virus/bacteria) *Route:* Intradermal *Formulation:* MVA.HW + PBS

Challenge: SIVmac251 *Route:* Intrarectal

Main Findings:
- High SIV gag specific-CTL response by immunization, capable of killing SIV-infected cells in vitro
- After intrarectal challenge with pathogenic SIVmac251, 2/3 vaccinated animals were infected
- Correlates of protective immunity not defined
- DNA prime-MVA boost regimen is an effective protocol for induction of CTLs in macaques

NHP.58 (11085589) **A vaccine strategy utilizing a combination of three different chimeric vectors which share specific vaccine antigens.**

Authors: Heeney JL, Koopman G, Rosenwirth B, Bogers W, van Dijk J, Nieuwenhuis I, Niphuis H, ten Haaft P, Hanke T, Rhodes G, Berglund P, Burny A, Bex F, Sutter G, Liljestrom P

Journal: J Med Primatol 2000 Aug;29(3-4):268-73.

Objectives: Immunogenicity. Overcomes an anti-vector immune response with chimeric vectors that have in common only the specific antigens for immunization.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: DNA.PTH.SIVmac.J5.gptnr *Type:* DNA *Route:* Intradermal *Formulation:* DNA.PTH.SIVmac.J5.gptnr + Saline

Vaccine Name: DNA.pND14-G1.SIVmac251.env *Type:* DNA *Route:* Intradermal *Formulation:* DNA.pND14-G1.SIVmac251.env + Saline

Vaccine Name: MVA.pUCII.SIVmac.J5 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular *Formulation:* MVA.pUCII.SIVmac.J5 + Saline

Vaccine Name: MVApIII-sp.SIVmac.J5.env *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular *Formulation:* MVApIII-sp.SIVmac.J5.env + Saline

Vaccine Name: SFVpSFVI.SIVmac.J5.gpetnr *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intravenous, Intradermal *Formulation:* SFVpSFVI.SIVmac.J5.gpetnr + Saline

Challenge: SIVmac32H.IXc *Route:* Intravenous

Main Findings:
- Anti-vector immune response to foreign genes of engineered vectors may preclude sufficient 'priming' or immunogenicity, or impair optimal 'boosting' upon repeated immunization

- Describes a new strategy that avoids increased anti-vector responses,allows the use of combinations of vectors to present the same or related antigen differently to the immune system and at alternative sites
- New strategy induces optimal type of immunity against the pathogen

NHP.59 (10906202) **Simian immunodeficiency virus (SIV) gag DNA-vaccinated rhesus monkeys develop secondary cytotoxic T-lymphocyte responses and control viral replication after pathogenic SIV infection.**

Authors: Egan MA, Charini WA, Kuroda MJ, Schmitz JE, Racz P, Tenner-Racz K, Manson K, Wyand M, Lifton MA, Nickerson CE, Fu T, Shiver JW, Letvin NL

Journal: J Virol 2000 Aug;74(16):7485-95.

Objectives: Challenge, Immunogenicity. To use plasmid DNA construct to elicit protective immunity in SIV/macaque model.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: V1R-SIV gag *Type:* DNA *Route:* Intramuscular *Formulation:* V1R-SIV gag + Saline

Challenge: SIVsmE660 *Route:* Intravenous

Main Findings:

- Soluble major histocompatibility class I/peptide tetramers and peptide-specific killing assays are used to monitor CD8(+) T-lymphocyte responses to a dominant SIV Gag epitope in rhesus monkeys
- Codon-optimized SIV gag DNA vaccine construct elicits high-frequency SIV-specific CTL response in peripheral blood and lymph node lymphocytes
- After IV challenge with SIVsm E660, gag plasmid DNA-vaccinated monkeys have better containment of viral replication by 50 dpc

NHP.60.1 (11039923) **Control of viremia and prevention of clinical AIDS in rhesus monkeys by cytokine-augmented DNA vaccination.**

Authors: Barouch DH, Santra S, Schmitz JE, Kuroda MJ, Fu TM, Wagner W, Bilska M, Craiu A, Zheng XX, Krivulka GR, Beaudry K, Lifton MA, Nickerson CE, Trigona WL, Punt K, Freed DC, Guan L, Dubey S, Casimiro D, Simon A, Davies ME, Chastain M, Strom TB, Gelman RS, Montefiori DC, Lewis MG, Emini EA, Shiver JW, Letvin NL

Journal: Science 2000 Oct 20;290(5491):486-92.

Objectives: Challenge, Immunogenicity. Reports the protective efficacy of vaccine-elicited immune responses against a pathogenic SHIV-89.6P challenge in rhesus monkeys.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac239 gag DNA *Type:* DNA *Route:* Intramuscular

Vaccine Name: HIV-1.89.6P env DNA *Type:* DNA *Route:* Intramuscular *Formulation:* HIV-1.89.6P env DNA + IL-2/lg plasmid, IL-2/lg protein

Challenge: SHIV89.6P *Route:* Intravenous

Main Findings:

- The monkeys that received the DNA vaccines plus IL-2/Ig protein or IL-2/Ig plasmid demonstrated markedly higher vaccine-elicited CTL responses than the animals that received the DNA vaccines alone
- All monkeys that received DNA vaccines augmented with IL-2/Ig were infected, demonstrated potent secondary CTL responses, stable CD4+ T cell counts, preserved virus-specific CD4+ T cell responses, low to undetectable setpoint viral loads, and no evidence of clinical disease or mortality by 140 dpc.
- After the final immunization at week 40, the vaccinated monkeys developed significant circulating p11C- and p41A-specific CD8+ T lymphocytes, in contrast with the control monkeys that had no detectable circulating tetramer-positive CD8+ T lymphocytes

NHP.60.2 (11797012) **Eventual AIDS vaccine failure in a rhesus monkey by viral escape from cytotoxic T lymphocytes.**

Authors: Barouch DH, Kunstman J, Kuroda MJ, Schmitz JE, Santra S, Peyerl FW, Krivulka GR, Beaudry K, Lifton MA, Gorgone DA, Montefiori DC, Lewis MG, Wolinsky SM, Letvin NL

Journal: Nature 2002 Jan 17;415(6869):335-9.

Objectives: Challenge.

Main Findings:

- Viral escape from CTL recognition can result in the long-term failure of partial immune protection to challenge (i.e. to control viral replication and prevent clinical disease progression)
- In a cohort of rhesus monkeys that were vaccinated and subsequently infected with a pathogenic hybrid SHIV, the frequency of viral sequence mutations within CTL epitopes correlated with the level of viral replication
- Viral escape from CTL recognition may be a major limitation of the CTL-based AIDS vaccines

NHP.60.3 (12021371) **Prior vaccination increases the epitopic breadth of the cytotoxic T-lymphocyte response that evolves in rhesus monkeys following a simian-human immunodeficiency virus infection.**

Authors: Santra S, Barouch DH, Kuroda MJ, Schmitz JE, Krivulka GR, Beaudry K, Lord CI, Lifton MA, Wyatt LS, Moss B, Hirsch VM, Letvin NL

Journal: J Virol 2002 Jun;76(12):6376-81.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac239 gag DNA *Type:* DNA *Route:* Intramuscular

Vaccine Name: HIV-1.89.6P env DNA *Type:* DNA *Route:* Intramuscular *Formulation:* HIV-1.89.6P env DNA + IL-2/lg plasmid, IL-2/lg protein

Challenge: SHIV89.6P *Route:*

Main Findings:

- rMVA vaccination elicited high-frequency CTL responses to dominant epitopes but with substantially lower frequency to subdominant epitopes
- Animals immunized with DNA plus IL-2/Ig plasmid showed higher frequency p41A-specific CTL responses than animals immunized with DNA alone and controls

NHP.61 (11044096) **Effective induction of simian immunodeficiency virus-specific systemic and mucosal immune responses in primates by vaccination with proviral DNA producing intact but noninfectious virions.**

Authors: Wang SW, Kozlowski PA, Schmelz G, Manson K, Wyand MS, Glickman R, Montefiori D, Lifson JD, Johnson RP, Neutra MR, Aldovini A

Journal: J Virol 2000 Nov;74(22):10514-22.

Objectives: Challenge, Immunogenicity. Reports a pilot evaluation of a DNA vaccine producing genetically inactivated SIV particles in primates, focuses on eliciting mucosal immunity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pVacc1 DNA *Type:* DNA *Routes:* Intrarectal, Intradermal (Gene Gun DNA-coated gold beads), Intradermal, Intramuscular *Formulation:* pVacc1 DNA + Liposomes + Saline

Challenge: SIVmac239 *Route:* Intrarectal

Main Findings:

- IgA in rectal secretions of macaques that received the DNA vaccine intradermally and at the rectal mucosa are higher than in natural infection
- CTL responses were low and sporadic
- After rectal challenge with cloned SIVmac239, some animals with high SIV-specific IgA levels became infected

- High levels of IgA alone are not sufficient to prevent the establishment of chronic infection, although mucosal IgA responses may reduce the infectivity of the initial viral inoculum

NHP.62 (11152527) **DNA vaccination with the human immunodeficiency virus type 1 SF162DeltaV2 envelope elicits immune responses that offer partial protection from simian/human immunodeficiency virus infection to CD8(+) T-cell-depleted rhesus macaques.**

Authors: Cherpelis S, Shrivastava I, Gettie A, Jin X, Ho DD, Barnett SW, Stamatatos L

Journal: J Virol 2001 Feb;75(3):1547-50.

Objectives: Challenge, Immunogenicity. To conduct DNA immunization of macaques with the SF162V2 envelope, then challenge with SHIV162P4.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: DNA.SF162ΔV2 gp140 *Type:* DNA *Routes:* Intradermal, Intramuscular

Vaccine Name: SF162ΔV2 gp140 protein *Type:* Recombinant Subunit Protein *Routes:* Intradermal, Intramuscular *Formulation:* SF162ΔV2 gp140 protein + MF59

Challenge: SHIV162P4 *Route:* Intravenous

Main Findings:

- Immunization elicited lymphoproliferative responses and potent neutralizing antibodies
- Animals were depleted of their CD8+ T lymphocytes and then challenged intravenously with SHIV162P4
- Compared to unvaccinated animals, vaccinated macaques had lower peak viremia levels, rapidly cleared plasma virus, and delayed seroconversion

NHP.63 (11884556) **Induction of mucosal protection against primary, heterologous simian immunodeficiency virus by a DNA vaccine.**

Authors: Fuller DH, Rajakumar PA, Wilson LA, Trichel AM, Fuller JT, Shipley T, Wu MS, Weis K, Rinaldo CR, Haynes JR, Murphey-Corb M

Journal: J Virol 2002 Apr;76(7):3309-17.

Objectives: Challenge, Immunogenicity. To analyze immunogenicity and protective efficacy of a DNA vaccine containing SIV strain 17E-Fr (SIV/17E-Fr) gag-pol-env in rhesus macaques.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIV/17E-Fr gag-pol-env *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal

Challenge: SIVDeltaB670 *Route:* Intrarectal

Main Findings:

- First report of mucosal protection against a primary pathogenic, heterologous isolate of SIV using a commercially viable vaccine approach
- Vaccinated and naive control monkeys were challenged intrarectally with SIV strain DeltaB670 (SIV/DeltaB670), whose env is 15% dissimilar to that of the vaccine strain
- Postchallenge, in 4/7 vaccinees no SIV viral RNA or DNA sequences were found in the peripheral blood, and anamnestic antibody responses were absent

NHP.64 (11085583) **Mucosal challenge of Macaca nemestrina with simian immunodeficiency virus (SIV) following SIV nucleocapsid mutant DNA vaccination.**

Authors: Gorelick RJ, Lifson JD, Yovandich JL, Rossio JL, Piatak M Jr, Scarzello AJ, Knott WB, Bess JW Jr, Fisher BA, Flynn BM, Henderson LE, Arthur LO, Benveniste RE

Journal: J Med Primatol 2000 Aug;29(3-4):209-19.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Vaccine Name: SIV(Mne)NCΔZF2 DNA *Type:* Live Attenuated Virus *Route:* Intramuscular

Vaccine Name: S8-NCΔZF2 *Type:* Live Attenuated Virus *Routes:* Subcutaneous, Intramuscular

Challenge: SIV(Mne) clone E11S *Route:* Intrarectal

Main Findings:

- Challenged mucosally, all 12 macaques became infected, the 4 immunized animals greatly restricted their viral replication
- One immunized animal that controlled replication remains antibody negative, no disease evident 46 wpc

NHP.65.1 (11090194) **Protection of Macaca nemestrina from disease following pathogenic simian immunodeficiency virus (SIV) challenge: utilization of SIV nucleocapsid mutant DNA vaccines with and without an SIV protein boost.**

Authors: Gorelick RJ, Benveniste RE, Lifson JD, Yovandich JL, Morton WR, Kuller L, Flynn BM, Fisher BA, Rossio JL, Piatak M Jr, Bess JW Jr, Henderson LE, Arthur LO

Journal: J Virol 2000 Dec;74(24):11935-49.

Objectives: Challenge, Immunogenicity. To evaluate SIV nucleocapsid mutant DNA vaccines with and without an SIV protein boost.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Vaccine Name: SIV(Mne)NCΔZF2 DNA *Type:* Live Attenuated Virus *Route:* Intramuscular

Vaccine Name: SIV(Mne) gp160Env protein *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Vaccine Name: Gag-Pol particles *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Challenge: SIV(Mne) clone E11S *Route:* Intravenous

Main Findings:

- Background: 11 pigtailed macaques were inoculated with nucleocapsid mutant SIV expressing DNA, intramuscularly (i.m.) in one study and i.m. and subcutaneously in another study. Six control animals received vector DNA lacking SIV sequences
- Post IV challenge, all control animals became infected and 3/4 developed progressive SIV disease
- 2 ypc, most immunized animals had low postacute levels of plasma SIV RNA, no CD4+ T-cell depletion or clinical evidence of progressive disease (see experiment 2 for additional information)

NHP.65.2 (11090194) **Protection of Macaca nemestrina from disease following pathogenic simian immunodeficiency virus (SIV) challenge: utilization of SIV nucleocapsid mutant DNA vaccines with and without an SIV protein boost.**

Authors: Gorelick RJ, Benveniste RE, Lifson JD, Yovandich JL, Morton WR, Kuller L, Flynn BM, Fisher BA, Rossio JL, Piatak M Jr, Bess JW Jr, Henderson LE, Arthur LO

Journal: J Virol 2000 Dec;74(24):11935-49.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Vaccine Name: SIV(Mne)NCΔZF2 DNA *Type:* Live Attenuated Virus *Routes:* Subcutaneous, Intramuscular

Vaccine Name: S8-NCΔZF2 *Type:* Live Attenuated Virus *Routes:* Subcutaneous, Intramuscular

Challenge: SIV(Mne) clone E11S *Route:* Intravenous

Main Findings:

- The vaccine induced only modest and inconsistent humoral responses and no cellular immune responses prior to challenge
- Following iv challenge with 20 animal infectious doses of the pathogenic SIV(Mne) in a long-term study, all control animals became infected and 3/4 animals developed progressive SIV disease leading to death
- All 11 NC mutant SIV DNA-immunized animals became infected following challenge

but decreased initial peak plasma SIV RNA levels compared to those of control animals

NHP.66 (11689679) **Vaccination with attenuated simian immunodeficiency virus by DNA inoculation.**

Authors: Kent SJ, Dale CJ, Preiss S, Mills J, Campagna D, Purcell DF

Journal: J Virol 2001 Dec;75(23):11930-4.

Objectives: Challenge, Immunogenicity. To evaluate attenuated proviral DNA vaccine in macaques.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Vaccine Name: SIVmac239 sbbvΔ3 DNA *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal, Intramuscular

Vaccine Name: SIVmac239 sbbvΔ3Delta5 DNA *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal, Intramuscular

Challenge: SIVmac251 *Route:* Intrarectal

Main Findings:

- Innoculated with wild-type simian immunodeficiency virus strain mac239 (SIV(mac239)) DNA or SIV(mac239) DNA containing a single deletion in the 3' nef-long terminal repeat overlap region (nef/LTR) led to sustained SIV infections and AIDS
- Injection of SIV(mac239) DNA containing identical deletions in both the 5' LTR and 3' nef/LTR resulted in attenuated SIV infections and substantial protection against subsequent mucosal SIV(mac251) challenge

NHP.67 (10869776) **Induction of protective immunity against pathogenic simian immunodeficiency virus by a foreign receptor-dependent replication of an engineered avirulent virus.**

Authors: Matano T, Kano M, Odawara T, Nakamura H, Takeda A, Mori K, Sato T, Nagai Y

Journal: Vaccine 2000 Aug 1;18(28):3310-8.

Objectives: Challenge, Immunogenicity. To develop a chimeric (SIV,Friend Murine leukemia virus) DNA vaccine to induce restricted replication of an avirulent virus.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: FMSIV *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intramuscular

Challenge: SIVmac239 *Route:* Intravenous

Main Findings:

- A novel strategy: a vaccine consisting of a chimeric SIV and a Friend murine leukemia virus, in which the SIV env is replaced with ecotropic Friend murine leukemia virus (FMLV) env to confine its replication to FMLV receptor (mCAT1)-expressing cells
- Macaques vaccinated with both the FMSIV DNA and the mCAT1-expression plasmid DNA generated SIV Gag-specific cellular immune responses and resistance against pathogenic SIVmac239 challenge
- Vaccination with FMSIV DNA alone was insufficient to prevent the disease onset

NHP.68 (11118363) **Induction of immune responses and break of tolerance by DNA against the HIV-1 coreceptor CCR5 but no protection from SIVsm challenge.**

Authors: Zuber B, Hinkula J, Vodros D, Lundholm P, Nilsson C, Morner A, Levi M, Benthin R, Wahren B

Journal: Virology 2000 Dec 20;278(2):400-11.

Objectives: Challenge, Immunogenicity. To explore genetic immunization to induce an immune response directed to CCR5 structures and break immunological tolerance toward endogenous CCR5.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: pcDNA3-CCR5 *Type:* DNA *Route:* Intradermal (Gene Gun DNA-coated gold beads) *Formulation:* pcDNA3-CCR5 + GM-CSF

Vaccine Name: pcDNA3--tet.CCR5 *Type:* DNA *Route:* Intradermal (Gene Gun DNA-coated gold beads) *Formulation:* pcDNA3--tet.CCR5 + GM-CSF

Vaccine Name: CCR5 peptides *Type:* Synthetic Protein/Peptide *Route:* Intramuscular *Formulation:* CCR5 peptides + GM-CSF, Ribilike adjuvant system (MPL, TMD,CWS) + Saline

Challenge: SIVsm *Route:* Intrarectal

Main Findings:

- Intramucosal immunization of cynomolgus macaques with CCR5 DNA followed by boosts with CCR5 peptides induced prominent IgG and IgA antibody responses
- The CCR5-specific antibodies neutralized the infectivity of primary human R5 HIV-1 strains, and the macaque SIVsm
- CCR5 gene and CCR5 peptide immunizations induced B- and T-cell responses
- Tolerance was broken against endogenous macaque CCR5
- Neither protection against nor enhancement of SIVsm infection was achieved

NHP.69 (10894297) **Elicitation of protective immunity against simian immunodeficiency virus infection by a recombinant Sendai virus expressing the Gag protein.**

Authors: Kano M, Matano T, Nakamura H, Takeda A, Kato A, Ariyoshi K, Mori K, Sata T, Nagai Y

Journal: AIDS 2000 Jun 16;14(9):1281-2.

Objectives: Challenge, Immunogenicity. To use recombinant SeV expressing the Gag antigen of SIV, SeV/SIVgag, to elicit protective immunity.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: F(+)SeV-gag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intranasal

Challenge: SIVmac239 *Route:* Intravenous

Main Findings:

- The vaccinated animals and controls were all infected by the challenge virus SIVmac239. Only animals immunized with SeV-SIV-gag were able to control infection by reducing the viral load to below detectable level.

NHP.70 (11689672) **Rapid appearance of secondary immune responses and protection from acute CD4 depletion after a highly pathogenic immunodeficiency virus challenge in macaques vaccinated with a DNA prime/Sendai virus vector boost regimen.**

Authors: Matano T, Kano M, Nakamura H, Takeda A, Nagai Y

Journal: J Virol 2001 Dec;75(23):11891-6.

Objectives: Challenge, Immunogenicity. To test the immunogenicity and protective effect of a SHIV-DNA prime vaccine followed by a single booster with a Gag-expressing Sendai virus (SeV-Gag).

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: F(+)SeV-gag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intranasal

Vaccine Name: FMSIV *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intramuscular *Formulation:* FMSIV + pCMVmCAT1, pCMVN

Challenge: SHIV89.6PD *Route:* Intravenous

Main Findings:

- All naive control macaques showed acute CD4(+) T-cell depletion at 2 wpc (iv SHIV89.6PD)
- All vaccinated macaques with prime/boost regimen were protected from depletion and showed greatly reduced peak viral loads
- Vaccination with DNA alone or SeV-Gag alone did not confer protection
- Differences in secondary responses between the protected and unprotected macaques was clear at 1 wpc
- Rapid secondary responses reduce peak viral loads and protect from acute CD4(+) T-cell depletion

NHP.71 (10983638) **Therapeutic immunization of HIV-infected chimpanzees using HIV-1 plasmid antigens and**

interleukin-12 expressing plasmids.

Authors: Boyer JD, Cohen AD, Ugen KE, Edgeworth RL, Bennett M, Shah A, Schumann K, Nath B, Javadian A, Bagarazzi ML, Kim J, Weiner DB

Journal: AIDS 2000 Jul 28;14(11):1515-22.

Objectives: Immunogenicity, Immunotherapy. To assess HIV-1 DNA vaccination and co-immunization with interleukin (IL)-12 and IL-10 as immunotherapy in the HIV-1 infected chimpanzee model system.

Species/Subspecies: Pan Troglodytes (Chimpanzee)

Vaccine Name: pCMN160 (HIV-1 MN env) *Type:* DNA *Route:* Intramuscular *Formulation:* pCMN160 (HIV-1 MN env) + pCIL-10, pCIL12

Vaccine Name: pCGag/Pol *Type:* DNA *Route:* Intramuscular *Formulation:* pCGag/Pol + pCIL-10, pCIL12

Challenge: HIV-1 IIIB *Route:*

Main Findings:

- No evidence of systemic toxicity associated with DNA immunization or the cytokine-expressing plasmids
- IL-12/HIV-1 DNA vaccinated animals enhanced proliferative responses to multiple HIV-1 antigens at multiple time points
- Animal co-immunized with HIV-1 and IL-10 did not have any changes in the proliferative responses
- Control chimpanzee demonstrated moderate increases in the proliferative responses to HIV-1 antigens

NHP.72 (9971763) **Acute effects of pathogenic simian-human immunodeficiency virus challenge on vaccine-induced cellular and humoral immune responses to Gag in rhesus macaques.**

Authors: Steger KK, Waterman PM, Pauza CD

Journal: J Virol 1999 Mar;73(3):1853-9.

Objectives: Challenge, Immunogenicity. To test immunization with recombinant Salmonella typhimurium (expressing Gag) or soluble Gag in adjuvant, by challenge with SHIV89.6PD (macaques).

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVhu *Type:* Live Attenuated Virus *Routes:* Intravenous, Intragastric, Intramuscular *Formulation:* SIVhu + Adjumer™

Challenge: SHIV89.6PD *Route:* Intrarectal

Main Findings:

- Virus infection accompanied by rapid losses of lymphoproliferative responses to Gag or phytohemagglutinin
- 8 wpc mitogen responses recovered to near normal levels but antigen-specific immunity remained low or undetectable
- Serum antibody levels elevated initially but soon dropped well below levels achieved by immunization
- Rapid depletion of preexisting Gag-specific CD4(+) T cells prevent or limit subsequent antiviral cellular and humoral immune responses during acute SHIV infection

NHP.73 (10461832) **Combined systemic and mucosal immunization with microsphere-encapsulated inactivated simian immunodeficiency virus elicits serum, vaginal, and tracheal antibody responses in female rhesus macaques.**

Authors: Israel ZR, Gettie A, Ishizaka ST, Mishkin EM, Staas J, Gilley R, Montefiori D, Marx PA, Eldridge JH

Journal: AIDS Res Hum Retroviruses 1999 Aug 10;15(12):1121-36.

Objectives: Challenge, Immunogenicity. To determine the efficacy of immunization with microsphere-encapsulated whole inactivated SIV by combined systemic and mucosal administration to protect female rhesus macaques against vaginal challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac251.whole inactivated *Type:* Whole (killed) Inactivated Virus *Routes:* Intratracheal, Oral, Intramuscular

Vaccine Name: vvrgp140 *Type:* DNA *Routes:* Oral

Challenge: SIVmac251 *Route:* Vaginal or perivaginal

Main Findings:

- Intramuscular priming resulted in strong IgG and modest IgA response
- Intratracheal boosting following intramuscular priming resulted in high bronchial alveolar wash IgG and less pronounced IgA
- IgG was present in the animals immunized intramuscularly boosted either intramuscularly or intratracheally
- No neutralizing antibody to homologous SIVmac251 in response to the immunization with the whole inactivated SIV vaccine
- On vaginal challenge none of the immunized groups was infected at a lesser frequency than the unimmunized controls

NHP.74 (10438051) **Induction of mucosal antibody responses by microsphere-encapsulated formalin-inactivated simian immunodeficiency virus in a male urethral challenge model.**

Authors: Ishizaka ST, Israel ZR, Gettie A, Mishkin EM, Staas JK, Gilley RM, Dailey PJ, Montefiori DC, Marx PA, Eldridge JH

Journal: Vaccine 1999 Jul 16;17(22):2817-25.

Objectives: Challenge, Immunogenicity. To test use of microsphere-encapsulated formalin-inactivated SIV particles against mucosal SIV challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Whole inactivated SIVmac239 (encapsulated) *Type:* Whole (killed) Inactivated Virus *Routes:* Intratracheal, Intramuscular

Challenge: SIVmac251 *Route:* Urethral

Main Findings:

- Macaques, primed intramuscularly, boosted tracheally, had strong Iga response to SIV vaccine
- The bulk of antibody response was against non-envelope epitopes
- No neutralizing antibody observed
- Intraurethral challenge with cell-free rhesus-grown virus showed no evidence of protection against challenge
- Microsphere-based immunization raises local and system responses, but does not provide sufficient immunity to protect against mucosal challenge

NHP.75 (10074183) **Comparison of immunity generated by nucleic acid-, MF59-, and ISCOM-formulated human immunodeficiency virus type 1 vaccines in Rhesus macaques: evidence for viral clearance.**

Authors: Verschoor EJ, Mooij P, Oostermeijer H, van der Kolk M, ten Haaft P, Verstrepen B, Sun Y, Morein B, Akerblom L, Fuller DH, Barnett SW, Heeney JL

Journal: J Virol 1999 Apr;73(4):3292-300.

Objectives: Challenge, Immunogenicity. To compare the kinetics of T-helper immune responses in rhesus monkeys by 3 HIV vaccine strategies: a rgp120SF2 expressed in vivo by DNA immunization or when it was delivered as a subunit protein vaccine formulated with the MF59 adjuvant or by ISCOMs.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pUCgp120SF2-gold particle *Type:* DNA *Route:* Intradermal (Gene Gun DNA-coated gold beads)

Vaccine Name: HIV-1SF2 rgp120 *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* HIV-1SF2 rgp120 + MF59, ISCOM(s)™

Main Findings:
- Virus-neutralizing antibodies against HIV-1SF2 reached similar titers in the two rgp120SF2 protein-immunized groups, with different kinetics, while nab were delayed and low in the DNA-immunized animals
- rgp120/ISCOM-immunized animals rapidly developed marked IL-2, IFN-gamma (type 1-like), and IL-4 responses that peaked after the second immunization
- Protection challenge with SHIV was observed in the two groups receiving the rgp120 subunit vaccines. Half of the animals in the ISCOM group were completely protected from infection

NHP.76 (1708168) **Recombinant virus vaccine-induced SIV-specific CD8+ cytotoxic T lymphocytes.**

Authors: Shen L, Chen ZW, Miller MD, Stallard V, Mazzara GP, Panicali DL, Letvin NL

Journal: Science 1991 Apr 19;252(5004):440-3.

Objectives: Immunogenicity. To determine whether a genetically restricted live recombinant virus, the vaccinia-simian immunodeficiency virus of macaques (SIVmac) could generate a T lymphocyte-mediated antiviral response in a primate.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: rVaccinia-SIVmac-env.gagpol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intradermal

Main Findings:
- Vaccinia-SIVmac vaccination elicited an SIVmac Gag-specific, CD8+ CTL response in rhesus monkeys
- The rhesus monkey major histocompatibility complex (MHC) class I gene product restricting this CTL response was defined
- Both the vaccinated and control SIVmac-infected monkeys that shared this MHC class I gene product developed CTLs with the same Gag epitope specificity
- The findings support the use of recombinant virus vaccines for the prevention of HIV infections in humans

NHP.77 (10506654) **Accelerated clearance of SHIV in rhesus monkeys by virus-like particle vaccines is dependent on induction of neutralizing antibodies.**

Authors: Notka F, Stahl-Hennig C, Dittmer U, Wolf H, Wagner R

Journal: Vaccine 1999 Sep;18(3-4):291-301.

Objectives: Challenge, Immunogenicity. To investigate efficacy of recombinant, insect cell derived SIV Pr56(gag) virus-like particles modified either by inserting HIV-1 Gp160 derived peptides into the Pr56(gag) precursor or by integrating the complete HIV-1 gp120 in the particle membrane.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIV Pr56gag VLP-type II *Type:* Virus-like Particle *Route:*

Vaccine Name: SFV- Pr56gag VLP-type II *Type:* Live Virus *Route:*

Vaccine Name: SFV-SIV Pr56gag VLP-type I *Type:* Virus-like Particle *Route:*

Challenge: SHIV-4.vpu+ *Route:* Intravenous

Main Findings:
- All vaccinated monkeys became infected upon challenge with SHIV-4, but animals vaccinated with VLPs presenting the complete gp120 cleared virus faster than nonimmunized controls
- Observed virus elimination significantly correlated with an anamnesticantibody response and accelerated appearance of neutralizing antibodies postchallenge

NHP.78 (10725402) **Vaccination with tat toxoid attenuates disease in simian/HIV-challenged macaques.**

Authors: Pauza CD, Trivedi P, Wallace M, Ruckwardt TJ, Le Buanec H, Lu W, Bizzini B, Burny A, Zagury D, Gallo RC

Journal: Proc Natl Acad Sci U S A 2000 Mar 28;97(7):3515-9.

Objectives: Challenge, Immunogenicity. To study the role of tat by immunizing macaques with chemically inactivated tat toxoid and challenging animals intrarectally with SHIV89.6PD.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: inactivated Tat toxoid *Type:* Other *Routes:* Intradermal, Intramuscular *Formulation:* inactivated Tat toxoid + Adjumer™

Vaccine Name: rVaccinia-gp160 *Type:* Recombinant Vector (virus/bacteria) *Route:* Intradermal

Vaccine Name: soluble gp160 *Type:* Purified Viral Products *Route:* Intramuscular

Vaccine Name: biologically active Tat protein *Type:* Purified Viral Products *Routes:* Intradermal, Intramuscular *Formulation:* biologically active Tat protein + Adjumer™

Challenge: SHIV89.6PD *Route:* Intrarectal

Main Findings:

- Immune animals had significantly attenuated disease with lowered viral RNA, interferon-Alpha, and chemokine receptor expression (CXCR4 and CCR5) on CD4+ T cells, features linked to in vitro effects of Tat
- Immunization with Tat toxoid inhibits key steps in viral pathogenesis

NHP.79 (10936096) **Evaluation of immune responses induced by HIV-1 gp120 in rhesus macaques: effect of vaccination on challenge with pathogenic strains of homologous and heterologous simian human immunodeficiency viruses.**

Authors: Kumar A, Lifson JD, Silverstein PS, Jia F, Sheffer D, Li Z, Narayan O

Journal: Virology 2000 Aug 15;274(1):149-64.

Objectives: Challenge, Immunogenicity. To evaluate monomeric recombinant gp120 of HIV-1(LAI) (rgp120) vaccines against (SHIV(KU-2) and SHIV(89.6)P.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Monomeric rgp120 *Type:* Recombinant Subunit Protein *Route:* Intradermal *Formulation:* Monomeric rgp120 + Freund′s Complete Adjuvant

Challenge: SHIV-KU2, SHIV89.6P *Route:* Intravenous

Main Findings:

- All 8 vaccinated macaques developed high antibody titers against rgp120 that reacted efficiently with envelope proteins of homologous SHIVKU-2 and poorly with the SHIV89.6P envelope
- Vaccinated macaques showed anamnestic antibody and T-helper cell responses, but T-helper responses were short-lived
- After challenge, level of productive virus replication was indistinguishable between vaccine and control groups, suggesting that rgp120 did not confer protection against virus replication

NHP.80 (10756013) **Evidence for viral virulence as a predominant factor limiting human immunodeficiency virus vaccine efficacy.**

Authors: Mooij P, Bogers WM, Oostermeijer H, Koornstra W, Ten Haaft PJ, Verstrepen BE, Van Der Auwera G, Heeney JL

Journal: J Virol 2000 May;74(9):4017-27.

Objectives: Challenge, Immunogenicity. Using vaccination with CCR5 binding envelope of HIV-1W6.1D to determine if virus virulence or genetic distance had a greater impact on HIV-1 vaccine efficacy against SHIV challenge (rhesus macaques).

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: rgp120W6.1D *Type:* Recombinant Subunit Protein *Route:*

Challenge: SHIV.W6.1D, SHIV.SF13, SHIVHan2, SHIV89.6P *Route:*

Main Findings:

- Protection from either of the divergent SHIVsf13 or SHIVhan2 challenges was

demonstrated in the majority of the vaccinated animals
- Second challenge with the virulent SHIV89.6p achieved protection in only one of the previously protected vaccinees
- Immunization beneficial to viral load and CD4+ T-cell counts, but failed to protect from infection

NHP.81 (11689887) **Protection of rhesus macaques against disease progression from pathogenic SHIV-89.6PD by vaccination with phage-displayed HIV-1 epitopes.**

Authors: Chen X, Scala G, Quinto I, Liu W, Chun TW, Justement JS, Cohen OJ, vanCott TC, Iwanicki M, Lewis MG, Greenhouse J, Barry T, Venzon D, Fauci AS

Journal: Nat Med 2001 Nov;7(11):1225-31.

Objectives: Challenge, Immunogenicity. To test an array of HIV-specific epitopes that behave as antigenic mimics (mimotopes) of conformational epitopes of gp120 and gp41 proteins for clades A-F.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: gp120/gp41 mimotopes *Type:* Synthetic Protein/Peptide *Route:* Intramuscular *Formulation:* gp120/gp41 mimotopes + QS-21

Challenge: SHIV89.6PD *Route:* Intravenous

Main Findings:
- Upon intravenous challenge with 60 MID50 of pathogenic SHIV-89.6PD, phage-borne epitopes elicit envelope-specific antibody responses
- 4/5 mimotope-immunized monkeys had lower levels of peak viremia, followed by viral set points of undetectable or transient levels of viremia, mild decline of CD4+ T cells, protection from progression to AIDS-like illness

NHP.82.1 (10196297) **Protection of Macaques against pathogenic simian/human immunodeficiency virus 89.6PD by passive transfer of neutralizing antibodies.**

Authors: Mascola JR, Lewis MG, Stiegler G, Harris D, VanCott TC, Hayes D, Louder MK, Brown CR, Sapan CV, Frankel SS, Lu Y, Robb ML, Katinger H, Birx DL

Journal: J Virol 1999 May;73(5):4009-18.

Objectives: Challenge, Immunogenicity. Used a chimeric SHIV based on the envelope of a primary isolate (HIV-89.6) to perform passive-transfer experiments and study the role of anti-envelope antibodies in protection (rhesus macaques).

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Monoclonal antibody 2G12 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name: Monoclonal antibody 2F5 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name: HIVIG *Type:* Passive Antibody *Route:* Intravenous

Challenge: SHIV89.6PD *Route:* Intravenous

Main Findings:
- 3/6 animals given HIVIG/2F5/2G12 were completely protected; the remaining 3 animals became SHIV infected but displayed reduced plasma viremia and near normal CD4(+)-cell counts
- 1/3 monkeys given 2F5/2G12 exhibited only transient evidence of infection; 2/3 had marked reductions in viral load
- All monkeys that received HIVIG, 2F5, or 2G12 alone became infected and developed high-level plasma viremia
- General correlation between in vitro neutralization and protection

NHP.82.2 (10196297) **Protection of Macaques against pathogenic simian/human immunodeficiency virus 89.6PD by passive transfer of neutralizing antibodies.**

Authors: Mascola JR, Lewis MG, Stiegler G, Harris D, VanCott TC, Hayes D, Louder MK, Brown CR,

Sapan CV, Frankel SS, Lu Y, Robb ML, Katinger H, Birx DL

Journal: J Virol 1999 May;73(5):4009-18.

Objectives: Challenge, Immunogenicity, Passive Immunization. Used a chimeric SHIV based on the envelope of a primary isolate (HIV-89.6) to perform passive-transfer experiments and study the role of anti-envelope antibodies in protection.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Monoclonal antibody 2G12 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name: Monoclonal antibody 2F5 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name: HIVIG *Type:* Passive Antibody *Route:* Intravenous

Challenge: SHIV89.6PD *Route:* Intravenous

NHP.83 (10772996) **Passive infusion of immune serum into simian immunodeficiency virus-infected rhesus macaques undergoing a rapid disease course has minimal effect on plasma viremia.**

Authors: Binley JM, Clas B, Gettie A, Vesanen M, Montefiori DC, Sawyer L, Booth J, Lewis M, Marx PA, Bonhoeffer S, Moore JP

Journal: Virology 2000 Apr 25;270(1):237-49.

Objectives: Immunotherapy, Passive Immunization. To investigate the role of passive immunization in controling viremia and disease progression in infected macaques.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVIG-1 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name: SIVIG-2 *Type:* Passive Antibody *Route:* Intravenous

Main Findings:

- Despite restoring anti-SIV titers to levels typical of macaques with a normal disease course, SIVIG had only a modest effect on plasma SIV RNA and cell-associated viral load
- The kinetics of the viremia changes are inconsistent with neutralization of new cycles of infection. More likely, perhaps unexpectedly, is that infused antibodies killed SIV-infected cells, via an effector mechanism such as antibody-dependent cellular cytotoxicity.

NHP.84 (10468614) **Postexposure immunoprophylaxis of primary isolates by an antibody to HIV receptor complex.**

Authors: Wang CY, Sawyer LS, Murthy KK, Fang X, Walfield AM, Ye J, Wang JJ, Chen PD, Li ML, Salas MT, Shen M, Gauduin MC, Boyle RW, Koup RA, Montefiori DC, Mascola JR, Koff WC, Hanson CV

Journal: Proc Natl Acad Sci U S A 1999 Aug 31;96(18):10367-72.

Objectives: Immunotherapy. To evaluate neutralizing activity of mAb B4, a monoclonal antibody directed against HIV receptor complex.

Species/Subspecies: Pan Troglodytes (Chimpanzee)

Vaccine Name: mAb B4 *Type:* Passive Antibody *Route:*

Challenge: HIV-1.DH12 *Route:* Intravenous

Main Findings:

- mAb B4 preferentially neutralized primary HIV-1 isolates, including syncytium-inducing(si) and non-si phenotypes, for subtypes A-G and HIV-2, SIV, SHIV
- Neutralization demonstrated in both pre- and postinfection models
- Administration of mAb B4 after infectious challenge totally interrupted the infection of hu-PBL-severe combined immunodeficient mice by PBL-grown HIV-1 and the infection of chimpanzees by chimp-adapted HIV-1

NHP.85 (10655110) **Human neutralizing monoclonal antibodies of the IgG1 subtype protect against mucosal simian-human immunodeficiency virus infection.**

Authors: Baba TW, Liska V, Hofmann-Lehmann R, Vlasak J, Xu W, Ayehunie S, Cavacini LA, Posner MR,

Katinger H, Stiegler G, Bernacky BJ, Rizvi TA, Schmidt R, Hill LR, Keeling ME, Lu Y, Wright JE, Chou TC, Ruprecht RM

Journal: Nat Med 2000 Feb;6(2):200-6.

Objectives: Challenge, Passive Immunization. To evaluate triple combination of the human IgG1 monoclonal antibodies F105, 2G12 and 2F5, which neutralize SHIV-vpu+, a chimeric simian-human virus that encodes the env gene of HIV-IIIB, to develop immunoprophylaxis against intrapartum HIV-1 transmission

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: F105/2G12/2F5 mab *Type:* Passive Antibody *Route:* Intravenous

Challenge: SHIV-vpu+ *Route:* Intravenous, Oral

Main Findings:

- Four pregnant macaques treated with a triple combination of mab F105, 2G12 and 2F5 were protected from SHI-vpu+ challenge
- Infants treated with the mab triple combination at birth and and challenged orally: no evidence of infection in any infant during 6 months of follow-up
- Epitopes recognized by the three monoclonal antibodies are important determinants for achieving substantial protection

NHP.86.1 (9930869) **Neutralizing antibody directed against the HIV-1 envelope glycoprotein can completely block HIV-1/SIV chimeric virus infections of macaque monkeys.**

Authors: Shibata R, Igarashi T, Haigwood N, Buckler-White A, Ogert R, Ross W, Willey R, Cho MW, Martin MA

Journal: Nat Med 1999 Feb;5(2):204-10.

Objectives: Challenge, Passive Immunization. To assess whether HIV-1 envelope-specific antibodies confer resistance against primate lentivirus infections (pigtailed macaques).

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Vaccine Name: Anti-HIV-1 ch4750 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name: Anti-HIV-1 ch1206 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name: Anti-HIV-1 ch911 *Type:* Passive Antibody *Route:* Intravenous

Challenge: SHIV-MD14YE (DH12) *Route:* Intravenous

Main Findings:

- In pigtailed macaques passively immunized with HIV-1 specific antibodies from chimpanzees, anti-SHIV neutralizing activity is the absolute requirement for antibody-mediated protection
- Ti ter in plasma for complete protection of SHIV-challenged macaques in range of 1:5-1:8
- HIV-1-specific nab studied are able to bind to native gp120 present on infectious virus particles
- Administration of non-neutralizing anti-HIV IgG neither inhibited nor enhanced a subsequent SHIV infection.

NHP.86.2 (9930869) **Neutralizing antibody directed against the HIV-1 envelope glycoprotein can completely block HIV-1/SIV chimeric virus infections of macaque monkeys.**

Authors: Shibata R, Igarashi T, Haigwood N, Buckler-White A, Ogert R, Ross W, Willey R, Cho MW, Martin MA

Journal: Nat Med 1999 Feb;5(2):204-10.

Objectives: Challenge, Immunogenicity, Passive Immunization.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Vaccine Name: Anti-HIV-1 ch1206 *Type:* Passive Antibody *Route:* Intravenous

Challenge: SHIV-MD14YE (DH12) *Route:* Intravenous

NHP.87 (10082123) **Passively administered neutralizing serum that protected macaques against infection with parenterally inoculated pathogenic simian-human immunodeficiency virus failed to protect against mucosally inoculated virus.**

Authors: Joag SV, Li Z, Wang C, Foresman L, Jia F, Stephens EB, Zhuge W, Narayan O

Journal: AIDS Res Hum Retroviruses 1999 Mar 1;15(4):391-4.

Objectives: Challenge, Immunogenicity, Passive Immunization. To determine whether passive immunization with neutralizing serum would protect macaques against infection with pathogenic SHIV following oral inoculation of the virus.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Vaccine Name: Anti-SHIV Plasma *Type:* Passive Antibody *Route:* Intravenous

Challenge: SHIV.KU1 *Route:* Oral

Main Findings:

- Ten pigtail macaques were inoculated orally with one animal infectious dose of SHIV(KU-1). Four of the 10 had been given pooled anti-SHIV plasma (15 ml/kg) 24 hr earlier, 4 others were given the same dose of anti-SHIV plasma 2 hr after virus challenge, and the 2 remaining animals were used as controls
- The neutralizing antibodies failed to protect macaques against infection after mucosal challenge with SHIV(KU-1).

NHP.88 (11907251) **Tat-vaccinated macaques do not control simian immunodeficiency virus SIVmac239 replication.**

Authors: Allen TM, Mortara L, Mothe BR, Liebl M, Jing P, Calore B, Piekarczyk M, Ruddersdorf R, O'Connor DH, Wang X, Wang C, Allison DB, Altman JD, Sette A, Desrosiers RC, Sutter G, Watkins DI

Journal: J Virol 2002 Apr;76(8):4108-12.

Objectives: Challenge, Immunogenicity. To assess the role of Tat-specific CTL in controlling pathogenic SIVmac239 replication after using a DNA-prime, vaccinia virus Ankara-boost vaccine regimen

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: MVA-SIV239tat *Type:* Recombinant Vector (virus/bacteria) *Route:* Intradermal

Vaccine Name: MVA-SIVSL8-tat28-35 *Type:* Recombinant Vector (virus/bacteria) *Route:* Intradermal

Vaccine Name: MVA-SIV251 32H tat *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intrarectal, Intradermal *Formulation:* MVA-SIV251 32H tat + PBS

Challenge: SIVmac239 *Route:* Intrarectal

Main Findings:

- Despite the induction of Tat-specific CTL, there was no significant reduction in either peak or viral set point in animals immunized with a DNA-prime, vaccinia virus Ankara-boost vaccine regimen and challenged with SIVmac239 compared to controls

NHP.89 (12021347) **Critical role for Env as well as Gag-Pol in control of a simian-human immunodeficiency virus 89.6P challenge by a DNA prime/recombinant modified vaccinia virus Ankara vaccine.**

Authors: Amara RR, Smith JM, Staprans SI, Montefiori DC, Villinger F, Altman JD, O'Neil SP, Kozyr NL, Xu Y, Wyatt LS, Earl PL, Herndon JG, McNicholl JM, McClure HM, Moss B, Robinson HL

Journal: J Virol 2002 Jun;76(12):6138-46.

Objectives: Challenge, Immunogenicity. To test Gag-Pol DNA priming and Gag-Pol rMVA boosting to evaluate the contribution of anti-Env immune responses to viral control.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pGA1-gag-pol DNA vaccine *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal *Formulation:* pGA1-gag-pol DNA vaccine + PBS

Vaccine Name: rMVA SIV239 gag-pol *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular *Formulation:* rMVA SIV239 gag-pol + PBS

Challenge: SHIV89.6P *Route:* Intrarectal

Main Findings:

- Gag-specific T cell response to a gag-pol DNA vaccine was similar to those raised against the gag-pol-env vaccine and were capable of controlling challenge infection with SHIV89.6P
- The control of the SHIV 89.6P challenge was delayed and inconsistent in the Gag-Pol-vaccinated group and all of the animals underwent severe and, in most cases, sustained loss of CD4(+) cells
- Most of the lost CD4(+) cells in the Gag-Pol-vaccinated group were uninfected cells, suggesting that the rapid appearance of binding antibody for Env in Gag-Pol-Env-vaccinated animals helped protect uninfected CD4(+) cells from Env-induced apoptosis

NHP.90.1 (12009868) **Comparison of vaccine strategies using recombinant env-gag-pol MVA with or without an oligomeric Env protein boost in the SHIV rhesus macaque model.**

Authors: Earl PL, Wyatt LS, Montefiori DC, Bilska M, Woodward R, Markham PD, Malley JD, Vogel TU, Allen TM, Watkins DI, Miller N, Moss B

Journal: Virology 2002 Mar 15;294(2):270-81.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: rMVASIV239gagpol.HIV89.6env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name: Oligomeric HIV-1.89.6 gp140 *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Challenge: SHIV89.6 *Route:* Intravenous

Main Findings:

- All control and vaccinated animals except one became infected. However, the levels of viremia were as follows: controls >rMVA alone > rMVA >protein. The differences were statistically significant between immunized and control groups but not between the two immunized groups
- A relationship between vaccine-induced antibody titers and reduction in virus burden was observed

NHP.90.2 (12009868) **Comparison of vaccine strategies using recombinant env-gag-pol MVA with or without an oligomeric Env protein boost in the SHIV rhesus macaque model.**

Authors: Earl PL, Wyatt LS, Montefiori DC, Bilska M, Woodward R, Markham PD, Malley JD, Vogel TU, Allen TM, Watkins DI, Miller N, Moss B

Journal: Virology 2002 Mar 15;294(2):270-81.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: rMVASIV239gagpol.HIV89.6env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name: Oligomeric HIV-1.89.6 gp140 *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Challenge: SHIV89.6P *Route:* Intravenous

Main Findings:

- All animals became infected
- The vaccinated group exhibited a 5-fold reduction in peak viremia and a 10-fold reduction in the postacute phase viremia in comparison to the controls
- All of the controls required euthanasia by 10 mpc. A relationship between vaccine-induced antibody titers and reduction in virus burden was observed in both studies
- Immunization with MVA/SHIV89.6 alone or with a protein boost stimulated both arms

of the immune system and resulted in significant control of viremia and delayed progression to disease after challenge with SHIV-89.6P.

NHP.92 (12111421) **Characterization of simian and human immunodeficiency chimeric viruses re-isolated from vaccinated macaque monkeys after challenge infection.**

Authors: Kwofie TB, Miura T, Ibuki K, Enose Y, Suzuki H, Ui M, Kuwata T, Hayami M

Journal: Arch Virol 2002 Jun;147(6):1091-104.

Objectives: Challenge, Immunogenicity. To examine the biological properties of circulating viruses whose replication has been suppressed in vaccinated monkeys.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- Monkeys vaccinated with nef-deleted SHIVs were either fully or partially protected against challenge with acute pathogenic SHIV-89.6 P.
- Though the vaccination did not completely prevent the replication of the challenge virus in the monkeys it did contain the challenge virus by suppressing the pathogenic variants

NHP.93 (12100017) **Spontaneous production of RANTES and antigen-specific IFN-gamma production in macaques vaccinated with SHIV-4 correlates with protection against SIVsm challenge.**

Authors: Ahmed RK, Makitalo B, Karlen K, Nilsson C, Biberfeld G, Thorstensson R

Journal: Clin Exp Immunol 2002 Jul;129(1):11-8.

Objectives: Challenge, Immunogenicity. To investigate the production of beta-chemokines in eight cynomolgus macaques vaccinated with non-pathogenic SHIV-4 in relation to protection against pathogenic SIVsm challenge.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: SHIV-4 *Type:* Live Virus *Route:* Intravenous

Challenge: SIVsm *Route:* Intrarectal

Main Findings:

- 2/8 vaccinated monkeys were completely protected and one was partially protected against the challenge virus
- The monkeys that resisted infectious SIVsm virus challenge showed higher spontaneous beta-chemokine production by peripheral blood mononuclear cells and had higher numbers of antigen-induced IFN-gamma secreting cells compared to the non-protected animals.
- The genetic background of the host and/or environmental factors are involved in the chemokine production and beta-chemokines contribute to protection against HIV/SIV infection

NHP.94 (1281660) **Vaccination of macaques with SIV conserved envelope peptides suppressed infection and prevented disease progression and transmission.**

Authors: Shafferman A, Lewis MG, McCutchan FE, Benveniste RE, Jahrling PB, Hickman RL, Lai CY, Burke DS, Eddy GA

Journal: AIDS Res Hum Retroviruses 1992 Aug;8(8):1483-7.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVenv-Bgal peptides *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* SIVenv-Bgal peptides + Freund′s Complete Adjuvant

Challenge: SIV(Mne) clone E11S *Route:* Intravenous

Main Findings:

- Vaccinated macaques became transiently viremic following challenge with SIVmne
- Lymph nodes from all vaccinated macaques remain SIV-PCR positive
- Lymph nodes and whole blood from vaccinated macaques challenged with SIV could not

transmit SIV to naive macaques

NHP.95.1 (1433263) **Comparison of protection from homologous cell-free vs cell-associated SIV challenge afforded by inactivated whole SIV vaccines.**

Authors: Heeney JL, de Vries P, Dubbes R, Koornstra W, Niphuis H, ten Haaft P, Boes J, Dings ME, Morein B, Osterhaus AD

Journal: J Med Primatol 1992 Feb-May;21(2-3):126-30.

Objectives: Challenge, Immunogenicity. To determine if SIV vaccines could protect against challenge with PBMCs from an SIV infected rhesus monkeys.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- 100% SIV vaccinated animals challenged with the 11-88 cell-free stock of SIVmac32H were protected, whereas only 50% of the SIV vaccinated monkeys receiving the same infectious dose of the 1XC cell stock were protected.

NHP.95.2 (1466991) **Comparison of protection afforded by whole virus ISCOM versus MDP adjuvanted formalin-inactivated SIV vaccines from IV cell-free or cell-associated homologous challenge.**

Authors: Osterhaus A, de Vries P, Morein B, Akerblom L, Heeney J

Journal: AIDS Res Hum Retroviruses 1992 Aug;8(8):1507-10.

Objectives: Challenge, Immunogenicity. To test SIV-ISCOM and SIV-MDP adjuvanted vaccines for their potential to induce protection from intravenous homologous SIV challenge in rhesus monkeys.

Main Findings:

- 7/7 monkeys vaccinated 4x over a 4-month period with the SIV-ISCOM or the SIV-MDP vaccine were protected from developing viremia during a three-month observation period since intravenous challenge with 10 MID50 cell-free SIVmac251(32H)
- 2/4 and 2/4 monkeys in 2 other groups of 4 monkeys vaccinated in the same way with either of these vaccines, then challenged (intravenously with 10 MID50 of SIVmac251(32H)-infected PBMC of a rhesus monkey) were protected
- All the control animals vaccinated with measles virus ISCOMS or MDP adjuvanted measles virus antigen were infected upon challenge
- Conclusion: vaccinated previously unchallenged nonhuman primates can be protected from infection with lentivirus-infected PBMC from another animal. Serological analysis indicated that SIV-specific serum antibody titers were considerably higher in SIV-ISCOM vaccinated animals than in the SIV-MDP vaccinated animals.

NHP.96 (1346285) **Intrarectal challenge of macaques vaccinated with formalin-inactivated simian immunodeficiency virus.**

Authors: Cranage MP, Baskerville A, Ashworth LA, Dennis M, Cook N, Sharpe S, Farrar G, Rose J, Kitchin PA, Greenaway PJ

Journal: Lancet 1992 Feb 1;339(8788):273-4.

Objectives: Challenge, Immunogenicity. To test the immunogenicity and efficacy of a formalin-inactivated SIV in rhesus macaques.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- 4 rhesus macaques vaccinated with a formalin-inactivated SIV given intramuscularly were protected from challenge up to 10 mpc

NHP.97 (1466966) **Immunization of rhesus monkeys with high- and low-dose Tween-ether-disrupted SIVMAC.**

Authors: Voss G, Stahl-Hennig C, Petry H, Coulibaly C, Nick S, Fuchs D, Wachter H, Luke W, Hunsmann G

Journal: AIDS Res Hum Retroviruses 1992 Aug;8(8):1397-400.

Objectives: Challenge, Immunogenicity. To test the immunogenicity and protection from challenge induced by a low dose of tween-ether-disrupted SIVmac251.32H.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac251/32H (Tween/Ether) *Type:* Whole (killed) Inactivated Virus *Route:* *Formulation:* SIVmac251/32H (Tween/Ether) + Alum

Challenge: SIVmac251(32H) *Route:*

Main Findings:
- 3/3 naive controls infected 14 dpc (increased neopterin levels correlated with infection)
- 4/7 protected from infection

NHP.98 (10759543) **Augmentation of immune responses to HIV-1 and simian immunodeficiency virus DNA vaccines by IL-2/Ig plasmid administration in rhesus monkeys.**

Authors: Barouch DH, Craiu A, Kuroda MJ, Schmitz JE, Zheng XX, Santra S, Frost JD, Krivulka GR, Lifton MA, Crabbs CL, Heidecker G, Perry HC, Davies ME, Xie H, Nickerson CE, Steenbeke TD, Lord CI, Montefiori DC, Strom TB, Shiver JW, Lewis MG, Letvin NL

Journal: Proc Natl Acad Sci U S A 2000 Apr 11;97(8):4192-7.

Objectives: Immunogenicity. To investigate whether DNA vaccine-elicited immune responses in rhesus monkeys could be augmented by using either an IL-2/Ig fusion protein or a plasmid expressing IL-2/Ig.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac239 gag DNA *Type:* DNA *Route:* Intramuscular *Formulation:* SIVmac239 gag DNA + Saline

Vaccine Name: HIV-1.89.6P env DNA *Type:* DNA *Route:* Intramuscular *Formulation:* HIV-1.89.6P env DNA + IL-2/lg plasmid, IL-2/lg protein + Saline

Main Findings:
- The administration of both IL-2/Ig protein and IL-2/Ig plasmid induced a significant and sustained in vivo activation of peripheral T cells in the vaccinated monkeys
- The monkeys that received IL-2/Ig plasmid generated 30-fold higher Env-specific antibody titers and 5-fold higher Gag-specific, tetramer-positive CD8+ T cell levels than the monkeys receiving the DNA vaccines alone
- IL-2/Ig protein also augmented the vaccine-elicited immune responses, but less effectively than IL-2/Ig plasmid
- Augmentation of the immune responses by IL-2/Ig was evident after the primary immunization and increased with subsequent boost immunizations

NHP.99.1 (11713828) **Cytokine-induced augmentation of DNA vaccine-elicited SIV-specific immunity in rhesus monkeys.**

Authors: Barouch DH, Letvin NL

Journal: Dev Biol (Basel) 2000;104:85-92.

Objectives: Immunogenicity. To investigate the ability of an IL-2/lg cytokine fusion protein and a plasmid expressing IL-2/lg to augment immune responses in rhesus monkeys induced by DNA vaccines encoding SIV gag and HIV-1 env 89.6P.

Main Findings:
- Both IL-2/lg protein and IL-2/lg plasmid augment DNA vaccine-elicited antibody and CTL responses
- The most consistent and dramatic augmentation was observed using the IL-2/lg plasmid

NHP.99.2 (1466966) **Immunization of rhesus monkeys with high- and low-dose Tween-ether-disrupted SIVMAC.**

Authors: Voss G, Stahl-Hennig C, Petry H, Coulibaly C, Nick S, Fuchs D, Wachter H, Luke W, Hunsmann G

Journal: AIDS Res Hum Retroviruses 1992 Aug;8(8):1397-400.

Objectives: Challenge, Immunogenicity. To test the immunogenicity and protection from challenge induced by a HIGH dose of tween-ether-disrupted SIVmac251.32H.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac251/32H (Tween/Ether) *Type:* Whole (killed) Inactivated Virus *Route:* *Formulation:* SIVmac251/32H (Tween/Ether) + Alum

Challenge: SIVmac251(32H) *Route:*

Main Findings:
- 3/3 naive historic controls infected 14 dpc
- 4/5 protected from infection

NHP.100 (11085584) **Maturation of envelope-specific antibody responses to linear determinants in monkeys inoculated with attenuated SIV.**

Authors: Cole KS, Paliotti MJ, Murphey-Corb M, Montelaro RC

Journal: J Med Primatol 2000 Aug;29(3-4):220-30.

Objectives: Immunogenicity. To characterize the evolution of antibody responses to define linear determinants of the SIV envelope protein

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIV 17E-CL *Type:* Recombinant Live Attenuated Virus *Route:* Intravenous

Main Findings:
- Antibodies to certain envelope peptide domains have different patterns of antibody maturation to distinct linear envelope antigenic determinants
- Potential for domain-specific serology to produce a high-resolution characterization of SIV-specific antibody responses that can be used to evaluate experimental vaccine responses and to identify potential immune correlates of protection

NHP.101 (10954580) **Induction of mucosal homing virus-specific CD8(+) T lymphocytes by attenuated simian immunodeficiency virus.**

Authors: Cromwell MA, Veazey RS, Altman JD, Mansfield KG, Glickman R, Allen TM, Watkins DI, Lackner AA, Johnson RP

Journal: J Virol 2000 Sep;74(18):8762-6.

Objectives: Immunogenicity. To determine if virus-specific CD8+ lymphocytes induced in rhesus macaques by immunization with attenuated SIV express the mucosa-homing receptor α4β7 (and traffic to the intestinal mucosa).

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac251ΔNef *Type:* Live Attenuated Virus *Route:* Intravenous

Main Findings:
- Virus-specific CD8+ T cells are induced by immunization with attenuated SIV express α4β7 and home to mucosal sites, whereas those induced by a DNA-MVA vaccine lack expression of the intestinal homing receptor
- SIV-specific CD8+ T lymphocytes expressing α4β7 by a vaccine approach that replicates in mucosal tissue suggest that induction of virus-specific lymphocytes that are able to home to mucosal sites may be an important characteristic of a successful AIDS vaccine.

NHP.102 (10856795) **Anti-major histocompatibility complex antibody responses in macaques via intradermal DNA immunizations.**

Authors: Dela Cruz CS, MacDonald KS, Barber BH

Journal: Vaccine 2000 Jul 15;18(27):3152-65.

Objectives: Immunogenicity. To determine if DNA immunization with class I and class II MHC-encoding plasmids elicite xenogeneic and allogeneic antibody response against conformationally intact MHC molecules in rhesus macaques.

Species/Subspecies: Macaca mulatta (Rhesus macaque), Macaca fascicularis (cynomolgus macaque)

Main Findings:
- Intradermal immunizations of non-human primates with plasmid DNA encoding human MHC alleles can safely elicit xenogeneic anti-MHC antibody responses
- DNA encoding a specific macaque allogeneic MHC induced anti-allogeneic MHC antibodies production

NHP.103 (10763887) **Control of viral replication and disease onset in cynomolgus monkeys by HIV-1 TAT vaccine.**

Authors: Ensoli B, Cafaro A

Journal: J Biol Regul Homeost Agents 2000 Jan-Mar;14(1):22-6.

Objectives: Challenge, Immunogenicity. To test the hypothesis that humoral and cellular anti-Tat immunity have a protective role and may control disease progression.

Main Findings:
- High titers of anti-Tat antibodies capable of neutralizing Tat activity and the in vitro infection with the SHIV89.6P, Tat-specific proliferation, CTLs, TNFalpha production and skin tests were detected in the vaccinated monkeys
- Upon challenge with the highly pathogenic SHIV89.6P (10 MID50, i.v.), 5/7 of the vaccinated monkeys showed no signs of infection nor CD4+-T cell decline over 19 months of follow-up, whereas 3/3 controls were highly infected

NHP.104 (10729127) **Evidence for recombination of live, attenuated immunodeficiency virus vaccine with challenge virus to a more virulent strain.**

Authors: Gundlach BR, Lewis MG, Sopper S, Schnell T, Sodroski J, Stahl-Hennig C, Uberla K

Journal: J Virol 2000 Apr;74(8):3537-42.

Objectives: Challenge, Immunogenicity. To increase the immunogenicity of the vaccine virus with IL-2 and to investigate whether a recombination event between the vaccine and challenge viruses could explain the negative effect of vaccination with live, attenuated immunodeficiency viruses.

Main Findings:
- Detection of recombination between a live attenuated vaccine and the challenge strain resulting in a more adverse clinical outcome in vaccinated animals
- 3 of the vaccinated macaques developed higher set point viral load levels than unvaccinated control monkeys. 2 of these vaccinated monkeys developed AIDS, while the control monkeys infected in parallel remained asymptomatic
- Emergence of more-virulent recombinants of live, attenuated viruses and less-aggressive wild-type viruses is an additional risk of live, attenuated immunodeficiency virus vaccines.

NHP.105 (11713807) **DNA vaccine protection against challenge with simian/human immunodeficiency virus 89.6 in rhesus macaques.**

Authors: Habel A, Chanel C, Le Grand R, Martinon F, Couillin L, Moog C, Doms R, Gauduin MC, Hurtrel B, Guillet JG, Aubertin AM, Girard M

Journal: Dev Biol (Basel) 2000;104:101-5.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- 6/6 control monkeys became infected with challenge strain (SHIV89.6, 750 TCID50)
- In monkeys immunized with DNA only: 5/6 had challenge virus recovered by co-cultivation; in the DNA-protein group 2/6 were culture positive
- Rechallenge using 600TCID50 of pathogenic SHIV-89.6P. A rapid CD4 cell count decline in the 4 control monkeys as well as in the monkey vaccinated with DNA only, but not 4 animals immunized with DNA + protein
- No virus was recovered from PBMC in two of these monkeys, and viral RNA loads in

plasma were greatly reduced in three of them as compared with the controls. Absence of virus in PBMC was ascertained by whole blood transfusion to naive recipients. Altogether, this shows that the DNA prime-protein boost vaccine regimen could provide some protection against mucosal SHIV infection in rhesus monkeys, whereas DNA alone was ineffective

NHP.106 (10792505) **Up-regulation of beta-chemokines and down-modulation of CCR5 co-receptors inhibit simian immunodeficiency virus transmission in non-human primates.**

Authors: Lehner T, Wang Y, Cranage M, Tao L, Mitchell E, Bravery C, Doyle C, Pratt K, Hall G, Dennis M, Villinger L, Bergmeier L

Journal: Immunology 2000 Apr;99(4):569-77.

Objectives: Challenge, Immunogenicity. To evaluate in vivo the mechanism of protection from SIV that involves up-regulation of chemokines, which bind and may down-modulate the CCR5 coreceptors, thereby preventing transmission.

Species/Subspecies: -

Vaccine Name: rSIV-gp120 protein *Type:* Recombinant Subunit Protein *Route:* Subcutaneous

Vaccine Name: Recombinant p27 *Type:* Recombinant Subunit Protein *Route:* Subcutaneous

Challenge: SIVmac220 *Route:* Intrarectal

Main Findings:

- Immunization induced significant increases in the concentrations of CD8 cell-derived suppressor factor (CD8SF), regulated on activation normal T cells expressed and secreted (RANTES), macrophage inflammatory protein (MIP)1 and MIP1, and down-modulation of the proportion of cells expressing CCR5 ($r = 0.737$, $P < 0.05$).
- In vivo immunization up-regulates chemokines, which may down-modulate CCR5 coreceptors, and both functions are significantly correlated with the viral load.

NHP.107 (12359422) **Immunization of Macaques with Live Simian Human Immunodeficiency Virus (SHIV) Vaccines Conferred Protection Against AIDS Induced by Homologous and Heterologous SHIVs and Simian Immunodeficiency Virus.**

Authors: Kumar A, Mukherjee S, Shen J, Buch S, Li Z, Adany I, Liu Z, Zhuge W, Piatak M, Lifson J, McClure H, Narayan O

Journal: Virology 2002 Sep 30;301(2):189.

Objectives: Challenge, Immunogenicity. To evaluate the vaccine potential of SHIVs attenuated by deletion of viral accessory genes.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: DeltavpuDeltaNefSHIV-4 *Type:* Live Attenuated Virus *Route:* Subcutaneous

Vaccine Name: DeltavpuSHIV-ppc *Type:* Live Attenuated Virus *Routes:* Oral, Subcutaneous

Challenge: SHIV-KU2, SIVmacR71, SHIV89.6P *Route:* Intrarectal

Main Findings:

- No virological evidence of productive infection with the vaccine strains
- 7/7 animals developed binding as well as neutralizing antibodies
- Virus-specific CTLs that recognized homologous as well as heterologous pathogenic SHIVs and SIV, and also soluble inhibitory factors that blocked the in vitro replication of the vaccine strains and different challenge viruses
- 2/2 control animals were infected, succumbed to AIDS upon challenge
- 7/7 vaccinees were also infected with challenge viruses, but peak VL were 2-5 lower than in the control and later plasma viral RNA became undetectable in vaccinees (in lymph nodes of 6/7 vaccinees, SHIV89.6P in 5/7, and SHIVKU in 3/7 animals)

NHP.108 (10839807) **Effects of in vivo CD8(+) T cell depletion on virus replication in rhesus macaques immunized**

with a live, attenuated simian immunodeficiency virus vaccine.

Authors: Metzner KJ, Jin X, Lee FV, Gettie A, Bauer DE, Di Mascio M, Perelson AS, Marx PA, Ho DD, Kostrikis LG, Connor RI

Journal: J Exp Med 2000 Jun 5;191(11):1921-31.

Objectives: Challenge, Immunogenicity. To investigate the role of CD8(+) T lymphocytes in controlling replication of live, attenuated simian immunodeficiency virus (SIV) as part of a vaccine study to examine the correlates of protection in the SIV/rhesus macaque model.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac251Δnef *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge: SIVmac251 *Route:* Intravenous

Main Findings:

- CD8+ T cell depletion was associated with a 1-2 log increase in SIVmac239-nef plasma viremia
- Control of SIVmac239-nef replication was temporally associated with the recovery of CD8+ T cells between days 8 and 10. The challenge virus, SIVmac251, was not detectable in either the plasma or lymph nodes after depletion of CD8+ T cells
- CD8+ T cells play an important role in controlling replication of live, attenuated SIV in vivo

NHP.109 (10612675) **Simian immunodeficiency virus-specific cytotoxic T lymphocytes and protection against challenge in rhesus macaques immunized with a live attenuated simian immunodeficiency virus vaccine.**

Authors: Nixon DF, Donahoe SM, Kakimoto WM, Samuel RV, Metzner KJ, Gettie A, Hanke T, Marx PA, Connor RI

Journal: Virology 2000 Jan 5;266(1):203-10.

Objectives: Challenge, Immunogenicity. To examine the role of SIV-specific CTLs in macaques immunized with an attenuated strain of simian immunodeficiency virus (SIVmac239Deltanef) in protection against pathogenic challenge with SIVmac251.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac239-Δnef *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge: SIVmac251 *Route:* Intravenous

Main Findings:

- Attenuated SIVmac239Deltanef can elicit specific CTL precursor cells (CTLp), but no correlation was observed between breadth or strength of CTLp response to structural proteins SIV-Env, -Gamg or -Pol and protection against infection
- The low level of Mamu-A*01/p11C, C-M-specific CTLs induced through attenuated SIVmac239Deltanef vaccination increased in the absence of detectable SIVmac251 or SIVmac239Deltanef proviral DNA

NHP.110 (9371609) **Identification of the V1 region as a linear neutralizing epitope of the simian immunodeficiency virus SIVmac envelope glycoprotein.**

Authors: Jurkiewicz E, Hunsmann G, Schaffner J, Nisslein T, Luke W, Petry H

Journal: J Virol 1997 Dec;71(12):9475-81.

Objectives: Immunogenicity. To investigate the role of the V1 in neutralization.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

NHP.111 (10644340) **Antiretroviral therapy during primary immunodeficiency virus infection can induce persistent suppression of virus load and protection from heterologous challenge in rhesus macaques.**

Authors: Rosenwirth B, ten Haaft P, Bogers WM, Nieuwenhuis IG, Niphuis H, Kuhn EM, Bischofberger N,

Heeney JL, Uberla K

Journal: J Virol 2000 Feb;74(4):1704-11.

Objectives: Challenge, Immunogenicity. To study rhesus macaques with the pathogenic simian/human immunodeficiency virus RT-SHIV and treat them with the antiretroviral drug (R)-9-(2-phosphonylmethoxypropyl)adenine (PMPA) for 8 weeks starting 7 or 14 days postinfection.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: RT-SHIV *Type:* Live Virus *Route:* Intravenous

Main Findings:

- Rhesus macaques inoculated with the pathogenic RT-SHIV then treated with the antiretroviral drug (R)-9-(2-phosphonylmethoxypropyl)adenine (PMPA) for 8 weeks starting 7 or 14 days postinfection, showed suppressed viral replication efficiently
- Suppression of viral replication was transient in 4/6 monkeys
- The challenge of the monkeys with better out come with SIV(8980) shows that both monkeys proved to be protected against the heterologous virus

NHP.112 (9765452) **Oral immunization of macaques with attenuated vaccine virus induces protection against vaginally transmitted AIDS.**

Authors: Joag SV, Liu ZQ, Stephens EB, Smith MS, Kumar A, Li Z, Wang C, Sheffer D, Jia F, Foresman L, Adany I, Lifson J, McClure HM, Narayan O

Journal: J Virol 1998 Nov;72(11):9069-78.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque), Macaca (sp)

Vaccine Name: DeltavpuDeltaNefSHIV-4 *Type:* Live Attenuated Virus *Route:* Subcutaneous

Vaccine Name: DeltavpuSHIV-ppc *Type:* Live Attenuated Virus *Routes:* Oral, Subcutaneous

Challenge: SHIV.KU1 *Route:* Oral, Vaginal or perivaginal

Main Findings:

- 4/4 controls developed low CD4+ T-cell counts (<200/µl) and AIDS
- 12/12 vaccinees became infected with SHIVKU-1, and two in group 1 developed a persistent productive infection followed by development of AIDS in one. The other 10 maintained almost complete control over virus replication.
- First demonstration of protection against virulent SHIV administered by the intravaginal route. Thus, sexually transmitted HIV disease can be prevented by parenteral or oral immunization.

NHP.113 (11054270) **Characterization of immune escape viruses from a macaque immunized with live-virus vaccine and challenged with pathogenic SHIVKU-1.**

Authors: Stipp HL, Kumar A, Narayan O

Journal: AIDS Res Hum Retroviruses 2000 Oct 10;16(15):1573-80.

Objectives: Challenge. To characterize immune escape viruses (SHIV(KU-1/105w52) and SHIV(KU-1/105w98)) from a macaque immunized with DeltavpuDeltanef SHIV-4 and challenged with pathogenic SHIV(KU-1).

Main Findings:

- The two newly identified escape variant viruses could not be neutralized by anti-SHIV(KU-1)-specific neutralizing antibodies and were poorly recognized by challenge virus-specific CTLs
- Sequence analysis of the gene encoding gp120 revealed several mutations in the protein that might have contributed to the development of the immune-escape viruses

NHP.114 (10888354) **Protective immune responses induced by a non-pathogenic simian/human immunodeficiency virus (SHIV) against a challenge of a pathogenic SHIV in monkeys.**

Authors: Yoshino N, Ami Y, Someya K, Ando S, Shinohara K, Tashiro F, Lu Y, Honda M

Journal: Microbiol Immunol 2000;44(5):363-72.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: SHIV-NM3n *Type:* Live Attenuated Virus *Route:*

Challenge: SHIV89.6 *Route:* Intravenous

Main Findings:

- After the heterologous virus challenge, all of the vaccinees were completely protected from SHIV challenge
- The inhibition of CD4+ cell depletion was associated with maintaining the proliferative response of helper T-cells against SIV p27 in the vaccinated animals following the pathogenic virus challenge
- Decline of CD28+ cells, the increase in CD95+ cells, and the enhancement of in vitro apoptosis in PBMC were inhibited in the non-pathogenic virus-inoculated animals

NHP.115 (11348720) **Enhanced simian immunodeficiency virus-specific immune responses in macaques induced by priming with recombinant Semliki Forest virus and boosting with modified vaccinia virus Ankara.**

Authors: Nilsson C, Makitalo B, Berglund P, Bex F, Liljestrom P, Sutter G, Erfle V, ten Haaft P, Heeney J, Biberfeld G, Thorstensson R

Journal: Vaccine 2001 May 14;19(25-26):3526-36.

Objectives: Challenge, Immunogenicity. To investigate the the immunogenicity and protection from challenge of two vector-based vaccines, either given alone or in a prime-boost regimen.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Main Findings:

- Generally, antibody responses, T-cell proliferative responses and cytotoxic T-cell responses remained low or undetectable in vaccinees receiving MVA-SIVmac or SFV-SIVmac alone, in contrast with monkeys who first received SFV-SIVmac twice and then were boosted with MVA-SIVmac
- No evidence of protection was seen against an intrarectal heterologous SIVsm challenge given 3 months after the last immunization

NHP.116 (11514733) **In situ hybridization and immunolabelling study of the early replication of simian immunodeficiency virus (SIVmacJ5) in vivo.**

Authors: Canto-Nogues C, Jones S, Sangster R, Silvera P, Hull R, Cook R, Hall G, Walker B, Stott EJ, Hockley D, Almond N

Journal: J Gen Virol 2001 Sep;82(Pt 9):2225-34.

Objectives: Pathogenicity. To determine the distribution of virus-infected cells in cynomolgus macaques following intravenous challenge with 1000 TCID50 of the wild-type simian immunodeficiency virus SIVmacJ5 (stock J5C).

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Challenge: SIVmac251(32H) *Route:* Intravenous

Main Findings:

- Following intravenous inoculation with SIVmacJ5, all macaques became infected, as determined by virus isolation and/or DNA PCR
- At day 4 post-infection detection of the virus was sporadic. By 7 dpc significant SIV loads were detected in the blood and lymphoid tissues by DNA PCR and virus co-cultivation. Large numbers of cells expressing SIV RNA were detected in mesenteric lymph nodes by ISH and significantly fewer ($P<0.05$) in the spleen
- A major site of the initial replication of SIV is gut-associated lymphoid tissue

NHP.117 (11983253) **Passive immunization with human neutralizing monoclonal antibodies: correlates of protective immunity against HIV.**

Authors: Xu W, Hofmann-Lehmann R, McClure HM, Ruprecht RM

Journal: Vaccine 2002 May 6;20(15):1956-60.

Objectives: Challenge, Immunogenicity, Passive Immunization. To determine the value of passive immunization to protect rhesus macaque against SHIV challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: F105/2G12/2F5 mab *Type:* Passive Antibody *Route:* Intravenous

Challenge: SHIV89.6P, SHIV-vpu+ *Route:* Intravenous, Oral

Main Findings:

- Passive immunization with synergistic combinations of human monoclonal antibodies (mAbs) directed against conserved epitopes of the HIV envelope completely protected 13/16 rhesus monkeys challenged intravenously or orally with chimeric simian-humanimmunodeficiency virus (SHIV) strains; partial protection was seen in another 2
- A high degree of protection was seen among orally challenged neonates

NHP.118 (11752703) **A DNA/MVA-based candidate human immunodeficiency virus vaccine for Kenya induces multi-specific T cell responses in rhesus macaques.**

Authors: Wee EG, Patel S, McMichael AJ, Hanke T

Journal: J Gen Virol 2002 Jan;83(Pt 1):75-80.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pTHr.HIVA DNA *Type:* DNA *Routes:* Intradermal, Intramuscular

Vaccine Name: MVA.HIVA *Type:* DNA *Route:* Intradermal

Main Findings:

- The very same vaccines that had entered clinical trials in Oxford and Nairobi (plasmid pTHr.HIVA DNA and recombinant modified vaccinia virus Ankara MVA.HIVA in a prime-boost protocol) induced cellular immune responses specific for multiple HIV-derived epitopes in rhesus macaques

NHP.119 (11752704) **Induction of anti-simian immunodeficiency virus cellular and humoral immune responses in rhesus macaques by peptide immunogens: correlation of CTL activity and reduction of cell-associated but not plasma virus load following challenge.**

Authors: Vogel TU, Beer BE, zur Megede J, Ihlenfeldt HG, Jung G, Holzammer S, Watkins DI, Altman JD, Kurth R, Norley S

Journal: J Gen Virol 2002 Jan;83(Pt 1):81-91.

Objectives: Challenge, Immunogenicity. To test the ability of branched peptide constructs to induce humoral and celular response against SIV infection in rhesus macaques.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: P3CSS CTL *Type:* Synthetic Protein/Peptide *Route:* Subcutaneous

Vaccine Name: V2-P3CSS *Type:* Synthetic Protein/Peptide *Route:* Subcutaneous *Formulation:* V2-P3CSS + MONTANIDE ISA 51

Vaccine Name: V2-MAP *Type:* Synthetic Protein/Peptide *Routes:* Subcutaneous, Intramuscular *Formulation:* V2-MAP + RIBI, MONTANIDE ISA 51

Vaccine Name: V4.32-MAP *Type:* Synthetic Protein/Peptide *Routes:* Subcutaneous, Intramuscular *Formulation:* V4.32-MAP + RIBI, MONTANIDE ISA 51

Challenge: SIV mac251 (European) stock 5 *Route:* Intravenous

Main Findings:

- Although none of the monkeys were protected from infection, most demonstrated an anamnestic CTL response with epitope-specific CTL precursor frequencies reaching as

high as 1 in 20 total PBMC as measured by limiting dilution CTL assay or 25% of all CD8+ T-cells using tetrameric MHC-I/peptide complexes
- A significant inverse correlation between the levels of CTLp and the number of infected cells in circulation. However, no such correlation with the plasma viral load (RNA copies/ml) was evident.

NHP.120 (12009295) **Evaluation of SIV library vaccines with genetic cytokines in a macaque challenge.**

Authors: Sykes KF, Lewis MG, Squires B, Johnston SA

Journal: Vaccine 2002 May 22;20(17-18):2382-95.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIV Random-GLV *Type:* DNA *Routes:* Intradermal, Intramuscular

Vaccine Name: SIV-Run-Cyt. GLV *Type:* DNA *Routes:* Intradermal, Intramuscular

Vaccine Name: SIV Diected GLV *Type:* DNA *Routes:* Intradermal, Intramuscular

Challenge: SIVmac251 *Route:* Intravenous

Main Findings:
- 8/12 animals in the three test groups showed some anti-SIV immune response, whereas the controls did not
- Six months after priming, monkeys were intravenously challenged with virulent SIVmac251: All were infected but animals in two groups vaccinated with SIV libraries showed a trend toward lower viral-loads, mitigated clinical disease, and higher survival rates than controls
- Significantly, co-administering the GMCSF and IL-12-encoding plasmids worsened the measures of protection

NHP.121 (11907220) **Outcome of simian-human immunodeficiency virus strain 89.6p challenge following vaccination of rhesus macaques with human immunodeficiency virus Tat protein.**

Authors: Silvera P, Richardson MW, Greenhouse J, Yalley-Ogunro J, Shaw N, Mirchandani J, Khalili K, Zagury JF, Lewis MG, Rappaport J

Journal: J Virol 2002 Apr;76(8):3800-9.

Objectives: Challenge, Immunogenicity. To investigate whether vaccination with biologically active Tat or inactive Tat toxoid derived from HIV-1(IIIB) and SHIV strain 89.6p would induce protective immunity in rhesus macaques.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: HIV-1 HXBc2 Tat Toxoid *Type:* Other *Route:* Intramuscular

Vaccine Name: SHIV89.6P tat toxoid *Type:* Other *Route:* Intramuscular

Vaccine Name: HIV-1 HXBc2 Tat *Type:* Purified Viral Products *Route:* Intramuscular

Vaccine Name: SHIV89.6P tat *Type:* Purified Viral Products *Route:* Intramuscular

Challenge: SHIV89.6P *Route:* Intravenous

Main Findings:
- Vaccination induced high titers of anti-Tat immunoglobulin G in all immunized animals by week 7, but titers were somewhat lower in the 89.6p Tat group
- Tat-specific T-helper responses were detected in 50% of immunized animals
- T-cell epitopes appeared to map within amino acids (aa) 1 to 24 and aa 37 to 66
- Tat-specific gamma interferon responses were detected in CD4+ and/or CD8+ T lymphocytes in 11/16 immunized animals on the day of challenge
- All animals became infected upon intravenous challenge with 30 AID50 of SHIV 89.6p, and there were no significant differences in viral loads or CD4+ T-cell counts between immunized and control animals.

NHP.123 (11823518) **Recombinant canarypox vaccine-elicited CTL specific for dominant and subdominant simian immunodeficiency virus epitopes in rhesus monkeys.**

Authors: Santra S, Schmitz JE, Kuroda MJ, Lifton MA, Nickerson CE, Lord CI, Pal R, Franchini G, Letvin NL

Journal: J Immunol 2002 Feb 15;168(4):1847-53.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: ALVAC-SIV-gpe (vcp180) *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intrarectal, Intramuscular, Intranasal

Challenge: SIVmac251 *Route:* Intrarectal

Main Findings:
- Following a series of five immunizations, memory gag-specific (not pol) CTL responses specific were demonstrated in vaccinated monkeys
- Following challenge with SIVmac251, the vaccinated animals developed high frequency CTL responses specific for the dominant Gag epitope, associated with the early containment of viral replication
- The vaccinees, but not the control animals, developed CTL responses to the subdominant Pol epitope that were detectable only after containment of early viremia

NHP.124 (12076047) **DNA prime/protein boost vaccine strategy in neonatal macaques against simian human immunodeficiency virus.**

Authors: Rasmussen RA, Hofmann-Lehman R, Montefiori DC, Li PL, Liska V, Vlasak J, Baba TW, Schmitz JE, Kuroda MJ, Robinson HL, McClure HM, Lu S, Hu SL, Rizvi TA, Ruprecht RM

Journal: J Med Primatol 2002 Feb;31(1):40-60.

Objectives: Challenge, Immunogenicity.

Main Findings:
- Following SHIV-vpu+ challenge, containment of infection was observed in 4/15 animals given DNA priming/protein boost vaccination and in 3/4 animals given gp160 boosts only
- Rechallenge with homologous virus of 6 animals that contained the first challenge virus resulted in rapid viral clearance or low viral loads
- Upon additional rechallenge with heterologous, pathogenic SHIV89.6P, 4/6 animals maintained normal CD4+ T-cell counts with no or limited SHIV89.6P infection
- Humoral and cellular immune mechanisms may have contributed to the containment of SHIV89.6P; however, viral interference with SHIV-vpu+ could also have played a role
- Immunogenicity and efficacy of candidate AIDS vaccines are not affected when vaccination is initiated during infancy as compared with later in life.

NHP.125 (11907330) **Immunization with recombinant modified vaccinia virus Ankara can modify mucosal simian immunodeficiency virus infection and delay disease progression in macaques.**

Authors: Nilsson C, Sutter G, Walther-Jallow L, ten Haaft P, Akerblom L, Heeney J, Erfle V, Bottiger P, Biberfeld G, Thorstensson R

Journal: J Gen Virol 2002 Apr;83(Pt 4):807-18.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: rMVA (SIVsm) gagpolenv *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name: Native SIV gp148 env *Type:* Purified Viral Products *Route:* Intramuscular

Vaccine Name: SIVmac251 p27 *Type:* Purified Viral Products *Route:* Intramuscular *Formulation:* SIVmac251 p27 + ISCOM(s)™

Challenge: SIVsm *Route:* Intrarectal

Main Findings:

- At the time of challenge, antibody titers to SIV Env and lymphocyte proliferation responses to whole viral antigen were highest in vaccinees receiving MVA-SIVsm with protein immunizations
- One immunized animal was completely protected from intrarectal challenge SIVsm
- A prolonged survival time was observed in 2/4 monkeys in each of the groups immunized with MVA-SIVsm, in 2 monkeys given MVA-SIVsm followed by protein and in 3/4 monkeys given wild-type MVA, compared with naive controls
- Immunization with MVA-SIVsm, as well as wild-type MVA alone, seemed to delay disease progression after mucosal SIV infection in a proportion of the monkeys

NHP.126 (11751978) **Vaccine protection against functional CTL abnormalities in simian human immunodeficiency virus-infected rhesus monkeys.**

Authors: McKay PF, Schmitz JE, Barouch DH, Kuroda MJ, Lifton MA, Nickerson CE, Gorgone DA, Letvin NL

Journal: J Immunol 2002 Jan 1;168(1):332-7.

Objectives: Challenge, Immunogenicity. To assess cytokine production by virus-specific CTL in the rhesus monkey model for AIDS to determine its contribution to the functional impairment of CTL.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: HIV-1.89.6P env DNA *Type:* DNA *Route:* Intramuscular *Formulation:* HIV-1.89.6P env DNA + IL-2/lg protein

Vaccine Name: SIVmac239 gag DNA *Type:* DNA *Route:* Intramuscular *Formulation:* SIVmac239 gag DNA + IL-2/lg plasmid

Challenge: SIVmac251 (J5), SHIV89.6, SHIV89.6P *Route:* Intravenous

Main Findings:

- CTL from monkeys infected with nonpathogenic isolates of simian and simian-human immunodeficiency virus expressed high levels of IFN-gamma, TNF-alpha, and IL-2 after in vitro exposure to a nonspecific mitogen or the optimal peptide representing a dominant virus-specific CTL epitope
- CTL from vaccinated monkeys that effectively controlled the replication of a highly pathogenic simian-human immunodeficiency virus isolate following challenge demonstrated a preserved capacity to produce these cytokines

NHP.127 (12743287) **Comparative immunogenicity in rhesus monkeys of DNA plasmid, recombinant vaccinia virus, and replication-defective adenovirus vectors expressing a human immunodeficiency virus type 1 gag gene.**

Authors: Casimiro DR, Chen L, Fu TM, Evans RK, Caulfield MJ, Davies ME, Tang A, Chen M, Huang L, Harris V, Freed DC, Wilson KA, Dubey S, Zhu DM, Nawrocki D, Mach H, Troutman R, Isopi L, Williams D, Hurni W, Xu Z, Smith JG, Wang S, Liu X, Guan L, Long R, Trigona W, Heidecker GJ, Perry HC, Persaud N, Toner TJ, Su Q, Liang X, Youil R, Chastain M, Bett AJ, Volkin DB, Emini EA, Shiver JW

Journal: J Virol 2003 Jun;77(11):6305-13.

Objectives: Immunogenicity. To evaluate an MVA vector and a replication-defective adenovirus serotype 5

(Ad5) vector, each expressing the same codon-optimized HIV-1 gag gene for immunogenicity in rhesus monkeys.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- The Ad5-gag vector was the most effective in eliciting anti-Gag CTL; the vaccine produced both CD4(+) and CD8(+) T-cell responses, with the latter consistently being the dominant component
- Of the formulations tested, the DNA-CRL1005 vaccine primed T-cell responses most effectively and provided the best overall immune responses after boosting with Ad5-gag
- Conclusion: An immunization strategy for humans that is based on the adenovirusvector and in which existing adenovirus immunity may be overcome by combined immunization with adjuvanted DNA and adenovirus vector boosting.

NHP.128 (11751749) **Prime-boost immunization generates a high frequency, high-avidity CD8(+) cytotoxic T lymphocyte population.**

Authors: Estcourt MJ, Ramsay AJ, Brooks A, Thomson SA, Medveckzy CJ, Ramshaw IA

Journal: Int Immunol 2002 Jan;14(1):31-7.

Objectives: Challenge, Immunogenicity. To study a 'prime-boost' immunization with DNA vaccines and recombinant poxvirus vectors that generates high frequencies of CTL.

Main Findings:
- The 'prime-boost' immunization with DNA vaccines and recombinant poxvirus vectors generated high frequencies of cytotoxic T lymphocytes (CTL) that recognize target cells expressing very low levels of specific antigen; these cells persist for at least 6 months at levels representing approximately 10% of the CD8(+) T cell population
- Prime-boost immunized animals were capable of eliminating target cells expressing 10- to 100-fold less immunogenic peptide than mice given either vector alone
- Viral challenge led to rapid expansion of CTL effectors in prime-boost groups, to levels representing >30% of total CD8(+) T cell numbers.

NHP.129 (12208982) **Sustained Peptide-Specific Gamma Interferon T-Cell Response in Rhesus Macaques Immunized with Human Immunodeficiency Virus gag DNA Vaccines.**

Authors: Caulfield MJ, Wang S, Smith JG, Tobery TW, Liu X, Davies ME, Casimiro DR, Fu TM, Simon A, Evans RK, Emini EA, Shiver J

Journal: J Virol 2002 Oct 1;76(19):10038-43.

Objectives: Immunogenicity. To examine the influence of dose and method of antigen delivery on the dynamics and durability of T-cell responses to candidate human immunodeficiency virus (HIV) vaccines.

Main Findings:
- Cell-mediated immune (CMI) response in rhesus macaques persisted for at least 18 months following a four-dose vaccination regimen
- The plasmid vaccine, with or without CRL8623, was immunogenic in macaques; however, the form coadministered with adjuvant exhibited improved T-cell responses, with a bias toward more antigen-specific CD8(+) T cells
- Broad and durable CMI response to HIV DNA vaccines can be induced in a relevant nonhuman primate model

NHP.131 (12127792) **Protection by intranasal immunization of a nef-deleted, nonpathogenic SHIV against intravaginal challenge with a heterologous pathogenic SHIV.**

Authors: Enose Y, Ui M, Miyake A, Suzuki H, Uesaka H, Kuwata T, Kunisawa J, Kiyono H, Takahashi H, Miura T, Hayami M

Journal: Virology 2002 Jul 5;298(2):306-16.

Objectives: Challenge, Immunogenicity. To examine the possibility of using an attenuated virus for mucosal immunization, four female macaques were intranasally or intravenously administered with a

chimeric simian-human immunodeficiency virus with a deleted nef gene (SHIV-dn).

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SHIV-dn *Type:* Live Attenuated Virus *Routes:* Intravenous, Intranasal

Challenge: SHIV89.6P *Route:* Vaginal or perivaginal

Main Findings:

- Although all the monkeys had anti-HIV-1 antibodies with neutralizing activity in the plasma, the intranasally immunized monkeys had much higher levels of HIV-1 Env-specific IgG and IgA antibodies in mucosal secretions compared with the intravenously immunized monkeys
- 3/4 intranasally immunized monkeys were completely protected from intravaginal challenge with a pathogenic virus, SHIV-89.6P, whereas only 1 intravenously immunized monkey was protected
- Intranasal immunization of an attenuated virus can induce the protective efficacy against intravaginal infection

NHP.132 (12097576) **Different patterns of immune responses but similar control of a simian-human immunodeficiency virus 89.6P mucosal challenge by modified vaccinia virus Ankara (MVA) and DNA/MVA vaccines.**

Authors: Amara RR, Villinger F, Staprans SI, Altman JD, Montefiori DC, Kozyr NL, Xu Y, Wyatt LS, Earl PL, Herndon JG, McClure HM, Moss B, Robinson HL

Journal: J Virol 2002 Aug;76(15):7625-31.

Objectives: Challenge, Immunogenicity. To evaluate the ability of the MVA component of this vaccine to serve as both a prime and a boost for an AIDS vaccine.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIV-HIV89.6 DNA vaccine *Type:* DNA *Routes:* Intradermal, Intramuscular *Formulation:* SIV-HIV89.6 DNA vaccine + PBS

Vaccine Name: rMVA 89.6 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intravenous, Intradermal, Intramuscular *Formulation:* rMVA 89.6 + PBS

Challenge: SHIV89.6P *Route:* Intrarectal

Main Findings:

- Compared to the DNA/MVA vaccine, the MVA-only vaccine raised less than one-tenth the number of vaccine-specific T cells but 10-fold-higher titers of binding antibody for Env
- Postchallenge, the animals vaccinated with MVA alone increased their CD8 cell numbers to levels that were similar to those seen in DNA/MVA-vaccinated animals
- By 5 wpc, the MVA-only-vaccinated animals had achieved as good control of the viral infection as the DNA/MVA group

NHP.133 (11085582) **SHIV89.6P pathogenicity in cynomolgus monkeys and control of viral replication and disease onset by human immunodeficiency virus type 1 Tat vaccine.**

Authors: Cafaro A, Caputo A, Maggiorella MT, Baroncelli S, Fracasso C, Pace M, Borsetti A, Sernicola L, Negri DR, Ten Haaft P, Betti M, Michelini Z, Macchia I, Fanales-Belasio E, Belli R, Corrias F, Butto S, Verani P, Titti F, Ensoli B

Journal: J Med Primatol 2000 Aug;29(3-4):193-208.

Objectives: Challenge, Immunogenicity.

Main Findings:

- A vaccine based on the Tat protein of HIV blocks primary infection with SHIV89.6P and prevents the CD4 T cell decline and disease onset in cynomolgus monkeys
- No signs of virus replication were found in five out of seven vaccinated macaques for almost 1 year of follow-up
- Since the inoculated virus is shown to be highly pathogenic in cynomolgus macaques, the

results indicate efficacy of Tat vaccination in protection against highly pathogenic virus challenge
- There was a correlation of protection with a cytotoxic T cell response

NHP.134 (10482571) **Role of immune responses against the envelope and the core antigens of simian immunodeficiency virus SIVmne in protection against homologous cloned and uncloned virus challenge in Macaques.**

Authors: Polacino PS, Stallard V, Klaniecki JE, Pennathur S, Montefiori DC, Langlois AJ, Richardson BA, Morton WR, Benveniste RE, Hu SL

Journal: J Virol 1999 Oct;73(10):8201-15.

Objectives: Challenge, Immunogenicity. To examine (i) the effect of priming by recombinant vaccinia virus; (ii) the role of surface antigen gp130; and (iii) the role of core antigens (Gag and Pol) in eliciting protective immunity.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: Recombinant vaccinia virus vac-gp160 (v-SE5) *Type:* Recombinant Vector (virus/bacteria) *Route:* Scarification

Vaccine Name: Recombinant vaccinia gp130 (v-SE6) *Type:* Recombinant Vector (virus/bacteria) *Route:* Scarification

Vaccine Name: Recombinant vaccinia gagpol (v-SG11) *Type:* Recombinant Vector (virus/bacteria) *Route:* Scarification

Vaccine Name: Recombinant vaccinia gagpolenv (v-SGE14) *Type:* Recombinant Vector (virus/bacteria) *Route:* Scarification

Vaccine Name: rgp160 *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Vaccine Name: Recombinant gp130 *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Vaccine Name: Recombinant gagpol particles *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Vaccine Name: Recombinant gagpolenv particles *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Challenge: SIV(Mne) clone E11S *Route:* Intravenous

Main Findings:
- Priming with recombinant vaccinia virus was more effective than subunit antigen in eliciting protective responses
- While both gp130 and gp160 elicited similar levels of SIV-specific antibodies, gp130 was not as effective as gp160 in protection, indicating a possible role for the transmembrane protein in presenting functionally important epitopes
- Although animals immunized with core antigens failed to generate any neutralizing antibody and were infected upon challenge, their virus load was 50- to 100-fold lower than that of the controls
- Complete protection against intravenous infection by the pathogenic uncloned SIVmne was achieved by immunization with both the envelope and the core antigens

NHP.135 (10203053) **Protection from pathogenic SIV challenge using multigenic DNA vaccines.**

Authors: Haigwood NL, Pierce CC, Robertson MN, Watson AJ, Montefiori DC, Rabin M, Lynch JB, Kuller L, Thompson J, Morton WR, Benveniste RE, Hu SL, Greenberg P, Mossman SP

Journal: Immunol Lett 1999 Mar;66(1-3):183-8.

Objectives: Challenge, Immunogenicity. To compare the efficacy of DNA immunization alone and in combination with subunit protein boosts.

Main Findings:
- Humoral immune responses were stronger in the macaques receiving subunit boosts
- Significant Nab titers to SIVmne detected in one of the subunit-boosted animals and in none of the DNA-only animals prior to challenge
- T-cell proliferative responses to gp160 and to Gag were detected in all immunized

animals after three immunizations, and these responses increased after four immunizations

NHP.136 (9930869) **Neutralizing antibody directed against the HIV-1 envelope glycoprotein can completely block HIV-1/SIV chimeric virus infections of macaque monkeys.**

Authors: Shibata R, Igarashi T, Haigwood N, Buckler-White A, Ogert R, Ross W, Willey R, Cho MW, Martin MA

Journal: Nat Med 1999 Feb;5(2):204-10.

Objectives: Challenge, Immunogenicity, Passive Immunization. To assess whether human immunodeficiency virus type 1 (HIV-1) envelope-specific antibodies confer resistance against primate lentivirus infections

Main Findings:

- Passive immunization of pig-tailed macaques with IgG purified from multiply infected HIV-1+ chimpanzees followed by intravenous challenge with a SHIV (env derived form HIV-1DH12)
- Anti-SHIV neutralizing activity is the absolute requirement for antibody-mediated protection in vivo
- Administration of non-neutralizing anti-HIV IgG neither inhibited nor enhanced a subsequent SHIV infection

NHP.137 (9863867) **Live attenuated simian immunodeficiency virus (SIV)mac in macaques can induce protection against mucosal infection with SIVsm.**

Authors: Nilsson C, Makitalo B, Thorstensson R, Norley S, Binninger-Schinzel D, Cranage M, Rud E, Biberfeld G, Putkonen P

Journal: AIDS 1998 Dec 3;12(17):2261-70.

Objectives: Challenge, Immunogenicity. To investigate whether vaccination of macaques with attenuated simian immunodeficiency virus (SIV)macC8 could induce long-term protective immunity against rectal exposure to SIVsm and intravenous exposure to the more divergent HIV-2

Main Findings:

- At the time of challenge, 8/10 vaccinees were PCR-positive for SIVmacC8 DNA but no virus could be isolated from peripheral blood mononuclear cells
- After SIVsm challenge, 3/6 vaccinees were repeatedly SIVsm PCR-negative. In 1/3 infected monkeys, the challenge virus was initially suppressed but the monkey ultimately developed AIDS after increased replication of the pathogenic virus. Monkeys protected from initial challenge remained uninfected after rechallenge
- Infection with SIV did not protect from challenge with HIV-2
- All controls became infected with either SIVsm or HIV-2
- At the time of challenge the vaccinees had neutralizing antibodies to SIVmac but no demonstrable cross-neutralizing antibodies to SIVsm or HIV-2
- Titers of antigen-binding or neutralizing antibodies did not correlate with protection
- Cytotoxic T-cell responses to SIV Gag/Pol and virus-specific T-cell proliferative responses were low

NHP.138 (9747945) **Presence of circulating CTL induced by infection with wild-type or attenuated SIV and their correlation with protection from pathogenic SHIV challenge.**

Authors: Vogel TU, Fournier J, Sherring A, Ko D, Parenteau M, Bogdanovic D, Mihowich J, Rud EW

Journal: J Med Primatol 1998 Apr-Jun;27(2-3):65-72.

Objectives: Challenge, Immunogenicity. To evaluate the role of CTLs in the protection from challenge with pathogenic SHIV in macaques vaccinated with attenuated virus.

Main Findings:

- SIVmacC8-vaccinated monkeys demonstrated a broader CTL response than the SIVmacJ5-infected animals

- CTL against some proteins in SIVmacC8-vaccinated monkeys became progressively more difficult to detect through the day of challenge
- Neither the presence of circulating CTL nor the CTL precursor frequency against any of the tested proteins correlated with the outcome of the challenge when SIVmacJ5- and SIVmacC8-infected animals were analyzed together
- Only the protected animal had detectable CTL precursors with moderate frequencies against all three tested proteins at the day of challenge

NHP.139 (9814958) **Prime-boost immunization strategies against HIV.**

Authors: Barnett SW, Klinger JM, Doe B, Walker CM, Hansen L, Duliege AM, Sinangil FM

Journal: AIDS Res Hum Retroviruses 1998 Oct;14 Suppl 3:S299-309.

Objectives: Passive immunotherapy.

NHP.140 (14498984) **Comparison of virology and immunology in SHIV 89.6 proviral DNA and virus-inoculated rhesus macaques.**

Authors: Busch M, Lu D, Fritts L, Lifson JD, Miller CJ

Journal: J Med Primatol 2003 Aug;32(4-5):240-6.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SHIV89.6 *Type:* Live Virus *Routes:* Intravenous, Vaginal or perivaginal, Intranasal

Vaccine Name: pMA SHIV89.6 *Type:* DNA *Routes:* Targeted Lymph node immunization, Intradermal, Intramuscular, Intranasal *Formulation:* pMA SHIV89.6 + Saline, Tris-EOTA 8.0

NHP.141 (9811775) **Vaccine protection against a heterologous, non-syncytium-inducing, primary human immunodeficiency virus.**

Authors: Robert-Guroff M, Kaur H, Patterson LJ, Leno M, Conley AJ, McKenna PM, Markham PD, Richardson E, Aldrich K, Arora K, Murty L, Carter L, Zolla-Pazner S, Sinangil F

Journal: J Virol 1998 Dec;72(12):10275-80.

Objectives: Challenge, Immunogenicity. Follow up study: to challenge the three previously protected chimpanzees a third time, with the heterologous primary isolate HIV-15016.

Species/Subspecies: Pan Troglodytes (Chimpanzee)

Vaccine Name: AD4-gp160(MN) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intranasal

Vaccine Name: CHO cell-expressed HIV-1SF2 gp120 *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* CHO cell-expressed HIV-1SF2 gp120 + MF59, MTP-PE

Challenge: HIV-1.SF2, HIV-1.5016 *Route:* Intravenous

Main Findings:

- Following challenge with HIV-1.5016, complete protection in 1/3 chimpanzees previously protected against low- and high-dose HIV-1SF2 exposures after immunization with an adenovirus-HIV-1MN gp160 priming-HIV-1SF2 gp120 boosting regimen
- At challenge, the protected chimpanzee exhibited broad humoral immunity, including neutralizing antibody activity.

NHP.142 (9811759) **Enhanced T-cell immunogenicity and protective efficacy of a human immunodeficiency virus type 1 vaccine regimen consisting of consecutive priming with DNA and boosting with recombinant fowlpox virus.**

Authors: Kent SJ, Zhao A, Best SJ, Chandler JD, Boyle DB, Ramshaw IA

Journal: J Virol 1998 Dec;72(12):10180-8.

Objectives: Challenge, Immunogenicity. To evaluate a consecutive immunization strategy involving priming with DNA and boosting with rFPV vaccines encoding common HIV-1 antigens.

Main Findings:
- A dramatic boosting effect on DNA vaccine-primed HIV-1-specific helper and cytotoxic T-lymphocyte responses, but a decline in HIV-1 antibody titers, was observed following rFPV immunization
- The vaccine regimen protected macaques from an intravenous HIV-1 challenge, with the resistance most likely mediated by T-cell responses

NHP.143 (9765452) **Oral immunization of macaques with attenuated vaccine virus induces protection against vaginally transmitted AIDS.**

Authors: Joag SV, Liu ZQ, Stephens EB, Smith MS, Kumar A, Li Z, Wang C, Sheffer D, Jia F, Foresman L, Adany I, Lifson J, McClure HM, Narayan O

Journal: J Virol 1998 Nov;72(11):9069-78.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca (sp)

Main Findings:
- Six adult macaques immunized subcutaneously with DeltavpuDeltanefSHIV-4 (vaccine 1), and six were immunized orally with DeltavpuSHIVPPc (vaccine 2). Both viruses caused infection in all inoculated animals, but whereas vaccine 1 virus caused only a nonproductive type of infection, vaccine 2 virus replicated productively but transiently for a 6- to 10-week period
- The 12/12 vaccinated animals became infected with the challenge virus SHIVKU-1, and two in group 1 developed a persistent productive infection followed by development of AIDS in one. The other 10 have maintained almost complete control over virus replication even though spliced viral RNA was detected in lymph nodes

NHP.144 (1466990) **Inactivated whole SIV vaccine in macaques: evaluation of protective efficacy against challenge with cell-free virus or infected cells.**

Authors: Johnson PR, Montefiori DC, Goldstein S, Hamm TE, Zhou J, Kitov S, Haigwood NL, Misher L, London WT, Gerin JL, et al.

Journal: AIDS Res Hum Retroviruses 1992 Aug;8(8):1501-5.

Objectives: Challenge, Immunogenicity. To evaluate the protective efficacy against challenge with cell-free virus or infected cells.

NHP.146 (1466992) **Prevention of HIV-2 and SIVSM infection in cynomolgus monkeys by active or passive immunization.**

Authors: Biberfield G, Putkonen P, Thorstensson R, Norrby E

Journal: AIDS Res Hum Retroviruses 1992 Aug;8(8):1511-3.

Objectives: Challenge, Immunogenicity, Passive Immunization.

Main Findings:
- Protection against homologous HIV-2 infection was demonstrated in 2/2 monkeys immunized with a Triton-X100-treated whole HIV-2SBL-6669 vaccine in incomplete Freund's adjuvant and in 2/4 monkeys immunized with a formalin-inactivated whole HIV-2 vaccine in RIBI adjuvant
- Monkeys preinfected with a live poorly replicating HIV-2 strain were shown to develop cross-protection against SIV-induced disease
- HIV-2 and SIVsm infection in cynomolgus monkeys can be prevented by passive immunization.

NHP.147 (1470916) **Cellular proteins bound to immunodeficiency viruses: implications for pathogenesis and**

vaccines.

Authors: Arthur LO, Bess JW Jr, Sowder RC 2nd, Benveniste RE, Mann DL, Chermann JC, Henderson LE

Journal: Science 1992 Dec 18;258(5090):1935-8.

Main Findings:
- Retracted from public display

NHP.148 (1470917) **Protective effects of a live attenuated SIV vaccine with a deletion in the nef gene.**

Authors: Daniel MD, Kirchhoff F, Czajak SC, Sehgal PK, Desrosiers RC

Journal: Science 1992 Dec 18;258(5090):1938-41.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac239ΔNef *Type:* Live Attenuated Virus *Route:* Intramuscular

Challenge: SIVmac239, SIVmac251 *Route:* Intravenous

Main Findings:
- Rhesus monkeys vaccinated with live SIV deleted in nef were completely protected against challenge by intravenous inoculation of live, pathogenic SIV
- 2/2 naive controls infected 14 dpc and dead of SAIDS 252 dpc
- 2/2 vaccinees protected from increased viral load and disease and remain healthy >208 wpc (>4 years)
- 2/2 vaccinees protected from infection >208 wpc (>4 years)

NHP.149.1 (1677743) **Prevention of HIV-2 and SIVsm infection by passive immunization in cynomolgus monkeys.**

Authors: Putkonen P, Thorstensson R, Ghavamzadeh L, Albert J, Hild K, Biberfeld G, Norrby E

Journal: Nature 1991 Aug 1;352(6334):436-8.

Objectives: Challenge, Passive Immunization. To determine whether a transfer of antibodies can prevent HIV-2 and SIVsm (SIV of sooty mangabey origin) infection in cynomolgus monkeys.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: Anti-HIV-2 *Type:* Passive Antibody *Route:* Intravenous

Challenge: HIV-2.SBL6669 *Route:* Intravenous

Main Findings:
- All 6 control animals treated with normal monkey serum or no serum (n = 39) became infected by the challenge virus
- 5/7 animals pretreated with antibody-containing serum at a dose of 9 ml kg-1 resisted infection
- Conclusion: passively transferred antibodies can protect against a low-dose lentivirus challenge in a nonhuman primate.

NHP.149.2 (1677743) **Prevention of HIV-2 and SIVsm infection by passive immunization in cynomolgus monkeys.**

Authors: Putkonen P, Thorstensson R, Ghavamzadeh L, Albert J, Hild K, Biberfeld G, Norrby E

Journal: Nature 1991 Aug 1;352(6334):436-8.

Objectives: Challenge, Passive Immunization.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: DNA Vaccine pNL432-ZF1* *Type:* DNA *Routes:* Intravenous, Intramuscular

Vaccine Name: Anti-HIV-2 *Type:* Passive Antibody *Route:* Intravenous

Main Findings:
- Antibody titers declined to undetectable level after challenge
- Active infection did not occur during 6-10 months of follow up in 3/4 passively immunized monkeys

NHP.150.1 (8986737) **Resistance of neonatal monkeys to live attenuated vaccine strains of simian immunodeficiency virus.**

Authors: Wyand MS, Manson KH, Lackner AA, Desrosiers RC

Journal: Nat Med 1997 Jan;3(1):32-6.

Objectives: Challenge, Immunogenicity, Passive Immunization.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- High viral loads and disease were observed in only 2 of 18 neonatal monkeys infected with gene-deleted vaccine strains of simian immunodeficiency virus
- Pathogenicity was restricted to neonates born to unvaccinated mothers and that received extremely high doses of vaccine virus orally
- No in utero transmission of vaccine virus was observed in 4 neonates born to mothers vaccinated during the second trimester
- Conclusion: Live attenuated vaccine approach should remain a viable option for preventing HIV infection and disease in high-risk human populations

NHP.150.2 (8986737) **Resistance of neonatal monkeys to live attenuated vaccine strains of simian immunodeficiency virus.**

Authors: Wyand MS, Manson KH, Lackner AA, Desrosiers RC

Journal: Nat Med 1997 Jan;3(1):32-6.

Objectives: Challenge, Passive Immunization.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac239Δ3 *Type:* Live Attenuated Virus *Routes:* Intravenous, Oral, Intraplacental

Main Findings:

- 0/4 cases of vertical transmission of SIVmac239Δ3
- Maternal antibody dd not prevent transmission of the autologous challenge in 3/4 neonates

NHP.151 (1733103) **Immunization with tween-ether-treated SIV adsorbed onto aluminum hydroxide protects monkeys against experimental SIV infection.**

Authors: Stahl-Hennig C, Voss G, Nick S, Petry H, Fuchs D, Wachter H, Coulibaly C, Luke W, Hunsmann G

Journal: Virology 1992 Feb;186(2):588-96.

Objectives: Challenge, Immunogenicity. To study immunogenicity and protective values of tween-ether-disrupted SIVmac251/32H adsorbed onto aluminum hydroxide immunization in monkeys.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac251/32H (Tween/Ether) *Type:* Whole (killed) Inactivated Virus *Route:* Intravenous *Formulation:* SIVmac251/32H (Tween/Ether) + Alum

Challenge: SIVmac251(32H) *Route:* Intravenous

Main Findings:

- 4/7 immunized animals did not show any signs of virus replication and therefore appeared to be protected
- Nonvaccinated control animals and the vaccine failures showed a rise in their urinary neopterin concentrations 1 to 2 weeks after infection
- After the challenge, control animals and infected vaccinees showed a primary or secondary antibody response while antibody titers declined in virus-negative animals
- Specific cytotoxic T-lymphocytes were not present prior to challenge

NHP.152.1 (1741059) **Prevention of HIV-1 infection in chimpanzees by gp120 V3 domain-specific monoclonal antibody.**

Authors: Emini EA, Schleif WA, Nunberg JH, Conley AJ, Eda Y, Tokiyoshi S, Putney SD, Matsushita S,

Cobb KE, Jett CM, et al.

Journal: Nature 1992 Feb 20;355(6362):728-30.

Objectives: Challenge, Passive Immunization. To demonstrate the protective efficacy of anti-V3 domain antibody in vivo.

Species/Subspecies: Pan Troglodytes (Chimpanzee)

Vaccine Name: Cβ1 anti-V3 *Type:* Passive Antibody *Route:* Intravenous

Challenge: SIVmac251(32H) *Route:* Intravenous

Main Findings:
- 1/1 control chimpanzee infected
- 1/1 protected from infection >336 dpc

NHP.152.2 (1741059) **Prevention of HIV-1 infection in chimpanzees by gp120 V3 domain-specific monoclonal antibody.**

Authors: Emini EA, Schleif WA, Nunberg JH, Conley AJ, Eda Y, Tokiyoshi S, Putney SD, Matsushita S, Cobb KE, Jett CM, et al.

Journal: Nature 1992 Feb 20;355(6362):728-30.

Objectives: Challenge, Immunotherapy. To demonstrate the protective efficacy of anti-V3 post challenge with live virus

Species/Subspecies: Pan Troglodytes (Chimpanzee)

Vaccine Name: Cβ1 anti-V3 *Type:* Passive Antibody *Route:* Intravenous

Challenge: SIVmac251(32H) *Route:* Intravenous

Main Findings:
- 1 OF 1 CONTROL CHIMPANZEE INFECTED 56 DPC
- 1 OF 1 PROTECTED FROM INFECTION >224 DPC

NHP.153 (9593009) **Passive immunization of newborn rhesus macaques prevents oral simian immunodeficiency virus infection.**

Authors: Van Rompay KK, Berardi CJ, Dillard-Telm S, Tarara RP, Canfield DR, Valverde CR, Montefiori DC, Cole KS, Montelaro RC, Miller CJ, Marthas ML

Journal: J Infect Dis 1998 May;177(5):1247-59.

Objectives: Challenge, Passive Immunization. To determine if passively acquired antiviral antibodies modulate virus transmission and disease progression in human pediatric AIDS.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- Untreated neonates became infected after oral SIV inoculation and had high viremia, and most animals developed fatal AIDS within 3 months
- In contrast, SIV hyperimmune serum given subcutaneously prior to oral SIV inoculation protected 6 newborns against infection
- When SIV hyperimmune serum was given to 3 newborns 3 weeks after oral SIV inoculation, viremia was not reduced, and all 3 infants died within 3 months of age due to AIDS and immune-complex disease
- Conclusion: passively acquired anti-HIV IgG may decrease perinatal HIV transmission.

NHP.154 (1871125) **Protection of macaques with a simian immunodeficiency virus envelope peptide vaccine based on conserved human immunodeficiency virus type 1 sequences.**

Authors: Shafferman A, Jahrling PB, Benveniste RE, Lewis MG, Phipps TJ, Eden-McCutchan F, Sadoff J, Eddy GA, Burke DS

Journal: Proc Natl Acad Sci U S A 1991 Aug 15;88(16):7126-30.

Objectives: Challenge, Immunogenicity. To evaluate envelope peptide vaccine based on conserved HIV-1 sequences.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVenv-Bgal peptides *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* SIVenv-Bgal peptides + Freund′s Complete Adjuvant

Challenge: SIV(Mne) clone E11S *Route:* Intravenous

Main Findings:

- After challenge with virulent virus, controls became virus positive and developed gradually rising antibody titers to SIV over 63 weeks
- Immunized macaques developed a postchallenge anamnestic response to SIVenv antigens within 3-6 weeks followed by a gradual, fluctuating decline in SIV antibody titers and partial or total suppression of detectable SIV
- Virus suppression correlated with prechallenge neutralizing antibody titers

NHP.155 (1883540) **Efficacy of SIV/deltaB670 glycoprotein-enriched and glycoprotein-depleted subunit vaccines in protecting against infection and disease in rhesus monkeys.**

Authors: Murphey-Corb M, Montelaro RC, Miller MA, West M, Martin LN, Davison-Fairburn B, Ohkawa S, Baskin GB, Zhang JY, Miller GB, et al.

Journal: AIDS 1991 Jun;5(6):655-62.

Objectives: Challenge, Immunogenicity. To define the role of virion components in the induction of protective immunity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- Immunization with the glycoprotein-enriched preparation prevented infection in 2/4 monkeys, whereas the glycoprotein-depleted vaccine failed to prevent infection in all 4 vaccinates tested
- Glycoprotein-depleted vaccine appeared to moderate the progression of SIV-induced disease compared with non-immunized infected control monkeys inoculated with the same challenge dose
- Conclusion: subunit vaccines containing sufficient quantities of viral glycoproteins can protect against SIV infection, whereas subunit vaccines composed predominantly of viral core proteins cannot

NHP.156 (1907354) **Prevention of HIV-1 IIIB infection in chimpanzees by CD4 immunoadhesin.**

Authors: Ward RH, Capon DJ, Jett CM, Murthy KK, Mordenti J, Lucas C, Frie SW, Prince AM, Green JD, Eichberg JW

Journal: Nature 1991 Aug 1;352(6334):434-6.

Objectives: Challenge, Passive Immunization. To evaluate the CD4 immunoadhesin (CD4-IgG) in the protection against HIV-1 infection in chimpanzees.

Species/Subspecies: Pan Troglodytes (Chimpanzee)

Vaccine Name: CHO-SIVgp120 *Type:* DNA *Routes:* Intravenous, Intramuscular

Vaccine Name: CD4 Immunoadhesin (CD4-IgG) *Type:* Other *Routes:* Intravenous, Intramuscular

Main Findings:

- Pretreatment with CD4-IgG can prevent the infection of chimpanzees with HIV-1

NHP.157.1 (1979369) **Preliminary report: protection of cynomolgus macaques against simian immunodeficiency virus by fixed infected-cell vaccine.**

Authors: Stott EJ, Chan WL, Mills KH, Page M, Taffs F, Cranage M, Greenaway P, Kitchin P

Journal: Lancet 1990 Dec 22-29;336(8730):1538-41.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: Fixed inactivated SIVmac251 infected cells *Type:* Whole (killed) Inactivated Virus *Route:*

Subcutaneous *Formulation:* Fixed inactivated SIVmac251 infected cells + Quil-A + PBS

Challenge: SIVmac251 *Route:* --

Main Findings:

- Upon challenged with 10 MID50 of SIVmac251, virus and proviral DNA were not found in any of the vaccinated cynomolgus macaques immunized with with inactivated SIV-infected cells and 'Quil-A' as adjuvant
- Virus was repeatedly isolated from unvaccinated animals on at least 5 separate occasions and proviral DNA was detected in circulating lymphocytes by polymerase chain reaction amplification (Trials 1,2)
- In animals previously infected, vaccination regimen did not eliminate virus (Trial 3)

NHP.157.2 (1979369) **Preliminary report: protection of cynomolgus macaques against simian immunodeficiency virus by fixed infected-cell vaccine.**

Authors: Stott EJ, Chan WL, Mills KH, Page M, Taffs F, Cranage M, Greenaway P, Kitchin P

Journal: Lancet 1990 Dec 22-29;336(8730):1538-41.

Objectives: Challenge, Immunogenicity. see experiment 1 (except the challenge was carried out at week 18)

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: Fixed inactivated SIVmac251 infected cells *Type:* Whole (killed) Inactivated Virus *Route:* Subcutaneous *Formulation:* Fixed inactivated SIVmac251 infected cells + Quil-A + PBS

Challenge: SIVmac251 *Route:* Subcutaneous

Main Findings:

- See Experiment 1

NHP.157.3 (1979369) **Preliminary report: protection of cynomolgus macaques against simian immunodeficiency virus by fixed infected-cell vaccine.**

Authors: Stott EJ, Chan WL, Mills KH, Page M, Taffs F, Cranage M, Greenaway P, Kitchin P

Journal: Lancet 1990 Dec 22-29;336(8730):1538-41.

Objectives: Immunotherapy. To evaluate whether a vaccine would reduce the course of SIV infection in animals already infected with the live virus and have active progressive infection.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: Fixed inactivated SIVmac251 infected cells *Type:* Whole (killed) Inactivated Virus *Route:* Subcutaneous *Formulation:* Fixed inactivated SIVmac251 infected cells + Quil-A + PBS

Challenge: SHIV.DH12R-PS1 *Route:* --

Main Findings:

- The vaccine that protected from challenge in Trial 1 and 2, did little to eliminate the virus in already infected animals.

NHP.158 (1979745) **Infection of cynomolgus monkeys with HIV-2 protects against pathogenic consequences of a subsequent simian immunodeficiency virus infection.**

Authors: Putkonen P, Thorstensson R, Albert J, Hild K, Norrby E, Biberfeld P, Biberfeld G

Journal: AIDS 1990 Aug;4(8):783-9.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Main Findings:

- At the time of SIV challenge the HIV-2-infected monkeys had neutralizing antibodies against HIV-2, but virus could no longer be recovered from their PBMCs and no clinical symptoms or decrease in CD4+ lymphocytes were observed
- Protection from challenge with SIVsm including SIV-induced immunodeficiency (no decrease of CD4+ lymphocytes) and lymphadenopathy was observed in HIV-2-infected monkeys for 9 months post challenge

- 4 naive control monkeys that were inoculated with the same dose of SIV became persistently infected and developed a decrease of the absolute numbers of CD4+ cells and showed a marked lymphadenopathy.

NHP.159 (1988952) **Immunization of chimpanzees confers protection against challenge with human immunodeficiency virus.**

Authors: Girard M, Kieny MP, Pinter A, Barre-Sinoussi F, Nara P, Kolbe H, Kusumi K, Chaput A, Reinhart T, Muchmore E, et al.

Journal: Proc Natl Acad Sci U S A 1991 Jan 15;88(2):542-6.

Objectives: Challenge, Immunogenicity. To evaluate protection against challenge with human immunodeficiency virus in immunized chimpanzees.

Species/Subspecies: Pan Troglodytes (Chimpanzee)

Main Findings:

- After 6 months of follow-up, immunized chimpanzees appeared uninfected by serologic and virologic criteria, including polymerase chain reaction analysis and failure to isolate virus from peripheral blood lymphocytes, bone marrow, and lymph node tissue
- Of 2 chimpanzees monitored for 1 yr, virus was isolated initially from 1 animal at 32 weeks, but the second chimpanzee was virus negative by all assays through 12 mo; the third animal has remained virus negative through 9 mo of follow-up

NHP.160 (2078406) **Vaccine protection of rhesus macaques against simian immunodeficiency virus infection.**

Authors: Carlson JR, McGraw TP, Keddie E, Yee JL, Rosenthal A, Langlois AJ, Dickover R, Donovan R, Luciw PA, Jennings MB, et al.

Journal: AIDS Res Hum Retroviruses 1990 Nov;6(11):1239-46.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque), Macaca (sp)

Main Findings:

- Method: Rhesus macaques were immunized with an inactivated whole SIVmac vaccine and muramyl dipeptide (MDP), incomplete Freund's adjuvant (IFA), or aqueous suspension were challenged intravenously with 0.1 TCID50 of cell-free SIVmac
- Virus was readily recovered from the PBMCs of 10/10 controls
- 3/3 animals that received the vaccine with MDP were protected from challenge
- 1/2 animals that received the vaccine with IFA were protected from challenge
- 1/3 animals that received the aqueous vaccine were protected from challenge

NHP.161 (2127681) **Yeast-expressed p55 precursor core protein of human immunodeficiency virus type 1 does not elicit protective immunity in chimpanzees.**

Authors: Emini EA, Schleif WA, Quintero JC, Conard PG, Eichberg JW, Vlasuk GP, Lehman ED, Polokoff MA, Schaeffer TF, Schultz LD, et al.

Journal: AIDS Res Hum Retroviruses 1990 Nov;6(11):1247-50.

Objectives: Challenge, Immunogenicity.

NHP.162 (11282197) **Vaccination with DNA containing tat coding sequences and unmethylated CpG motifs protects cynomolgus monkeys upon infection with simian/human immunodeficiency virus (SHIV89.6P).**

Authors: Cafaro A, Titti F, Fracasso C, Maggiorella MT, Baroncelli S, Caputo A, Goletti D, Borsetti A, Pace M, Fanales-Belasio E, Ridolfi B, Negri DR, Sernicola L, Belli R, Corrias F, Macchia I, Leone P, Michelini Z, ten Haaft P, Butto S, Verani P, Ensoli B

Journal: Vaccine 2001 Apr 6;19(20-22):2862-77.

Objectives: Challenge.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: pCV-tat *Type:* DNA *Routes:* Intradermal, Intramuscular *Formulation:* pCV-tat + Saline, PBS

Main Findings:

- A Tat-expressing vector (pCV-tat), expressing the HIV-1 BH10 isolate Tat gene, and containing unmethylated CpG dinucleotides, induced an anti-Tat CTL response that was protective in containing primary infection with SHIV89.6P.

NHP.163 (11282197) **Vaccination with DNA containing tat coding sequences and unmethylated CpG motifs protects cynomolgus monkeys upon infection with simian/human immunodeficiency virus (SHIV89.6P).**

Authors: Cafaro A, Titti F, Fracasso C, Maggiorella MT, Baroncelli S, Caputo A, Goletti D, Borsetti A, Pace M, Fanales-Belasio E, Ridolfi B, Negri DR, Sernicola L, Belli R, Corrias F, Macchia I, Leone P, Michelini Z, ten Haaft P, Butto S, Verani P, Ensoli B

Journal: Vaccine 2001 Apr 6;19(20-22):2862-77.

Objectives: Challenge, Immunogenicity. To verify whether a DNA vaccine utilizing the tat gene expressed by a vector containing defined unmethylated CpG sequences would be capable of enhancing antigen-specific CTL responses against Tat and inducing an effective protection against AIDS.

Main Findings:

- Intramuscular inoculation of the pCV-tat contained primary infection with the highly pathogenic SHIV89.6P virus preventing the CD4+ T cell decline in all the vaccinated monkeys
- Undetectable virus replication and negative virus isolation correlatedin all cases with the presence of anti-Tat CTLs
- CD8-mediated non cytolytic antiviral activity was present in all protected animals
- CpG-rich tat DNA vaccine may represent a promising candidate for preventive and therapeutic vaccination against AIDS

NHP.164 (9747943) **The role of type-1 and type-2 T-helper immune responses in HIV-1 vaccine protection.**

Authors: Heeney JL, van Gils ME, van der Meide P, de Giuli Morghen C, Ghioni C, Gimelli M, Raddelli A, Davis D, Akerblom L, Morein B

Journal: J Med Primatol 1998 Apr-Jun;27(2-3):50-8.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: HIV-1.SF2 gp120/p24 Recombinant *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* HIV-1.SF2 gp120/p24 Recombinant + ISCOM(s)™

Vaccine Name: V2.V3.HIV-1.SF2 Synth.peptides *Type:* Synthetic Protein/Peptide *Route:* Intramuscular

Challenge: SHIV.SF13 *Route:* Intravenous

NHP.165 (9733821) **Env-independent protection induced by live, attenuated simian immunodeficiency virus vaccines.**

Authors: Gundlach BR, Reiprich S, Sopper S, Means RE, Dittmer U, Matz-Rensing K, Stahl-Hennig C, Uberla K

Journal: J Virol 1998 Oct;72(10):7846-51.

Objectives: Challenge, Immunogenicity.

Main Findings:

- In contrast to the results with naive control monkeys, no challenge virus could be isolated from the SIV-IL2- and SIVNU-infected macaques
- Challenge virus sequences detected by nested PCR in some of the vaccinated macaques
- 4 vaccinated macaques were rechallenged with an SIV-murine leukemia virus (MLV) hybrid were protected from productive infection with the SIV-MLV hybrid in the absence

of measurable Nab, while 2 naive control monkeys were readily infected
- Chemokine inhibition and receptor interference phenomena were not involved in protection
- Conclusion: protective responses induced by live attenuated SIV vaccines can be independent of host immune reactions directed against Env.

NHP.166 (9718118) **Neutralizing antibodies administered before, but not after, virulent SHIV prevent infection in macaques.**

Authors: Foresman L, Jia F, Li Z, Wang C, Stephens EB, Sahni M, Narayan O, Joag SV

Journal: AIDS Res Hum Retroviruses 1998 Aug 10;14(12):1035-43.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- 3/6 macaques inoculated with anti-SHIV plasma and challenged 24 hr later with approximately 300 AID of SHIV(KU-2), completely resisted infection with SHIV(KU-2). A fourth animal failed to yield infectious virus, but DNA extracted from its peripheral blood mononuclear cells (PBMC) and lymph nodes had viral sequences
- 2/6 vaccinees had partial control of infection
- 6/6 macaques given the same dose of anti-SHIV plasma 18 hr after exposure to virus became infected
- 2/2 macaques given anti-SHIV plasma only 2 hr after exposure to virus became infected

NHP.167 (9718117) **Fine specificity of anti-V3 antibodies induced in chimpanzees by HIV candidate vaccines.**

Authors: Coeffier E, Girard M, Barre-Sinoussi F, Meignier B, Muchmore E, Fultz PN, LeClerc C

Journal: AIDS Res Hum Retroviruses 1998 Aug 10;14(12):1023-34.

Objectives: Challenge, Immunogenicity. To assess the specificity of the anti-V3 antibody responses induced in chimpanzees immunized by various human immunodeficiency type 1 (HIV-1) candidate vaccines and challenged by heterologous strains of HIV-1.

Species/Subspecies: Pan Troglodytes (Chimpanzee)

NHP.168 (8896498) **Immunogenicity and protective efficacy of a human immunodeficiency virus type 2 recombinant canarypox (ALVAC) vaccine candidate in cynomolgus monkeys.**

Authors: Andersson S, Makitalo B, Thorstensson R, Franchini G, Tartaglia J, Limbach K, Paoletti E, Putkonen P, Biberfeld G

Journal: J Infect Dis 1996 Nov;174(5):977-85.

Objectives: Challenge, Immunogenicity. To investigate the efficacy of a recombinant HIV-2 canarypox (ALVAC HIV-2) vaccine candidate given alone or in combination with HIV-2 envelope gp125 or HIV-2 V3 synthetic peptides in cynomolgus monkeys.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Main Findings:
- High antibody titers to HIV-2 gp125 and significant lymphocyte proliferative responses to killed HIV-2 virions demonstrated in monkeys given booster immunizations with gp125
- Neutralizing antibody titers were low
- 3/12 monkeys generated HIV-2-specific cytotoxic T lymphocytes prior to viral challenge
- 4/10 monkeys immunized with ALVAC HIV-2 plus HIV-2 gp125 or V3 peptides were protected.

NHP.169 (9714241) **In vivo resistance to simian immunodeficiency virus superinfection depends on attenuated virus dose.**

Authors: Cranage MP, Sharpe SA, Whatmore AM, Polyanskaya N, Norley S, Cook N, Leech S, Dennis MJ,

Hall GA

Journal: J Gen Virol 1998 Aug;79 (Pt 8):1935-44.

NHP.170 (8892959) **Failure of a human immunodeficiency virus type 1 (HIV-1) subtype B-derived vaccine to prevent infection of chimpanzees by an HIV-1 subtype E strain.**

Authors: Girard M, Yue L, Barre-Sinoussi F, van der Ryst E, Meignier B, Muchmore E, Fultz PN

Journal: J Virol 1996 Nov;70(11):8229-33.

NHP.171 (8892046) **In vivo protective anti-HIV immune responses in non-human primates through DNA immunization.**

Authors: Boyer JD, Wang B, Ugen KE, Agadjanyan M, Javadian A, Frost P, Dang K, Carrano RA, Ciccarelli R, Coney L, Williams WV, Weiner DB

Journal: J Med Primatol 1996 Jun;25(3):242-50.

NHP.172 (9696847) **Temporal analyses of virus replication, immune responses, and efficacy in rhesus macaques immunized with a live, attenuated simian immunodeficiency virus vaccine.**

Authors: Connor RI, Montefiori DC, Binley JM, Moore JP, Bonhoeffer S, Gettie A, Fenamore EA, Sheridan KE, Ho DD, Dailey PJ, Marx PA

Journal: J Virol 1998 Sep;72(9):7501-9.

NHP.173 (8827215) **Protection against mucosal SIVsm challenge in macaques infected with a chimeric SIV that expresses HIV type 1 envelope.**

Authors: Quesada-Rolander M, Makitalo B, Thorstensson R, Zhang YJ, Castanos-Velez E, Biberfeld G, Putkonen P

Journal: AIDS Res Hum Retroviruses 1996 Jul 20;12(11):993-9.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Main Findings:

- 4/4 immunized monkeys were infected with the vaccine virus
- All monkeys developed neutralizing antibodies to HIV-1 and high antibody titers to HIV-1 env glycoproteins, but no Nabs to SIVsm
- After a follow-up period of 1 year, 2/4 SHIV-infected monkeys were completely protected against SIVsm infection
- 2/2 SHIV-immunized and infected with the challenge virus, but were able to control this infection
- CTL in 1/4 of the immunized animals
- All 6 control animals yielded virus repeatedly after SIVsm challenge and 3 of them showed declining CD4 cell counts

NHP.174 (8827214) **Multiple immunizations with attenuated poxvirus HIV type 2 recombinants and subunit boosts required for protection of rhesus macaques.**

Authors: Myagkikh M, Alipanah S, Markham PD, Tartaglia J, Paoletti E, Gallo RC, Franchini G, Robert-Guroff M

Journal: AIDS Res Hum Retroviruses 1996 Jul 20;12(11):985-92.

Objectives: Challenge, Immunogenicity. To study macaques immunized twice with NYVAC or ALVAC recombinants carrying HIV-2 env, gag, and pol genes, then boosted either with an additional recombinant immunization or an HIV-2 gp160 protein.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: ALVAC/vCP153 HIV-2 gag,pol,env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name: HIV-2 gp160 *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* HIV-2 gp160 + Rehydragel HPA

Challenge: HIV-2.SBL6669 *Route:* Intravenous

Main Findings:

- Macaques primed with ALVAC recombinant exhibited sporadic T cell proliferative activity, and all but one failed to develop neutralizing antibodies
- In contrast, macaques primed with NYVAC recombinants had no T cell proliferative activity but exhibited neutralizing antibody titers (highest in the three recombinant group) that declined by the time of challenge
- None of the macaques exhibited significant CTL activity
- Following challenge at 32 weeks with HIV-2SBL6669 all macaques became infected. Thus, immunization regimen was not sufficient to confer protective immunity in the HIV-2 rhesus macaque model
- Delayed infection in macaques immunized with the NYVAC-HIV-2 recombinant may have been associated with the development of memory B cells capable of providing a neutralizing antibody response on challenge.

NHP.175 (9614868) **Cytotoxic T cells and neutralizing antibodies induced in rhesus monkeys by virus-like particle HIV vaccines in the absence of protection from SHIV infection.**

Authors: Wagner R, Teeuwsen VJ, Deml L, Notka F, Haaksma AG, Jhagjhoorsingh SS, Niphuis H, Wolf H, Heeney JL

Journal: Virology 1998 May 25;245(1):65-74.

NHP.176 (8811357) **Attenuated SIV imparts immunity to challenge with pathogenic spleen-derived SIV but cannot prevent repair of the nef deletion.**

Authors: Stahl-Hennig C, Dittmer U, Nisslein T, Pekrun K, Petry H, Jurkiewicz E, Fuchs D, Wachter H, Rud EW, Hunsmann G

Journal: Immunol Lett 1996 Jun;51(1-2):129-35.

NHP.177 (8811354) **Recombinant subunit vaccines as an approach to study correlates of protection against primate lentivirus infection.**

Authors: Hu SL, Polacino P, Stallard V, Klaniecki J, Pennathur S, Travis BM, Misher L, Kornas H, Langlois AJ, Morton WR, Benveniste RE

Journal: Immunol Lett 1996 Jun;51(1-2):115-9.

Objectives: Challenge, Immunogenicity.

NHP.178 (8811353) **Passive immune globulin therapy in the SIV/macaque model: early intervention can alter disease profile.**

Authors: Haigwood NL, Watson A, Sutton WF, McClure J, Lewis A, Ranchalis J, Travis B, Voss G, Letvin NL, Hu SL, Hirsch VM, Johnson PR

Journal: Immunol Lett 1996 Jun;51(1-2):107-14.

NHP.179 (9543435) **A clinically relevant HIV-1 subunit vaccine protects rhesus macaques from in vivo passaged simian-human immunodeficiency virus infection.**

Authors: Mooij P, van der Kolk M, Bogers WM, ten Haaft PJ, Van Der Meide P, Almond N, Stott J, Deschamps M, Labbe D, Momin P, Voss G, Von Hoegen P, Bruck C, Heeney JL

Journal: AIDS 1998 Mar 26;12(5):F15-22.

NHP.180 (8806509) **Fetal or neonatal infection with attenuated simian immunodeficiency virus results in protective immunity against oral challenge with pathogenic SIVmac251.**

Authors: Otsyula MG, Miller CJ, Tarantal AF, Marthas ML, Greene TP, Collins JR, van Rompay KK, McChesney MB

Journal: Virology 1996 Aug 1;222(1):275-8.

NHP.181 (8794330) **Intrarectal transmission of simian immunodeficiency virus in rhesus macaques: selective amplification and host responses to transient or persistent viremia.**

Authors: Trivedi P, Horejsh D, Hinds SB, Hinds PW II, Wu MS, Salvato MS, Pauza CD

Journal: J Virol 1996 Oct;70(10):6876-83.

NHP.182 (8794312) **The consequence of passive administration of an anti-human immunodeficiency virus type 1 neutralizing monoclonal antibody before challenge of chimpanzees with a primary virus isolate.**

Authors: Conley AJ, Kessler JA II, Boots LJ, McKenna PM, Schleif WA, Emini EA, Mark GE III, Katinger H, Cobb EK, Lunceford SM, Rouse SR, Murthy KK

Journal: J Virol 1996 Oct;70(10):6751-8.

NHP.183 (9461191) **Reduction in SIV replication in rhesus macaques infused with autologous lymphocytes engineered with antiviral genes.**

Authors: Donahue RE, Bunnell BA, Zink MC, Metzger ME, Westro RP, Kirby MR, Unangst T, Clements JE, Morgan RA

Journal: Nat Med 1998 Feb;4(2):181-6.

NHP.184 (8676459) **Resistance of previously infected chimpanzees to successive challenges with a heterologous intraclade B strain of human immunodeficiency virus type 1.**

Authors: Shibata R, Siemon C, Cho MW, Arthur LO, Nigida SM Jr, Matthews T, Sawyer LA, Schultz A, Murthy KK, Israel Z, Javadian A, Frost P, Kennedy RC, Lane HC, Martin MA

Journal: J Virol 1996 Jul;70(7):4361-9.

NHP.185.1 (8673922) **Protective mucosal immunity elicited by targeted iliac lymph node immunization with a subunit SIV envelope and core vaccine in macaques.**

Authors: Lehner T, Wang Y, Cranage M, Bergmeier LA, Mitchell E, Tao L, Hall G, Dennis M, Cook N, Brookes R, Klavinskis L, Jones I, Doyle C, Ward R

Journal: Nat Med 1996 Jul;2(7):767-75.

Objectives: Challenge, Immunogenicity. To evaluate a novel route of immunization (the targeted iliac lymph node-TILN) aiming close to the iliac lymph nodes draining the genitorectal mucosa.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: rSIV-gp120 protein *Type:* Recombinant Subunit Protein *Routes:* Subcutaneous, Targeted Lymph node immunization *Formulation:* rSIV-gp120 protein + Alum

Vaccine Name: Recombinant p27 *Type:* Recombinant Subunit Protein *Routes:* Subcutaneous, Targeted Lymph node immunization *Formulation:* Recombinant p27 + Alum

Challenge: SIVmac251(32H) *Route:* Intrarectal

Main Findings:

- Rectal challenge with the SIVmac 32H J5 molecular clone induced total protection in 4/7

macaques immunized by targeted iliac lymph node (TILN), compared with infection in 13/14 unimmunized macaques or immunized by other routes (P = 0.025)(experiment 1 and experiment 2)
- Protection was associated with significant increase in the iliac lymph nodes of IgA antibody-secreting cells to p27 (P < 0.02), CD8-suppressor factor (P < 0.01), and the chemokines RANTES and MIP-1 beta (P < 0.01).

NHP.185.2 (8680896) **Protective mucosal immunity elicited by targeted iliac lymph node immunization with a subunit SIV envelope and core vaccine in macaques.**

Authors: Lu Y, Salvato MS, Pauza CD, Li J, Sodroski J, Manson K, Wyand M, Letvin N, Jenkins S, Touzjian N, Chutkowski C, Kushner N, LeFaile M, Payne LG, Roberts B

Journal: J Acquir Immune Defic Syndr Hum Retrovirol 1996 Jun 1;12(2):99-106.

Objectives: Challenge, Immunogenicity. To evaluate a novel route of immunization (the targeted iliac lymph node-TILN) aiming close to the iliac lymph nodes draining the genitorectal mucosa.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: rSIV-gp120 protein *Type:* Recombinant Subunit Protein *Routes:* Intrarectal, Subcutaneous, Targeted Lymph node immunization, Intradermal, Intramuscular *Formulation:* rSIV-gp120 protein + Alum

Vaccine Name: Recombinant p27 *Type:* Recombinant Subunit Protein *Routes:* Intrarectal, Subcutaneous, Targeted Lymph node immunization, Intradermal, Intramuscular *Formulation:* Recombinant p27 + Alum

Challenge: SIVmac251 (J5) *Route:* Intrarectal

Main Findings:
- Rectal challenge with the SIVmac 32H J5 molecular clone induced total protection in 4/7 macaques immunized by targeted iliac lymph node (TILN), compared with infection in 13/14 unimmunized macaques or immunized by other routes (P = 0.025)(experiment 1 and experiment 2)
- Protection was associated with significant increase in the iliac lymph nodes of IgA antibody-secreting cells to p27 (P < 0.02), CD8-suppressor factor (P < 0.01), and the chemokines RANTES and MIP-1 beta (P < 0.01).

NHP.186 (8648707) **Vaccine protection by a triple deletion mutant of simian immunodeficiency virus.**

Authors: Wyand MS, Manson KH, Garcia-Moll M, Montefiori D, Desrosiers RC

Journal: J Virol 1996 Jun;70(6):3724-33.

Objectives: Challenge, Immunogenicity.

NHP.187 (9445041) **Selection of virus variants and emergence of virus escape mutants after immunization with an epitope vaccine.**

Authors: Mortara L, Letourneur F, Gras-Masse H, Venet A, Guillet JG, Bourgault-Villada I

Journal: J Virol 1998 Feb;72(2):1403-10.

NHP.188 (9449524) **Vaccine evaluation studies of replication-defective SIVsmB7.**

Authors: Kraiselburd EN, Salaman A, Beltran M, Rivera M, Oliver J, Kessler M, Knezevich M, Rodriguez A, Bilska M, Montefiori D, Torres-Bauza LJ, Martinez I

Journal: Cell Mol Biol (Noisy-le-grand) 1997 Nov;43(7):915-24.

NHP.189 (8648735) **Simian immunodeficiency virus DNA vaccine trial in macaques.**

Authors: Lu S, Arthos J, Montefiori DC, Yasutomi Y, Manson K, Mustafa F, Johnson E, Santoro JC, Wissink

J, Mullins JI, Haynes JR, Letvin NL, Wyand M, Robinson HL
Journal: J Virol 1996 Jun;70(6):3978-91.

NHP.190 (8648204) **Vaccination of pregnant macaques protects newborns against mucosal simian immunodeficiency virus infection.**
Authors: Van Rompay KK, Otsyula MG, Tarara RP, Canfield DR, Berardi CJ, McChesney MB, Marthas ML
Journal: J Infect Dis 1996 Jun;173(6):1327-35.
Objectives: Challenge, Immunogenicity.

NHP.191 (8642649) **Construction and characterization of replication-competent simian immunodeficiency virus vectors that express gamma interferon.**
Authors: Giavedoni LD, Yilma T
Journal: J Virol 1996 Apr;70(4):2247-51.

NHP.192 (8627782) **Vaginal transmission of chimeric simian/human immunodeficiency viruses in rhesus macaques.**
Authors: Lu Y, Brosio P, Lafaile M, Li J, Collman RG, Sodroski J, Miller CJ
Journal: J Virol 1996 May;70(5):3045-50.

NHP.193 (8605050) **Resistance of chimpanzees immunized with recombinant gp120SF2 to challenge by HIV-1SF2.**
Authors: el-Amad Z, Murthy KK, Higgins K, Cobb EK, Haigwood NL, Levy JA, Steimer KS
Journal: AIDS 1995 Dec;9(12):1313-22.
Objectives: Challenge, Immunogenicity. To determine whether vaccination with recombinant HIV-1SF2 gp120 in a novel oil-in-water adjuvant emulsion, MF59, protects chimpanzees against challenge with HIV-1SF2, the homologous virus isolate.
Species/Subspecies: Pan Troglodytes (Chimpanzee)
Vaccine Name: CHO cell-expressed HIV-1SF2 gp120 *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* CHO cell-expressed HIV-1SF2 gp120 + MF59, MTP-PE
Challenge: HIV-1.SF2 *Route:* Intravenous
Main Findings:
- 1/2 vaccinated animals showed no serologic or virologic evidence of infection suggesting a complete sterilizing protection from challenge in 1 animal and a transient infection in the other animal
- Both control animals showed evidence of seroconversion in ELISA and Western blot assays; virus was detected in the early, acute phase of infection of both control animals by plasma RNA PCR, virus culture and PBMC DNA PCR assays.

NHP.194.1 (8623530) **Protection from pathogenic SIVmac challenge following short-term infection with a nef-deficient attenuated virus.**
Authors: Norley S, Beer B, Binninger-Schinzel D, Cosma C, Kurth R
Journal: Virology 1996 May 1;219(1):195-205.
Objectives: Challenge, Immunogenicity. To determine if protection could be achieved against challenge with a "swarm" of SIVmac251-32H produced in monkey cells and if protection could be demonstrated after a short period of infection with the attenuated virus.
Species/Subspecies: Macaca mulatta (Rhesus macaque)
Vaccine Name: SIVmac251, 32H, (C8) *Type:* Live Attenuated Virus *Route:* Intravenous
Challenge: SIVmac251(32H) *Route:* Intravenous

Main Findings:
- 3/4 monkeys challenged at 10 weeks and 3/4 challenged at 20 weeks were protected from productive superinfection
- No apparent correlation between the levels of binding or neutralizing antibodies on the day of challenge and subsequent protection

NHP.194.2 (8623530) **Protection from pathogenic SIVmac challenge following short-term infection with a nef-deficient attenuated virus.**

Authors: Norley S, Beer B, Binninger-Schinzel D, Cosma C, Kurth R

Journal: Virology 1996 May 1;219(1):195-205.

Objectives: Challenge, Immunogenicity. To determine the breadth of protection afforded by immunization with live attenuated virus

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac251 *Type:* Live Virus *Routes:* Intravenous, Mucosal

Vaccine Name: SIVmac251, 32H, (C8) *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge: SIVsm *Route:* Intrarectal, Intravenous, Intravenous

Main Findings:
- Animals previously immunized with live attenuated SIVmac251 then with the wild type SIVmac251 were protected from infection with SIVsm
- The virus load was 2-3 orders of magnitude lower than the control animals

NHP.195 (8680896) **Utility of SHIV for testing HIV-1 vaccine candidates in macaques.**

Authors: Lu Y, Salvato MS, Pauza CD, Li J, Sodroski J, Manson K, Wyand M, Letvin N, Jenkins S, Touzjian N, Chutkowski C, Kushner N, LeFaile M, Payne LG, Roberts B

Journal: J Acquir Immune Defic Syndr Hum Retrovirol 1996 Jun 1;12(2):99-106.

NHP.196 (8605046) **Protection from HIV-1 envelope-bearing chimeric simian immunodeficiency virus (SHIV) in rhesus macaques infected with attenuated SIV: consequences of challenge.**

Authors: Bogers WM, Niphuis H, ten Haaft P, Laman JD, Koornstra W, Heeney JL

Journal: AIDS 1995 Dec;9(12):F13-8.

Objectives: Challenge, Immunogenicity.

NHP.197 (9444999) **Induction of neutralizing antibodies to T-cell line-adapted and primary human immunodeficiency virus type 1 isolates with a prime-boost vaccine regimen in chimpanzees.**

Authors: Zolla-Pazner S, Lubeck M, Xu S, Burda S, Natuk RJ, Sinangil F, Steimer K, Gallo RC, Eichberg JW, Matthews T, Robert-Guroff M

Journal: J Virol 1998 Feb;72(2):1052-9.

NHP.198 (8537682) **Protection of MN-rgp120-immunized chimpanzees from heterologous infection with a primary isolate of human immunodeficiency virus type 1.**

Authors: Berman PW, Murthy KK, Wrin T, Vennari JC, Cobb EK, Eastman DJ, Champe M, Nakamura GR, Davison D, Powell MF, Bussiere J, Francis DP, Matthews T, Gregory TJ, Obijeski JF

Journal: J Infect Dis 1996 Jan;173(1):52-9.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Pan Troglodytes (Chimpanzee)

Vaccine Name: HIV-1.MN.rgp120 *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* HIV-1.MN.rgp120 + Alum

Vaccine Name: SIVsmE660 *Type:* Live Virus *Routes:* Intravenous, Mucosal

Main Findings:
- The control animal was infected by the challenge virus: viral infection was detected in the control animal by viral culture, PCR, and multiple serologic assays beginning 2 weeks after infection
- 3/3 animals immunized with gp120 were not infected (during 12 months of follow-up)
- No neutralization activity in gp120 immunized animals
- Conclusions: (1) Immunization with recombinant gp120 derived from a T cell-adapted isolate prevented infection by a heterologous primary isolate of HIV-1. (2) In vitro virus neutralization assays utilizing primary isolates cultured in PBMC may be imperfect indicators of protection in vivo

NHP.199 (9420212) **Administration of an anti-CD8 monoclonal antibody interferes with the clearance of chimeric simian/human immunodeficiency virus during primary infections of rhesus macaques.**

Authors: Matano T, Shibata R, Siemon C, Connors M, Lane HC, Martin MA

Journal: J Virol 1998 Jan;72(1):164-9.

NHP.200 (8493576) **Protection against vaginal SIV transmission with microencapsulated vaccine.**

Authors: Marx PA, Compans RW, Gettie A, Staas JK, Gilley RM, Mulligan MJ, Yamshchikov GV, Chen D, Eldridge JH

Journal: Science 1993 May 28;260(5112):1323-7.

Objectives: Challenge, Immunogenicity. To study the immunogenicity and protection confered by formalin inactivated SIV macaques.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac251 (encapsulated) *Type:* Whole (killed) Inactivated Virus *Routes:* Intratracheal, Oral, Intramuscular *Formulation:* SIVmac251 (encapsulated) + DL-PGL

Challenge: SIVmac251 *Route:* Vaginal or perivaginal

Main Findings:
- 5/6 macaques immunized with formalin-treated SIV in biodegradable microspheres by the intramuscular plus oral or plus intratracheal route were protected against vaginal challenge
- Oral immunization alone did not protect
- After a second vaginal challenge, 3/4 intramuscularly primed and mucosally boosted macaques remained protected

NHP.201.1 (9419166) **Induction of Th2 cytokine expression for p27-specific IgA B cell responses after targeted lymph node immunization with simian immunodeficiency virus antigens in rhesus macaques.**

Authors: Kawabata S, Miller CJ, Lehner T, Fujihashi K, Kubota M, McGhee JR, Imaoka K, Hiroi T, Kiyono H

Journal: J Infect Dis 1998 Jan;177(1):26-33.

Objectives: Immunogenicity. To determine if there is an association between the isotype of SIV-specific B cell responses and the profile of Th1 and Th2 cytokine expression.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: rSIV-gp120 protein *Type:* Recombinant Subunit Protein *Routes:* Intrarectal, Subcutaneous, Targeted Lymph node immunization, Intradermal, Intramuscular *Formulation:* rSIV-gp120 protein + Alum, Rehydragel HPA

Vaccine Name: Whole inactivated SIVmac251 *Type:* Whole (killed) Inactivated Virus *Route:* Targeted Lymph node immunization *Formulation:* Whole inactivated SIVmac251 + Rehydragel HPA

Vaccine Name: Recombinant p27 *Type:* Recombinant Subunit Protein *Routes:* Intrarectal, Subcutaneous, Targeted Lymph node immunization, Intradermal, Intramuscular *Formulation:* Recombinant p27 + Alum, Rehydragel HPA

Main Findings:
- In rhesus macaques immunized with SIV antigens, when CD4+ T cells purified from antigen-stimulated PBMCs were analyzed, the levels of Th2 cytokine production were gradually increased after the second and third immunizations with no change of interferon-gamma
- The main isotype following the second and third immunization was IgG
- Induction of Th2 type responses in TLN-immunized rhesus macaques reflects the sequence of initial induction of SIV-specific IgG-producing cells followed by IgA-secreting cells.

NHP.201.2 (9456249) **Targeted lymph-node immunization with whole inactivated simian immunodeficiency virus (SIV) or envelope and core subunit antigen vaccines does not reliably protect rhesus macaques from vaginal challenge with SIVmac251.**

Authors: Lu X, Kiyono H, Lu D, Kawabata S, Torten J, Srinivasan S, Dailey PJ, McGhee JR, Lehner T, Miller CJ

Journal: AIDS 1998 Jan 1;12(1):1-10.

Objectives: Challenge, Immunogenicity. To investigate protection from challenge by recombinant subunit protein inoculation targeting iliac lymph node.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: rSIV-gp120 protein *Type:* Recombinant Subunit Protein *Routes:* Intrarectal, Subcutaneous, Targeted Lymph node immunization, Intradermal, Intramuscular *Formulation:* rSIV-gp120 protein + Alum, Rehydragel HPA

Vaccine Name: Whole inactivated SIVmac251 *Type:* Whole (killed) Inactivated Virus *Route:* Targeted Lymph node immunization *Formulation:* Whole inactivated SIVmac251 + Rehydragel HPA

Vaccine Name: Recombinant p27 *Type:* Recombinant Subunit Protein *Routes:* Intrarectal, Subcutaneous, Targeted Lymph node immunization, Intradermal, Intramuscular *Formulation:* Recombinant p27 + Alum, Rehydragel HPA

Challenge: SIVmac251 *Route:* Vaginal or perivaginal

Main Findings:
- High-titer SIV-specific IgG antibodies in serum in all animals immunized with recombinant subunit proteins inoculated by (targeted) iliac lymph node immunization
- Upon intravaginal challenge with SIVmac251, all animals became virus isolation-positive, except 1 animal immunized with SIV p27 and gp120
- Conclusion: Reliable protection from vaginal transmission of SIV was not achieved by the targeted lymph node immunization procedure

NHP.202 (9395361) **DNA vaccination as anti-human immunodeficiency virus immunotherapy in infected chimpanzees.**

Authors: Boyer JD, Ugen KE, Chattergoon M, Wang B, Shah A, Agadjanyan M, Bagarazzi ML, Javadian A, Carrano R, Coney L, Williams WV, Weiner DB

Journal: J Infect Dis 1997 Dec;176(6):1501-9.

Objectives: Immunogenicity, Immunotherapy. To evaluate the role of DNA vaccine as anti-HIV immunotherapy in infected chimpanzees.

Species/Subspecies: Pan Troglodytes (Chimpanzee)

Vaccine Name: pCMN160 HIV-1.MN env-rev *Type:* DNA *Route:* Intramuscular *Formulation:* pCMN160 HIV-1.MN env-rev + Bupivacaine

Challenge: HIV-1 IIIB *Route:* Intravenous

Main Findings:
- Two HIV-1-infected chimpanzees were vaccinated with plasmid pCMN160-HIV-1.MN.env-rev demonstrated enhanced humoral responses, decrease in viral load to background levels from week 20

- The control chimpanzee was subsequently vaccinated with pCMN160 following the inoculation with a control sham plasmid, had the antibody responses increased and, as in the first animal, and the virus load decreased
- Conclusion: the immune response has a direct impact on HIV-1 replication in chimpanzees

NHP.203 (8427714) **Studies on the specificity of the vaccine effect elicited by inactivated simian immunodeficiency virus.**

Authors: Cranage MP, Polyanskaya N, McBride B, Cook N, Ashworth LA, Dennis M, Baskerville A, Greenaway PJ, Corcoran T, Kitchin P, et al.

Journal: AIDS Res Hum Retroviruses 1993 Jan;9(1):13-22.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac251, 32H, (C8) *Type:* Whole (killed) Inactivated Virus *Route:* Intramuscular *Formulation:* SIVmac251, 32H, (C8) + Rehydragel HPA, SAF-1

Vaccine Name: HIV-1 GB8 *Type:* Whole (killed) Inactivated Virus *Route:* Intramuscular *Formulation:* HIV-1 GB8 + SAF-1

Challenge: SIVsmB670, SIVmac251(32H) *Route:* Intravenous

Main Findings:

- Partially purified SIVmac protected macaques from intravenous challenge with homologous and heterologous SIV grown on human cells but not on monkey grown cells
- HIV-1 grown on human C8166 T cell line protected macaques against challenge with human cell-grown SIVmac
- All vaccinated macaques had anti-cell antibodies

NHP.204 (8427039) **Immune response of chimpanzees after immunization with the inactivated whole immunodeficiency virus (HIV-1), three different adjuvants and challenge.**

Authors: Niedrig M, Gregersen JP, Fultz PN, Broker M, Mehdi S, Hilfenhaus J

Journal: Vaccine 1993;11(1):67-74.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Pan troglodytes troglodytes (chimpanzee)

Vaccine Name: Whole inactivated HIV-1 IIIB *Type:* Whole (killed) Inactivated Virus *Route:* Intramuscular *Formulation:* Whole inactivated HIV-1 IIIB + Rehydragel HPA, BWZL

Vaccine Name: Recombinant HIV-1 gag core (p24,p15) antigen *Type:* Recombinant Subunit Protein *Route:* Subcutaneous

Vaccine Name: Recombinant HIV-1 env gp160 antigen *Type:* Recombinant Subunit Protein *Routes:* Subcutaneous, Intramuscular

Challenge: HIV-1.LAI *Route:* Intravenous

Main Findings:

- Weak and inconsistent responses were observed in animals that received HIV-1 formulated with alum as adjuvant, whereas HIV-1 formulated with incomplete Freund's adjuvant or an experimental adjuvant (BWZL) induced good humoral and cellular immune responses to the virus
- The 3 animals that received HIV-1 with the BWZL adjuvant generated overall the best immune responses
- Upon challenge with infectious HIV-1, despite good humoral and cell-mediated immunity, all 3 immunized animals and a control animal became infected within 4 weeks

NHP.205.1 (9343211) **An adenovirus-simian immunodeficiency virus env vaccine elicits humoral, cellular, and mucosal immune responses in rhesus macaques and decreases viral burden following vaginal challenge.**

Authors: Buge SL, Richardson E, Alipanah S, Markham P, Cheng S, Kalyan N, Miller CJ, Lubeck M, Udem S, Eldridge J, Robert-Guroff M

Journal: J Virol 1997 Nov;71(11):8531-41.

Objectives: Challenge, Immunogenicity. To investigate the immunogenicity of an adenovirus expressing SIV env and its ability to protect rhesus macaques against vaginal challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Ad5hr-SIVenv *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Oral, Intranasal *Formulation:* Ad5hr-SIVenv + Water, PBS

Vaccine Name: Native SIV gp120 *Type:* Purified Viral Products *Routes:* Intratracheal, Intramuscular *Formulation:* Native SIV gp120 + SAF-1 + PBS

Challenge: SIVmac251 *Route:* Vaginal or perivaginal

Main Findings:

- The vaccine induced SIV-specific neutralizing antibodies and HIV gp120 binding IgG and IgA detected in nasal and rectal secretions
- SIV-specific IgGs were also observed in vaginal secretions and saliva
- T-cell proliferative responses to SIV gp140 and T-helper epitopes were sporadically detected in all immunized macaques
- Following vaginal challenge with SIVmac251, transient or persistent infection resulted in both immunized and control monkeys
- Conclusion: Ad5hr-SIV env recombinant and gp120 subunit induces strong humoral, cellular, and mucosal immunity in rhesus macaques

NHP.205.2 (12021334) **Rhesus macaque resistance to mucosal simian immunodeficiency virus infection is associated with a postentry block in viral replication.**

Authors: Peng B, Voltan R, Lim L, Edghill-Smith Y, Phogat S, Dimitrov DS, Arora K, Leno M, Than S, Woodward R, Markham PD, Cranage M, Robert-Guroff M

Journal: J Virol 2002 Jun;76(12):6016-26.

Objectives: Challenge. To investigate the mechanism of resistance to challenge of an unvaccinated control rhesus macaque.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Challenge: SIVmac251(32H), SIVmac251 *Route:* Intrarectal, Vaginal or perivaginal

Main Findings:

- Rhesus macaque 359, a vaccine control animal, resisted 2 successive intravaginal challenges with SIVmac251 (and failed to seroconvert) an additional intrarectal SIVmac32H challenge
- Resistance of this macaque to SIV infection was not due to a high level of CD8+ suppressor activity but to an inherent resistance of its CD4+ T cells
- Resistance is due to a postentry block in viral replication and implicates a cellular inhibitory mechanism in its CD4+ T cells.

NHP.205.3 (10438833) **Factors associated with slow disease progression in macaques immunized with an adenovirus-simian immunodeficiency virus (SIV) envelope priming-gp120 boosting regimen and challenged vaginally with SIVmac251.**

Authors: Buge SL, Murty L, Arora K, Kalyanaraman VS, Markham PD, Richardson ES, Aldrich K, Patterson LJ, Miller CJ, Cheng SM, Robert-Guroff M

Journal: J Virol 1999 Sep;73(9):7430-40.

Objectives: Challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Ad5hr-SIVenv *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Oral, Intranasal *Formulation:* Ad5hr-SIVenv + Water, Saline, PBS

Vaccine Name: Native SIV gp120 *Type:* Purified Viral Products *Routes:* Intratracheal, Intramuscular *Formulation:* Native SIV gp120 + SAF-1 + Saline, PBS

Challenge: SIVmac251 *Route:* Vaginal or perivaginal

Main Findings:
- Reboosting and re-challenge of macaques vaccinated and challenged in trials 205.1 and 205.2 again resulted in partial protection from pathogenicity of challenge.

NHP.206 (8411103) **Immunization of Macaca fascicularis with inactivated SIV preparations: challenge with human- or monkey-derived SIV and the effects of a longer immunization schedule.**

Authors: Titti F, Koanga Mogtomo ML, Borsetti A, Geraci A, Sernicola L, Panzini G, Turillazzi GP, Baroncelli S, Giovannetti A, Zamarchi R, et al.

Journal: J Med Primatol 1993 Feb-May;22(2-3):110-8.

Objectives: Challenge, Immunogenicity. To compare two human-derived SIVmac251 whole virus vaccines, a long vs short immunization schedule, and two different challenge viruses.

Main Findings:
- Both vaccines induced protection after challenge with human-derived SIVmac251/32H
- No difference between the 2 schedules of immunization
- 5/7 were protected following the first challenge (human-derived)
- No protection was observed in monkeys that were reboosted and rechallenged with monkey-derived SIVmac251

NHP.207 (9343164) **Live, attenuated simian immunodeficiency virus vaccines elicit potent resistance against a challenge with a human immunodeficiency virus type 1 chimeric virus.**

Authors: Shibata R, Siemon C, Czajak SC, Desrosiers RC, Martin MA

Journal: J Virol 1997 Nov;71(11):8141-8.

Objectives: Challenge, Immunogenicity. To ask what protection live attenuated vaccines can provide against SHIVdh12 challenge. A long term follow up.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIMmac239Δ2 *Type:* Live Attenuated Virus *Route:* Intravenous

Vaccine Name: SIVmac239Δ3 *Type:* Live Attenuated Virus *Routes:* Intravenous, Oral, Intraplacental

Challenge: SHIV.MD1 *Route:* Intravenous

Main Findings:
- 3 rhesus macaques, previously immunized with SIVΔ3 or SIVΔ2, then challenged with 30,000 TCID50 dose of SHIV.DH12 controlled the SHIV infection by reducing the viral load to barely detectable levels
- Only SIV sequences, derived from the vaccine, could be amplified from numerous tissue samples collected at the conclusion of the experiment, 60 weeks postchallenge, but SHIV-specific sequences (viz., HIV-1 env) could not
- Live attenuated SIV vaccines provide strong long-term protection even against challenge strains with highly divergent envelope sequences.

NHP.208 (8363756) **Protection of monkeys by a split vaccine against SIVmac depends upon biological properties of the challenge virus.**

Authors: Stahl-Hennig C, Voss G, Dittmer U, Coulibaly C, Petry H, Makoschey B, Cranage MP, Aubertin AM, Luke W, Hunsmann G

Journal: AIDS 1993 Jun;7(6):787-95.

Objectives: Challenge, Immunogenicity. To investigate the role of the anti-cellular immune response in the protection of rhesus macaques against infection with SIVmac and to determine the biological differences between SIV challenge stocks grown either on human T-cell lines or on monkey PBMC.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Main Findings:

- Protection from virus challenge with C8166-grown SIVmac251/32H or SIVmac251/MPBMC did not correlate with anti-cellular antibodies or proliferative T-cell reactivities
- Control animals infected with SIVmac251/MPBMC showed high persistent antigenaemia and high plasma virus titres
- Neither the antibody nor the proliferative T-cell response to SIVmac correlates with protection from virus challenge. In contrast to SIVmac251/32H grown on C8166 cells, the MPBMC-grown challenge virus SIVmac251 appears to belong to the 'rapid-high' phenotype, possibly explaining the lack of protection against this SIV

NHP.209 (9333153) **Superinfection with human immunodeficiency virus type 2 can reactivate virus production in baboons but is contained by a CD8 T cell antiviral response.**

Authors: Locher CP, Blackbourn DJ, Barnett SW, Murthy KK, Cobb EK, Rouse S, Greco G, Reyes-Teran G, Brasky KM, Carey KD, Levy JA

Journal: J Infect Dis 1997 Oct;176(4):948-59.

Objectives: Challenge, Immunogenicity. To assess resistance to superinfection by human immunodeficiency virus.

Main Findings:

- Background: Asymptomatic baboons previously infected with HIV-2, were first challenged with homologous virus (HIV-2UC2 or HIV-2UC14) and later with heterologous virus (HIV-2UC12)
- After both virus inoculations, either resistance to viral infection or a transient viremia was observed
- The original virus was recovered in 3 baboons, suggesting that reactivation of a latent infection occurred on heterologous challenge and that HIV-2 superinfection is blocked by processes established during prior infection
- Low antibody titers and low levels of virus neutralization
- Suppression of HIV-1 replication was observed attributed to CD8 T cells

NHP.210 (8312055) **In vitro spontaneous production of anti-SIV antibodies is a reliable tool in the follow-up of protection of SIV-vaccinated monkeys.**

Authors: Zamarchi R, Veronese ML, Titti F, Geraci A, Verani P, Rossi GB, Amadori A, Chieco-Bianchi L

Journal: AIDS Res Hum Retroviruses 1993 Nov;9(11):1139-44.

Objectives: Challenge, Immunogenicity. To assess the reliability of the spontaneous in vitro synthesis of simian immunodeficiency virus (SIV)-specific antibodies as a marker in the monitoring of protection in SIV-vaccinated animals

Main Findings:

- Background: Macaca fascicularis monkeys were immunized with formalin-inactivated SIVmac251 or SIVmac251/32H, and challenged with human-derived (SIVmac251/32H) or monkey-derived live SIV
- Immunized animals were protected against human-derived SIV challenge
- No spontaneous in vitro synthesis of anti-SIV antibody was observed in nonstimulated PBMC cultures over a 4-month follow-up
- Human cell-grown SIVmac251 immunization did not afford protection against monkey-derived SIV, and all the animals became infected and showed spontaneous in vitro synthesis of anti-SIV antibodies

NHP.211 (9315483) **Gene gun-based nucleic acid immunization alone or in combination with recombinant vaccinia vectors suppresses virus burden in rhesus macaques challenged with a heterologous SIV.**

Authors: Fuller DH, Simpson L, Cole KS, Clements JE, Panicali DL, Montelaro RC, Murphey-Corb M, Haynes JR

Journal: Immunol Cell Biol 1997 Aug;75(4):389-96.

Objectives: Challenge, Immunogenicity. To evaluate the ability of gene gun-based DNA immunization alone or in combination with recombinant vaccinia vectors to elicit protective immune responses in rhesus macaques challenged with a pathogenic heterologous SIV.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- Geometric mean end-point IgG titres in the DNA + VAC and VAC + DNA groups were substantially higher than the responses seen in the VAC + VAC and DNA + DNA groups, demonstrating a synergistic relationship between DNA-based vaccines and recombinant vaccinia virus-based vaccines
- The vaccines did not prevent infection
- All vaccine groups showed significant virus load reductions from 7 to 56 days post challenge when compared to controls
- DNA + DNA group developed the lowest prechallenge antibody responses and the most significant reduction (200-fold) in virus load was associated with this group. In addition, a significant delay in CD4+ T cell loss relative to controls was observed in the DNA + DNA group.

NHP.212 (9271187) **Mechanisms of protection induced by attenuated simian immunodeficiency virus. IV. Protection against challenge with virus grown in autologous simian cells.**

Authors: Almond N, Corcoran T, Hull R, Walker B, Rose J, Sangster R, Silvera K, Silvera P, Cranage M, Rud E, Stott EJ

Journal: J Med Primatol 1997 Feb-Apr;26(1-2):34-43.

Objectives: Challenge, Immunogenicity. To test the mechanism of protection provided by live attenuated SIV.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Main Findings:

- Background: 8 animals infected with live attenuated SIV then challenged with wild-type grown in autologous and heterologous cells
- Animals infected with attenuated SIV are protected against wild-type SIV grown in autologous or heterologous cells
- Live attenuated SIV protects by the induction of allogeneic antibodies is not tenable

NHP.213 (8217348) **Lymphoproliferative responses in macaques immunized with inactivated SIV vaccine.**

Authors: Teng XC, Ashworth LA, Sharpe SA, Dennis MJ, Cranage MP

Journal: AIDS Res Hum Retroviruses 1993 Aug;9(8):799-801.

Objectives: Challenge, Immunogenicity. To examine the lymphoproliferative response of macaques immunized with inactivated, partially purified SIVmac32H grown in C8166 cells.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- Animals vaccinated with partially purified C8166 cell-grown SIVmac32H in alum adjuvant (Group 1) were protected from initial challenge with SIVmac32H but became infected when rechallenged with SIVmac251
- No association could be demonstrated between protection from challenge and lymphoproliferative response to one particular antigen tested against

NHP.214 (9266989) **Macaques infected with attenuated simian immunodeficiency virus resist superinfection with virulence-revertant virus.**

Authors: Sharpe SA, Whatmore AM, Hall GA, Cranage MP

Journal: J Gen Virol 1997 Aug;78 (Pt 8):1923-7.

Objectives: Challenge, Immunogenicity. To examine the protective values of live attenuated virus vaccine to protect against revertant autologous strains.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- 3 macaques already infected with the attenuated molecular clone SIVmacC8 were resistant to superinfection with virulent virus that arose in vivo following repair of a 12 bp attenuating lesion in the nef/3' LTR
- 4 naive animals became infected following inoculation with blood taken from the macaque in which virulent virus arose

NHP.215 (9266988) **Mechanisms of protection induced by attenuated simian immunodeficiency virus. I. Protection cannot be transferred with immune serum.**

Authors: Almond N, Rose J, Sangster R, Silvera P, Stebbings R, Walker B, Stott EJ

Journal: J Gen Virol 1997 Aug;78 (Pt 8):1919-22.

Objectives: Challenge, Passive Immunization. To evaluate the role in protection induced by live attenuated SIVmacC8 against SIVmajJ5 challenge.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: Anti-SIVmacC8 *Type:* Passive Antibody *Route:* Intraperitoneal

Challenge: SIVmacJ5M *Route:* ND

Main Findings:
- 4/4 control animals were infected as indicated by the test at 14 dpc
- 2 of passively immunized animals were protected from infection at 14 dpc but were shown to be infected thereafter
- The failure of passive immunization to transfer protection indicates that serum components alone are not sufficient to mediate the potent protection obtained using live attenuated vaccines

NHP.216 (8198872) **Reduced virus load in rhesus macaques immunized with recombinant gp160 and challenged with simian immunodeficiency virus.**

Authors: Ahmad S, Lohman B, Marthas M, Giavedoni L, el-Amad Z, Haigwood NL, Scandella CJ, Gardner MB, Luciw PA, Yilma T

Journal: AIDS Res Hum Retroviruses 1994 Feb;10(2):195-204.

Objectives: Challenge, Immunogenicity. To evaluate the potential of SIVmac239 gp160 expressed by recombinant vaccinia virus (vSIVgp160) and baculovirus (bSIVgp160) to protectively immunize rhesus macaques against intravenous infection with pathogenic SIVmac isolates.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- Binding antibodies to gp130 were induced in all animals following immunization with SIVgp160
- Immunization did not induce neutralizing antibodies up to 1 week prior to virus challenge
- No protection from challenge: All animals became infected after i.v. inoculation with 1-10 AID50 of either challenge virus

NHP.217 (8198871) **Passive immunization of cynomolgus macaques with immune sera or a pool of neutralizing monoclonal antibodies failed to protect against challenge with SIVmac251.**

Authors: Kent KA, Kitchin P, Mills KH, Page M, Taffs F, Corcoran T, Silvera P, Flanagan B, Powell C, Rose J, et al.

Journal: AIDS Res Hum Retroviruses 1994 Feb;10(2):189-94.

Objectives: Passive Immunization.

NHP.218 (9256490) **Potent, protective anti-HIV immune responses generated by bimodal HIV envelope DNA plus protein vaccination.**

Authors: Letvin NL, Montefiori DC, Yasutomi Y, Perry HC, Davies ME, Lekutis C, Alroy M, Freed DC, Lord CI, Handt LK, Liu MA, Shiver JW

Journal: Proc Natl Acad Sci U S A 1997 Aug 19;94(17):9378-83.

Objectives: Challenge, Immunogenicity. To study prime-boost regimen using HIV-1 env DNA and synthetic protein and neutralizing antibodies in nonhuman primate species.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- HIV-1 Env protein as a boosting immunogen generates a high titer neutralizing antibody response in rhesus macaques
- HIV-1 env DNA (multiple doses) followed by a final immunization with HIV-1 env DNA plus HIV-1 Env protein (env gene from HXBc2 clone of HIV IIIB; Env protein from parental HIV IIIB) completely protects monkeys from infection after i.v. challenge with a chimeric virus expressing HIV-1 env (HXBc2) on a simian immmunodeficiency virus (SIV-MAC239) backbone (SHIV-HXBc2)

NHP.219 (8179961) **Immune responses induced by prototype vaccines for AIDS in rhesus monkeys.**

Authors: Ohkawa S, Wilson LA, Larosa G, Javaherian K, Martin LN, Murphey-Corb M

Journal: AIDS Res Hum Retroviruses 1994 Jan;10(1):27-38.

Objectives: Challenge, Immunogenicity. To profile humoral and cell mediated immune response induced by immunization with candidate vaccines consisting of recombinant SIV gp110 with SAF-M adjuvant or rgp140+FA adjuvant.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- All the monkeys were infected after intravenous challenge
- 16 days following infection, viral antigenemia was reduced in both groups of vaccinates compared to controls
- After 23 days antigenemia in the gp110 + SAF-M group remained at the same level as on day 16, whereas antigenemia in the gp140 + FA group was significantly reduced further than the level observed on day 16
- Both vaccines induced high ELISA titers of IgG antibody against rgp140
- gp110 +/- SAF-M (not gp140 + FA) induced high titers of neutralizing antibody

NHP.220 (9223408) **Anti-major histocompatibility complex antibody responses to simian B cells do not protect macaques against SIVmac infection.**

Authors: Polyanskaya N, Sharpe S, Cook N, Leech S, Banks J, Dennis M, Hall G, Stott J, Cranage M

Journal: AIDS Res Hum Retroviruses 1997 Jul 20;13(11):923-31.

Objectives: Challenge, Immunogenicity. To investigate the efficacy of alloimmunization with simian B cells expressing high level of MHC class I and class II molecules to confer protection against systemic challenge with SIVmac.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- Antibody responses to allogeneic MHC molecules do not protect against infection with immunodeficiency lentiviruses

NHP.221 (8176640) **Long-standing protection of macaques against cell-free HIV-2 with a HIV-2 iscom vaccine.**

Authors: Putkonen P, Bjorling E, Akerblom L, Thorstensson R, Lovgren K, Benthin L, Chiodi F, Morein B, Biberfeld G, Norrby E, et al.

Journal: J Acquir Immune Defic Syndr 1994 Jun;7(6):551-9.

Objectives: Challenge, Immunogenicity. To investigate the capacity of two immunostimulating-complex (iscom) formulations including inactivated native HIV-2 viral proteins and selected peptides to induce protective immunity against HIV-2 in a nonhuman primate.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Main Findings:
- 3/4 immunized macaques were protected from challenge
- 4/4 control macaques became readily infected with challenge virus
- 1/3 protected animals showed an anamnestic antibody response to a dominating antigenic site
- The vaccine-protected monkeys were subsequently resistant to rechallenge infection at 12, 15, and 18 months after the first challenge, suggesting that a reasonable duration of protective immunity had been induced by the vaccine

NHP.222 (9188572) **Evolution of envelope-specific antibody responses in monkeys experimentally infected or immunized with simian immunodeficiency virus and its association with the development of protective immunity.**

Authors: Cole KS, Rowles JL, Jagerski BA, Murphey-Corb M, Unangst T, Clements JE, Robinson J, Wyand MS, Desrosiers RC, Montelaro RC

Journal: J Virol 1997 Jul;71(7):5069-79.

Objectives: Challenge, Immunogenicity.

Main Findings:
- The establishment of long-term protective immunity in general parallels the absence of further detectable changes in antibody responses and a maintenance of relatively constant antibody titer, avidity, conformational dependence, and the presence of neutralizing antibody for at least 2 years postinoculation
- Attenuated SIV vaccine and whole virus elicited mature antibody response
- Envelope subunit vaccines elicited in general immature antibody response characterized by poor reactivity with native envelope proteins, low avidity, low conformational dependence, and the absence of neutralization activity against the challenge strain

NHP.223 (8107246) **Incomplete protection, but suppression of virus burden, elicited by subunit simian immunodeficiency virus vaccines.**

Authors: Israel ZR, Edmonson PF, Maul DH, O'Neil SP, Mossman SP, Thiriart C, Fabry L, Van Opstal O, Bruck C, Bex F, et al.

Journal: J Virol 1994 Mar;68(3):1843-53.

Objectives: Challenge, Immunogenicity. To compare the efficacy of immunization with either SIV Env glycoprotein, Gag-Env, or whole inactivated virus, with or without recombinant live vaccinia vector priming, in protecting rhesus macaques from challenge with SIVmac251 clone BK28.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- Sterilizing immunity was induced only by whole inactivated vaccine
- Abortive infection (strong immunity) was observed in 2 animals (one VV-Env and one Gag-Env)
- Suppression of infection (incomplete or partial immunity) occurred in the 8/12 of subunit-vaccinated animals
- Active infection developed in all controls and 2/3 VV-Gag-Env-immunized animals

NHP.224 (8046353) **Major histocompatibility complex class I-associated vaccine protection from simian immunodeficiency virus-infected peripheral blood cells.**

Authors: Heeney JL, van Els C, de Vries P, ten Haaft P, Otting N, Koornstra W, Boes J, Dubbes R, Niphuis H, Dings M, et al.

Journal: J Exp Med 1994 Aug 1;180(2):769-74.

Objectives: Challenge, Immunogenicity. To evaluate the effectiveness of vaccine protection from infected cells from another individual of the same species.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- 50% of the SIV-vaccinated animals were protected from challenge
- 50% SIV-vaccinees were unprotected and rapidly progressed to AIDS
- Protection was unrelated to either total antibody titers to human cells, used in the production of the vaccine, to HLA antibodies, or to virus neutralizing activity
- All animals protected against cell-associated virus challenge were those which were SIV vaccinated and which shared the MHC class I allele (Mamu-A26) with the donor of the infected cells
- CTL specific for SIV envelope protein were detected in 3/4 protected animals vs. 1/4 unprotected animals, suggesting a possible role of MHC class I-restricted CTL in protection from infected blood cells.

NHP.225 (9185593) **Challenge of chimpanzees immunized with a recombinant canarypox-HIV-1 virus.**

Authors: Girard M, van der Ryst E, Barre-Sinoussi F, Nara P, Tartaglia J, Paoletti E, Blondeau C, Jennings M, Verrier F, Meignier B, Fultz PN

Journal: Virology 1997 May 26;232(1):98-104.

Objectives: Challenge, Immunogenicity. To evaluate the potential protective efficacy of a live recombinant HIV-1 canarypox vaccine candidate.

Species/Subspecies: Pan Troglodytes (Chimpanzee)

Main Findings:
- Vaccination against HIV-1(IIIB(LAI)) or HIV-1(MN) did not protect animals from challenge with heterologous cell-free HIV-1(DH12)
- 1/2 chimpanzees vaccinated 5 times with ALVAC-HIV-1 vCP250 and challenged by iv injection of PBMC from an HIV-1(IIIB(LAI))-infected chimpanzee were protected
- After booster inoculation 5 months post-challenge, both animals were re-challenged with HIV-1(DH12) and neither animal had neutralizing antibodies to HIV-1(DH12) and neither was protected from infection
- ALVAC-HIV-1 vCP250 expresses HIV-1(IIIB(LAI))gp120/TM, gag and protease gene products

NHP.226 (9142121) **Protection of chimpanzees from high-dose heterologous HIV-1 challenge by DNA vaccination.**

Authors: Boyer JD, Ugen KE, Wang B, Agadjanyan M, Gilbert L, Bagarazzi ML, Chattergoon M, Frost P, Javadian A, Williams WV, Refaeli Y, Ciccarelli RB, McCallus D, Coney L, Weiner DB

Journal: Nat Med 1997 May;3(5):526-32.

Objectives: Challenge, Immunogenicity. To examine the immunogenicity and efficacy of of an HIV-1 DNA vaccine encoding env, rev, gag/pol in a chimpanzee model system.

Species/Subspecies: Pan Troglodytes (Chimpanzee)

Main Findings:
- The immunized animals developed specific cellular and humoral immune responses
- The DNA constructs induced protection from the establishment of infection with a heterologous challenge (HIV-1 SF2)
- Control animal was infected

NHP.227 (9135877) **Live attenuated SIV vaccines are not effective in a postexposure vaccination model.**

Authors: Linhart H, Gundlach BR, Sopper S, Dittmer U, Matz-Rensing K, Kuhn EM, Muller J, Hunsmann G, Stahl-Hennig C, Uberla K

Journal: AIDS Res Hum Retroviruses 1997 May 1;13(7):593-9.

Objectives: Challenge, Immunogenicity, Immunotherapy. To evaluate the value of live attenuated vaccine therapeutic immunization.

Species/Subspecies: -

Main Findings:

- 4/4 controls (vaccinated with delta nef only - i.e., without the SIV IL-2 construct) were infected
- 0/4 vaccinees protected from increased viral loads
- 0/4 vaccinees protected from infection
- All coinfected macaques had a high viral load, and some of them developed AIDS-like symptoms and pathological alterations rapidly
- In the presence of pathogenic SIV, both live attenuated SIV vaccines did not protect from disease in this postexposure vaccination model

NHP.228 (7986590) **Induction of antigen-specific killer T lymphocyte responses using subunit SIVmac251 gag and env vaccines containing QS-21 saponin adjuvant.**

Authors: Newman MJ, Munroe KJ, Anderson CA, Murphy CI, Panicali DL, Seals JR, Wu JY, Wyand MS, Kensil CR

Journal: AIDS Res Hum Retroviruses 1994 Jul;10(7):853-61.

Objectives: Challenge, Immunogenicity. To increase the immunogenicity of recombinant subunit vaccine (SIVmac251 gag and env) with QS-21 adjuvant.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- Antigen-specific killer cell responses could be induced by a subunit vaccine formulated with the QS-21 saponin adjuvant that was detected was mediated by both CD4+ and CD8+ lymphocytes
- Despite the presence of these killer cells, all of the animals became infected with the SIVmac251 on experimental challenge
- The characteristics of the responses suggested that the effector cells were T lymphocytes, expressing either CD4 or CD8

NHP.229 (9123856) **Macaques infected with live attenuated SIVmac are protected against superinfection via the rectal mucosa.**

Authors: Cranage MP, Whatmore AM, Sharpe SA, Cook N, Polyanskaya N, Leech S, Smith JD, Rud EW, Dennis MJ, Hall GA

Journal: Virology 1997 Mar 3;229(1):143-54.

Objectives: Challenge, Immunogenicity. To determine if protection against systemic challenge in the SIVmac model of AIDS extends to intrarectal mucosal challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- 4 macaques previously infected with the attenuated SIVmacC8 resisted superinfection with SIVmacJ5, following intrarectal inoculation
- Immunization with live attenuated SIV protected 4 macaques from intrarectal challenge with SHIV (composed of SIVmac239 expressing the HXBc2 env, tat, and rev genes)
- In protected animals, SIV-specific CTL were detected in gut-associated lymph nodes and may have a role in limiting superinfection following mucosal exposure

NHP.230.1 (7986589) **High-titer immune responses elicited by recombinant vaccinia virus priming and particle boosting are ineffective in preventing virulent SIV infection.**

Authors: Daniel MD, Mazzara GP, Simon MA, Sehgal PK, Kodama T, Panicali DL, Desrosiers RC

Journal: AIDS Res Hum Retroviruses 1994 Jul;10(7):839-51.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- Method: Monkeys primed with a recombinant vaccinia virus expressing SIV Gag, Pol,

and Env polypeptides +/- SIV particles boost in adjuvant
- Despite the induction of vigorous immune responses, 17/18 rhesus monkeys became infected on challenge with a low dose of virulent SIVmac
- Vaccination may have diminished SIV burdens and rates of CD4+ cell declines in some of the animals
- Vaccinated/challenged/infected animals eventually developed fatal disease similar to control animals

NHP.230.2 (7986589) **High-titer immune responses elicited by recombinant vaccinia virus priming and particle boosting are ineffective in preventing virulent SIV infection.**

Authors: Daniel MD, Mazzara GP, Simon MA, Sehgal PK, Kodama T, Panicali DL, Desrosiers RC

Journal: AIDS Res Hum Retroviruses 1994 Jul;10(7):839-51.

Objectives: Challenge, Immunogenicity. To evaluate the ability of two different vaccinia virus recombinant to elicit immune response and to protect macaques against challenge.

NHP.230.3 (7986589) **High-titer immune responses elicited by recombinant vaccinia virus priming and particle boosting are ineffective in preventing virulent SIV infection.**

Authors: Daniel MD, Mazzara GP, Simon MA, Sehgal PK, Kodama T, Panicali DL, Desrosiers RC

Journal: AIDS Res Hum Retroviruses 1994 Jul;10(7):839-51.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

NHP.231 (7966239) **Efficacy of inactivated whole HIV-2 vaccines with various adjuvants in cynomolgus monkeys.**

Authors: Putkonen P, Nilsson C, Walther L, Ghavamzadeh L, Hild K, Broliden K, Biberfeld G, Thorstensson R

Journal: J Med Primatol 1994 Feb-May;23(2-3):89-94.

NHP.232 (9108105) **Vaccine effect using a live attenuated nef-deficient simian immunodeficiency virus of African green monkeys in the absence of detectable vaccine virus replication in vivo.**

Authors: Beer B, Baier M, zur Megede J, Norley S, Kurth R

Journal: Proc Natl Acad Sci U S A 1997 Apr 15;94(8):4062-7.

Objectives: Challenge, Immunogenicity. To test a live attenuated virus vaccine (SIVagm3-Delta nef)) in its natural host (African green monkey).

Species/Subspecies: Cercopithecus aetiops (African Green monkeys)

Main Findings:
- Preinoculated African green monkeys showed drastic decreases in virus load or were protected from challenge
- Vaccine protection occurred in the absence of detectable vaccine virus replication and humoral immune response, suggesting a protective cellular immune response similar to that associated with subinfectious or abortive infections
- SIVagm3(delta)nef replication was delayed marginally in vitro, but highly attenuated in vivo

NHP.233 (7966237) **Immunization with whole inactivated vaccine protects from infection by SIV grown in human but not macaque cells.**

Authors: Goldstein S, Elkins WR, London WT, Hahn A, Goeken R, Martin JE, Hirsch VM

Journal: J Med Primatol 1994 Feb-May;23(2-3):75-82.

Objectives: Challenge, Immunogenicity. To determine whether the species of origin of the cell line used to generate virus stock influenced the degree of protection mediated by WI-SIV vaccine.

Species/Subspecies: Macaca (sp)

Main Findings:

- Two groups of animals were vaccinated then challenged with either SIV-Human or SIV-Macaque virus
- All SIV-Human vaccinees were protected from infection, and all SIV-Macaque vaccinees became infected
- Difference between the two groups is due to cellular proteins in the virus preparation rather than the pathogenic or genetic properties of the virus< li>
- No virus was isolated from PBMC of macaques challenged with SIV-Human during the course of the study

NHP.234 (7966232) **Passive immunization of macaques against SIV infection.**

Authors: Gardner MB, Rosenthal A, Jennings M, Yee JA, Antipa L, MacKenzie M

Journal: J Med Primatol 1994 Feb-May;23(2-3):164-74.

Objectives: Challenge, Passive Immunization. To evaluate the mechanism responsible for protection achieved by an inactivated whole SIV vaccine and to test antiviral effect against SIV challenge of inactivated plasma or purified Ig.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- Plasma from a monkey that had been protected by an inactivated-whole SIV(mac) vaccine conferred protection to animals challenged iv 4-18 hours later with 10 AID50 of homologous cell-free virus
- Plasma or purified immunoglobulin (Ig) from SIVmac infected asymptomatic monkeys failed to protect any recipients, and may have enhanced infection and accelerated disease
- Anti-SIV Ig administered 24 hours post challenge may have enhanced infection.

NHP.235 (7966226) **Cellular immune responses in rhesus macaques infected rectally with low dose simian immunodeficiency virus.**

Authors: Salvato MS, Emau P, Malkovsky M, Schultz KT, Johnson E, Pauza CD

Journal: J Med Primatol 1994 Feb-May;23(2-3):125-30.

Objectives: Challenge, Immunogenicity. To test hypothesis that cellular immune responses in previously-infected animals are a correlate of protection.

Species/Subspecies: -

Main Findings:

- Monkeys infected rectally with low dose of SIV were resistant to high dose challenge with SIV
- PBMC from 2/4 challenged monkeys were unable to support SIV replication in vitro unless cultures were depleted of CD8+ lymphocytes
- Monkeys that survived high dose rectal infection with SIV also suppressed virus replication in cultured PBMC
- Virus-suppressive activity of PBMC may be an important correlate of protective immunity in AIDS

NHP.236 (7887023) **Protection of rhesus macaques from SIV infection by immunization with different experimental SIV vaccines.**

Authors: de Vries P, Heeney JL, Boes J, Dings ME, Hulskotte EG, Dubbes R, Koornstra W, ten Haaft P, Akerblom L, Eriksson S, et al.

Journal: Vaccine 1994 Nov;12(15):1443-52.

Objectives: Challenge, Immunogenicity. To compare the immunogenicity and efficacy of an inactivated whole

SIVmac (32H) preparation adjuvanted with muramyl dipeptide (SIV-MDP) and a gp120-enriched SIVmac (32H) ISCOM preparation (SIV-ISCOM).

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- Higher SIV-specific serum antibody titres were found in the SIV-MDP-immunized monkeys than in the SIV-ISCOM-immunized ones
- 4/4 SIV-MDP- and 4/4 SIV-ISCOM-immunized monkeys were protected against intravenous challenge
- 2/2 in each control group were infected with the challenge virus
- 0/4 in each vaccinee group were protected after reboost and rechallenge with 10 MID50 of the same virus produced in PBMC from a rhesus macaque.
- SIV-ISCOM-immunized animals of PBMC-only (Group B) did not develop clinical symptoms during observation period, unlike most other animals in this trial
- Both SIV preparations induced low VN antibody titres, possibly caused by denatured form of gp120after formaldehyde or acid treatment in both vaccine preparations.

NHP.237 (9032322) **Rhesus macaques previously infected with simian/human immunodeficiency virus are protected from vaginal challenge with pathogenic SIVmac239.**

Authors: Miller CJ, McChesney MB, Lu X, Dailey PJ, Chutkowski C, Lu D, Brosio P, Roberts B, Lu Y

Journal: J Virol 1997 Mar;71(3):1911-21.

Objectives: Challenge, Immunogenicity. To determine if a previous infection with SHIV 89.6 by vaginal inoculation could protect animals from vaginal challenge with pathogenic SIV.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- 5 Rhesus macaques infected intravaginally with SHIV89.6 then challenged intravaginally with pathogenic SIV-mac239 had low or undetectable viral RNA levels in plasma compared to control animals
- 3/5 of the SHIV-immunized animals remained virus isolation negative for more than 8 months, while 2 became virus isolation positive
- The presence of SIV Gag-specific cytotoxic T lymphocytes in peripheral blood mononuclear cells and SIV-specific antibodies in cervicovaginal secretions at the time of challenge was associated with resistance to pathogenic SIV infection after vaginal challenge.

NHP.238 (9000087) **Rapid development of vaccine protection in macaques by live-attenuated simian immunodeficiency virus.**

Authors: Stahl-Hennig C, Dittmer U, Nisslein T, Petry H, Jurkiewicz E, Fuchs D, Wachter H, Matz-Rensing K, Kuhn EM, Kaup FJ, Rud EW, Hunsmann G

Journal: J Gen Virol 1996 Dec;77 (Pt 12):2969-81.

Objectives: Challenge, Immunogenicity. To investigate the efficacy the nature of the immune protection induced of a nef-deleted mutant of SIVmac32H called pC8.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- All monkeys infected with pC8 live attenuated virus became persistently infected, exhibiting low cell-associated viral loads, but strong cellular and strong humoral antiviral responses
- 2/8 pC8-infected monkeys developed an immunodeficiency and were not challenged with complete replenishment of the deletion
- 6 monkeys, 2 preinfected for 42 weeks and 4 for 22 weeks, were challenged with pathogenic spleen-derived SIV; complete protection was achieved in 4 vaccinees
- Protection from challenge virus infection or a delayed disease development seemed to be associated with a sustained SIV-specific T helper cell response after challenge

- Conclusion: sterilizing immunity against superinfection with pathogenic SIV can be induced even after a relatively short waiting period of 22 weeks

NHP.239 (2157886) **Inactivated simian immunodeficiency virus vaccine failed to protect rhesus macaques from intravenous or genital mucosal infection but delayed disease in intravenously exposed animals.**

Authors: Sutjipto S, Pedersen NC, Miller CJ, Gardner MB, Hanson CV, Gettie A, Jennings M, Higgins J, Marx PA

Journal: J Virol 1990 May;64(5):2290-7.

Objectives: Challenge, Immunogenicity. To test efficacy of a whole-virus vaccine inactivated with psoralen and UV light.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac HUT-78 ((Psoralem-UV) *Type:* Whole (killed) Inactivated Virus *Route:* *Formulation:* SIVmac HUT-78 ((Psoralem-UV) + Threonyl muramyl dipeptide (TMDP)

Challenge: SIVmac (not determined) *Route:* Urethral, Vaginal or perivaginal, Mucosal

Main Findings:

- The vaccine elicited humoral immune response prior to challenge
- All immunized animals became infected after challenge, but their clinical course was delayed compared with controls
- Route of infection affected disease course, with animals infected by the iv route more likely to develop acute form of SIV than those infected by the genital mucosal route
- Concentration of challenge did not affect outcome; vaccinated animals did not fare any better following minimal mucosal challenge than a much greater iv infection

NHP.240 (2164591) **Immunization with a live, attenuated simian immunodeficiency virus (SIV) prevents early disease but not infection in rhesus macaques challenged with pathogenic SIV.**

Authors: Marthas ML, Sutjipto S, Higgins J, Lohman B, Torten J, Luciw PA, Marx PA, Pedersen NC

Journal: J Virol 1990 Aug;64(8):3694-700.

Objectives: Challenge, Immunogenicity. Tp test the potential of virulence-attenuated virus to protect against iv challenge with a pathogenic SIV(MAC) strain.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac1A11 *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge: SIVmac (not determined) *Route:* Intravenous

Main Findings:

- Live SIVmacIAII is immunogenic, did not induce disease, but failed to protect against moderately high dose of pathogenic virus
- Immunization prevented severe, early disease and prolonged the lives of monkeys subsequently infected with pathogenic SIV
- Within 1-6 weeks iv inoculated animals developed transient viremia without clinical disease and persistent humoral antibody response
- Time until severe clinical symptoms: 267-304 days in immunized monkeys, 38-227 days PC in naive controls

NHP.241 (2370678) **Antibody-mediated in vitro neutralization of human immunodeficiency virus type 1 abolishes infectivity for chimpanzees.**

Authors: Emini EA, Nara PL, Schleif WA, Lewis JA, Davide JP, Lee DR, Kessler J, Conley S, Matsushita S, Putney SD, et al.

Journal: J Virol 1990 Aug;64(8):3674-8.

Objectives: Challenge, Immunogenicity. To determine whether antibody against the HIV-1 V3 loop can abolish infectivity of HIV-1 in chimpanzees.

Species/Subspecies: Pan Troglodytes (Chimpanzee)

Main Findings:
- Antibody to the gp120 principal neutralization determinant (V3 loop) prevented HIV-1 infection in vitro and inhibited infection in vivo

NHP.242 (2455898) **Human immunodeficiency virus type 1 challenge of chimpanzees immunized with recombinant envelope glycoprotein gp120.**

Authors: Berman PW, Groopman JE, Gregory T, Clapham PR, Weiss RA, Ferriani R, Riddle L, Shimasaki C, Lucas C, Lasky LA, et al.

Journal: Proc Natl Acad Sci U S A 1988 Jul;85(14):5200-4.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Pan troglodytes troglodytes (chimpanzee)

Vaccine Name: rgp120 *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* rgp120 + Rehydragel HPA

Challenge: HIV-1 IIIB *Route:* Intravenous

Main Findings:
- The recombinant gp120 was effective in eliciting cellular and humoral immunity as well as immunologic memory
- Anti-rgp120 antibodies reacted with authentic viral gp120 in immunological blot assays and were able to neutralize HIV-1 infectivity in vitro
- Sera from the rgp120-immunized animals were able to neutralize HIV-1 pseudotypes of vesicular stomatitis virus prepared from the IIIB isolate, from which the gene encoding rgp120 was derived, as well as two heterologous isolates, ARV-2 and RF
- The immune response elicited against the rgp120 was not effective in preventing viral infection after intravenous challenge with HIV-1

NHP.243 (2370678) **Antibody-mediated in vitro neutralization of human immunodeficiency virus type 1 abolishes infectivity for chimpanzees.**

Authors: Emini EA, Nara PL, Schleif WA, Lewis JA, Davide JP, Lee DR, Kessler J, Conley S, Matsushita S, Putney SD, et al.

Journal: J Virol 1990 Aug;64(8):3674-8.

Objectives: Challenge, Immunogenicity. To determine whether antibody against the HIV-1 V3 loop can abolish infectivity of HIV-1 in chimpanzees.

Species/Subspecies: Pan Troglodytes (Chimpanzee)

Main Findings:
- Antibody to the gp120 prinicpal neutralization determinant (V3 loop) prevented HIV-1 infection in vitro and inhibited infection in vivo

NHP.244 (2470398) **Cell-mediated immune proliferative responses to HIV-1 of chimpanzees vaccinated with different vaccinia recombinant viruses.**

Authors: Van Eendenburg JP, Yagello M, Girard M, Kieny MP, Lecocq JP, Muchmore E, Fultz PN, Riviere Y, Montagnier L, Gluckman JC

Journal: AIDS Res Hum Retroviruses 1989 Feb;5(1):41-50.

Objectives: Immunogenicity. To compare proliferative responses to HIV and to vaccinia virus antigens of lymphocytes taken at various times from chimpanzees vaccinated with recombinant vaccinia virus expressing different HIV genes.

Species/Subspecies: Pan Troglodytes (Chimpanzee)

Main Findings:
- Irrespective of the HIV gene utilized, lymphocyte proliferation to HIV was usually weak and rapidly decreased after each inoculation, contrasting with strong and sustained responses to vaccinia virus

- IL-2-producing VV did not lead to increased responsiveness
- Reactivity to soluble purified gp160, but not to p25, could be detected in PBL from animals that had received both VV160 and VV25, while immunization with VVF resulted in a significant response to this protein in 1/2 animals

NHP.245.1 (2548210) **Vaccine protection against simian immunodeficiency virus infection.**

Authors: Desrosiers RC, Wyand MS, Kodama T, Ringler DJ, Arthur LO, Sehgal PK, Letvin NL, King NW, Daniel MD

Journal: Proc Natl Acad Sci U S A 1989 Aug;86(16):6353-7.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Whole inactivated SIVmac251 *Type:* Whole (killed) Inactivated Virus *Routes:* Targeted Lymph node immunization, Intramuscular *Formulation:* Whole inactivated SIVmac251 + Rehydragel HPA, Squalene 2

Challenge: SIVmac251 *Route:* Intravenous

Main Findings:

- 2/6 vaccinated monkeys showed no evidence of infection following the live virus challenge
- Transfusion of 10 ml of whole blood from these 2 into uninfected, naive rhesus monkeys did not result in infection of the recipients, providing further support for the lack of infection in the 2 previously vaccinated animals
- 4/4 unvaccinated control monkeys inoculated with live SIV became infected and 3 of these died with AIDS 118-258 days after infection (in contrast with 1/6 vaccinated monkeys)
- 4/4 naive controls infected and developed SAIDS
- 4/4 naive controls infected and diseased
- 0/4 vaccinees protected from infection
- 1/4 protected from increased viral load and disease to 930 dpc

NHP.245.2 (2548210) **Vaccine protection against simian immunodeficiency virus infection.**

Authors: Desrosiers RC, Wyand MS, Kodama T, Ringler DJ, Arthur LO, Sehgal PK, Letvin NL, King NW, Daniel MD

Journal: Proc Natl Acad Sci U S A 1989 Aug;86(16):6353-7.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Whole inactivated SIVmac251 *Type:* Whole (killed) Inactivated Virus *Routes:* Targeted Lymph node immunization, Intramuscular *Formulation:* Whole inactivated SIVmac251 + Rehydragel HPA, Squalene 2, Threonyl muramyl dipeptide (TMDP), SAF-1

Challenge: SIVmac251 *Route:* Intramuscular

NHP.245.3 (2548210) **Vaccine protection against simian immunodeficiency virus infection.**

Authors: Desrosiers RC, Wyand MS, Kodama T, Ringler DJ, Arthur LO, Sehgal PK, Letvin NL, King NW, Daniel MD

Journal: Proc Natl Acad Sci U S A 1989 Aug;86(16):6353-7.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Whole inactivated SIVmac251 *Type:* Whole (killed) Inactivated Virus *Routes:* Targeted Lymph node immunization, Intramuscular *Formulation:* Whole inactivated SIVmac251 +

Rehydragel HPA, Squalene 2, Threonyl muramyl dipeptide (TMDP), Interleukin-2, SAF-1

Challenge: SIVmac251 *Route:* Intramuscular

NHP.247 (2555541) **Challenge of chimpanzees (Pan troglodytes) immunized with human immunodeficiency virus envelope glycoprotein gp120.**

Authors: Arthur LO, Bess JW Jr, Waters DJ, Pyle SW, Kelliher JC, Nara PL, Krohn K, Robey WG, Langlois AJ, Gallo RC, et al.

Journal: J Virol 1989 Dec;63(12):5046-53.

Objectives: Challenge, Immunogenicity. To determine the efficacy of the immunization of a gp120 immunization to prevent infection from homologous HIV-1 IIIB challenge in chimpanzees.

Species/Subspecies: Pan troglodytes troglodytes (chimpanzee)

Vaccine Name: HIV-1 IIIB gp120 *Type:* Purified Viral Products *Route:* Intramuscular *Formulation:* HIV-1 IIIB gp120 + QS-21

Challenge: HIV-1 IIIB *Route:* Intravenous

Main Findings:

- 2/2 animals became infected with HIV, indicating that the immune response elicited by immunization with gp120 formulated in alum was not effective in preventing infection with HIV-1

NHP.248 (2555923) **A formalin-inactivated whole SIV vaccine confers protection in macaques.**

Authors: Murphey-Corb M, Martin LN, Davison-Fairburn B, Montelaro RC, Miller M, West M, Ohkawa S, Baskin GB, Zhang JY, Putney SD, et al.

Journal: Science 1989 Dec 8;246(4935):1293-7.

Objectives: Challenge, Immunotherapy. Evaluate capacity of formalin-inactivated whole virus vaccine to prevent infection and/or block development of SIV.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: $SIV/Delta_{B670}$ *Type:* Whole (killed) Inactivated Virus *Route:* Intramuscular *Formulation:* $SIV/Delta_{B670}$ + Alum, Threonyl muramyl dipeptide (TMDP)

Challenge: SIVDeltaB670 *Route:* Intravenous

Main Findings:

- Immunization with formalin-inactivated whole SIV potentiated with either MDP or MDP combined with alum protected 9/9 juvenile rhesus monkeys against disease for at least 1 year after challenge.
- A high dose of highly purified material was used for all immunizations.
- The vaccine contained all major virion proteins.
- A rest period sufficient to establish appropriate memory cells was allowed before exposure to live virus.

NHP.249 (3475581) **Effect of immunization with a vaccinia-HIV env recombinant on HIV infection of chimpanzees.**

Authors: Hu SL, Fultz PN, McClure HM, Eichberg JW, Thomas EK, Zarling J, Singhal MC, Kosowski SG, Swenson RB, Anderson DC, et al.

Journal: Nature 1987 Aug 20-26;328(6132):721-3.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Pan troglodytes troglodytes (chimpanzee)

Vaccine Name: Chimp anti-HIV IgG *Type:* Passive Antibody *Route:*

Challenge: LAV-1 or NY5 *Route:* Intravenous

Main Findings:

- Although HIV-specific antibody and T-cell responses were elicited by immunization, virus was isolated from lymphocytes of all challenged chimpanzees, indicating that

immunization did not prevent infection by HIV
- Among the animals that received a higher dose of LAV-1, 1/2 control chimpanzees, but none of the 4 v-env5-immunized chimpanzees developed substantial and persistent lymphadenopathy

NHP.250 (7584989) **Early suppression of SIV replication by CD8+ nef-specific cytotoxic T cells in vaccinated macaques.**

Authors: Gallimore A, Cranage M, Cook N, Almond N, Bootman J, Rud E, Silvera P, Dennis M, Corcoran T, Stott J, et al.

Journal: Nat Med 1995 Nov;1(11):1167-73.

Objectives: Challenge, Immunogenicity. To evaluate potential of subunit vaccine (nef) to elicit protection with nef-specific CTLs.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Main Findings:
- Strong CTL responses substantially reduce viral load and appear to clear infection
- Early decline in viraemia, observed in both vaccinated and unvaccinated control animals was associated with the development of virus-specific CTL activity and not with the presence of virus-specific neutralizing antibodies

NHP.251 (7585061) **HIV-1 recombinant poxvirus vaccine induces cross-protection against HIV-2 challenge in rhesus macaques.**

Authors: Abimiku AG, Franchini G, Tartaglia J, Aldrich K, Myagkikh M, Markham PD, Chong P, Klein M, Kieny MP, Paoletti E, et al.

Journal: Nat Med 1995 Apr;1(4):321-9.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- Background: Rhesus macaques immunized with attenuated vaccinia or canarypox HIV-1 recombinants and boosted with HIV-1 protein subunits formulated in alum, then challenged with HIV-2.SBL6669
- Following challenge with HIV-2SBL6669, 3/8 immunized macaques resisted infection for 6 months and another exhibited significantly delayed infection, whereas all 3 naive controls became infected
- Immunizations elicited both humoral and cellular immune responses with no clear correlation with protection

NHP.252 (7585217) **Long-term protection against SIV-induced disease in macaques vaccinated with a live attenuated HIV-2 vaccine.**

Authors: Putkonen P, Walther L, Zhang YJ, Li SL, Nilsson C, Albert J, Biberfeld P, Thorstensson R, Biberfeld G

Journal: Nat Med 1995 Sep;1(9):914-8.

Objectives: Challenge, Immunogenicity. To test the ability of a live attenuated human immunodeficiency virus type 2 (HIV-2) vaccine to protect cynomolgus monkeys against superinfection with a pathogenic simian immunodeficiency virus (SIVsm).

Main Findings:
- 3/4 monkeys vaccinated with live HIV-2 were protected against immunosuppression and SIV-induced disease during more than 5 years of follow-up
- The quality of the immunity was permissive for infection, but monkeys that survived showed restricted viral replication in peripheral blood and lymph nodes
- Protection against a pathogenic heterologous primate lentivirus is possible

- Vaccine can prevent disease in vaccinated monkeys even if infection is not prevented

NHP.253 (7625117) **Heterologous HIV-2 challenge of rhesus monkeys immunized with recombinant vaccinia viruses and purified recombinant HIV-2 proteins.**

Authors: Vogt G, le Grand R, Vaslin B, Boussin F, Auboyer MH, Riviere Y, Putkonen P, Sonigo P, Kieny MP, Girard M, et al.

Journal: Vaccine 1995 Feb;13(2):202-8.

Objectives: Challenge, Immunogenicity. To analyze the role of anti-envelope immunity in the protection of rhesus monkeys against an HIV-2 intravenous challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- None of the animals was protected in spite of high humoral immune responses on day of challenge as determined by ELISA and Western Blot assays

NHP.254 (7521918) **Vaccine-induced neutralizing antibodies directed in part to the simian immunodeficiency virus (SIV) V2 domain were unable to protect rhesus monkeys from SIV experimental challenge.**

Authors: Schlienger K, Montefiori DC, Mancini M, Riviere Y, Tiollais P, Michel ML

Journal: J Virol 1994 Oct;68(10):6578-88.

Objectives: Challenge, Immunogenicity. To analyze the role of an SIV V2 vaccine as an effective region to boost SIV-neutralizing antibodies and to protect against live SIV challenge.

Main Findings:
- 2 rhesus macaques primed with vaccinia virus recombinants expressing the surface glycoprotein gp140 of SIVmac then given booster with the SIVmac V2 domain: The 2 vaccinated macaques exhibited SIV-neutralizing antibodies (part of which directed specifically to the V2 region) after primer injections that were enhanced by the V2/HBsAg injections
- Animals not protected against homologous challenge with SIVmac251.BK28
- Vaccinees had higher viral loads than control animals after challenge

NHP.255 (7632466) **In vivo administration of CD4-specific monoclonal antibody: effect on provirus load in rhesus monkeys chronically infected with the simian immunodeficiency virus of macaques.**

Authors: Reimann KA, Cate RL, Wu Y, Palmer L, Olson D, Waite BC, Letvin NL, Burkly LC

Journal: AIDS Res Hum Retroviruses 1995 Apr;11(4):517-25.

Objectives: Immunotherapy, Passive Immunization. To study the potential role of monoclonal antibodies specific for CD4 as an AIDS therapy.

Main Findings:
- 6 infected monkeys treated with anti-CD4 MAb demonstrated a significant decrease in SIVmac provirus level after 9 days (3 had >800 CD4 cell/microliter and developed strong antimouse Ig response that prevented further treatment; the remaining 3 monkeys had <800 CD4 cell/microliter and failed to develop antimouse Ig antibody response)
- 4 control monkeys that received a control MAb of irrelevant specificity for 9-22 days showed either no significant change or a transient increase in SIVmac provirus.

NHP.256 (7666524) **Vaccine-induced protection of chimpanzees against infection by a heterologous human immunodeficiency virus type 1.**

Authors: Girard M, Meignier B, Barre-Sinoussi F, Kieny MP, Matthews T, Muchmore E, Nara PL, Wei Q, Rimsky L, Weinhold K, et al.

Journal: J Virol 1995 Oct;69(10):6239-48.

NHP.257 (7666529) **Vaccine-induced virus-neutralizing antibodies and cytotoxic T cells do not protect macaques from experimental infection with simian immunodeficiency virus SIVmac32H (J5).**

Authors: Hulskotte EG, Geretti AM, Siebelink KH, van Amerongen G, Cranage MP, Rud EW, Norley SG, de Vries P, Osterhaus AD

Journal: J Virol 1995 Oct;69(10):6289-96.

NHP.258.1 (7707496) **Cross-protective immune responses induced in rhesus macaques by immunization with attenuated macrophage-tropic simian immunodeficiency virus.**

Authors: Clements JE, Montelaro RC, Zink MC, Amedee AM, Miller S, Trichel AM, Jagerski B, Hauer D, Martin LN, Bohm RP, et al.

Journal: J Virol 1995 May;69(5):2737-44.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- Rhesus macaques inoculated with an attenuated macrophage-tropic recombinant of SIVmac239 (SIV/17E-Cl) exhibited vigorous type-specific nab responses restricted to SIV/17E-Cl by 2 weeks postinfection
- Cross-reactive neutralizing antibodies emerged by 7 months, which neutralized not only SIV/17E-Cl but also the heterologous primary isolate SIV/DeltaB670
- Challenge of SIV/17E-Cl-infected monkeys with SIV/DeltaB670: protective responses associated with cross-reactive neutralizing antibodies
- Passive transfer of sera from SIV/17E-Cl-infected animals passively protected 2/4 naive recipients.

NHP.258.2 (7707496) **Cross-protective immune responses induced in rhesus macaques by immunization with attenuated macrophage-tropic simian immunodeficiency virus.**

Authors: Clements JE, Montelaro RC, Zink MC, Amedee AM, Miller S, Trichel AM, Jagerski B, Hauer D, Martin LN, Bohm RP, et al.

Journal: J Virol 1995 May;69(5):2737-44.

Objectives: Challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- Challenge of SIV/17E-Cl-infected monkeys with SIV/DeltaB670: protective responses associated with cross-reactive neutralizing antibodies

NHP.258.3 (7707496) **Cross-protective immune responses induced in rhesus macaques by immunization with attenuated macrophage-tropic simian immunodeficiency virus.**

Authors: Clements JE, Montelaro RC, Zink MC, Amedee AM, Miller S, Trichel AM, Jagerski B, Hauer D, Martin LN, Bohm RP, et al.

Journal: J Virol 1995 May;69(5):2737-44.

Objectives: Passive Immunization.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- Passive transfer of sera from SIV/17E-Cl-infected animals passively protected 2/4 naive recipients.

NHP.259 (7707540) **Macaques immunized with HLA-DR are protected from challenge with simian immunodeficiency virus.**

Authors: Arthur LO, Bess JW Jr, Urban RG, Strominger JL, Morton WR, Mann DL, Henderson LE, Benveniste RE

Journal: J Virol 1995 May;69(5):3117-24.

Objectives: Challenge, Immunogenicity. To identify the potential antigens involved in protection induced by the immunization with uninfected human cells against the challenge with SIV propagated in human cells.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Main Findings:

- All macaques immunized with beta 2M and HLA class I developed high antibody titers to beta 2M, BUT were not protected from a subsequent challenge with infectious SIV grown in human cells
- The macaques immunized with class II protein (HLA-DR) and mock virus developed antibodies to class II protein and were protected from the intravenous infectious virus challenge
- The protection seen with human class II protein did not extend to protection from infection with SIV containing macaque class II proteins
- Immunization with a purified cellular protein can protect from virus infection

NHP.260 (7752758) **Protection by attenuated simian immunodeficiency virus in macaques against challenge with virus-infected cells.**

Authors: Almond N, Kent K, Cranage M, Rud E, Clarke B, Stott EJ

Journal: Lancet 1995 May 27;345(8961):1342-4.

NHP.261 (7865285) **Vaccine protection and reduced virus load from heterologous macaque-propagated SIV challenge.**

Authors: Heeney JL, Holterman L, ten Haaft P, Dubbes R, Koornstra W, Teeuwsen V, Bourquin P, Norley S, Niphuis H

Journal: AIDS Res Hum Retroviruses 1994;10 Suppl 2:S117-21.

NHP.262 (7884874) **A vaccine-elicited, single viral epitope-specific cytotoxic T lymphocyte response does not protect against intravenous, cell-free simian immunodeficiency virus challenge.**

Authors: Yasutomi Y, Koenig S, Woods RM, Madsen J, Wassef NM, Alving CR, Klein HJ, Nolan TE, Boots LJ, Kessler JA, et al.

Journal: J Virol 1995 Apr;69(4):2279-84.

NHP.263 (7818809) **T-cell proliferation to subinfectious SIV correlates with lack of infection after challenge of macaques.**

Authors: Clerici M, Clark EA, Polacino P, Axberg I, Kuller L, Casey NI, Morton WR, Shearer GM, Benveniste RE

Journal: AIDS 1994 Oct;8(10):1391-5.

NHP.265 (11090194) **Protection of Macaca nemestrina from disease following pathogenic simian immunodeficiency virus (SIV) challenge: utilization of SIV nucleocapsid mutant DNA vaccines with and without an SIV protein boost.**

Authors: Gorelick RJ, Benveniste RE, Lifson JD, Yovandich JL, Morton WR, Kuller L, Flynn BM, Fisher BA, Rossio JL, Piatak M Jr, Bess JW Jr, Henderson LE, Arthur LO

Journal: J Virol 2000 Dec;74(24):11935-49.

Objectives: Challenge, Immunogenicity. To use molecular clones (that express nucleocapsid deletion mutant SIVs that are replication defective but capable of completing virtually all of the steps of a single viral infection cycle) in a vaccine challenge study.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Vaccine Name: SIV(Mne)NCΔZF2 DNA *Type:* Live Attenuated Virus *Routes:* Subcutaneous, Intramuscular

Vaccine Name: S8-NCΔZF2 *Type:* Live Attenuated Virus *Routes:* Subcutaneous, Intramuscular

Challenge: SIV(Mne) clone E11S *Route:* Intravenous

Main Findings:

- 11/11 animals immunized with nucelocapside mutant SIV DNA; immunized animals became infected following challenge but typically showed decreased initial peak plasma SIV RNA levels compared to those of control animals; all control animals became infected and 3/4 animals developed progressive SIV disease leading to death
- Only modest and inconsistent humoral responses and no cellular immune responses were observed prior to challenge
- Immunization of macaques with DNA that codes for replication-defective but structurally complete virions appears to protect from or at least delay the onset of AIDS after infection with a pathogenic immunodeficiency virus

NHP.266 (12390544) **Protection by SIV VLP DNA prime/protein boost following mucosal SIV challenge is markedly enhanced by IL-12/GM-CSF co-administration.**

Authors: O'Neill E, Martinez I, Villinger F, Rivera M, Gascot S, Colon C, Arana T, Sidhu M, Stout R, Montefiori DC, Martinez M, Ansari AA, Israel ZR, Kraiselburd E

Journal: J Med Primatol 2002 Aug;31(4-5):217-27.

Objectives: Challenge, Immunogenicity. To induce and enhance antiviral responses using a DNA prime/virus-like particles (VLP) protein boost strategy adjuvanted with interleukin (IL)-12/GM-CSF in rhesus macaques challenged with simian immunodeficiency virus (SIV).

Main Findings:

- All except 1 immunized monkey became infected
- All immunized monkeys showed a marked reduction of acute viral peaks
- Reduction of viral load set points was only achieved in groups whose prime-boost immunizations were supplemented with IL-12/GM-CSF (prime) and/or with IL-12 (boost)
- Control of viremia correlated with lack of disease progression and survival
- Detection of virus in rectal washes at 1 year post-challenge was only successful in monkeys whose immunizations did not include cytokine adjuvant, but these loads did not correlate with plasma viral loads

NHP.267 (2190095) **Protection of chimpanzees from infection by HIV-1 after vaccination with recombinant glycoprotein gp120 but not gp160.**

Authors: Berman PW, Gregory TJ, Riddle L, Nakamura GR, Champe MA, Porter JP, Wurm FM, Hershberg RD, Cobb EK, Eichberg JW

Journal: Nature 1990 Jun 14;345(6276):622-5.

Objectives: Challenge, Immunogenicity. To study chimpanzees that were immunized with recombinant forms of the HIV-1 glycoproteins gp120 and gp160 produced in Chinese hamster ovary cells, and then challenged with HIV-1.

Species/Subspecies: Pan Troglodytes (Chimpanzee)

Vaccine Name: rgp120 *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* rgp120 + Rehydragel HPA

Vaccine Name: rsgp160 *Type:* Recombinant Subunit Protein *Route:*

Challenge: HIV-1 IIIB *Route:*

Main Findings:

- The control and the 2 animals immunized with the gp160 variant became infected within 7 weeks of challenge
- The 2 animals immunized with the gp120 variant have shown no signs of infection after more than 6 months
- Conclusion: recombinant gp120, formulated in an adjuvant approved for human use, can

elicit protective immunity against a homologous strain of HIV-1

NHP.268.1 (10812220) **Minimization of chronic plasma viremia in rhesus macaques immunized with synthetic HIV-1 Tat peptides and infected with a chimeric simian/human immunodeficiency virus (SHIV33).**

Authors: Goldstein G, Manson K, Tribbick G, Smith R

Journal: Vaccine 2000 Jun 15;18(25):2789-95.

Objectives: Challenge, Immunogenicity. To study the effect of Tat on HIV-1 replication in vivo during acute, chronic asymptomatic and AIDS stages of infection by comparisons of plasma viremia in Tat-immunized or control monkeys challenged with SHIV33 or SHIV33A.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Synthetic tat *Type:* Synthetic Protein/Peptide *Route:* Intramuscular *Formulation:* Synthetic tat + Diphtheria toxoid, Freund′s Complete Adjuvant

Challenge: SHIV33, SHIV33A *Route:* Intravenous

Main Findings:

- Immunization of monkeys with tat affected the outcome of challenge: chronic plasma viremia became undetectable or minimized in Tat-immunized asymptomatic SHIV33-infected monkeys while the high viral loads of acute infection or SHIV33A-induced simian AIDS were unaffected by Tat immunization
- Active or passive immunotherapies targeting Tat provide potential approaches to controlling chronic HIV-1 viremia and preventing AIDS

NHP.268.2 (10812220) **Minimization of chronic plasma viremia in rhesus macaques immunized with synthetic HIV-1 Tat peptides and infected with a chimeric simian/human immunodeficiency virus (SHIV33).**

Authors: Goldstein G, Manson K, Tribbick G, Smith R

Journal: Vaccine 2000 Jun 15;18(25):2789-95.

Objectives: Challenge, Immunogenicity. To study the effect of Tat on HIV-1 replication in vivo during acute, chronic asymptomatic and AIDS stages of infection by comparisons of plasma viremia in Tat-immunized or control monkeys challenged with SHIV33 or SHIV33A

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- See NHP.268

NHP.269 (10074165) **Protection of macaques against intrarectal infection by a combination immunization regimen with recombinant simian immunodeficiency virus SIVmne gp160 vaccines.**

Authors: Polacino P, Stallard V, Montefiori DC, Brown CR, Richardson BA, Morton WR, Benveniste RE, Hu SL

Journal: J Virol 1999 Apr;73(4):3134-46.

Objectives: Challenge, Immunogenicity. To examine the protective efficacy of recombinant simian immunodeficiency virus SIVmne envelope (gp160) vaccines against mucosal challenge by the cloned homologous virus E11S clone and the uncloned SIVmne.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: Recombinant vaccinia virus vac-gp160 (v-SE5) *Type:* Recombinant Vector (virus/bacteria) *Route:* Scarification

Vaccine Name: gp160/BSC-40 *Type:* Purified Viral Products *Route:* Intramuscular

Challenge: SIV(Mne) clone E11S, SIV(Mne) Cell-free *Route:* Intrarectal

Main Findings:

- Protection correlates with high levels of SIV-specific antibodies
- 4/4 vaccinees developed low levels of SIV-specific antibody responses after the

recombinant vaccinia virus immunization; level increased 10-30 fold by boost envelop subunit
- After intrarectal challenge with E11S, all 3 control animals became persistently infected, whereas 3/4 immunized macaques were completely protected

NHP.270.1 (11514732) **Induction of simian immunodeficiency virus (SIV)-specific CTL in rhesus macaques by vaccination with modified vaccinia virus Ankara expressing SIV transgenes: influence of pre-existing anti-vector immunity.**

Authors: Sharpe S, Polyanskaya N, Dennis M, Sutter G, Hanke T, Erfle V, Hirsch V, Cranage M

Journal: J Gen Virol 2001 Sep;82(Pt 9):2215-23.

NHP.270.2 (11514732) **Induction of simian immunodeficiency virus (SIV)-specific CTL in rhesus macaques by vaccination with modified vaccinia virus Ankara expressing SIV transgenes: influence of pre-existing anti-vector immunity.**

Authors: Sharpe S, Polyanskaya N, Dennis M, Sutter G, Hanke T, Erfle V, Hirsch V, Cranage M

Journal: J Gen Virol 2001 Sep;82(Pt 9):2215-23.

NHP.274 (12490410) **Equivalent Immunogenicity of the Highly Attenuated Poxvirus-Based ALVAC-SIV and NYVAC-SIV Vaccine Candidates in SIVmac251-Infected Macaques.**

Authors: Hel Z, Nacsa J, Tsai WP, Thornton A, Giuliani L, Tartaglia J, Franchini G

Journal: Virology 2002 Dec 5;304(1):125-34.

Objectives: Challenge, Immunogenicity, Immunotherapy. To compare the immunogenicity of two vaccine candidates, the canarypox-based ALVAC-SIV-gag-pol-env and the vaccinia-based NYVAC-SIV-gag-pol-env, in rhesus macaques infected with SIVmac251 and treated with ART by 2 weeks postinfection.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: NYVAC-SIV-gag-pol-env (NYVAC-SIV-gpe) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name: ALVAC-SIV-gpe (vcp180) *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intrarectal, Intramuscular, Intranasal

Challenge: SIVmac251 (561) *Route:* Intravenous

Main Findings:
- Both ALVAC-SIV-gpe and NYVAC-SIV-gpe vaccine candidates induced and/or enhanced a virus-specific CD8+ T cell response to a similar extent, as demonstrated by tetramer staining of Gag-specific CD8+ T cells
- Both vaccines elicited comparable lymphoproliferative responses (LPRs) to the SIV p27 Gag and gp120 Env proteins
- The vaccine was given after infection and initiation of HAART, as a therapeutic vaccine, not as protection from infection.

NHP.275 (9234548) **SIV DNA vaccine trial in macaques: post-challenge necropsy in vaccine and control groups.**

Authors: Lu S, Manson K, Wyand M, Robinson HL

Journal: Vaccine 1997 Jun;15(8):920-3.

Objectives: Challenge. To study histopathologic findings from 9 macaques in a simian immunodeficiency virus (SIV) DNA vaccine trial evaluating the ability of a 5-plasmid DNA vaccine to protect against an uncloned SIVmac251 challenge (Lu et al., J. Virol. 1996, 70, 3978-3991).

Species/Subspecies: Macaca (sp)

Vaccine Name: DNA-SIV *Type:* DNA *Routes:* Intravenous, Intradermal (Gene Gun DNA-coated gold beads),

Intramuscular

Main Findings:
- 3 vaccinated and 1 control macaques developed disease and were sacrificed in the first year following challenge
- Diseased and clinically "normal" animals had developed typical SIV-related lymphoid changes, inflammatory disorders and opportunistic infections (all but 1 vaccinated animal and both controls)
- The ability to contain challenge was superior in animals immunized by 3 routes (iv,im and gene gun) as compared to those that received the control DNA or DNA vaccine by gene gun only.

NHP.276 (12396607) **Evaluation in rhesus macaques of Tat and rev-targeted immunization as a preventive vaccine against mucosal challenge with SHIV-BX08.**

Authors: Verrier B, Le Grand R, Ataman-Onal Y, Terrat C, Guillon C, Durand PY, Hurtrel B, Aubertin AM, Sutter G, Erfle V, Girard M

Journal: DNA Cell Biol 2002 Sep;21(9):653-8.

Objectives: Challenge, Immunogenicity. To evaluate whether vaccination with Tat or Tat and Rev could significantly reduce viral load in nonhuman primates.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SFV-tat *Type:* Recombinant Vector (virus/bacteria) *Route:* Subcutaneous

Vaccine Name: SFV-rev *Type:* Recombinant Vector (virus/bacteria) *Route:* Subcutaneous

Vaccine Name: MVA-tat *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name: MVA-rev *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name: DNA-pCI-tat *Type:* DNA *Routes:* Intradermal, Intramuscular

Vaccine Name: DNA-pCI-rev *Type:* DNA *Routes:* Intradermal, Intramuscular *Formulation:* DNA-pCI-rev + pCIL12

Challenge: SHIV-BX08 *Route:* Intrarectal

Main Findings:
- The immunization strategy by priming with either DNA or SFV seemed to be equivalent, but the additive or synergistic effect of a rev vaccine could not be clearly established
- None of the animals was protected from infection
- Peak viremia was reduced more than 200-fold compared to sham controls in one third (6/18) of vaccinated macaques
- 4/6 protected animals did not seroconvert

NHP.277 (12396606) **Immunogenicity of HIV-1 IIIB and SHIV 89.6P Tat and Tat toxoids in rhesus macaques: induction of humoral and cellular immune responses.**

Authors: Richardson MW, Mirchandani J, Silvera P, Regulier EG, Capini C, Bojczuk PM, Hu J, Gracely EJ, Boyer JD, Khalili K, Zagury JF, Lewis MG, Rappaport J

Journal: DNA Cell Biol 2002 Sep;21(9):637-51.

Objectives: Challenge, Immunogenicity. To compare immune responses in rhesus macaques immunized with unmodified HIV-1 IIIB Tat, SHIV89.6P Tat, and carboxymethylated IIIB and 89.6P Tat toxoids.

Main Findings:
- Immunization with either IIIB or 89.6P preparation induced high titer and broadly cross-reactive serum anti-Tat IgG that recognized HIV-1 subtype-E and SIVmac251 Tat
- Proliferative responses to Tat toxoids corresponding to the immunogen were evident in vitro in both IIIB and 89.6P groups
- All animals were infected upon intravenous challenge with 30 MID(50) of SHIV89.6P and outcome of vaccine groups was not different from controls
- Tat specific CD8+ T-cell responses may not appropriately recognize infected cells in vivo

in rhesus macaque model

NHP.278 (12477432) **Co-immunization of rhesus macaques with plasmid vectors expressing IFN-gamma, GM-CSF, and SIV antigens enhances anti-viral humoral immunity but does not affect viremia after challenge with highly pathogenic virus.**

Authors: Lena P, Villinger F, Giavedoni L, Miller CJ, Rhodes G, Luciw P

Journal: Vaccine 2002 Dec 19;20 Suppl 4:A69-79.

Objectives: Challenge, Immunogenicity. To investigate the adjuvant capacity of

Main Findings:

- Proliferative responses significantly enhanced by co-immunization with the cytokines GM-CSF and interferon-γ
- 12 immunized monkeys and 6 naive controls, were challenged by the oral mucosal route with the uncloned and highly pathogenic SIVmac251 and became infected
- Plasma viremia set points were not different in co-immunized group and the non-immunized control group
- Monkeys vaccinated with equivalent amounts of empty vector plasmid (i.e. no cytokine inserts) along with plasmids expressing viral antigens demonstrated a slight but significant decrease in acute viremia compared to non-immunized controls ($P<0.02$)
- Conclusion: results underscore the need for further testing of cytokines as vaccine adjuvants in relevant animal models.

NHP.279 (12396605) **Potent, persistent cellular immune responses elicited by sequential immunization of rhesus macaques with Ad5 host range mutant recombinants encoding SIV Rev and SIV Nef.**

Authors: Patterson LJ, Malkevitch N, Zhao J, Peng B, Robert-Guroff M

Journal: DNA Cell Biol 2002 Sep;21(9):627-35.

NHP.280 (12396604) **Design and in vivo immunogenicity of a polyvalent vaccine based on SIVmac regulatory genes.**

Authors: Hel Z, Tryniszewska E, Tsai WP, Johnson JM, Harrod R, Fullen J, Kalyanaraman VS, Altman JD, McNally J, Karpova T, Felber BK, Tartaglia J, Franchini G

Journal: DNA Cell Biol 2002 Sep;21(9):619-26.

NHP.281 (12391256) **Vaccination of macaques with long-standing SIVmac251 infection lowers the viral set point after cessation of antiretroviral therapy.**

Authors: Tryniszewska E, Nacsa J, Lewis MG, Silvera P, Montefiori D, Venzon D, Hel Z, Parks RW, Moniuszko M, Tartaglia J, Smith KA, Franchini G

Journal: J Immunol 2002 Nov 1;169(9):5347-57.

Objectives: Immunotherapy, Chemotherapy. Tested ART, ART plus therapeutic vaccine, ART plus therapeutic vaccine plus IL-2, ART plus IL-2.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- Therapeutic vaccines reduced average viral load at set point, but not peak viral load following cessation of ART. Addition of IL-2 to therapeutic vaccine produced virus-specific proliferative responses lower than therapeutic vaccine alone.

NHP.282 (12391187) **Containment of simian immunodeficiency virus infection in vaccinated macaques: correlation with the magnitude of virus-specific pre- and postchallenge CD4+ and CD8+ T cell responses.**

Authors: Hel Z, Nacsa J, Tryniszewska E, Tsai WP, Parks RW, Montefiori DC, Felber BK, Tartaglia J, Pavlakis GN, Franchini G

Journal: J Immunol 2002 Nov 1;169(9):4778-87.

NHP.283 (12388726) **Both mucosal and systemic routes of immunization with the live, attenuated NYVAC/simian immunodeficiency virus SIV(gpe) recombinant vaccine result in gag-specific CD8(+) T-cell responses in mucosal tissues of macaques.**

Authors: Stevceva L, Alvarez X, Lackner AA, Tryniszewska E, Kelsall B, Nacsa J, Tartaglia J, Strober W, Franchini G

Journal: J Virol 2002 Nov;76(22):11659-76.

NHP.284 (12388710) **Elicitation of simian immunodeficiency virus-specific cytotoxic T lymphocytes in mucosal compartments of rhesus monkeys by systemic vaccination.**

Authors: Baig J, Levy DB, McKay PF, Schmitz JE, Santra S, Subbramanian RA, Kuroda MJ, Lifton MA, Gorgone DA, Wyatt LS, Moss B, Huang Y, Chakrabarti BK, Xu L, Kong WP, Yang ZY, Mascola JR, Nabel GJ, Carville A, Lackner AA, Veazey RS, Letvin NL

Journal: J Virol 2002 Nov;76(22):11484-90.

NHP.285 (12388697) **Live, attenuated simian immunodeficiency virus SIVmac-M4, with point mutations in the Env transmembrane protein intracytoplasmic domain, provides partial protection from mucosal challenge with pathogenic SIVmac251.**

Authors: Shacklett BL, Shaw KE, Adamson LA, Wilkens DT, Cox CA, Montefiori DC, Gardner MB, Sonigo P, Luciw PA

Journal: J Virol 2002 Nov;76(22):11365-78.

NHP.286 (12359453) **Systemic infection and limited replication of SHIV vaccine virus in brains of macaques inoculated intracerebrally with infectious viral DNA.**

Authors: Smith MS, Niu Y, Li Z, Adany I, Pinson DM, Liu ZQ, Berry T, Sheffer D, Jia F, Narayan O

Journal: Virology 2002 Sep 15;301(1):130-5.

NHP.287 (12359438) **A simian immunodeficiency virus nef peptide is a dominant cytotoxic T lymphocyte epitope in Indian-origin rhesus monkeys expressing the common MHC class I allele mamu-A*02.**

Authors: Newberg MH, Kuroda MJ, Charini WA, Miura A, Lord CI, Schmitz JE, Gorgone DA, Lifton MA, Kuus-Reichel K, Letvin NL

Journal: Virology 2002 Sep 30;301(2):365-73.

NHP.288 (12239328) **Effects of cytotoxic T lymphocytes (CTL) directed against a single simian immunodeficiency virus (SIV) Gag CTL epitope on the course of SIVmac239 infection.**

Authors: Allen TM, Jing P, Calore B, Horton H, O Connor DH, Hanke T, Piekarczyk M, Ruddersdorf R, Mothe BR, Emerson C, Wilson N, Lifson JD, Belyakov IM, Berzofsky JA, Wang C, Allison DB, Montefiori DC, Desrosiers RC, Wolinsky S, Kunstman KJ, Altman JD, Sette A, McMichael AJ, Watkins DI

Journal: J Virol 2002 Oct;76(20):10507-11.

NHP.289 (12239289) **Slowly declining levels of viral RNA and DNA in DNA/recombinant modified vaccinia virus Ankara-vaccinated macaques with controlled simian-human immunodeficiency virus SHIV-89.6P challenges.**

Authors: Tang Y, Villinger F, Staprans SI, Amara RR, Smith JM, Herndon JG, Robinson HL

Journal: J Virol 2002 Oct;76(20):10147-54.

NHP.290 (12111423) **Infection of macaques with chimeric simian and human immunodeficiency viruses containing Env from subtype F.**

Authors: Kuwata T, Takemura T, Takehisa J, Miura T, Hayami M

Journal: Arch Virol 2002 Jun;147(6):1121-32.

NHP.291 (12502824) **Nonneutralizing antibodies to the CD4-binding site on the gp120 subunit of human immunodeficiency virus type 1 do not interfere with the activity of a neutralizing antibody against the same site.**

Authors: Herrera C, Spenlehauer C, Fung MS, Burton DR, Beddows S, Moore JP

Journal: J Virol 2003 Jan;77(2):1084-91.

Objectives: Passive Immunization. To investigate whether nonneutralizing monoclonal antibodies to the gp120 subunit of env glycoprotein complex of HIV-1 can interfere with HIV-1 neutralization by another anti-gp120 MAb

Main Findings:
- REMOVE THIS

NHP.293 (1708168) **Recombinant virus vaccine-induced SIV-specific CD8+ cytotoxic T lymphocytes.**

Authors: Shen L, Chen ZW, Miller MD, Stallard V, Mazzara GP, Panicali DL, Letvin NL

Journal: Science 1991 Apr 19;252(5004):440-3.

NHP.294 (12477823) **Immunization of newborn rhesus macaques with simian immunodeficiency virus (SIV) vaccines prolongs survival after oral challenge with virulent SIVmac251.*****

Authors: Van Rompay KK, Greenier JL, Cole KS, Earl P, Moss B, Steckbeck JD, Pahar B, Rourke T, Montelaro RC, Canfield DR, Tarara RP, Miller C, McChesney MB, Marthas ML

Journal: J Virol 2003 Jan;77(1):179-90.

Objectives: Challenge, Immunogenicity. To evaluate immunization of infant macaques at birth and 3 weeks of age with either MVA-SIV Gag, Pol, and Env or live-attenuated SIVmac1A11.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: rMVA SIVmac239 gagpolenv *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intramuscular, Intranasal

Vaccine Name: SIVmac1A11 *Type:* Live Attenuated Virus *Routes:* Intravenous, Oral, Intranasal

Vaccine Name: Anti-SIVmac251 *Type:* Passive Antibody *Route:* Intraplacental

Challenge: SIVmac251 *Route:* Oral

Main Findings:
- Upon challenge with virulent SIVmac251, all animals became infected
- The immunized animals mounted better antiviral antibody responses, controlled virus levels more effectively, and had a longer disease-free survival than the unvaccinated infected monkeys
- Maternal antibodies did not significantly reduce the efficacy of the MVA-SIVgpe vaccine

NHP.295 (11000207) **Intrinsic susceptibility of rhesus macaque peripheral CD4(+) T cells to simian immunodeficiency virus in vitro is predictive of in vivo viral replication.**

Authors: Goldstein S, Brown CR, Dehghani H, Lifson JD, Hirsch VM

Journal: J Virol 2000 Oct;74(20):9388-95. To evaluate possible correlation between relative viremia after SIV challenge and susceptibility of PBMC in in-vitro SIV infection.

Main Findings:
- Following intravenous infection of macaques with SIVsmE543-3, the wide range in

plasma viremia followed the same rank order as the relative susceptibility established by in vitro studies
- Significant correlation between plasma viremia at 2-8 wpi and in vitro susceptibility ($P < 0.05$)
- Simian T-lymphotropic virus type 1 appears to enhance susceptibility to SIV infection
- Intrinsic susceptibility of CD4+ target cells influences early virus replication patterns in vivo

NHP.296 (12502820) **Prevention of Disease Induced by a Partially Heterologous AIDS Virus in Rhesus Monkeys by Using an Adjuvanted Multicomponent Protein Vaccine**

Authors: Voss G, Manson K, Montefiori D, Watkins DI, Heeney J, Wyand M, Cohen J, Bruck C

Journal: J Virol 2003 Jan;77(2):1049-58.

Objectives: Challenge. To assess the efficacy of a recombinant human immunodeficiency virus type 1 (HIV-1) gp120, NefTat fusion protein, and simian immunodeficiency virus (SIV) Nef formulated in the clinically tested adjuvant AS02A.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Recombinant gp120 *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Vaccine Name: Nef-Tat *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Vaccine Name: SIV Nef *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Main Findings:
- Multiantigen subunit protein vaccine was able to prevent the development of disease induced in rhesus monkeys by a partially heterologous AIDS virus
- Upon challenge of genetically unselected rhesus monkeys with the highly pathogenic and partially heterologous SIV/HIV strain SHIV89.6p, the vaccine was able to reduce virus load and protect the animals from a decline in CD4-positive cells
- Vaccination prevented the development of AIDS for more than 2.5 years

NHP.297 (12502815) **Increased mucosal transmission but not enhanced pathogenicity of the CCR5-tropic, simian AIDS-inducing simian/human immunodeficiency virus SHIV(SF162P3) maps to envelope gp120.**

Authors: Hsu M, Harouse JM, Gettie A, Buckner C, Blanchard J, Cheng-Mayer C

Journal: J Virol 2003 Jan;77(2):989-98.

Objectives: Pathogenicity. To determine whether envelope glycoprotein gp120 is responsible for increased pathogenesis and transmissibility of the SHIV-SF162P3.

Main Findings:
- See NHP.312

NHP.298 (12477842) **Importance of B-cell responses for immunological control of variant strains of simian immunodeficiency virus.**

Authors: Johnson WE, Lifson JD, Lang SM, Johnson RP, Desrosiers RC

Journal: J Virol 2003 Jan;77(1):375-81.

Objectives: Immunogenicity, Pathogenicity. To compare the pathogenicity of three variants of cloned simian immunodeficiency virus strain 239 (SIV239).

Main Findings:
- All 3 cloned strains (M5, DeltaV1-V2 and 316) of SIVmac239 were capable of significant levels of fusion independent of CD4, and all 3 were considerably more sensitive to antibody-mediated neutralization than the parent strain from which they were derived
- The 3 clones induce viral loads at peak height around day 14 that are indistinguishable from or only slightly less than those observed in monkeys infected with the parental SIV239 strain

- Viral loads at the set point 20 to 50 weeks after infection, however, were more than 400- to 10,000-fold lower with the variant strains
- Depletion of B cells around the time of infection with M5 resulted in less effective immunological control and much higher viral loads at the set point in 2/3 monkeys.

NHP.299 (12496959) **Therapeutic dendritic-cell vaccine for simian AIDS.**

Authors: Lu W, Wu X, Lu Y, Guo W, Andrieu JM

Journal: Nat Med 2003 Jan;9(1):27-32.

Objectives: Immunogenicity, Immunotherapy. To investigate the ability of a vaccination with chemically inactivated SIV-pulsed dendritic cells to induce cellular and humoral immunity in SIV infected rhesus monkey model.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: AT-2 inactivated SIV-loaded DC *Type:* Cell/Tissue *Route:* Subcutaneous *Formulation:* AT-2 inactivated SIV-loaded DC + RPMI-1640

Main Findings:

- Chemically inactivated SIV-pulsed dendritic cells induced an effective and durable SIV-specific cellular and humoral immunity in SIV-infected rhesus monkeys
- After 3 immunizations made at 2-week intervals, the animals exhibited a 50-fold decrease of SIV DNA and a 1,000-fold decrease of SIV RNA in peripheral blood with reduced viral load levels maintained over the remaining 34 weeks

NHP.300 (12531331) **A Gag-Pol/Env-Rev SIV239 DNA vaccine improves CD4 counts, and reduce viral loads after pathogenic intrarectal SIV(mac)251 challenge in Rhesus Macaques.**

Authors: Muthumani K, Bagarazzi M, Conway D, Hwang DS, Manson K, Ciccarelli R, Israel Z, Montefiori DC, Ugen K, Miller N, Kim J, Boyer J, Weiner DB

Journal: Vaccine 2003 Jan 30;21(7-8):629-37.

Objectives: Challenge, Immunogenicity. To study plasmid vaccines supplemented by IL-2 Ig cytokine gene adjuvants or boosted by recombinant MVA vectors expressing relevant SIV and HIV antigens.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pGagpol/EnvRev SIV239 DNA *Type:* DNA *Route:* Intramuscular *Formulation:* pGagpol/EnvRev SIV239 DNA + Bupivacaine-HCl + PBS

Challenge: SIVmac251 *Route:* Intrarectal

Main Findings:

- The immunization strategy employed in this study prevented CD4(+) T-cell loss and lowered viral loads following pathogenic challenge
- Using a pathogenic SIV251 rhesus mucosal challenge model, pGag/Pol+pEnv/Rev plasmid vaccines could not prevent SIVinfection: vaccinated animals exhibited significant improvement in control of viral challenge and protection against CD4(+) T-cell loss compared to control animals.

NHP.301 (12526038) **Human and simian immunodeficiency virus-infected chimpanzees do not have increased intracellular levels of beta-chemokines in contrast to infected humans.**

Authors: Ondoa P, Vereecken C, Fransen K, Colebunders R, Van Der Groen G, Heeney JL, Kestens L

Journal: J Med Virol 2003 Mar;69(3):297-305.

Objectives: Immunogenicity, Pathogenicity. To explain why chimpanzees infected with HIV-1 or SIVcpz are relatively resistant to AIDS.

Species/Subspecies: Pan Troglodytes (Chimpanzee)

Main Findings:

- In humans, the percentage of B-chemokine-positive cells was significantly higher in CD8+ T and natural killer (NK) cells than in CD4+ T cells in both uninfected and HIV-1-

infected individuals
- In the presence of HIV-1 infection, however, both CD8+ and CD4+ T cell subsets contained significantly more B-chemokine-positive cells than in the absence of infection
- In chimpanzees, the percentage of B-chemokine-positive CD8+ T and NK cells was significantly higher than in uninfected humans
- In contrast to humans, infection of chimpanzees with either HIV-1 or with SIVcpz was not associated with increased numbers of B-chemokine-positive cells

NHP.302 (12393472) **Impact of simian immunodeficiency virus (SIV) infection on lymphocyte numbers and T-cell turnover in different organs of rhesus monkeys.**

Authors: Sopper S, Nierwetberg D, Halbach A, Sauer U, Scheller C, Stahl-Hennig C, Matz-Rensing K, Schafer F, Schneider T, ter Meulen V, Muller JG

Journal: Blood 2003 Feb 15;101(4):1213-9.

NHP.303 (12502833) **Control of viremia and prevention of simian-human immunodeficiency virus-induced disease in rhesus macaques immunized with recombinant vaccinia viruses plus inactivated simian immunodeficiency virus and human immunodeficiency virus type 1 particles.**

Authors: Willey RL, Byrum R, Piatak M, Kim YB, Cho MW, Rossio Jr JL Jr, Bess Jr J Jr, Igarashi T, Endo Y, Arthur LO, Lifson JD, Martin MA

Journal: J Virol 2003 Jan;77(2):1163-74.

Objectives: Challenge, Immunogenicity. To evaluate the protective efficacy of a vaccine regimen that uses recombinant vaccinia viruses expressing SIV and HIV-1 structural proteins in combination with intact inactivated SIV and HIV-1 particles.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: rVV-SIVmacgag/pol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intradermal

Vaccine Name: rVV-HIV-1.DH12env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intradermal

Vaccine Name: AT-2 rx SIVmac239 *Type:* Live Attenuated Virus *Route:* Intramuscular *Formulation:* AT-2 rx SIVmac239 + QS-21

Vaccine Name: AT-2 rx HIV-1.DH12 *Type:* Live Attenuated Virus *Route:* Intramuscular *Formulation:* AT-2 rx HIV-1.DH12 + QS-21

Challenge: SHIV.DH12R-PS1 *Route:* Intravenous

Main Findings:
- Following virus challenge, control animals experienced a rapid and complete loss of CD4(+) T cells, sustained high viral loads, and developed clinical disease by 17 to 21 weeks
- All the vaccinated monkeys became infected, displayed reduced post-peak viremia, had no significant loss of CD4(+) T cells, and have remained healthy for more than 15 mpc
- CD8(+) T-cell and nab responses demonstrated in vaccinated animals following challenge
- Immunologic control of infection was incomplete (no sterilizing protection) by 22 wpc

NHP.304 (12556683) **Post-exposure prophylaxis with human monoclonal antibodies prevented SHIV89.6P infection or disease in neonatal macaques**

Authors: Ferrantelli F, Hofmann-Lehmann R, Rasmussen RA, Wang T, Xu W, Li PL, Montefiori DC, Cavacini LA, Katinger H, Stiegler G, Anderson DC, McClure HM, Ruprecht RM.

Journal: AIDS 2003 Feb 14;17(3):301-309

Objectives: Challenge, Immunotherapy, Passive Immunization. To develop passive immunization with human neutralizing monoclonal antibodies against mother-to-child transmission of HIV during delivery and through breastfeeding.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Monoclonal antibody 2G12 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name: Monoclonal antibody 2F5 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name: Monoclonal antibody 4E10 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name: IgG1 b12 *Type:* Passive Antibody *Route:* Intravenous

Challenge: SHIV89.6P *Route:* Oral

Main Findings:

- 2/4 macaque infants treated with neutralizing mAbs showed no evidence of infection; the other 2 maintained normal CD4 T cell counts
- In contrast, all control animals became highly viremic and had profound CD4 T cell losses; 3/4 died from AIDS within 1.5-6 weeks of the challenge.
- Conclusions: Passive immunization with this quadruple neutralizing mAbs combination may represent a promising approach to prevent peri- and postnatal HIV transmission.

NHP.305 (12545074) **Live attenuated, nef-deleted SIV is pathogenic in most adult macaques after prolonged observation.**

Authors: Hofmann-Lehmann R, Vlasak J, Williams AL, Chenine AL, McClure HM, Anderson DC, O'Neil S, Ruprecht RM

Journal: AIDS 2003 Jan 24;17(2):157-66.

Objectives: Immunogenicity, Pathogenicity. To demonstrate the pathogenicity of a live attenuated SIV (SIVmac239Δ3).

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac239Δ3 (cell-infected) *Type:* Cell/Tissue *Route:* Intravenous

Vaccine Name: SIVmac239Δ3 *Type:* Live Attenuated Virus *Routes:* Intravenous, Oral, Intra-amniotic, Intraplacental

Main Findings:

- 11/11 rhesus macaques vaccinated with SIVmac239δ3 developed signs of immune dysfunction
- 11/11 vaccinated animals had inverted CD4:CD8 ratio
- 7/11 (64%) had persistent recurrent viremia
- Other signs of immune dysfunction included decreased CD4, low CD4CD29 lymphocyte subsets, low anti-gag antibodies, etc.
- 2/11 (18%) vaccinees developed AIDS
- Conclusion: Live attenuated virus can cause immune dysfunction in vaccinees and similar live attenuated HIV seems contraindicated for mass vaccination of humans.

NHP.306.1 (11797011) **Replication-incompetent adenoviral vaccine vector elicits effective anti-immunodeficiency-virus immunity.**

Authors: Shiver JW, Fu TM, Chen L, Casimiro DR, Davies ME, Evans RK, Zhang ZQ, Simon AJ, Trigona WL, Dubey SA, Huang L, Harris VA, Long RS, Liang X, Handt L, Schleif WA, Zhu L, Freed DC, Persaud NV, Guan L, Punt KS, Tang A, Chen M, Wilson KA, Collins KB, Heidecker GJ, Fernandez VR, Perry HC, Joyce JG, Grimm KM, Cook JC, Keller PM, Kresock DS, Mach H etc

Journal: Nature 2002 Jan 17;415(6869):331-5.

Objectives: Challenge, Immunogenicity. To compare vaccine vector delivery systems: 3 formulations of a plasmid DNA vector (MVA) and a replication incompetent adenovirus type 5 vector expressing SIV gag protein.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pV1R-SIVmac239-gag *Type:* DNA *Route:* Intramuscular *Formulation:* pV1R-SIVmac239-gag + Rehydragel HPA, CRL1005, MPL™ + PBS

Vaccine Name: MVA-SIVgag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name: Ad5-SIVgag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Challenge: SHIV89.6P *Route:* Intravenous

Main Findings:
- A replication-incompetent Ad5 vector, used either alone or as a booster inoculation after priming with a DNA vector elicited the most effective response
- After challenge with a pathogenic SHIV, the animals immunized with Ad5 vector exhibited the most pronounced attenuation of the virus infection
- The replication-defective adenovirus is a promising vaccine vector for development of an HIV-1 vaccine

NHP.306.2 (11797011) **Replication-incompetent adenoviral vaccine vector elicits effective anti-immunodeficiency-virus immunity.**

Authors: Shiver JW, Fu TM, Chen L, Casimiro DR, Davies ME, Evans RK, Zhang ZQ, Simon AJ, Trigona WL, Dubey SA, Huang L, Harris VA, Long RS, Liang X, Handt L, Schleif WA, Zhu L, Freed DC, Persaud NV, Guan L, Punt KS, Tang A, Chen M, Wilson KA, Collins KB, Heidecker GJ, Fernandez VR, Perry HC, Joyce JG, Grimm KM, Cook JC, Keller PM, Kresock DS, Mach H etc

Journal: Nature 2002 Jan 17;415(6869):331-5. To compare vaccine vector delivery systems: 3 formulations of a plasmid DNA vector (MVA) and a replication incompetent adenovirus type 5 vector expressing SIV gag protein.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pV1R-SIVmac239-gag *Type:* DNA *Route:* Intramuscular *Formulation:* pV1R-SIVmac239-gag + Rehydragel HPA, CRL1005, MPL™ + PBS

Vaccine Name: MVA-SIVgag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* MVA-SIVgag + PBS

Vaccine Name: Ad5-SIVgag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* Ad5-SIVgag + PBS

Challenge: SHIV89.6P *Route:* Intravenous

NHP.308 (12551977) **Mucosal priming of simian immunodeficiency virus-specific cytotoxic T-lymphocyte responses in rhesus macaques by the Salmonella type III secretion antigen delivery system.**

Authors: Evans DT, Chen LM, Gillis J, Lin KC, Harty B, Mazzara GP, Donis RO, Mansfield KG, Lifson JD, Desrosiers RC, Galan JE, Johnson RP

Journal: J Virol 2003 Feb;77(4):2400-9.

Objectives: Challenge, Immunogenicity. To test attenuated strains of Salmonella expressing fragments of the SIV Gag protein fused to the type III-secreted SopE protein for the ability to prime virus-specific CTL responses in rhesus macaques.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: rSalmonella typhimurium-SIVgag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intragastric

Vaccine Name: rSalmonella typhi-SIVgag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intragastric

Vaccine Name: MVA-SIVmac239gag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intragastric

Challenge: SIVmac239 *Route:* Intrarectal

Main Findings:
- Strong Gag-specific CTL responses were consistently detected, and tetramer staining revealed the expansion of Gag181-189-specific CD8+ T-cell responses in peripheral blood also in lymphocytes isolated from the colon
- A significant percentage of the Gag181-189-specific T-cell population in each animal also expressed the intestinal homing receptor α4ß7
- Salmonella-primed/MVA-boosted animals did not exhibit improved control of virus replication following a rectal challenge with SIVmac239

NHP.309 (12573592) **Replication, immunogenicity, and protective properties of live-attenuated simian immunodeficiency viruses expressing interleukin-4 or interferon-gamma.**

Authors: Stahl-Hennig C, Gundlach BR, Dittmer U, ten Haaft P, Heeney J, Zou W, Emilie D, Sopper S, Uberla K

Journal: Virology 2003 Jan 20;305(2):473-85.

Objectives: Challenge, Immunogenicity, Pathogenicity. To study the effect of interferon-γ and interleukin-4 on viral load, immunogenicity, and protective properties of Nef-lacking mutants of SIV-expressing SIV-IL4 or SIV-IFN.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIV-IL4 *Type:* Live Attenuated Virus *Route:* Intravenous *Formulation:* SIV-IL4 + IL-4

Vaccine Name: SIV-IFN *Type:* Live Attenuated Virus *Route:* Intravenous *Formulation:* SIV-IFN + Interferon-γ

Challenge: SIVmac239/nef-open *Route:* Intravenous

Main Findings:

- During the acute phase of infection, the cell-associated viral load, but not the plasma viral RNA load, was approximately 10-fold lower in SIV-IFN-infected macaques than in SIV-IL4-infected animals
- The viral load declined to hardly detectable levels 4 months postinfection in all animals
- The titers and affinity of SIV antibodies were higher in SIV-IL4-infected macaques than in SIV-IFN-infected animals
- Subsequent challenge with SHIV revealed protection in the absence of neutralizing antibodies

NHP.310 (12477812) **Increased virus replication and virulence after serial passage of human immunodeficiency virus type 2 in baboons.**

Authors: Locher CP, Witt SA, Herndier BG, Abbey NW, Tenner-Racz K, Racz P, Kiviat NB, Murthy KK, Brasky K, Leland M, Levy JA

Journal: J Virol 2003 Jan;77(1):77-83.

Objectives: Pathogenicity. To enhance the pathogenicity of HIV-2 in order to shorten the amount of time to the development of disease in baboons.

Species/Subspecies: Papio cynocephalus (Baboon)

Challenge: HIV-2 (UC2-12741), HIV-2 (UC2-11999), HIV-2 (UC2-10568), HIV-2 (UC2-11966), HIV-2 (UC2-12281), HIV-2 (UC2-9429) *Route:* Intravenous

Main Findings:

- After these serial passages, virus levels in plasma, peripheral blood mononuclear cells (PBMC) and lymphatic tissues in the acutely infected baboons were increased
- Within 1 year of the HIV-2 infection, all of the inoculated baboons showed specific signs of AIDS-related disease progression within the lymphatic tissues, such as vascular proliferation and lymphoid depletion
- HIV-2(UC2) isolate recovered after several serial passages in baboons will be useful in future studies of AIDS pathogenesis and vaccine development by using this animal model

NHP.312 (12502815) **Increased mucosal transmission but not enhanced pathogenicity of the CCR5-tropic, simian AIDS-inducing simian/human immunodeficiency virus SHIV(SF162P3) maps to envelope gp120.**

Authors: Hsu M, Harouse JM, Gettie A, Buckner C, Blanchard J, Cheng-Mayer C

Journal: J Virol 2003 Jan;77(2):989-98.

Objectives: Pathogenicity. To determine whether envelope glycoprotein gp120 is responsible for increased pathogenesis and transmissibility of the $SHIV_{SF162P3}$.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Challenge: $SHIV_{SF162-PC}$ *Route:* Intravenous, Vaginal or perivaginal

Main Findings:
- $SHIV_{SF162-PC}$ was as infectious as $SHIV_{SF162}$, and intermediate in pathogenicity between $SHIV_{SF162}$ and $SHIV_{SF162-P3}$
- Fusogenic capacity and inhibition by T-20 fusion inhibitor were also assayed
- Compared to wild-type SHIV(SF162) gp120, P3 gp120 conferred in vitro neutralization resistance and increased entry efficiency of the virus, but was compromised in its fusion-inducing capacity
- In vivo, SHIV(SF162PC) infected 2/2 and 2/3 rhesus macaques by the intravenous and intravaginal routes, respectively
- Although peak viremia reached 10^6 to 10^7 RNA copies per ml of plasma in some infected animals and was associated with depletion of gut-associated CD4(+) lymphocytes, none of the animals maintained a viral set point that would be predictive of progression to disease

NHP.313.1 (12663776) **Global Dysfunction of CD4 T-Lymphocyte Cytokine Expression in Simian-Human Immunodeficiency Virus/SIV-Infected Monkeys Is Prevented by Vaccination.**

Authors: McKay PF, Barouch DH, Schmitz JE, Veazey RS, Gorgone DA, Lifton MA, Williams KC, Letvin NL

Journal: J Virol 2003 Apr 15;77(8):4695-4702.

Objectives: Challenge, Immunogenicity. To assess the functional capacity of CD4+ T lymphocytes in rhesus monkeys both prospectively during the course of a simian immunodeficiency virus (SIV) infection and in a cohort of SIV/SHIV-infected animals with nonprogressive disease.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- Loss of the capacity of peripheral blood CD4+ T lymphocytes to express cytokines was first detected in SIV-infected monkeys during the peak of viral replication during primary infection and persisted thereafter
- Infected monkeys with progressive disease had peripheral blood CD4+ T lymphocytes that expressed significantly less cytokine than infected monkeys that had undetectable viral loads and intact CD4+ T-lymphocyte counts
- CD4+ T lymphocytes from vaccinated monkeys that effectively controlled the replication of a highly pathogenic immunodeficiency virus isolate following a challenge had a preserved functional capacity

NHP.313.2 (12663776) **Global Dysfunction of CD4 T-Lymphocyte Cytokine Expression in Simian-Human Immunodeficiency Virus/SIV-Infected Monkeys Is Prevented by Vaccination.**

Authors: McKay PF, Barouch DH, Schmitz JE, Veazey RS, Gorgone DA, Lifton MA, Williams KC, Letvin NL

Journal: J Virol 2003 Apr 15;77(8):4695-4702.

Objectives: Pathogenicity. To compare the CD+ T cell profile in progressor and nonprogressor rhesus monkeys infected with SIV/SHIV.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- Small difference between the cytokine expression profiles of the peripheral blood CD4+ T lymphocytes from normal monkeys and those from SIV/SHIV-infected clinical nonprogressor monkeys

NHP.318 (10803879) **Multi-envelope HIV vaccine safety and immunogenicity in small animals and chimpanzees.**

Authors: Lockey TD, Slobod KS, Caver TE, D'Costa S, Owens RJ, McClure HM, Compans RW, Hurwitz JL

Journal: Immunol Res 2000;21(1):7-21.

Objectives: Immunogenicity. To compare the multi envelope vaccine vs. those containing a single component, inoculated by cutaenous or subcutaenous route.

Species/Subspecies: Pan Troglodytes (Chimpanzee)

Main Findings:
- Cutaenous lesions were not required to elicit HIV-1 envelope or vaccinia virus-humoral immune response
- Antibody responses could be substantially enhanced with envelope booster immunization
- Immune response to envelope protein persisted to >1 year
- Multi-envelope vaccines are more immunogenic than those containing a single envelope component

NHP.319 (12706101) **Evidence for immune-mediated reduction of viral replication in Macaca nemestrina mucosally immunized with inactivated SHIV(89.6).**

Authors: Ambrose Z, Thompson J, Larsen K, Kuller L, Panicali DL, Clements JD, Agy M, Montefiori DC, Hu SL, Bosch ML

Journal: Virology 2003 Mar 30;308(1):178-90.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: vT107 *Type:* Recombinant Vector (virus/bacteria) *Route:* Scarification

Vaccine Name: vAbT394 *Type:* Recombinant Vector (virus/bacteria) *Route:* Scarification

Vaccine Name: AT-2-Inactivated SHIV89.6 *Type:* Whole (killed) Inactivated Virus *Routes:* Intragastric, Intranasal

Challenge: SHIV89.6 *Route:* Vaginal or perivaginal

Main Findings:
- Anti-SHIV T-cell responses were significant only in primed and boosted animals (group 2). Primed and boosted animals also showed significantly decreased viral loads compared to boosted only.

NHP.320 (9371609) **Identification of the V1 region as a linear neutralizing epitope of the simian immunodeficiency virus SIVmac envelope glycoprotein.**

Authors: Jurkiewicz E, Hunsmann G, Schaffner J, Nisslein T, Luke W, Petry H

Journal: J Virol 1997 Dec;71(12):9475-81.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIV-Mac-32H *Type:* Live Virus *Route:*

Vaccine Name: SIV-Mac-MPBMC *Type:* Live Virus *Route:*

Vaccine Name: oligomeric gp130 *Type:* Synthetic Protein/Peptide *Route:*

Main Findings:
- Rhesus macaques infected with clone Mac32H or immunized with Mac gp130 developed neutralizing antibodies directed at an epitope in the V1 region of Env.

NHP.321 (12719603) **Induction of broad and potent anti-human immunodeficiency virus immune responses in rhesus macaques by priming with a DNA vaccine and boosting with protein-adsorbed polylactide coglycolide microparticles.**

Authors: Otten G, Schaefer M, Greer C, Calderon-Cacia M, Coit D, Kazzaz J, Medina-Selby A, Selby M, Singh M, Ugozzoli M, Zur Megede J, Barnett SW, O'Hagan D, Donnelly J, Ulmer J

Journal: J Virol 2003 May 15;77(10):6087-92.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pCMV-gag-mod *Type:* DNA *Route:* Intramuscular *Formulation:* pCMV-gag-mod + Saline

Vaccine Name: HIV-IIIB-p55gag-VLP *Type:* Virus-like Particle *Route:* Intramuscular *Formulation:* HIV-IIIB-p55gag-VLP + LTK63 + Saline

Vaccine Name: p55Gag *Type:* Purified Viral Products *Route:* Intramuscular *Formulation:* p55Gag + LTK63, PLG + Saline

Main Findings:

- Priming with Gag DNA and boosting with Gag protein adsorbed to polylactide coglycolide microparticles produced a stronger and broader immune response than either vaccine alone.

NHP.322 (12867656) **DNA vaccination of macaques by a full-genome simian/human immunodeficiency virus type 1 plasmid chimera that produces non-infectious virus particles.**

Authors: Akahata W, Ido E, Akiyama H, Uesaka H, Enose Y, Horiuchi R, Kuwata T, Goto T, Takahashi H, Hayami M

Journal: J Gen Virol 2003 Aug;84(Pt 8):2237-2244.

Objectives: Challenge, Immunogenicity. To evaluate the immunogenicity and protection from chanllenge of a full-genome SHIV plasmid in rhesus monkeys.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pSHIV-NM-3rn ZF1* *Type:* DNA *Route:* Intramuscular *Formulation:* pSHIV-NM-3rn ZF1* + Bupivacaine + PBS

Challenge: SHIV-NM-3rN *Route:* Intravenous

Main Findings:

- High CTL activity in vaccinees
- In all macaques vaccinated, peak plasma virus loads after homologous challenge with SHIV were 2 to 3 orders of magnitude lower than those of the naive controls, and virus loads fell below the level of detection at 6 weeks post-challenge suggesting that the vaccination regime in this study was partially effective

NHP.323 (12919751) **Convergent evolution of SIV env after independent inoculation of rhesus macaques with infectious proviral DNA.**

Authors: Buckley KA, Li PL, Khimani AH, Hofmann-Lehmann R, Liska V, Anderson DC, McClure HM, Ruprecht RM

Journal: Virology 2003 Aug 1;312(2):470-80.

Objectives: Pathogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac239Δ3 *Type:* Live Attenuated Virus *Routes:* Intravenous, Intramuscular *Formulation:* SIVmac239Δ3 + Saline

Vaccine Name: SIVmac239Δ3+ *Type:* Live Attenuated Virus *Route:* Intramuscular *Formulation:* SIVmac239Δ3+ + Saline

Vaccine Name: pSIVNef-TPA *Type:* DNA *Route:* Intramuscular *Formulation:* pSIVNef-TPA + Saline

Main Findings:

- Rhesus macaques innoculated with SIV-MAC239, MAC239-delta3 or Mac239-delta3+ pathogenic revertant of delta3, each developed similar mutations, indicative of convergent evolution, in env.

NHP.324.1 (12922139) **Boosting of SIV-specific immune responses in rhesus macaques by repeated administration of Ad5hr-SIVenv/rev and Ad5hr-SIVgag recombinants.**

Authors: Zhao J, Lou Y, Pinczewski J, Malkevitch N, Aldrich K, Kalyanaraman VS, Venzon D, Peng B, Patterson LJ, Edghill-Smith Y, Woodward R, Pavlakis GN, Robert-Guroff M

Journal: Vaccine 2003 Sep 8;21(25-26):4022-35.

Objectives: Challenge. To evaluate ELISPOT reactivity to Gag, Env and Rev proteins after each of 2

innoculations with Adenovirus-Env-Rev and Adenovirus-Gag vectors.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Ad5hr-SIVenv *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Oral, Intranasal *Formulation:* Ad5hr-SIVenv + Water, Saline, PBS

Vaccine Name: Ad5hr-SIVmac239gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Oral, Intranasal *Formulation:* Ad5hr-SIVmac239gag + Saline

Challenge: SIVmac251 *Route:* Intrarectal

Main Findings:

- Vaccination with 2 Ad4hr vectors containing SIV-smH4 Env-Rev and SIV-Mac239 Gag was followed by ELISPOT cellular immune response detection, and antibody titre of humoral responses
- The second inoculation significantly boosted both responses
- Second paper described intrarectal challenge with SIV-Mac251 at week 42
- All animals developed persistent infection, but viral burden at peak viremia was reduced (14 fold; $P < 0.0001$) in vaccinated animals as compared to controls
- Viremia at set point was not significantly reduced in vaccinated animals compared to controls.

NHP.324.1 (12857905) **Improved protection of rhesus macaques against intrarectal simian immunodeficiency virus SIV(mac251) challenge by a replication-competent Ad5hr-SIVenv/rev and Ad5hr-SIVgag recombinant priming/gp120 boosting regimen.**

Authors: Zhao J, Pinczewski J, Gomez-Roman VR, Venzon D, Kalyanaraman VS, Markham PD, Aldrich K, Moake M, Montefiori DC, Lou Y, Pavlakis GN, Robert-Guroff M

Journal: J Virol 2003 Aug;77(15):8354-65.

NHP.325 (12097576) **Different patterns of immune responses but similar control of a simian-human immunodeficiency virus 89.6P mucosal challenge by modified vaccinia virus Ankara (MVA) and DNA/MVA vaccines.**

Authors: Amara RR, Villinger F, Staprans SI, Altman JD, Montefiori DC, Kozyr NL, Xu Y, Wyatt LS, Earl PL, Herndon JG, McClure HM, Moss B, Robinson HL

Journal: J Virol 2002 Aug;76(15):7625-31.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIV-HIV89.6 DNA vaccine *Type:* DNA *Routes:* Intradermal, Intramuscular *Formulation:* SIV-HIV89.6 DNA vaccine + PBS

Vaccine Name: rMVA 89.6 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intravenous, Intradermal, Intramuscular *Formulation:* rMVA 89.6 + PBS

Challenge: SHIV89.6P *Route:* Intrarectal

Main Findings:

- Although individual animals in DNA/MVA and MVA/MVA groups had varying levels of antibody and CD8 T-cell response, all controlled challenge virus, as measured by viral load and decline in CD4 T-cells, equally well post challenge.

NHP.326 (12915583) **Protective Efficacy of an AIDS Vaccine, a Single DNA Priming Followed by a Single Booster with a Recombinant Replication-Defective Sendai Virus Vector, in a Macaque AIDS Model.**

Authors: Takeda A, Igarashi H, Nakamura H, Kano M, Iida A, Hirata T, Hasegawa M, Nagai Y, Matano T

Journal: J Virol 2003 Sep 1;77(17):9710-9715.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: F(+)SeV-gag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intranasal

Vaccine Name: CMV SHIV dEN *Type:* DNA *Route:* Intramuscular
Challenge: SHIV89.6PD *Route:* Intravenous

NHP.327.1 (14970317) **Early protection against pathogenic virus infection at a mucosal challenge site after vaccination with attenuated simian immunodeficiency virus.**

Authors: Tenner-Racz K, Hennig CS, Uberla K, Stoiber H, Ignatius R, Heeney J, Steinman RM, Racz P
Journal: Proc Natl Acad Sci U S A 2004 Feb 17;.
Objectives: Challenge, Immunogenicity. Exp 1: To investigate long-term protection induced by live attenuated delta deleted SIV.
Species/Subspecies: Macaca mulatta (Rhesus macaque)
Vaccine Name: SIVDeltaNU *Type:* Live Attenuated Virus *Routes:* Intravenous, Other
Challenge: SIVmac251 *Route:* Other
Main Findings:

- Experiment 1 and experiment 2: A traumatic application of attenuated SIVmac239Deltanef vaccine to the tonsils of rhesus macaques provided protection against challenge 26 weeks later with infectious SIVmac251 applied through this route
- 10/10 vaccinees did not show significantly raised RNA levels in the plasma or increase in infected cells in lymphoid tissue after challenge (exp. 2)
- Vaccine virus was found in the tonsils of all vaccinees, but challenge virus was only detected at this portal of entry in 4/10 monkeys
- During tonsillar SIVDeltanef vaccination, infection is blocked early at the entry portal

NHP.327.2 (14970317) **Early protection against pathogenic virus infection at a mucosal challenge site after vaccination with attenuated simian immunodeficiency virus.**

Authors: Tenner-Racz K, Hennig CS, Uberla K, Stoiber H, Ignatius R, Heeney J, Steinman RM, Racz P
Journal: Proc Natl Acad Sci U S A 2004 Feb 17;.
Objectives: Challenge, Immunogenicity. To investigate short-term protection induced by live attenuated delta deleted SIV.
Species/Subspecies: Macaca mulatta (Rhesus macaque)
Vaccine Name: SIVDeltaNU *Type:* Live Attenuated Virus *Routes:* Intravenous, Other
Challenge: SIVmac251 *Route:*

NHP.328 (12885879) **Potent, persistent induction and modulation of cellular immune responses in rhesus macaques primed with Ad5hr-simian immunodeficiency virus (SIV) env/rev, gag, and/or nef vaccines and boosted with SIV gp120.**

Authors: Patterson LJ, Malkevitch N, Pinczewski J, Venzon D, Lou Y, Peng B, Munch C, Leonard M, Richardson E, Aldrich K, Kalyanaraman VS, Pavlakis GN, Robert-Guroff M
Journal: J Virol 2003 Aug;77(16):8607-20.
Species/Subspecies: Macaca mulatta (Rhesus macaque)
Vaccine Name: Ad5hr-SIVenv *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Oral, Intranasal *Formulation:* Ad5hr-SIVenv + Water, Saline, PBS
Vaccine Name: Recombinant HIV-1 gag core (p24,p15) antigen *Type:* Recombinant Subunit Protein *Routes:* Intratracheal, Subcutaneous *Formulation:* Recombinant HIV-1 gag core (p24,p15) antigen + PBS
Vaccine Name: Ad5hr-SIVmac239gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Oral, Intranasal *Formulation:* Ad5hr-SIVmac239gag + Saline, PBS
Vaccine Name: Ad5hr-SIVnefδ1-13 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Oral, Intranasal *Formulation:* Ad5hr-SIVnefδ1-13 + PBS
Vaccine Name: SIVmac251-gp120 *Type:* Purified Viral Products *Routes:* Intrarectal, Intramuscular, Intranasal

NHP.330 (12804847) **Specificity and effect on apoptosis of Tat antibodies from vaccinated and SHIV-infected rhesus macaques and HIV-infected individuals.**

Authors: Belliard G, Romieu A, Zagury JF, Dali H, Chaloin O, Le Grand R, Loret E, Briand JP, Roques B, Desgranges C, Muller S

Journal: Vaccine 2003 Jul 4;21(23):3186-99.

Objectives: Immunogenicity, Immunotherapy. To study the the recognition of several Tat mutants as well as various synthetic Tat fragments by anti-Tat monoclonal antibodies and by IgG antibodies in SHIV)-infected macaques (also human long-term survivals infected with HIV).

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Tat8-53 *Type:* Synthetic Protein/Peptide *Routes:* Intramuscular, Intranasal *Formulation:* Tat8-53 + Adju-Phos, MONTANIDE ISA 720, CpG 2006 + Saline

Vaccine Name: Tat1-20 *Type:* Synthetic Protein/Peptide *Routes:* Intramuscular, Intranasal *Formulation:* Tat1-20 + Adju-Phos, MONTANIDE ISA 720, CpG 2006 + Saline

Vaccine Name: Tat 19-53 *Type:* Synthetic Protein/Peptide *Routes:* Intramuscular, Intranasal *Formulation:* Tat 19-53 + Adju-Phos, MONTANIDE ISA 720, CpG 2006 + Saline

Vaccine Name: Tat 19-53m *Type:* Synthetic Protein/Peptide *Routes:* Intramuscular, Intranasal *Formulation:* Tat 19-53m + Adju-Phos, MONTANIDE ISA 720, CpG 2006 + Saline

Vaccine Name: Tat 1-61 *Type:* Synthetic Protein/Peptide *Routes:* Intramuscular, Intranasal *Formulation:* Tat 1-61 + MONTANIDE ISA 720 + Saline

Vaccine Name: Tat 44-61 *Type:* Synthetic Protein/Peptide *Routes:* Intramuscular, Intranasal *Formulation:* Tat 44-61 + MONTANIDE ISA 720 + Saline

Main Findings:

- Tat peptides innoculated into Rhesus macaques produced antibody responses capable of inhibiting functions of extracellular Tat protein

NHP.332 (9223407) **Protection of SIVmac-infected macaque monkeys against superinfection by a simian immunodeficiency virus expressing envelope glycoproteins of HIV type 1.**

Authors: Dunn CS, Hurtrel B, Beyer C, Gloeckler L, Ledger TN, Moog C, Kieny MP, Mehtali M, Schmitt D, Gut JP, Kirn A, Aubertin AM

Journal: AIDS Res Hum Retroviruses 1997 Jul 20;13(11):913-22.

Objectives: Challenge, Immunogenicity. To determine whether host immune responses to envelope glycoprotein are an essential component of the immunity to primate lentiviruses.

Main Findings:

- Superinfection of SIVmac-infected macaque monkeys with a large dose of SHIVsbg resulted in isolation of the chimeric SHIVsbg by coculture of PBMCs from 4/5 SIV-infected monkeys, but 3 animals were protected from extracellular SHIV viremia and did not seroconvert to HIV-1 glycoproteins
- In the 2 SIV-infected monkeys that did develop SHIV viremia, cell-associated viral load was reduced at least 100-fold

NHP.334 (12970419) **Cellular immunity elicited by human immunodeficiency virus type 1/ simian immunodeficiency virus DNA vaccination does not augment the sterile protection afforded by passive infusion of neutralizing antibodies.**

Authors: Mascola JR, Lewis MG, VanCott TC, Stiegler G, Katinger H, Seaman M, Beaudry K, Barouch DH, Korioth-Schmitz B, Krivulka G, Sambor A, Welcher B, Douek DC, Montefiori DC, Shiver JW, Poignard P, Burton DR, Letvin NL

Journal: J Virol 2003 Oct;77(19):10348-56.

NHP.335 (12850342) **Mucosal administration of three recombinant Mycobacterium bovis BCG-SIVmac251 strains**

to cynomolgus macaques induces rectal IgAs and boosts systemic cellular immune responses that are primed by intradermal vaccination.

Authors: Ruprecht RM, Ferrantelli F, Kitabwalla M, Xu W, McClure HM

Journal: Vaccine 2003 Jul 28;21(24):3370-3.

NHP.336 (12719580) **Molecular features of the broadly neutralizing immunoglobulin G1 b12 required for recognition of human immunodeficiency virus type 1 gp120.**

Authors: Zwick MB, Parren PW, Saphire EO, Church S, Wang M, Scott JK, Dawson PE, Wilson IA, Burton DR

Journal: J Virol 2003 May;77(10):5863-76.

NHP.339 (12359458) **Chimeric human papilloma virus-simian/human immunodeficiency virus virus-like-particle vaccines: immunogenicity and protective efficacy in macaques.**

Authors: Dale CJ, Liu XS, De Rose R, Purcell DF, Anderson J, Xu Y, Leggatt GR, Frazer IH, Kent SJ

Journal: Virology 2002 Sep 15;301(1):176-87.

Objectives: Challenge, Immunogenicity. To evaluate HPV-HIV VLPs for immunogenicity and protective immunity using a mucosal SHIV challenge model in macaques and to evaluate a DNA vaccine prime and HPV-HIV VLP boost approach to induce T cell mediated immunity in macaques.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Vaccine Name: Pooled SIVgag/HIVtat.rev DNA vaccine *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intramuscular

Vaccine Name: HPV/SHIV-VLP *Type:* Virus-like Particle *Routes:* Intrarectal, Intramuscular

Challenge: SHIV.229(mn) *Route:* Intrarectal

Main Findings:

- HPV L1 antibodies were induced in all immunized macaques
- Weak antibody or T cell responses to the chimeric SHIV antigens were detected only in animals receiving the DNA prime/HPV-SHIV VLP boost vaccine regimen
- Significant but partial protection from a virulent mucosal SHIV challenge was detected only in the prime/boosted macaques and not in animals receiving the HPV-SHIV VLP vaccines alone, with 3/5 prime/boosted animals retaining some CD4 T cells following challenge

NHP.340 (14498982) **Multigene DNA prime-boost vaccines for SHIV89.6P.**

Authors: Doria-Rose NA, Pierce CC, Hensel MT, Sutton WF, Sheikh N, Polacino P, Kuller L, Zhu YD, Hu SL, Anderson D, Haigwood NL

Journal: J Med Primatol 2003 Aug;32(4-5):218-28.

NHP.341 (14627745) **Transfer of neutralizing IgG to macaques 6 h but not 24 h after SHIV infection confers sterilizing protection: Implications for HIV-1 vaccine development.**

Authors: Nishimura Y, Igarashi T, Haigwood NL, Sadjadpour R, Donau OK, Buckler C, Plishka RJ, Buckler-White A, Martin MA

Journal: Proc Natl Acad Sci U S A 2003 Dec 9;100(25):15131-6.

Objectives: Challenge, Passive Immunization.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

NHP.344 (12519210) **Immune responses in baboons vaccinated with HIV-2 genetic expression libraries.**

Authors: Locher CP, Sykes KF, Blackbourn DJ, Johnston SA

Journal: J Med Primatol 2002 Dec;31(6):323-9.

Objectives: Challenge, Immunogenicity. To evaluate the effectiveness of an HIV-2 vaccine made from a genomic expression library in baboons.

Main Findings:
- HIV-2 expression library immunization induced HIV-2-specific memory responses but low levels of CD8+ cell anti-viral responses and neutralizing antibodies
- Immunization with HIV-2 expression library did not significantly alter the viral load in vaccinated animals compared to control group
- The approach does not provide protection in baboons against intravenous challenge with HIV-2

NHP.345 (14741150) **Avipox-based simian immunodeficiency virus (SIV) vaccines elicit a high frequency of SIV-specific CD4+ and CD8+ T-cell responses in vaccinia-experienced SIVmac251-infected macaques.**

Authors: Nacsa J, Radaelli A, Edghill-Smith Y, Venzon D, Tsai WP, Morghen Cde G, Panicali D, Tartaglia J, Franchini G

Journal: Vaccine 2004 Jan 26;22(5-6):598-607.

Objectives: Immunogenicity, Immunotherapy, Chemotherapy. To test the ability of ALVAC- or fowlpox-based SIV vaccines to boost SIV-specific CD4+ and CD8+ T-cell responses in 10 vaccinia-experienced macaques infected with SIVmac251.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac251 *Type:* Live Virus *Routes:* Intrarectal, Intravenous, Mucosal

Vaccine Name: FP-SIV-gp (FP74) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name: ALVAC-SIV-gp *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Main Findings:
- The 2 vaccine modalities effectively boosted both CD4+ and CD8+ SIV-specific T-cell response despite prior exposure to the vaccinia-derivative NYVAC vector, suggesting that sequential boosting with either avipox-based vector vaccine candidate is a realistic approach in immune therapy of HIV-1-infected individuals

NHP.346 (14645590) **Multispecific vaccine-induced mucosal cytotoxic T lymphocytes reduce acute-phase viral replication but fail in long-term control of simian immunodeficiency virus SIVmac239.**

Authors: Vogel TU, Reynolds MR, Fuller DH, Vielhuber K, Shipley T, Fuller JT, Kunstman KJ, Sutter G, Marthas ML, Erfle V, Wolinsky SM, Wang C, Allison DB, Rud EW, Wilson N, Montefiori D, Altman JD, Watkins DI

Journal: J Virol 2003 Dec;77(24):13348-60.

Objectives: Challenge, Immunogenicity. To ascertain the effect of vaccine-induced multispecific mucosal CTL.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- The vaccination induced virus-specific CTL and CD4+ helper T lymphocytes with CTL frequencies as high as 20,000/million peripheral blood mononuclear cells
- The final rMVA vaccination, delivered intravenously, engendered long-lived mucosal CTL
- Massive early anamnestic cellular immune responses controlled acute-phase viral replication; however, the 3 vaccinees were unable to control virus replication in the chronic phase
- Multispecific mucosal CTL, in the absence of neutralizing antibodies, can achieve a modicum of control over early viral replication but unable to control chronic-phase viral replication after a high-dose mucosal challenge with a pathogenic simian immunodeficiency virus

NHP.348.1 (14585346) **Immunogenicity in pig-tailed macaques of poliovirus replicons expressing HIV-1 and SIV antigens and protection against SHIV-89.6P disease.**

Authors: Fultz PN, Stallworth J, Porter D, Novak M, Anderson MJ, Morrow CD

Journal: Virology 2003 Oct 25;315(2):425-37.

Objectives: Immunogenicity. To determine whether poliovirus replicons expressing various HIV-1 Env and SIVmac239 Gag antigens would be immunogenic in macaques.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Vaccine Name: Polio (Sabin 1) -HIV-1.gag/env (1) *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intrarectal, Intranasal

Vaccine Name: Polio (Sabin 1) - HIV-1.gag/env (2) *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intrarectal, Intranasal

Vaccine Name: Polio (Sabin 2) - HIV-1.gag/env (3) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name: Polio (Sabin 2) - HIV-1.gag/env (4) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name: rgp140-env (HIV-1.89.6) *Type:* Recombinant Subunit Protein *Route:* Intramuscular

NHP.348.2 (14585346) **Immunogenicity in pig-tailed macaques of poliovirus replicons expressing HIV-1 and SIV antigens and protection against SHIV-89.6P disease.**

Authors: Fultz PN, Stallworth J, Porter D, Novak M, Anderson MJ, Morrow CD

Journal: Virology 2003 Oct 25;315(2):425-37.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Vaccine Name: rgp140-env (HIV-1.89.6) *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Vaccine Name: Polio-LAI/IIIB-Env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name: Polio- SIVmac239gag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Challenge: SHIV89.6P *Route:* Intravenous

NHP.349 (14585221) **Gp120-alum boosting of a Gag-Pol-Env DNA/MVA AIDS vaccine: poorer control of a pathogenic viral challenge.**

Authors: Buge SL, Ma HL, Amara RR, Wyatt LS, Earl PL, Villinger F, Montefiori DC, Staprans SI, Xu Y, Carter E, O'Neil SP, Herndon JG, Hill E, Moss B, Robinson HL, McNicholl JM

Journal: AIDS Res Hum Retroviruses 2003 Oct;19(10):891-900.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Soluble 89.6 gp120 protein *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* Soluble 89.6 gp120 protein + Alum

Vaccine Name: SIV-HIV89.6 DNA vaccine *Type:* DNA *Routes:* Intradermal, Intramuscular *Formulation:* SIV-HIV89.6 DNA vaccine + PBS

Vaccine Name: rMVA 89.6 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intravenous, Intradermal, Intramuscular *Formulation:* rMVA 89.6 + PBS

Challenge: SHIV89.6P *Route:* Intrarectal

NHP.350 (14583643) **Evaluation of simian immunodeficiency virus-specific immune responses induced by a defective proviral DNA vaccine in macaques.**

Authors: Takeda A, Nakamura H, Matano T

Journal: Jpn J Infect Dis 2003 Aug;56(4):172-3.

Objectives: Immunogenicity. To examine if macaques vaccinated with FMSIV DNA and an mCAT1-expression plasmid DNA (pCMVmCAT1) had SIV-specific T-cell levels significantly higher than control macaques vaccinated with replication-negative FMSIV DNA vaccine.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pCMVmCAT1 *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intramuscular

Vaccine Name: FMSIV *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intramuscular *Formulation:* FMSIV + pCMVmCAT1, pCMVN

Main Findings:

- SIV-specific CD4+ T cells and SIV-specific CD8+ T cells were efficiently induced in macaques vaccinated with FMSIV plus mCAT1 DNAs and levels of SIV-specific CD4+ T cells and SIV-specific CD8+ T cells in the group II macaques were significantly higher than those in the control group
- Macaques immunized with FMSIV plus pCMVmCAT1 had significantly higher levels of plasma anti-p27 antibodies than those in the control both at week 3 and week 8 after the initial vaccination

NHP.351 (14557642) **Multigene DNA priming-boosting vaccines protect macaques from acute CD4+-T-cell depletion after simian-human immunodeficiency virus SHIV89.6P mucosal challenge.**

Authors: Doria-Rose NA, Ohlen C, Polacino P, Pierce CC, Hensel MT, Kuller L, Mulvania T, Anderson D, Greenberg PD, Hu SL, Haigwood NL

Journal: J Virol 2003 Nov;77(21):11563-77.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

NHP.352 (14512560) **Microarray profiling of antibody responses against simian-human immunodeficiency virus: postchallenge convergence of reactivities independent of host histocompatibility type and vaccine regimen.**

Authors: Neuman de Vegvar HE, Amara RR, Steinman L, Utz PJ, Robinson HL, Robinson WH

Journal: J Virol 2003 Oct;77(20):11125-38.

NHP.353 (14505895) **Mucosal administration of three recombinant Mycobacterium bovis BCG-SIVmac251 strains to cynomolgus macaques induces rectal IgAs and boosts systemic cellular immune responses that are primed by intradermal vaccination.**

Authors: Mederle I, Le Grand R, Vaslin B, Badell E, Vingert B, Dormont D, Gicquel B, Winter N

Journal: Vaccine 2003 Oct 1;21(27-30):4153-66.

Objectives: Challenge, Immunogenicity. To investigate anti-SIV immune responses induced by intradermal vaccination of cynomolgus macaques with rBCG-SIV strains followed by a late mucosal booster dose.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: rBCG-SIV^3 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intrarectal, Oral, Intradermal

Challenge: SIVmac251 *Route:* Intrarectal

Main Findings:

- Intradermal immunization of cynomolgus macaques with a multi-component rBCG vaccine induces CTL responses targeted against 3 SIVmac251 antigens
- PBLs from rBCG-SIV3-immunized monkeys produce interferon-gamma in response to SIV antigens and production increases after the mucosal booster
- Anti-Gag IgAs are detected in rectal lavages of rBCG-SIV3-immunized monkeys only after the mucosal booster
- rBCG-SIV3 does not protect against a highly pathogenic SIVmac251 challenge despite

induction of anamnestic immune responses

NHP.354 (15096801) **Immunogenicity of HIV-1 Env and Gag in baboons using a DNA prime/boost regimen**

Authors: Leung L, Srivastava IK, Kan E, Legg H, Sun Y, Greer C, Montefiori DC, zur Megede J, Barnett SW

Journal: AIDS 2004 Apr 30;18(7):991-1001.

Objectives: Immunogenicity. To evaluate the immunogenicity of sequence-modified HIV env and gag in baboons using DNA prime and protein boost strategy.

Species/Subspecies: Papio cynocephalus (Baboon)

Vaccine Name: pCMV-gag-mod *Type:* DNA *Route:* Intramuscular *Formulation:* pCMV-gag-mod + MF59 + Saline

Vaccine Name: pCMVKm2-gp140mut *Type:* DNA *Route:* Intramuscular

Vaccine Name: CMVKm2-gp140TM *Type:* DNA *Route:* Intramuscular

Vaccine Name: o-gp140-US4 *Type:* Synthetic Protein/Peptide *Route:* Intramuscular *Formulation:* o-gp140-US4 + MF59

Vaccine Name: p55gagSF2 *Type:* DNA *Route:* Intramuscular

Vaccine Name: Chimp-anti-HIV-IgG *Type:* Passive Antibody *Route:* *Formulation:* Chimp-anti-HIV-IgG + MF59

Main Findings:

- Modest antibody responses and low or no lymphoproliferative responses were observed following multiple DNA immunizations
- Strong antibodies and substantial antigen-specific lymphoproliferative responses were seen following booster immunizations with oligomeric Env protein (o-gp140US4) in MF59
- Neutralizing antibody responses were scored against T cell line adapted HIV-1 strains after the protein boosters, but neutralizing responses were low or absent against homologous and heterologous primary isolate strains

NHP.361 (3413127) **Failure of a human immunodeficiency virus (HIV) immune globulin to protect chimpanzees against experimental challenge with HIV.**

Authors: Prince AM, Horowitz B, Baker L, Shulman RW, Ralph H, Valinsky J, Cundell A, Brotman B, Boehle W, Rey F, et al.

Journal: Proc Natl Acad Sci U S A 1988 Sep;85(18):6944-8.

Objectives: Challenge, Passive Immunization. To assess the possible efficacy of passive immunization against HIV using plasma from HIV seropositive donors.

Species/Subspecies: Pan Troglodytes (Chimpanzee)

Vaccine Name: HIVIG *Type:* Passive Antibody *Route:* Intravenous

Challenge: HIV-1 IIIB *Route:*

NHP.362 (1714748) **Immunization of chimpanzees with the HIV-1 glycoprotein gp160 induces long-lasting T-cell memory.**

Authors: Mannhalter JW, Pum M, Wolf HM, Kupcu Z, Barrett N, Dorner F, Eder G, Eibl MM

Journal: AIDS Res Hum Retroviruses 1991 May;7(5):485-93.

Objectives: Immunogenicity. To investigate the antigen-specific T-cell response to the recombinant HIV env gp160 and to test the effect of various adjuvant formulations on the efficiency of T-cell priming as well as on magnitude and longevity of the gp160-specific T-cell response.

Species/Subspecies: Pan Troglodytes (Chimpanzee)

Vaccine Name: rgp160 *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* rgp160 + Alum, Lipid-based Adjuvant

Main Findings:
- In combination with an appropriate adjuvant (lipid-based adjuvant or mineral carrier complex), immunization with recombinant gp160 led to the appearance of gp160-primed T cells
- The memory T-cell response toward the immunogen gp160 was substantial and long-lasting

NHP.363 (14963117) **Protection against mucosal simian immunodeficiency virus SIV(mac251) challenge by using replicating adenovirus-SIV multigene vaccine priming and subunit boosting.**

Authors: Patterson LJ, Malkevitch N, Venzon D, Pinczewski J, Gomez-Roman VR, Wang L, Kalyanaraman VS, Markham PD, Robey FA, Robert-Guroff M

Journal: J Virol 2004 Mar;78(5):2212-21.

Objectives: Challenge, Immunogenicity. To investigate a prime-boost strategy in macaques using priming with replicating adenovirus recombinants encoding SIV env/rev, gag, and/or nef genes, followed by boosting with SIV gp120 or an SIV polypeptide.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVIG-2 *Type:* Passive Antibody *Routes:* Intravenous, Intramuscular *Formulation:* SIVIG-2 + PBS

Vaccine Name: Ad5hr-SIVmac239gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Oral, Intranasal *Formulation:* Ad5hr-SIVmac239gag + Saline, PBS

Vaccine Name: Ad5hr-SIVnefδ1-13 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Oral, Intranasal *Formulation:* Ad5hr-SIVnefδ1-13 + PBS

Vaccine Name: Ad5hr-SIVsmH4 env/rev *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Oral, Intranasal

Vaccine Name: Mono-gp120H (89.6) *Type:* Recombinant Subunit Protein *Routes:* Intratracheal, Oral, Intramuscular, Intranasal *Formulation:* Mono-gp120H (89.6) + QS-21

Vaccine Name: HIV env_{MN}/rev(pCEnv) *Type:* DNA *Route:* Intramuscular *Formulation:* HIV env_{MN}/rev(pCEnv) + Bupivacaine, IL-2 in pCDNA3 + PBS

Vaccine Name: SIVmac251-gp120 *Type:* Purified Viral Products *Routes:* Intrarectal, Intramuscular, Intranasal *Formulation:* SIVmac251-gp120 + MPL-SE

Challenge: SIVmac251 *Route:* Intrarectal

Main Findings:
- Priming with replicating adenovirus recombinants encoding SIV env/rev, gag, and/or nef genes, followed by boosting with SIV gp120 or an SIV polypeptide mimicking the CD4 binding region of the envelope, protects rhesus macaques from intrarectal infection with the highly pathogenic SIV(mac251)
- Within immunization groups exhibiting significant protection, a subset (39%) of macaques have exhibited either no viremia, cleared viremia, or controlled viremia at the threshold of detection, now more than 40 weeks postchallenge
- Protection in macaques did not correlate with the Mamu A*01 allele

NHP.365 (14645581) **Intravenous inoculation of replication-deficient recombinant vaccinia virus DIs expressing simian immunodeficiency virus gag controls highly pathogenic simian-human immunodeficiency virus in monkeys.**

Authors: Izumi Y, Ami Y, Matsuo K, Someya K, Sata T, Yamamoto N, Honda M

Journal: J Virol 2003 Dec;77(24):13248-56.

Objectives: Challenge, Immunogenicity. To assess the immunogenicity and protection induced by immunization with rDIsSIVgag.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: Vaccinia-rDIsSIVgag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intravenous

Challenge: SHIV-C2/1 *Route:* Intravenous

Main Findings:
- Intravenous inoculation of 10^6 PFU of rDIsSIVGag in cynomologus macaques induced significant levels of gamma interferon (IFN-gamma) spot-forming cells (SFC) specific for SIV Gag
- Antigen-specific lymphocyte proliferative responses were also induced and were temporally associated with the peak of IFN-gamma SFC activity in each macaque
- CD4(+) T lymphocytes were maintained in the peripheral blood and lymphoid tissues of the immunized macaques after challenge with pathogenic SHIV

NHP.366 (15004179) **Control of Simian/Human Immunodeficiency Virus Viremia and Disease Progression after IL-2-Augmented DNA-Modified Vaccinia Virus Ankara Nasal Vaccination in Nonhuman Primates.**

Authors: Bertley FM, Kozlowski PA, Wang SW, Chappelle J, Patel J, Sonuyi O, Mazzara G, Montefiori D, Carville A, Mansfield KG, Aldovini A

Journal: J Immunol 2004 Mar 15;172(6):3745-3757.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pVacc4 DNA *Type:* DNA *Route:* Intranasal *Formulation:* pVacc4 DNA + IL-2/lg plasmid, IL-12 DNA + Saline

Vaccine Name: rMVA.SIVmac239gagpolHIVenv *Type:* Recombinant Vector (virus/bacteria) *Route:* Intranasal

Challenge: SHIV89.6P *Route:* Intranasal

Main Findings:
- The vaccine and challenge induced humoral responses, by the detection of both binding and neutralizing SHIV-specific IgG in plasma, and SHIV-specific IgA in rectal secretions
- After rectal challenge of vaccinated and naive animals with SHIV89.6P, all animals became infected. However a subset of animals was protected from CD4+ T cell loss and AIDS development
- SHIV DNA/MVA vaccine administered nasally can stimulate rectal antiviral IgA but was not effective at inducing antiviral systemic IgG
- IL-2/Ig or IL-12 DNA and the rMVA added to the vaccination did not result in significant differences in these humoral immune responses

NHP.367 (15003872) **Priming B cell-mediated anti-HIV envelope responses by vaccination allows for the long-term control of infection in macaques exposed to a R5-tropic SHIV.**

Authors: Buckner C, Gines LG, Saunders CJ, Vojtech L, Srivastava I, Gettie A, Bohm R, Blanchard J, Barnett SW, Safrit JT, Stamatatos L

Journal: Virology 2004 Mar 1;320(1):167-80.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- Antibodies elicited by the SF162gp140 immunogen recognize elements of the V1, V2, and V3 loops, the CD4-binding site, and the C1 and C2 regions on the homologous SF162 gp120
- Deletion of the V2 has a two-fold effect: 1) it alters the immunogenicity of the V3 and V1 loops, and 2) it renders the C5 region immunogenic
- Sterilizing immunity was not achieved
- All vaccinated animals effectively controlled and remained free of disease over 3 years of observation

NHP.368 (14980480) **Functional simian immunodeficiency virus Gag-specific CD8+ intraepithelial lymphocytes in**

the mucosae of SIVmac251- or simian-human immunodeficiency virus KU2-infected macaques.

Authors: Stevceva L, Moniuszko M, Alvarez X, Lackner AA, Franchini G

Journal: Virology 2004 Feb 20;319(2):190-200.

Objectives: Immunogenicity.

NHP.369 (14610180) **Simian-human immunodeficiency virus escape from cytotoxic T-lymphocyte recognition at a structurally constrained epitope.**

Authors: Peyerl FW, Barouch DH, Yeh WW, Bazick HS, Kunstman J, Kunstman KJ, Wolinsky SM, Letvin NL

Journal: J Virol 2003 Dec;77(23):12572-8.

NHP.370 (14550583) **Enhanced immunogenicity of SIV Gag DNA vaccines encoding chimeric proteins containing a C-terminal segment of Listeriolysin O.**

Authors: Ye L, Bu Z, Skeen MJ, Ziegler HK, Compans RW, Yang C

Journal: Virus Res 2003 Nov;97(1):7-16.

Objectives: Immunogenicity. Investigation of the potential of the C-terminal 59-amino acid segment of Listeriolysin O (LLO) in enhancing immune responses against the SIV Gag antigen in the context of DNA immunization.

NHP.371 (15018712) **Evaluation of combination DNA/replication-competent Ad-SIV recombinant immunization regimens in rhesus macaques.**

Authors: Malkevitch N, Rohne D, Pinczewski J, Aldrich K, Kalyanaraman VS, Letvin NL, Robert-Guroff M

Journal: AIDS Res Hum Retroviruses 2004 Feb;20(2):235-44.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Ad5hr-SIVsmH4 env/rev *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Oral, Intranasal

Vaccine Name: pCMV/SIVsmH4/rev-gp160 *Type:* DNA *Route:* Intradermal

Vaccine Name: HIV-1 IIIB gp120 *Type:* Purified Viral Products *Route:* Intramuscular *Formulation:* HIV-1 IIIB gp120 + QS-21

NHP.372 (14722263) **Simian immunodeficiency virus promoter exchange results in a highly attenuated strain that protects against uncloned challenge virus.**

Authors: Blancou P, Chenciner N, Ho Tsong Fang R, Monceaux V, Cumont MC, Guetard D, Hurtrel B, Wain-Hobson S

Journal: J Virol 2004 Feb;78(3):1080-92.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

NHP.373 (14593121) **High attenuation and immunogenicity of a simian immunodeficiency virus expressing a proteolysis-resistant inhibitor of NF-kappaB.**

Authors: Quinto I, Puca A, Greenhouse J, Silvera P, Yalley-Ogunro J, Lewis MG, Palmieri C, Trimboli F, Byrum R, Adelsberger J, Venzon D, Chen X, Scala G

Journal: J Biol Chem 2004 Jan 16;279(3):1720-8. Epub 2003 Oct 30.

NHP.374 (15016855) **Qualitative T-helper responses to multiple viral antigens correlate with vaccine-induced immunity to simian/human immunodeficiency virus infection.**

Authors: Mooij P, Nieuwenhuis IG, Knoop CJ, Doms RW, Bogers WM, Ten Haaft PJ, Niphuis H, Koornstra W, Bieler K, Kostler J, Morein B, Cafaro A, Ensoli B, Wagner R, Heeney JL

Journal: J Virol 2004 Apr;78(7):3333-42.

Objectives: Challenge, Immunogenicity. To determine whether immunization with multiple antigens can influence individual Th responses and increase protection relative to a single antigen.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pc-synTat (HIV-1IIIB) *Type:* DNA *Route:* Intramuscular

Vaccine Name: pc-syngp120 (SHIV-189.6p) *Type:* DNA *Route:* Intramuscular

Vaccine Name: pc-synGag (SIVmac239) *Type:* DNA *Route:* Intramuscular

Vaccine Name: HIV-189.6 Env gp140-ISCOM *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* HIV-189.6 Env gp140-ISCOM + ISCOM(s)™

Vaccine Name: SIVmac239 Gag-Pol-ISCOM *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* SIVmac239 Gag-Pol-ISCOM + ISCOM(s)™

Vaccine Name: tat protein *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* tat protein + ISCOM(s)™

Challenge: SHIV89.6P *Route:* Intravenous

NHP.375 (15047809) **Highly effective control of an AIDS virus challenge in macaques by using vesicular stomatitis virus and modified vaccinia virus Ankara vaccine vectors in a single-boost protocol.**

Authors: Ramsburg E, Rose NF, Marx PA, Mefford M, Nixon DF, Moretto WJ, Montefiori D, Earl P, Moss B, Rose JK

Journal: J Virol 2004 Apr;78(8):3930-40.

Objectives: Challenge, Immunogenicity. To compare the effectiveness of single prime-boost protocol consisting of VSV vectors expressing SHIV Env, Gag, and Pol proteins to that of VSV vector prime followed with a single boost with MVA expressing the same SHIV proteins.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

NHP.376 (15047820) **Induction of autoantibodies to CCR5 in macaques and subsequent effects upon challenge with an R5-tropic simian/human immunodeficiency virus.**

Authors: Chackerian B, Briglio L, Albert PS, Lowy DR, Schiller JT

Journal: J Virol 2004 Apr;78(8):4037-47.

Objectives: Challenge, Immunogenicity. To generate autoantibodies against CCR5 in macaques and to assess their role in protection from challenge with R5-tropic SHIV

Main Findings:

- 5 rhesus macaques injected with VLP-SA-EC1 developed antibodies against CCR5. IV challenge with SHIV resulted in infection, but some ability to control viremia.

NHP.377 (15140996) **Passive immunotherapy in simian immunodeficiency virus-infected macaques accelerates the development of neutralizing antibodies.**

Authors: Haigwood NL, Montefiori DC, Sutton WF, McClure J, Watson AJ, Voss G, Hirsch VM, Richardson BA, Letvin NL, Hu SL, Johnson PR

Journal: J Virol 2004 Jun;78(11):5983-95.

Objectives: Challenge, Passive immunotherapy.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVIG *Type:* Passive Antibody *Route:* Intravenous

Challenge: SIVsmE660 *Route:* Intravenous

Main Findings:
- SIVIG treatment significantly delayed disease
- Virus levels in PBMC and plasma predict disease outcome
- Gag-specific CTLs were detected in macaques surviving beyond 1 year
- Infused IgG delayed binding antibody and accelerated NAb production

NHP.378 (15149785) **Human immunodeficiency virus type 2 DNA vaccine provides partial protection from acute baboon infection.**

Authors: Locher CP, Witt SA, Ashlock BM, Polacino P, Hu SL, Shiboski S, Schmidt AM, Agy MB, Anderson DM, Staprans SI, Megede Jz J, Levy JA

Journal: Vaccine 2004 Jun 2;22(17-18):2261-72.

Objectives: Challenge, Immunogenicity. To determine if GM-CSF and B7-2 could boost immune responses to an HIV-2 DNA vaccine and help protect baboons against HIV-2 challenge by the intravaginal route

Species/Subspecies: Papio cynocephalus (Baboon)

Vaccine Name: HIV-2UC2.tat.nef.gag *Type:* DNA *Routes:* Intradermal, Intramuscular, Intranasal *Formulation:* HIV-2UC2.tat.nef.gag + B7-2

Challenge: HIV-2 (UC2-9429) *Route:* Vaginal or perivaginal

Main Findings:
- Baboons immunized with HIV-2 DNA vaccine with or without the genetic adjuvants had significant reductions in the viral loads in the peripheral blood mononuclear cells (PBMC) following challenge (P=0.028) while the reductions in their plasma viremia were suggestive of a protective effect (P=0.1)
- Partial protection against HIV-2 vaginal challenge, as measured by reduced viral load, can be achieved using only a DNA vaccine formulation

NHP.379 (15193413) **Enhancement of DNA vaccine potency in rhesus macaques by electroporation.**

Authors: Otten G, Schaefer M, Doe B, Liu H, Srivastava I, Megede Jz J, O'Hagan D, Donnelly J, Widera G, Rabussay D, Lewis MG, Barnett S, Ulmer JB

Journal: Vaccine 2004 Jun 23;22(19):2489-93.

NHP.380 (12551968) **Changes in the immunogenic properties of soluble gp140 human immunodeficiency virus envelope constructs upon partial deletion of the second hypervariable region.**

Authors: Srivastava IK, VanDorsten K, Vojtech L, Barnett SW, Stamatatos L

Journal: J Virol 2003 Feb;77(4):2310-20.

Objectives: Immunogenicity. To identify the envelope regions whose immunogenicity is altered following V2 loop deletion.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- Antibodies elicited by the SF162gp140 immunogen recognize elements of the V1, V2, and V3 loops, the CD4-binding site, and the C1 and C2 regions on the homologous SF162 gp120
- Deletion of the V2 has a two-fold effect: 1) it alters the immunogenicity of the V3 and V1 loops, and 2) it renders the C5 region immunogenic

NHP.381 (15220422) **Heterologous envelope immunogens contribute to AIDS vaccine protection in rhesus monkeys.**

Authors: Letvin NL, Huang Y, Chakrabarti BK, Xu L, Seaman MS, Beaudry K, Korioth-Schmitz B, Yu F, Rohne D, Martin KL, Miura A, Kong WP, Yang ZY, Gelman RS, Golubeva OG, Montefiori DC, Mascola JR, Nabel GJ

Journal: J Virol 2004 Jul;78(14):7490-7.

Objectives: Challenge, Immunogenicity. To evaluate a plasmid DNA prime-recombinant replication-defective adenovirus (ADV) boost immunization strategy for an HIV vaccine.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac239 gag-pol-nef *Type:* DNA *Route:* Intramuscular *Formulation:* SIVmac239 gag-pol-nef + PBS

Vaccine Name: rAd5-SIVmac239 gag/pol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd5-SIVmac239 gag/pol + PBS

Vaccine Name: gp145 DCFI 89.6P Env *Type:* DNA *Route:* Intramuscular *Formulation:* gp145 DCFI 89.6P Env + PBS

Vaccine Name: rAd-HxB2/BaL Env DCFI *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd-HxB2/BaL Env DCFI + PBS

Vaccine Name: gp140 DCFI (HxB2/BaL) Env *Type:* DNA *Route:* Intramuscular *Formulation:* gp140 DCFI (HxB2/BaL) Env + PBS

Vaccine Name: rAd5 89.6P Env (DCFI) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd5 89.6P Env (DCFI) + PBS

Challenge: SHIV89.6P *Route:* Intravenous

Main Findings:

- Vaccine regimens Gag-Pol-Nef immunogens that included the matched or mismatched Env immunogens conferred better protection against CD4+ T-lymphocyte loss than that seen with comparable regimens that did not include Env immunogens
- T-lymphocyte immunity to Env can broaden the protective cellular immune response to HIV despite significant sequence diversity of the strains of the Env immunogens and can contribute to immune protection in this AIDS vaccine model
- The control group had significantly higher peak viral loads than the vaccinated monkeys. However, the 3 groups of experimentally vaccinated monkeys did not differ significantly in their peak viral loads (P = 0.28, Kruskal-Wallis test)

NHP.382 (15210746) **Cytotoxic T Lymphocyte-based Control of Simian Immunodeficiency Virus Replication in a Preclinical AIDS Vaccine Trial.**

Authors: Matano T, Kobayashi M, Igarashi H, Takeda A, Nakamura H, Kano M, Sugimoto C, Mori K, Iida A, Hirata T, Hasegawa M, Yuasa T, Miyazawa M, Takahashi Y, Yasunami M, Kimura A, O'Connor DH, Watkins DI, Nagai Y

Journal: J Exp Med 2004 Jun 21;199(12):1709-18.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- 5/8 vaccinees controlled viral replication and had undetectable plasma viremia after 5 weeks of infection
- 5/8 macaques rapidly selected for CTL escape mutations in Gag, indicating that vaccine-induced CTLs successfully contained replication of the challenge virus
- Vaccine induction of highly effective CTLs can result in the containment of replication of a highly pathogenic immunodeficiency virus

NHP.384 (15242543) **Multiprotein HIV type 1 clade B DNA/MVA vaccine: construction, safety, and immunogenicity in Macaques.**

Authors: Smith JM, Amara RR, McClure HM, Patel M, Sharma S, Yi H, Chennareddi L, Herndon JG, Butera ST, Heneine W, Ellenberger DL, Parekh B, Earl PL, Wyatt LS, Moss B, Robinson HL

Journal: AIDS Res Hum Retroviruses 2004 Jun;20(6):654-65.

Objectives: Immunogenicity. To construct and test a Gag-Pol-Env DNA/MVA vaccine.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pGA2/JS2-HIV-1.gag.pol.env *Type:* DNA *Route:* Intramuscular

Vaccine Name: MVA/HIV 48 *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Main Findings:

- The vaccine constructs contain the gag region derived from HIV-1 HXB2 and do not include the zinc finger mutations found in pGA2/JS2; pol was from pGA2/JS2 including the RT mutations
- Safety: by abrogating reverse transcription, inactivating RNase H activity and strand transfer activity, Env gene was expression-deffective
- Safety: No adverse effects of the inoculations on the vaccinated monkeys
- Vaccine-elicited cellular as well as humoral immunity
- Vaccine-elicited T cells were at, or below, the level of detection following the DNA primes, rapidly expanded after the rMVA booster and then contracted into memory
- CD4 and CD8 epitopes are found throughout Gag and Env inserts of the vaccine
- The immunizations elicited only low levels of raised antibody

NHP.385 (9557706) **Recombinant vaccine-induced protection against the highly pathogenic simian immunodeficiency virus SIV(mac251): dependence on route of challenge exposure.**

Authors: Benson J, Chougnet C, Robert-Guroff M, Montefiori D, Markham P, Shearer G, Gallo RC, Cranage M, Paoletti E, Limbach K, Venzon D, Tartaglia J, Franchini G

Journal: J Virol 1998 May;72(5):4170-82.

Objectives: Challenge.

Main Findings:

- Vaccination with NYVAC-SIV-gpe carrying SIV-Mac-251 gag pol and env protected against intrarectal, but not intravenous infection with SIV-Mac-251, as determined by culture of virus. Viral loads were lower in vaccinated-infected than in non-vaccinated controls.

NHP.386 (15113931) **Induction of disease by a molecularly cloned highly pathogenic simian immunodeficiency virus/human immunodeficiency virus chimera is multigenic.**

Authors: Sadjadpour R, Theodore TS, Igarashi T, Donau OK, Plishka RJ, Buckler-White A, Martin MA

Journal: J Virol 2004 May;78(10):5513-9.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Challenge: SHIV-DH12clone7, SHIV-DH12clone8 *Route:* Intravenous

Main Findings:

- $SHIV_{DH12R\text{-}CLone7}$ induces rapid CD4 decline in rhesus macaques whereas the $SHIV_{DH12R}$ parental clone does not. Substitution of the clone 7 env into the nonpathogenic parental background did not confer pathogenicity. Amino acid changes in multiple genes were required for pathogenic effect.

NHP.387 (10570196) **Emergence of a highly pathogenic simian/human immunodeficiency virus in a rhesus macaque treated with anti-CD8 mAb during a primary infection with a nonpathogenic virus.**

Authors: Igarashi T, Endo Y, Englund G, Sadjadpour R, Matano T, Buckler C, Buckler-White A, Plishka R, Theodore T, Shibata R, Martin M

Journal: Proc Natl Acad Sci U S A 1999 Nov 23;96(24):14049-54.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Challenge: SHIV-MD14YE (DH12) *Route:* Intravenous

Main Findings:

- Mutations in many genes resulted in increased pathogenicity of the SHIV-DH12R clone.

NHP.388 (11861859) **Evolution of a human immunodeficiency virus type 1 variant with enhanced replication in pig-tailed macaque cells by DNA shuffling.**

Authors: Pekrun K, Shibata R, Igarashi T, Reed M, Sheppard L, Patten PA, Stemmer WP, Martin MA, Soong NW

Journal: J Virol 2002 Mar;76(6):2924-35.

Objectives: Pathogenicity.

Main Findings:

- A SHIV composed primarily of HIV-1 sequences with a SIV-Mac239 YE version of Nef was created and passaged to achieve a molecular clone that replicates in pig-tailed macaque PBMCs and can infect macaques. SIVMD17 accession number AF465242.

NHP.389 (9237701) **Infection and pathogenicity of chimeric simian-human immunodeficiency viruses in macaques: determinants of high virus loads and CD4 cell killing.**

Authors: Shibata R, Maldarelli F, Siemon C, Matano T, Parta M, Miller G, Fredrickson T, Martin MA

Journal: J Infect Dis 1997 Aug;176(2):362-73.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque), Macaca nemestrina (pigtailed macaque)

Challenge: SHIV-MD14YE (DH12), SHIV.MD1 *Route:* Intravenous

Main Findings:

- $SHIV_{MD1}$ carrying HIV-1 subtype B sequences from clones pNL43 (vpr) and DH12 (tat-nef) in a SIV_{Mac239} background, produced slower CD4+ T-cell decline in pig-tailed macaques than $SHIV_{MD14YE}$ in which the HIV-1 nef in $SHIV_{MD1}$ was replaced by SIV_{Mac239} nef with R17Y plus Q18E mutations.
- The nef with R17Y plus Q18E mutations had previously been shown to be determinants of pathogenicity in the SIV_{SMM9} to SIV_{PBJ14} series of viruses.

NHP.390 (8648760) **Requirements for lymphocyte activation by unusual strains of simian immunodeficiency virus.**

Authors: Du Z, Ilyinskii PO, Sasseville VG, Newstein M, Lackner AA, Desrosiers RC

Journal: J Virol 1996 Jun;70(6):4157-61.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- A single amino acid change in Nef R17Y was shown to be sufficient to confer pathogenicity to non-activated macaque T-cells in SIV_{Mac239} and that conversely, Y17R reversion in SIV_{PBJ14} eliminated the lymphocyteactivation phenotype of that highly pathogenic clone.
- YXXLXXXXXXXYXXL SH2-binding ITAM motif is created by R17Y mutation and abolished by Y28F mutation.

NHP.391 (10888632) **Short- and long-term clinical outcomes in rhesus monkeys inoculated with a highly pathogenic chimeric simian/human immunodeficiency virus.**

Authors: Endo Y, Igarashi T, Nishimura Y, Buckler C, Buckler-White A, Plishka R, Dimitrov DS, Martin MA

Journal: J Virol 2000 Aug;74(15):6935-45.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Challenge: SHIV.DH12R-PS1 *Route:* Intrarectal, Intravenous, Vaginal or perivaginal

Main Findings:

- $SHIV_{DH12R}$, derived from $SHIV_{MD14YE}$ by passage in rhesus macaque, induces CD4+ T-cell loss in rhesus macaques in a dose-dependent manner. The DH12R inoculum was uncloned, and higher doses apparently allow more antibody neutralization escape variants to survive.

NHP.392 (7769705) **Isolation and characterization of a syncytium-inducing, macrophage/T-cell line-tropic human immunodeficiency virus type 1 isolate that readily infects chimpanzee cells in vitro and in vivo.**

Authors: Shibata R, Hoggan MD, Broscius C, Englund G, Theodore TS, Buckler-White A, Arthur LO, Israel

Z, Schultz A, Lane HC, et al.

Journal: J Virol 1995 Jul;69(7):4453-62.

Objectives: Pathogenicity.

Species/Subspecies: Pan Troglodytes (Chimpanzee)

Challenge: HIV-1.DH12 *Route:* Intravenous

Main Findings:

- Of 23 different HIV-1 isolates tested, only one (DH12) was able to initiate infections in all chimpanzee PBMC cultures tested. The DH12 isolate was innoculated into three chimpanzees and was able to establish a robust infection with symptoms including lymphadenopathy and rashes.
- All DH12 clones sequenced had defective vpu genes, although the GenBank entry for the complete genome AF069140 was submitted with the ATA defective start codon corrected to ATG.

NHP.393 (7769705) **Isolation and characterization of a syncytium-inducing, macrophage/T-cell line-tropic human immunodeficiency virus type 1 isolate that readily infects chimpanzee cells in vitro and in vivo.**

Authors: Shibata R, Hoggan MD, Broscius C, Englund G, Theodore TS, Buckler-White A, Arthur LO, Israel Z, Schultz A, Lane HC, et al.

Journal: J Virol 1995 Jul;69(7):4453-62.

NHP.394 (11836389) **Determination of a statistically valid neutralization titer in plasma that confers protection against simian-human immunodeficiency virus challenge following passive transfer of high-titered neutralizing antibodies.**

Authors: Nishimura Y, Igarashi T, Haigwood N, Sadjadpour R, Plishka RJ, Buckler-White A, Shibata R, Martin MA

Journal: J Virol 2002 Mar;76(5):2123-30.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Vaccine Name: Chimp-anti-HIV-IgG *Type:* Passive Antibody *Route:* Intravenous *Formulation:* Chimp-anti-HIV-IgG + MF59

Challenge: SHIV.MD1 *Route:* Intravenous

Main Findings:

- Neutralizing antibodies from a chimpanzee infected with HIV-1 isolate DH12 can protect macaques from a SHIV containing the DH12 envelope gene. The recipient serum titre needed to protect 99% of macaques from 75 TCID50 IV inoculation was calculated to be 1:38.

NHP.395 (15356916) **CCR5 targeted SIV vaccination strategy preventing or inhibiting SIV infection.**

Authors: Bogers WM, Bergmeier LA, Oostermeijer H, ten Haaft P, Wang Y, Kelly CG, Singh M, Heeney JL, Lehner T

Journal: Vaccine 2004 Aug 13;22(23-24):2974-84.

Objectives: Challenge, Immunogenicity. To attempt to prevent SIV infection by (a) upregulating the three CC chemokines, (b) eliciting antibodies to CCR5 and (c) downmodulating the cell-surface expression of CCR5.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: HSP70-Baculovirus-infected cells.gp120-pGEX-3X.p27 *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* HSP70-Baculovirus-infected cells.gp120-pGEX-3X.p27 + CCR5 peptides

Challenge: SIVmac8980 *Route:* Intramuscular

Main Findings:

- Immunization with protein (HSP70) covalently linked to the CCR5 peptides, SIV gp120

and p27 protected rhesus monkeys from infection after challenge with SIVmac8980.

NHP.396 (15452269) **Heterologous human immunodeficiency virus type 1 priming-boosting immunization strategies involving replication-defective adenovirus and poxvirus vaccine vectors.**

Authors: Casimiro DR, Bett AJ, Fu TM, Davies ME, Tang A, Wilson KA, Chen M, Long R, McKelvey T, Chastain M, Gurunathan S, Tartaglia J, Emini EA, Shiver J

Journal: J Virol 2004 Oct;78(20):11434-8.

Objectives: Immunogenicity. To assess the ability of poxvirus vectors to boost Ad5-primed responses as a means of enhancing the levels of vaccine-elicited responses.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- Heterologous Ad5 priming-poxvirus boosting regimen induced a significantly greater immune response in rhesus monkeys than immunization elicited by homologous prime-boost regimens with the individual vectors or by a heterologous poxvirus priming-Ad5 boosting regimen

NHP.397 (15302953) **Macaques infected long-term with attenuated simian immunodeficiency virus (SIVmac) remain resistant to wild-type challenge, despite declining cytotoxic T lymphocyte responses to an immunodominant epitope.**

Authors: Sharpe SA, Cope A, Dowall S, Berry N, Ham C, Heeney JL, Hopkins D, Easterbrook L, Dennis M, Almond N, Cranage M

Journal: J Gen Virol 2004 Sep;85(Pt 9):2591-602.

Objectives: Challenge, Immunogenicity. To investigate mechanisms of protective immunity induced by live, attenuated SIV

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIV.GX2 *Type:* Live Attenuated Virus *Route:*

Challenge: SIVmac220 *Route:* Intravenous

Main Findings:

- 3 macaques immunized with live attenuated SIVmacGX2 were resistant to challenge with an uncloned pool of wild-type SIVmac220, whereas four naive controls became infected
- Both attenuated (vaccine) and wild-type (challenge) viruses induced a disseminated CD8+ T-cell response, which was of a higher magnitude in lymphoid tissues than in the periphery.

NHP.398 (9732063) **Rhesus macaques that become systemically infected with pathogenic SHIV 89.6-PD after intravenous, rectal, or vaginal inoculation and fail to make an antiviral antibody response rapidly develop AIDS.**

Authors: Lu Y, Pauza CD, Lu X, Montefiori DC, Miller CJ

Journal: J Acquir Immune Defic Syndr Hum Retrovirol 1998 Sep 1;19(1):6-18.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Challenge: SHIV89.6PD *Route:* Intrarectal, Intravenous, Vaginal or perivaginal

Main Findings:

- The pathogenicity of an uncloned stock of SHIV-89.6P was tested in 12 rhesus macaques. Two were injected IV, 6 were innoculated intravaginally, and 4 were innoculated intrarectally. Intraveinous inoculation resulted in peak viremia in 7 days vs 14 days for mucosal inoculation.

NHP.399 (12163269) **A novel chimeric Rev, Tat, and Nef (Retanef) antigen as a component of an SIV/HIV vaccine.**

Authors: Hel Z, Johnson JM, Tryniszewska E, Tsai WP, Harrod R, Fullen J, Tartaglia J, Franchini G

Journal: Vaccine 2002 Aug 19;20(25-26):3171-86.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- Retanef is a synthetic open reading frame encoding epitopes from Rev, Tat and Nef proteins. Inserted into the NYVAC vaccinia virus vector, and injected into naive macaques, it induced CTL responses. It also boosted responses 2 to 7-fold in previously infected macaques undergoing HAART.

NHP.400 (15258286) **Recombinant poxvirus boosting of DNA-primed rhesus monkeys augments peak but not memory T lymphocyte responses.**

Authors: Santra S, Barouch DH, Korioth-Schmitz B, Lord CI, Krivulka GR, Yu F, Beddall MH, Gorgone DA, Lifton MA, Miura A, Philippon V, Manson K, Markham PD, Parrish J, Kuroda MJ, Schmitz JE, Gelman RS, Shiver JW, Montefiori DC, Panicali D, Letvin NL

Journal: Proc Natl Acad Sci U S A 2004 Jul 27;101(30):11088-93. Epub 2004 Jul 16.

Objectives: Challenge, Immunogenicity. To assess the relative immunogenicity including a CTL response of vaccine regimens that included a cytokine-augmented plasmid DNA prime and a boost with DNA or recombinant pox vectors.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: HIV-1 89.6P Env gp140 (KB9) DNA *Type:* DNA *Route:* Intramuscular

Vaccine Name: SIV mac239 Gag DNA *Type:* DNA *Route:* Intramuscular

Vaccine Name: Recombinant fowlpox (rFPV).SHIV89.6P env *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular

Vaccine Name: Recombinant fowlpox (rFPV) SIVmac239 gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular

Vaccine Name: Recombinant MVA-SHIV89.6P env *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular

Vaccine Name: Recombinant MVA-SIVmac239 gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular

Vaccine Name: Recombinant vaccinia virus (rVac).SHIV89.6P Env *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular

Vaccine Name: Recombinant vaccinia virus (rVac).SIVmac239 gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular

Challenge: SHIV89.6P *Route:* Intravenous

Main Findings:
- Recombinant vaccinia virus, recombinant modified vaccinia Ankara (MVA), and recombinant fowlpox were comparable in their immunogenicity
- Whereas the magnitude of the peak vaccine-elicited T lymphocyte responses in the recombinant pox virus-boosted monkeys was substantially greater than that seen in the monkeys immunized with plasmid DNA alone, the magnitudes of recombinant pox boosted CTL responses decayed rapidly and were comparable to those of the DNA-alone-vaccinated monkeys by the time of viral challenge
- The memory T cell responses for the three vaccines were comparable
- Protection from clinical disease in all groups of experimentally vaccinated monkeys was similar
- The steady-state memory, rather than the peak effector vaccine-elicited T lymphocyte responses, may be the critical immune correlate of protection for a CTL-based HIV vaccine.

NHP.401 (15269383) **Enhanced cellular immunity and systemic control of SHIV infection by combined parenteral and mucosal administration of a DNA prime MVA boost vaccine regimen.**

Authors: Makitalo B, Lundholm P, Hinkula J, Nilsson C, Karlen K, Morner A, Sutter G, Erfle V, Heeney JL,

Wahren B, Biberfeld G, Thorstensson R

Journal: J Gen Virol 2004 Aug;85(Pt 8):2407-19.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: rMVA-tat,rev,nef *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intrarectal, Oral, Intramuscular *Formulation:* rMVA-tat,rev,nef + PBS

Vaccine Name: rVac-HIV1gp120 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intrarectal, Oral, Intramuscular *Formulation:* rVac-HIV1gp120 + PBS

Vaccine Name: HIV1-nef *Type:* DNA *Routes:* Intrarectal, Oral, Intramuscular *Formulation:* HIV1-nef + GM-CSF + PBS

Vaccine Name: HIV1-tat *Type:* DNA *Routes:* Intrarectal, Oral, Intramuscular *Formulation:* HIV1-tat + GM-CSF + PBS

Vaccine Name: HIV1-rev *Type:* DNA *Routes:* Intrarectal, Oral, Intramuscular *Formulation:* HIV1-rev + GM-CSF + PBS

Vaccine Name: HIV1-RT *Type:* DNA *Routes:* Intrarectal, Oral, Intramuscular *Formulation:* HIV1-RT + GM-CSF + PBS

Vaccine Name: HIV1-gag *Type:* DNA *Routes:* Intrarectal, Oral, Intramuscular *Formulation:* HIV1-gag + GM-CSF + PBS

Vaccine Name: HIV1-gp160 *Type:* DNA *Routes:* Intrarectal, Oral, Intramuscular *Formulation:* HIV1-gp160 + GM-CSF + PBS

Vaccine Name: MVA-SIVmacJ5 (gag-pol) *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intrarectal, Oral, Intramuscular *Formulation:* MVA-SIVmacJ5 (gag-pol) + PBS

Challenge: SHIV-4 *Route:* Intravenous

Main Findings:

- The immunogenicity and protective efficacy of a DNA and recombinant modified vaccinia Ankara (MVA) vaccine administered by two different routes were investigated. DNA expressing HIV-1 IIIB env, gag, RT, rev, tat and nef, and MVA expressing HIV-1 IIIB nef, tat and rev and simian immunodeficiency virus (SIV) macJ5 gag/pol and vaccinia HIV-1 env, were used as immunogens. Four cynomolgus macaques received DNA intramuscularly (i.m.) at month 0 and intrarectally (i.r.) and intra-orally (i.o.) at 2 months, followed by MVA i.m. at 4 months and i.r. and i.o. at 8 months. Another group of four monkeys received the same immunogens but only i.m. Overall, stronger cellular immune responses measured by ELISPOT and T-cell proliferation assay were detected in the group primed i.m. and boosted mucosally. Following homologous intravenous simian-human immunodeficiency virus (SHIV) challenge, one of eight vaccinated animals was completely protected. Four weeks post-challenge none of the monkeys immunized i.m. and i.r.+i.o., and only two out of four animals immunized i.m., demonstrated detectable plasma viral RNA levels. Thus, stronger cellular immune responses and reduction of challenge virus burden were demonstrated in animals immunized i.m. as well as mucosally, compared with animals immunized i.m. only.

NHP.402 (15308348) **Long-term protection against SHIV89.6P replication in HIV-1 Tat vaccinated cynomolgus monkeys.**

Authors: Maggiorella MT, Baroncelli S, Michelini Z, Fanales-Belasio E, Moretti S, Sernicola L, Cara A, Negri DR, Butto S, Fiorelli V, Tripiciano A, Scoglio A, Caputo A, Borsetti A, Ridolfi B, Bona R, ten Haaft P, Macchia I, Leone P, Pavone-Cossut MR, Nappi F, Ciccozzi M, Heeney J, Titti F, Cafaro A, Ensoli B

Journal: Vaccine 2004 Sep 3;22(25-26):3258-69.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: pCV-tat *Type:* DNA *Routes:* Intradermal, Intramuscular *Formulation:* pCV-tat + Bupivacaine,

p-Hydroxybenzoique acid methyl ester + Saline, PBS

Vaccine Name: tat protein *Type:* Recombinant Subunit Protein *Routes:* Subcutaneous, Intradermal, Intramuscular *Formulation:* tat protein + Alum, ISCOM(s)™, RIBI + Saline

Vaccine Name: Tat-ISCOM *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* Tat-ISCOM + PBS

Challenge: SHIV89.6P *Route:* Intravenous

Main Findings:

- Vaccination with a biologically active Tat protein or tat DNA contained infection up to week 104 after challenge with the highly pathogenic SHIV89.6P virus, preventing CD4 T-cell decline and disease onset. In contrast, virus persisted and replicated in peripheral blood mononuclear cells and lymph nodes of infected animals, two of which died. Tat-specific antibody, CD4 and CD8 T-cell responses were high and stable only in the animals controlling the infection. In contrast, Gag-specific antibody production and CD4 and CD8 T-cell responses were consistently and persistently positive only in the monkeys that did not control primary virus replication. These results indicate that vaccination with Tat protein or DNA induced long-term memory Tat-specific immune responses and controlled primary infection at its early stages allowing a long-term containment of virus replication and spread in blood and tissues.

NHP.403 (15105535) **Protective efficacy of a multicomponent vector vaccine in cynomolgus monkeys after intrarectal simian immunodeficiency virus challenge.**

Authors: Negri DR, Baroncelli S, Catone S, Comini A, Michelini Z, Maggiorella MT, Sernicola L, Crostarosa F, Belli R, Mancini MG, Farcomeni S, Fagrouch Z, Ciccozzi M, Boros S, Liljestrom P, Norley S, Heeney J, Titti F

Journal: J Gen Virol 2004 May;85(Pt 5):1191-201.

Objectives: Challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIV-MAC251 plasmid DNA cocktail *Type:* DNA *Route:* Intradermal *Formulation:* SIV-MAC251 plasmid DNA cocktail + Saline

Vaccine Name: rSFV-cocktail *Type:* Live Virus *Route:* Subcutaneous *Formulation:* rSFV-cocktail + Saline

Main Findings:

- A systemic polyvalent DNA/ SFV/MVA vaccine abrogated virus replication in three of the four vaccinated monkeys following mucosal challenge with SIVmac251, apparently by inducing robust T-cell immune responses.
- Only the immunized animals that had specific anamnestic responses to all vaccine antigens tested (Gag, Rev, Tat, Nef) were able to contain SIV infection.
- At 2 weeks post-challenge the levels of viral RNA in plasma were low to undetectable and by week 4 all monkeys had become and remained plasma viraemia negative.

NHP.404 (15320991) **Macaque dendritic cells infected with SIV-recombinant canarypox ex vivo induce SIV-specific immune responses in vivo.**

Authors: Villamide-Herrera L, Ignatius R, Eller MA, Wilkinson K, Griffin C, Mehlhop E, Jones J, Han SY, Lewis MG, Parrish S, Vancott TC, Lifson JD, Schlesinger S, Mascola JR, Pope M

Journal: AIDS Res Hum Retroviruses 2004 Aug;20(8):871-84.

Objectives: Immunogenicity. To explore whether immature and mature DCs infected with SIV-recombinant canarypox (vCP180) ex vivo could induce primary virus-specific immune responses in vivo

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: vCP180 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Subcutaneous, Intramuscular *Formulation:* vCP180 + Kehole Limpet Hemocyanin, Tetanus toxoid (TT) + PBS

Main Findings:

- Subcutaneous injected ex-vivo SIV-recombinant canarypox-infected dentritic cells safely

induce low-level SIV-specific immuneresponses in vivo
- SIV-recombinant canary pox-infected dentritic cells prime SIV-specific responses in vivo
- Partially matured DCs might provide only suboptimal immunostimulatory signals and thereby elicit less robust responses compared to immature DCs

NHP.405 (15654970) **DermaVir: a novel topical vaccine for HIV/AIDS.**

Authors: Lisziewicz J, Trocio J, Whitman L, Varga G, Xu J, Bakare N, Erbacher P, Fox C, Woodward R, Markham P, Arya S, Behr JP, Lori F

Journal: J Invest Dermatol 2005 Jan;124(1):160-9.

Objectives: Immunogenicity, Immunotherapy.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: DermaVir *Type:* DNA *Routes:* Subcutaneous, Other *Formulation:* DermaVir + PBS

Main Findings:
- In this paper, a novel immunization strategy called DermaVir is used to improve viral antigen presentation using dendritic cells (DC) in rhesus macaques. DermaVir contains plasmid DNA expressing all HIV proteins except integrase to induce immune responses with broad specificity. After topical application, DermaVir-transduced cells migrate from the skin to the draining lymph node and interdigitate as DermaVir-expressing, antigen-presenting DC. The immunogenicity of topical and ex vivo DC-based DermaVir vaccinations were compared in naive rhesus macaques. Both vaccinations induced simian immunodeficiency virus-specific CD4 helper and CD8 memory T cells detected by an in vivo skin test and an in vitro intracellular cytokine-based assay.

NHP.406 (15448353) **Vaccine protection from CD4+ T-cell loss caused by simian immunodeficiency virus (SIV) mac251 is afforded by sequential immunization with three unrelated vaccine vectors encoding multiple SIV antigens.**

Authors: Koopman G, Mortier D, Hofman S, Niphuis H, Fagrouch Z, Norley S, Sutter G, Liljestrom P, Heeney JL

Journal: J Gen Virol 2004 Oct;85(Pt 10):2915-24.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SFV-SIVmac *Type:* DNA *Route:* Subcutaneous *Formulation:* SFV-SIVmac + PBS

Vaccine Name: DNA.PTH.SIVmac.J5.gptnr *Type:* DNA *Route:* Intradermal *Formulation:* DNA.PTH.SIVmac.J5.gptnr + Saline, PBS

Vaccine Name: DNA.pND14-G1.SIVmac251.env *Type:* DNA *Route:* Intradermal *Formulation:* DNA.pND14-G1.SIVmac251.env + Saline, PBS

Vaccine Name: rMVA-SIVmac251 32H *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intrarectal, Intradermal, Intramuscular *Formulation:* rMVA-SIVmac251 32H + PBS

Challenge: SIVmac251 *Route:* Intrarectal

Main Findings:
- Three groups of Indian Rhesus macaques: Six animals received the DNA, MVA and SFV vectors expressing the SIV proteins Gag, Pol, Nef, Rev, Tat and Env; four animals received the empty DNA, MVA and SFV vectors (vector controls); two animals were not immunized (naı¨ve controls). Animals received four immunizations at 8-weekly intervals, starting with the DNA vector, followed by MVA, then SFV and finally a second MVA immunization. Eight weeks after the last immunization, all animals were challenged by intrarectal administration of 50 MID50 of the pathogenic SIVmac251 stock. All six immunized animals and the two naı¨ve-control animals became infected, as determined by RT-PCR analysis of plasma. However, only two of four vector-control animals became virus-positive. The same findings were obtained when the cell-associated virus load was measured. In addition, PBMCs from the two RT-PCR-negative animals were also SIV

DNA-negative.

NHP.407 (15326293) **Enhanced SIV replication and accelerated progression to AIDS in macaques primed to mount a CD4 T cell response to the SIV envelope protein.**

Authors: Staprans SI, Barry AP, Silvestri G, Safrit JT, Kozyr N, Sumpter B, Nguyen H, McClure H, Montefiori D, Cohen JI, Feinberg MB

Journal: Proc Natl Acad Sci U S A 2004 Aug 31;101(35):13026-31. Epub 2004 Aug 23.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: rVZV-SIVenv *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Intramuscular, Intranasal *Formulation:* rVZV-SIVenv + PBS

Challenge: SIVsmE660 *Route:* Intravenous

Main Findings:

- An attenuated recombinant varicella-zoster virus vaccine expressing the simian immunodeficiency virus (SIV) envelope (Env) elicited nonneutralizing Env-binding antibodies and little if any cytotoxic T lymphocyte responses in rhesus macaques (Macaca mulatta). After challenge with SIV, Env vaccinees manifested increased levels of SIV replication, more rapid CD4 depletion, and accelerated progression to AIDS compared with controls. Enhanced SIV replication correlated with increased CD4 T cell proliferation soon after SIV challenge, apparently the result of an anamnestic response to SIV antigens. Thus activation of virus-specific CD4 T cells at the time of exposure to a CD4 T cell-tropic lentivirus, in the absence of an effective CD8 response, may enhance virus replication and disease.

NHP.408 (15650171) **Vaccination of rhesus macaques with recombinant Mycobacterium bovis bacillus Calmette-Guerin Env V3 elicits neutralizing antibody-mediated protection against simian-human immunodeficiency virus with a homologous but not a heterologous V3 motif.**

Authors: Someya K, Cecilia D, Ami Y, Nakasone T, Matsuo K, Burda S, Yamamoto H, Yoshino N, Kaizu M, Ando S, Okuda K, Zolla-Pazner S, Yamazaki S, Yamamoto N, Honda M

Journal: J Virol 2005 Feb;79(3):1452-62.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: rBCG-Env V3 *Type:* Recombinant Vector (virus/bacteria) *Route:* Subcutaneous *Formulation:* rBCG-Env V3 + PBS

Challenge: SHIV89.6PD, SHIV-MN *Route:* Intravenous

Main Findings:

- This study examined immune responses elicited in rhesus macaques following vaccination with recombinant Mycobacterium bovis bacillus Calmette-Guerin expressing an HIV-1 Env V3 antigen (rBCG Env V3). The effect of vaccination on protection against challenge with either a simian-human immunodeficiency virus (SHIV-MN) or a highly pathogenic SHIV strain (SHIV-89.6PD) was also determined. Immunization with rBCG Env V3 elicited significant levels of NAb for the 24 weeks tested that were predominantly HIV-1 type specific. Sera from the immunized macaques neutralized primary HIV-1 isolates in vitro, including HIV-1BZ167/X4, HIV-1SF2/X4, HIV-1CI2/X4, and, to a lesser extent, HIV-1MNp/X4, all of which contain a V3 sequence homologous to that of rBCG Env V3. In contrast, neutralization was not observed against HIV-1SF33/X4, which has a heterologous V3 sequence. Furthermore, the viral load in the vaccinated macaques was significantly reduced following low-dose challenge with SHIV-MN, and early plasma viremia was markedly decreased after high-dose SHIV-MN challenge. While this response was not sufficient to provide protection against a pathogenic SHIV challenge, it was able to significantly reduce the viral load in macaques following challenge with a

nonpathogenic SHIV.

NHP.409 (15585086) **Immunogenicity of attenuated vesicular stomatitis virus vectors expressing HIV type 1 Env and SIV Gag proteins: comparison of intranasal and intramuscular vaccination routes.**

Authors: Egan MA, Chong SY, Rose NF, Megati S, Lopez KJ, Schadeck EB, Johnson JE, Masood A, Piacente P, Druilhet RE, Barras PW, Hasselschwert DL, Reilly P, Mishkin EM, Montefiori DC, Lewis MG, Clarke DK, Hendry RM, Marx PA, Eldridge JH, Udem SA, Israel ZR, Rose JK

Journal: AIDS Res Hum Retroviruses 2004 Sep;20(9):989-1004.

Objectives: Challenge, Immunogenicity. rVSV with SIV Gag and HIV Env, intravaginal challenge with SHIV89.6P

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: rVSV G(I)-HIV env and SIV gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intramuscular, Intranasal *Formulation:* rVSV G(I)-HIV env and SIV gag + PBS

Vaccine Name: VSV(GCh)-Env+Gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Oral, Intramuscular, Intranasal *Formulation:* VSV(GCh)-Env+Gag + PBS

Vaccine Name: VSV(GNJ)-Env+Gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Oral, Intramuscular, Intranasal *Formulation:* VSV(GNJ)-Env+Gag + PBS

Challenge: SHIV89.6PD *Route:* Vaginal or perivaginal

Main Findings:

- The ability of rVSV-based vaccine vectors expressing HIV-1 Env and SIV Gag proteins was evaluated, when given either intramuscularly (i.m.) or intranasally (i.n.), to elicit antigen-specific cellular and humoral immune responses, and to protect from a subsequent vaginal challenge with simian–human immunodeficiency virus (SHIV89.6P). Results demonstrate that macaques vaccinated by the i.n. route developed significantly higher antigen-specific cellular immune responses as determined by MHC class I tetramer staining, IFN-

NHP.410 (15356916) **CCR5 targeted SIV vaccination strategy preventing or inhibiting SIV infection.**

Authors: Bogers WM, Bergmeier LA, Oostermeijer H, ten Haaft P, Wang Y, Kelly CG, Singh M, Heeney JL, Lehner T

Journal: Vaccine 2004 Aug 13;22(23-24):2974-84.

Objectives: Challenge, Immunogenicity. Vaccinated with 70kDa Heatshock protein linked to SIV gp120 and p27; IV Challenge with SIVmac8980

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: CCR5 peptides *Type:* Synthetic Protein/Peptide *Routes:* Subcutaneous, Intramuscular *Formulation:* CCR5 peptides + GM-CSF, Ribilike adjuvant system (MPL, TMD,CWS) + Saline, PBS

Vaccine Name: HSP70-Baculovirus-infected cells.gp120-pGEX-3X.p27 *Type:* Recombinant Subunit Protein *Routes:* Subcutaneous, Intramuscular *Formulation:* HSP70-Baculovirus-infected cells.gp120-pGEX-3X.p27 + CCR5 peptides + PBS

Challenge: SIVmac8980 *Route:* Intravenous

Main Findings:

- In this study, the SIV CCR5 coreceptor was targeted in a combined CCR5-SIV antigen immunization strategy. Rhesus macaques were immunized i.m. with the 70 kDa heat shock protein (HSP70) covalently linked to the CCR5 peptides, SIV gpl20 and p27. Intravenous challenge with SIV mac 8980 prevented SIV infection or decreased the viral load with the CCR5-SIV combined vaccine. CC chemokines and antibodies which block and downmodulateCCR5 were induced, as well as immune responses to the subunit SIV antigens. This novel vaccination strategy complements cognate immunity to SIV with innate immunity to the CCR5 coreceptor of SIV.

NHP.411 (15478078) **Abrogation of attenuated lentivirus-induced protection in rhesus macaques by administration of depo-provera before intravaginal challenge with simian immunodeficiency virus mac239.**

Authors: Abel K, Rourke T, Lu D, Bost K, McChesney MB, Miller CJ

Journal: J Infect Dis 2004 Nov 1;190(9):1697-705. Epub 2004 Sep 24.

Objectives: Challenge, Immunogenicity, Pathogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SHIV89.6 *Type:* Live Virus *Routes:* Intravenous, Vaginal or perivaginal, Intranasal *Formulation:* SHIV89.6 + PBS

Challenge: SIVmac239 *Route:* Vaginal or perivaginal

Main Findings:

- The goal of the present study was to determine whether administration of Depo-Provera before IVAG challenge with SIV decreases the protective efficacy of infection with SHIV89.6. The rate of protection after IVAG challenge with SIVmac239 was significantly lower (P<.05), and the acute postchallenge plasma viral RNA levels were significantly higher (P<.006), in Depo-Provera-treated, SHIV89.6-immunized macaques than in Depo-Provera-naive, SHIV89.6-immunized macaques. In the primate model of sexual transmission of human immunodeficiency virus, treatment with progesterone before IVAG challenge with a pathogenic virus can decrease the efficacy of a model "vaccine."

NHP.412 (15650171) **Vaccination of rhesus macaques with recombinant Mycobacterium bovis bacillus Calmette-Guerin Env V3 elicits neutralizing antibody-mediated protection against simian-human immunodeficiency virus with a homologous but not a heterologous V3 motif.**

Authors: Someya K, Cecilia D, Ami Y, Nakasone T, Matsuo K, Burda S, Yamamoto H, Yoshino N, Kaizu M, Ando S, Okuda K, Zolla-Pazner S, Yamazaki S, Yamamoto N, Honda M

Journal: J Virol 2005 Feb;79(3):1452-62.

Objectives: Challenge.

NHP.413 (15627031) **Control of viral rebound through therapeutic immunization with DermaVir.**

Authors: Lisziewicz J, Trocio J, Xu J, Whitman L, Ryder A, Bakare N, Lewis MG, Wagner W, Pistorio A, Arya S, Lori F

Journal: AIDS 2005 Jan 3;19(1):35-43.

Objectives: Immunotherapy.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: DermaVir *Type:* DNA *Routes:* Intravenous, Subcutaneous, Other *Formulation:* DermaVir + PBS

Challenge: SIVmac251 *Route:*

Main Findings:

- A topical, DNA-based therapeutic immunization (DermaVir) was designed to express most of the regulatory and structural viral genes in dendritic cells. DermaVir alone and in combination with antiretroviral drugs was tested in chronically SIV-infected macaques.

DermaVir provided virological, immunological and clinical benefit for SIV-infected macaques during chronic infection and AIDS. In combination with antiretroviral drugs, DermaVir augmented SIV-specific T-cell responses and enhanced control of viral load rebound during treatment interruptions. The results indicate the feasibility of therapeutic immunization even in immune compromised hosts, and suggest that DermaVir can complement antiretroviral drugs to sustain suppression of HIV-1 replication.

NHP.414 (15448351) **Important B-cell epitopes for neutralization of human immunodeficiency virus type 1 Tat in serum samples of humans and different animal species immunized with Tat protein or peptides.**

Authors: Moreau E, Belliard G, Partidos CD, Pradezinsky F, Le Buanec H, Muller S, Desgranges C

Journal: J Gen Virol 2004 Oct;85(Pt 10):2893-901.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Tat1-20 *Type:* Synthetic Protein/Peptide *Routes:* Intramuscular, Intranasal *Formulation:* Tat1-20 + Adju-Phos, MONTANIDE ISA 720, CpG 2006 + Saline, PBS

Vaccine Name: Tat 1-61 *Type:* Synthetic Protein/Peptide *Routes:* Intramuscular, Intranasal *Formulation:* Tat 1-61 + MONTANIDE ISA 720 + Saline, PBS

Vaccine Name: Tat 44-61 *Type:* Synthetic Protein/Peptide *Routes:* Intramuscular, Intranasal *Formulation:* Tat 44-61 + MONTANIDE ISA 720 + Saline, PBS

Vaccine Name: rTat *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* rTat + PBS

Main Findings:

- Immunization of rhesus macaques with Tat protein or Tat peptides stimulated production of anti-Tat antibodies which could neutralize extracellular Tat-induced transactivation.

NHP.415 (15531036) **Evaluation in macaques of HIV-1 DNA vaccines containing primate CpG motifs and fowlpoxvirus vaccines co-expressing IFNgamma or IL-12.**

Authors: Dale CJ, De Rose R, Wilson KM, Croom HA, Thomson S, Coupar BE, Ramsay A, Purcell DF, Ffrench R, Law M, Emery S, Cooper DA, Ramshaw IA, Boyle DB, Kent SJ

Journal: Vaccine 2004 Nov 25;23(2):188-97.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Vaccine Name: rFPV-HIV gag/pol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rFPV-HIV gag/pol + PBS

Vaccine Name: rFPV-HIV gag/pol/IFNg *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rFPV-HIV gag/pol/IFNg + PBS

Vaccine Name: rFPV-HIV gag/pol/IL-12 *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rFPV-HIV gag/pol/IL-12 + PBS

Vaccine Name: pHIS-HIV-B *Type:* DNA *Route:* Intramuscular *Formulation:* pHIS-HIV-B + PBS

Challenge: LAI isolate K98227/W35 *Route:* Intravenous

Main Findings:

- A consecutive immunisation strategy involving priming with DNA and boosting with rFPV vaccines encoding multiple common HIV-1 antigens was evaluated in 30 macaques. The DNA vaccine vector included CpG immunostimulatory molecules, and rFPV vaccines were compared with rFPV vaccines co-expressing the pro-T cell cytokines IFNgamma or IL-12. Vaccines expressed multiple HIV-1 genes, mutated to remove active sites of the HIV proteins. The vaccines were well tolerated, and a significant enhancement of DNA-vaccine primed HIV-1 specific T lymphocyte responses was observed following rFPV boosting. Co-expression of IFNgamma or IL-12 by the rFPV vaccines did not further enhance immune responses. Non-sterilising protection from a non-pathogenic

HIV-1 challenge was observed.

NHP.416 (15557247) **Readily acquired secondary infections of human and simian immunodeficiency viruses following single intravenous exposure in non-human primates.**

Authors: ten Haaft P, Verschoor EJ, Verstrepen B, Niphuis H, Dubbes R, Koornstra W, Bogers W, Rosenwirth B, Heeney JL

Journal: J Gen Virol 2004 Dec;85(Pt 12):3735-45.

Objectives: Challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque), Pan Troglodytes (Chimpanzee)

Vaccine Name: SIVmac239ΔNef *Type:* Live Attenuated Virus *Routes:* Intravenous, Intramuscular

Vaccine Name: HIV-1LAI *Type:* Live Virus *Route:* Intravenous

Vaccine Name: SIVmac251ΔNef *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge: HIV-1 Han2, SIVmac8980 *Route:* Intravenous

NHP.417 (15671751) **Effects of virus burden and chemokine expression on immunity to SHIV in nonhuman primates.**

Authors: Waterman PM, Kitabwalla M, Hatfield GS, Evans PS, Lu Y, Tikhonov I, Bryant JL, Pauza CD

Journal: Viral Immunol 2004;17(4):545-57.

Objectives: Challenge.

Main Findings:

- Recombinant SHIVs were engineered to express macrophage inflammatory protein-1 alpha (MIP-1alpha), regulated upon activation, normal T-cell expressed and secreted (RANTES), or Lymphotactin (Ltn) in place of nef in SHIV89.6 (SHIV89.6-MIP-1alpha, SHIV89.6-RANTES, SHIV89.6-Ltn). The parental virus SHIV89.6 was included because it replicates to higher titer while still not causing disease.
- After pathogenic challenge with SHIV89.6pd, animals from groups that received recombinant (nef-deleted) viruses had peak viremia levels three orders of magnitude lower than unvaccinated controls and increased survival times.
- Animals that received the original SHIV89.6 (nef+) were highly resistant to both intrarectal and intravenous challenge with SHIV89.6PD, and showed no signs of disease.
- There were no differences in survival times comparing unvaccinated and SHIV89.6-dLtn (control) groups, indicating that nef deleted viruses did not provide durable protection in this model.
- The strongest protection was seen in animals with the highest replicating virus (SHIV89.6), and the lower effect on survival after SHIV89.6 nef-deleted vaccination, likely reflects differences in replication capacity.
- The protective effect of nef-deleted virus was partly restored by expressing Type 1 chemokines to augment viral immunity.

NHP.418 (15613305) **Neutralizing antibodies elicited by immunization of monkeys with DNA plasmids and recombinant adenoviral vectors expressing human immunodeficiency virus type 1 proteins.**

Authors: Mascola JR, Sambor A, Beaudry K, Santra S, Welcher B, Louder MK, Vancott TC, Huang Y, Chakrabarti BK, Kong WP, Yang ZY, Xu L, Montefiori DC, Nabel GJ, Letvin NL

Journal: J Virol 2005 Jan;79(2):771-9.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac239 gag-pol-nef *Type:* DNA *Route:* Intramuscular *Formulation:* SIVmac239 gag-pol-nef + Saline, PBS

Vaccine Name: rAd5-SIVmac239 gag/pol *Type:* Recombinant Vector (virus/bacteria) *Route:*

Intramuscular *Formulation:* rAd5-SIVmac239 gag/pol + Saline, PBS

Vaccine Name: gp145 DCFI 89.6P Env *Type:* DNA *Route:* Intramuscular *Formulation:* gp145 DCFI 89.6P Env + Saline, PBS

Vaccine Name: rAd-HxB2/BaL Env DCFI *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd-HxB2/BaL Env DCFI + Saline, PBS

Vaccine Name: gp140 DCFI (HxB2/BaL) Env *Type:* DNA *Route:* Intramuscular *Formulation:* gp140 DCFI (HxB2/BaL) Env + Saline, PBS

Vaccine Name: rAd5 89.6P Env (DCFI) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd5 89.6P Env (DCFI) + Saline, PBS

Challenge: SHIV89.6P *Route:* Intravenous

Main Findings:

- DNA plasmids and rAd5 vectors encoding the HIV-1 89.6P or chimeric HxB2/BaL envelope glycoprotein were used to immunize rhesus macaques.
- A single rAd5 immunization elicited anti-Env antibody responses, but there was little boosting with subsequent rAd5 immunizations.
- In contrast, rAd5 boosting of DNA-primed monkeys resulted in a rapid rise in antibody titers, including the development of anti-HIV-1 neutralizing antibodies.
- The potency and breadth of neutralization were evaluated by testing plasma against a panel of 14 clade B primary isolates. Moderate levels of plasma neutralizing activity were detected against about one-third of the viruses tested, and immunoglobulin G fractionation demonstrated that virus neutralization was antibody mediated.
- After a challenge with SHIV89.6P, an anamnestic neutralizing antibody response was observed, although the breadth of the response was limited to the subset of viruses that were neutralized after the primary immunization.

NHP.419 (15613296) **Analysis of pigtail macaque major histocompatibility complex class I molecules presenting immunodominant simian immunodeficiency virus epitopes.**

Authors: Smith MZ, Dale CJ, De Rose R, Stratov I, Fernandez CS, Brooks AG, Weinfurter J, Krebs K, Riek C, Watkins DI, O'connor DH, Kent SJ

Journal: J Virol 2005 Jan;79(2):684-95.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Challenge: SIVmac251 *Route:* Intravenous

Main Findings:

- The Gag p27 KP9 epitope (KKFGAEVVP; amino acids 29-37 in SMM239 p27) is presented by at least 15 of 36 outbread pigtailed macaques.
- Mane-A*10 was shown to be one of the alleles that presents the K9P epitope.
- K9P immunodominant responder animals had lower viral loads compared to macaques which did not respond to this epitope.

NHP.420 (15507782) **Stimulation of virus-specific T cell responses by dendritic cell vaccination in the chronic phase of simian AIDS models.**

Authors: Kato M, Igarashi H, Takeda A, Horie S, Higashihara E, Matano T

Journal: Jpn J Infect Dis 2004 Oct;57(5):220-3.

Objectives: Immunotherapy.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: inactivated SIVmac239 *Type:* Whole (killed) Inactivated Virus *Route:* Intravenous *Formulation:* inactivated SIVmac239 + autologous dendritic cells + PBS

Vaccine Name: inactivated SHIV89.6PD *Type:* Whole (killed) Inactivated Virus *Route:* Intravenous *Formulation:* inactivated SHIV89.6PD + autologous dendritic cells + PBS

Vaccine Name: inactivated SHIV(DH12R) *Type:* Whole (killed) Inactivated Virus *Route:* Intravenous *Formulation:* inactivated SHIV(DH12R) + autologous dendritic cells + PBS

Main Findings:
- Three rhesus macaques each with a different vaccine/challenge history were given a herapeutic vaccination with inactivated virus-pulsed autologous dendritic cells. CTL responses were augmented by treatment.

NHP.421 (15837216) **Induction of Gag-specific T-cell responses by therapeutic immunization with a Gag-expressing Sendai virus vector in macaques chronically infected with simian-human immunodeficiency virus.**

Authors: Kato M, Igarashi H, Takeda A, Sasaki Y, Nakamura H, Kano M, Sata T, Iida A, Hasegawa M, Horie S, Higashihara E, Nagai Y, Matano T

Journal: Vaccine 2005 May 2;23(24):3166-73.

Objectives: Immunotherapy.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: F(+)SeV-gag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intranasal *Formulation:* F(+)SeV-gag + PBS

Vaccine Name: pCMVmCAT1 *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intramuscular *Formulation:* pCMVmCAT1 + PBS

Vaccine Name: F(+)SeV-Tat *Type:* Recombinant Vector (virus/bacteria) *Route:* Intranasal *Formulation:* F(+)SeV-Tat + PBS

Vaccine Name: F(-)SeV-Gag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intranasal *Formulation:* F(-)SeV-Gag + PBS

Vaccine Name: FMSIV *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intramuscular *Formulation:* FMSIV + pCMVmCAT1, pCMVN + PBS

Challenge: SHIV89.6PD *Route:* Intravenous

Main Findings:
- Therapeutic immunization with a Sendai Virus vector encoding SIV-Mac239 Gag, of 5 Rhesus macaques chronically infected with SHIV89.6PD after various prophylactic vaccinations, with FMSIV-Tat or FMSIV-Gag plus mCAT1.
- CD8 T-cell responses were measured and appeared to broaden after the therapeutic vaccination.

NHP.422 (15527850) **Vaccination with live attenuated simian immunodeficiency virus for 21 days protects against superinfection.**

Authors: Stebbings R, Berry N, Stott J, Hull R, Walker B, Lines J, Elsley W, Brown S, Wade-Evans A, Davis G, Cowie J, Sethi M, Almond N

Journal: Virology 2004 Dec 5;330(1):249-60.

Objectives: Challenge.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: SIVmac251, 32H, (C8) *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge: SIVmacJ5M *Route:* Intravenous

Main Findings:
- Juvenile cynomolgus macaques immunized with SIV-mac-251-32H attenuated infectious molecular clone pC8 and challenged with SIV-mac-251-32H "wild type" infectious molecular clone J5 which differs only in the Nef gene. The vaccine strain has a 4 amino acid deletion and 2 other conservative amino acid changes in Nef.
- The main difference between 5 groups of vaccinated animals was time between vaccination and challenge ranging from 0 to 70 days. Increasing time lead to greater protection from superinfection.

NHP.423 (15557179) **A novel adjuvant for mucosal immunity to HIV-1 gp120 in nonhuman primates.**

Authors: Yoshino N, Lu FX, Fujihashi K, Hagiwara Y, Kataoka K, Lu D, Hirst L, Honda M, van Ginkel FW, Takeda Y, Miller CJ, Kiyono H, McGhee JR

Journal: J Immunol 2004 Dec 1;173(11):6850-7.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Monomeric rgp120 *Type:* Recombinant Subunit Protein *Routes:* Intradermal, Intranasal *Formulation:* Monomeric rgp120 + nCT native Cholera Toxin, Freund′s Complete Adjuvant + Saline

Vaccine Name: DNA-SIV *Type:* DNA *Routes:* Intravenous, Intradermal (Gene Gun DNA-coated gold beads), Intramuscular *Formulation:* DNA-SIV + non-toxic mutant E112K of Cholera Toxin mCT-E112K

Main Findings:

- A nontoxic mutant of cholera toxin (mCT-E112K) was found to be a safe and effective mucosal adjuvant for use with a nasal HIV vaccine.

NHP.424 (15564456) **Immunogenicity study of glycoprotein-deficient rabies virus expressing simian/human immunodeficiency virus SHIV89.6P envelope in a rhesus macaque.**

Authors: McKenna PM, Aye PP, Dietzschold B, Montefiori DC, Martin LN, Marx PA, Pomerantz RJ, Lackner A, Schnell MJ

Journal: J Virol 2004 Dec;78(24):13455-9.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: RVG dG-89.6P env *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intravenous, Subcutaneous, Intramuscular *Formulation:* RVG dG-89.6P env + PBS

Challenge: SHIV89.6P *Route:* Intravenous

Main Findings:

- An SHIV89.6P Env-only immunogen, based on a live-attenuated chimeric rhabdovirus construct, is capable of providing protection from disease in the SHIV89.6P model. Seroconversion to both envelope and RV proteins was seen following immunization, which shows this RV-based vector to be replication competent in vivo. The data further show that this animal had strong cellular and humoral responses to the SHIV89.6P challenge, which resulted in impressive suppression of plasma viremia. This control of viral replication has been maintained to 22 weeks postchallenge. To date, there has been no evidence of CD4 T-cell loss, and no adverse effects for this animal from either the vaccination or SHIV89.6P infection have been observed.

NHP.425 (15557247) **Readily acquired secondary infections of human and simian immunodeficiency viruses following single intravenous exposure in non-human primates.**

Authors: ten Haaft P, Verschoor EJ, Verstrepen B, Niphuis H, Dubbes R, Koornstra W, Bogers W, Rosenwirth B, Heeney JL

Journal: J Gen Virol 2004 Dec;85(Pt 12):3735-45.

Objectives: Challenge, Pathogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque), Pan Troglodytes (Chimpanzee)

Challenge: SIV8980, SIVmac239 delta nef, HIV-1 Han2, SIVmac251-BK28-delta nef, HIV-1.LAI *Route:* Intravenous

Main Findings:

- The aim of this study was to determine under what conditions secondary or superinfections of HIV or simian immunodeficiency virus (SIV) may be acquired under controlled settings in well-defined, non-human primate models. Retrospective analysis of macaques that had acquired apparent immunity upon infection with a defined attenuated SIV(mac) strain revealed that animals that were secondarily exposed to a new virus variant became infected with the new virus strain, but at low levels. Macaques infected

with SIV-Mac239-delta-Nef and chimpanzees infected with HIV-1 strain LAI were not protected from secondary infection. These findings reveal that secondary lentiviral infections may be acquired readily during different stages of primary infection.

NHP.426 (15588349) **Mucosal and systemic anti-HIV responses in rhesus macaques following combinations of intranasal and parenteral immunizations.**

Authors: Vajdy M, Singh M, Kazzaz J, Soenawan E, Ugozzoli M, Zhou F, Srivastava I, Bin Q, Barnett S, Donnelly J, Luciw P, Adamson L, Montefiori D, O'Hagan DT

Journal: AIDS Res Hum Retroviruses 2004 Nov;20(11):1269-81.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: HIV-1 p55 gag *Type:* DNA *Routes:* Intradermal, Intramuscular *Formulation:* HIV-1 p55 gag + PLG + PBS

Vaccine Name: o-gp140 *Type:* DNA *Routes:* Intradermal, Intramuscular *Formulation:* o-gp140 + PLG + PBS

Vaccine Name: p55gag-SF2 *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* p55gag-SF2 + PLG + PBS

Vaccine Name: p24 gag *Type:* Recombinant Subunit Protein *Route:* Intranasal *Formulation:* p24 gag + PBS

Vaccine Name: Delta-V2 gp140 oligomeric *Type:* Recombinant Subunit Protein *Routes:* Intramuscular, Intranasal *Formulation:* Delta-V2 gp140 oligomeric + MF59, LTK63, LTK72 + PBS

Main Findings:

- Four groups of 2 rhesus macaques each.
- The first group was immunized twice IM with plasmid DNA encoding HIV-1 gag (0.5 mg/dose) adsorbed onto PLG microparticles (PLG-DNA-gag) and plasmid DNA encoding HIV-1-env-gp140 (1 mg/dose) (PLG-DNA-gp140).
- The second group received an identical dose to the first group but the immunizations were through the ID route.
- The third group was immunized five times IN with HIV-1 Ogp140 protein (300 g/dose) and HIV-1 gag p24 protein (300 g/dose) plus LTK63 (100 g).
- The fourth group was immunized five times IN with HIV-1 Ogp140 protein (300 g/dose) and HIV-1 gag p24 protein (300 g/dose) plus LTR72 (100 g).
- Immunological responses were measured.
- The data showed that the combination of IN immunizations followed by a resting period and IM booster immunizations induced not only quantitatively higher plasma antibodies as measured by ELISA but also qualitatively better and more functional plasma antibodies for neutralization of HIV-1 virions.

NHP.427 (15721357) **Kinetics of expansion of SIV Gag-specific CD8+ T lymphocytes following challenge of vaccinated macaques.**

Authors: Abdel-Motal UM, Gillis J, Manson K, Wyand M, Montefiori D, Stefano-Cole K, Montelaro RC, Altman JD, Johnson RP

Journal: Virology 2005 Mar 15;333(2):226-38.

Objectives: Challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac239Δ3 *Type:* Live Attenuated Virus *Routes:* Intravenous, Oral, Intra-amniotic, Intraplacental *Formulation:* SIVmac239Δ3 + PBS

Challenge: SIVsmE660, SIVmac239 *Route:* Intravenous

Main Findings:

- Rhesus macaques vaccinated with the attenuated strain SIVmac239D3 and challenged with the pathogenic viruses SIVmac239 or SIVsmE660.
- Although all vaccinated animals were infected with challenge virus, peak levels of plasma

viremia in vaccinees were decreased by 1.5 to 2 logs as compared with naive controls. The observation that expansion of SIV-specific CD8+ T cells is delayed until 7 days or more after initial detection of viremia indicates limitations in the ability of CD8+ T cells to mediate protection against challenge.

NHP.428 (15589168) **T cell receptor recognition motifs govern immune escape patterns in acute SIV infection.**

Authors: Price DA, West SM, Betts MR, Ruff LE, Brenchley JM, Ambrozak DR, Edghill-Smith Y, Kuroda MJ, Bogdan D, Kunstman K, Letvin NL, Franchini G, Wolinsky SM, Koup RA, Douek DC

Journal: Immunity 2004 Dec;21(6):793-803.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Challenge: SIVmac251 *Route:* Intravenous

Main Findings:

- Rhesus macaques infected with SIV-MAC251.
- Escape mutations in CD8 T-cell epitopes were observed.

NHP.429 (15609225) **Multiple vaginal exposures to low doses of R5 simian-human immunodeficiency virus: strategy to study HIV preclinical interventions in nonhuman primates.**

Authors: Otten RA, Adams DR, Kim CN, Jackson E, Pullium JK, Lee K, Grohskopf LA, Monsour M, Butera S, Folks TM

Journal: J Infect Dis 2005 Jan 15;191(2):164-73. Epub 2004 Dec 9.

Objectives: Challenge, Chemotherapy. Although these were all naive animals, not vaccinated, the study established infective dose of SHIVSF162P3 via vaginal exposure.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Challenge: SHIV-SF162P3 *Route:* Vaginal or perivaginal

Main Findings:

- The efficacy of cellulose acetate phthalate (CAP) as a vaginal microbicide was evaluated by applying it to the vaginal vault of macaques (n = 4) 15 min before each weekly exposure to SHIVSF162P3.
- Dose-titration experiments indicated that 3 once-weekly exposures to 10 tissue culture infectious doses of SHIVSF162P3 resulted in consistent transmission of virus and establishment of systemic infection.
- CAP prevented infection in 12 of 13 possible chances for infection, over the course of 39 total exposures.

NHP.430 (15542208) **Vaccination with gp120-depleted HIV-1 plus immunostimulatory CpG oligodeoxynucleotides in incomplete Freund's adjuvant stimulates cellular and humoral immunity in rhesus macaques.**

Authors: Silvera P, Savary JR, Livingston V, White J, Manson KH, Wyand MH, Salk PL, Moss RB, Lewis MG

Journal: Vaccine 2004 Dec 21;23(6):827-39.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: HIV-1 inactivated antigen (gp120-depleted) *Type:* Whole (killed) Inactivated Virus *Route:* Intramuscular *Formulation:* HIV-1 inactivated antigen (gp120-depleted) + CpG 2006, IFA + PBS

Main Findings:

- This study investigated whether immunization of rhesus macaques with an inactivated gp 120-depleted HIV-1 immunogen, emulsified in incomplete Freund's adjuvant (IFA) together with immunostimulatory CpG-containing ODN (ODN 2006), would elicit HIV-specific cellular and humoral immune responses.

- High titer anti-p24 antibody levels were induced in all four immunized animals that were sustained 6 weeks after the fifth and final boost at 23 months.
- These anti-gag antibodies mapped to linear B-cell epitopes within the matrix (MA), capsid (CA), p2, nucleocapsid (NC) and p6 proteins of HIV-1 gag.

NHP.431 (15650426) **DNA/MVA vaccine for HIV type 1: effects of codon-optimization and the expression of aggregates or virus-like particles on the immunogenicity of the DNA prime.**

Authors: Smith JM, Amara RR, Campbell D, Xu Y, Patel M, Sharma S, Butera ST, Ellenberger DL, Yi H, Chennareddi L, Herndon JG, Wyatt LS, Montefiori D, Moss B, McClure HM, Robinson HL

Journal: AIDS Res Hum Retroviruses 2004 Dec;20(12):1335-47.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pGA2/JS2-HIV-1.gag.pol.env *Type:* DNA *Route:* Intramuscular *Formulation:* pGA2/JS2-HIV-1.gag.pol.env + PBS

Vaccine Name: MVA/HIV 48 *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* MVA/HIV 48 + PBS

Vaccine Name: pGA2/JS7 *Type:* DNA *Route:* Intramuscular *Formulation:* pGA2/JS7 + PBS

Vaccine Name: pGA1/JS8 *Type:* DNA *Route:* Intramuscular *Formulation:* pGA1/JS8 + PBS

Main Findings:

- This study assessed the ability of a codon-optimized Gag-expressing DNA and two noncodon-optimized Gag - Pol - Env-expressing DNAs to prime a modified vaccinia Ankara (MVA) booster dose in Rhesus macaques.
- Immunogenicity studies in macaques used one intramuscular prime with 600 mug of DNA and two intramuscular boosts with 1 x 108 pfu of MVA at weeks 8 and 30.
- The codon-optimized and noncodon-optimized DNAs proved similar in their ability to prime anti-Gag T cell responses.
- The aggregate and VLP-expressing Gag - Pol - Env DNAs also showed no significant differences in their ability to prime anti-Env Ab responses.
- The second MVA booster dose did not increase the peak CD4 and CD8 T cell responses, but increased anti-Env Ab titers by 40- to 90-fold.
- MVA-only immunizations elicited 10 - 100 times lower frequencies of T cells and 2 - 4 lower titers of anti-Env Ab than the Gag - Pol - Env DNA/MVA immunizations.

NHP.432 (15613324) **Novel adeno-associated virus vector vaccine restricts replication of simian immunodeficiency virus in macaques.**

Authors: Johnson PR, Schnepp BC, Connell MJ, Rohne D, Robinson S, Krivulka GR, Lord CI, Zinn R, Montefiori DC, Letvin NL, Clark KR

Journal: J Virol 2005 Jan;79(2):955-65.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: rAAV2/SIVRevRRE *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAAV2/SIVRevRRE + PBS

Vaccine Name: rAAV-SIVRevEnv *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAAV-SIVRevEnv + PBS

Vaccine Name: rAAV-SIVRT-Int *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAAV-SIVRT-Int + PBS

Vaccine Name: SIV-rev-gag-PR-dRT *Type:* DNA *Route:* Intramuscular *Formulation:* SIV-rev-gag-PR-dRT + PBS

Vaccine Name: SIV-rev-env *Type:* DNA *Route:* Intramuscular *Formulation:* SIV-rev-env + PBS

Vaccine Name: SIV-RT/IN *Type:* DNA *Route:* Intramuscular *Formulation:* SIV-RT/IN + PBS

Challenge: SIVsmE660 *Route:* Intravenous

Main Findings:

- Recombinant adeno-associated virus (rAAV) vectors expressing SIV genes were used in macaques.
- After a single intramuscular dose, rAAV/SIV vaccines elicited SIV-specific T cells and antibodies in macaques.
- Immunized animals were able to significantly restrict replication of a live, virulent SIV challenge.

NHP.433 (15795278) **Induction of humoral immune responses following vaccination with envelope-containing, formaldehyde-treated, thermally inactivated human immunodeficiency virus type 1.**

Authors: Poon B, Safrit JT, McClure H, Kitchen C, Hsu JF, Gudeman V, Petropoulos C, Wrin T, Chen IS, Grovit-Ferbas K

Journal: J Virol 2005 Apr;79(8):4927-35.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Inactivated HIV-1 virions *Type:* Whole (killed) Inactivated Virus *Route:* Intramuscular *Formulation:* Inactivated HIV-1 virions + QS-21

Vaccine Name: Inactivated HIV-1 (Env-depleted) virions *Type:* Whole (killed) Inactivated Virus *Route:* Intramuscular *Formulation:* Inactivated HIV-1 (Env-depleted) virions + QS-21

Main Findings:

- Treatment of virions with low-dose formaldehyde prior to thermal inactivation retains the association of viral envelope with virions.
- Juvenile rhesus macaques vaccinated with formaldehyde-treated, thermally inactivated virions produce antibodies capable of neutralizing heterologous strains of HIV in peripheral blood mononuclear cell-, MAGI cell-, and U87-based infectivity assays.

NHP.434 (15709015) **Multiclade human immunodeficiency virus type 1 envelope immunogens elicit broad cellular and humoral immunity in rhesus monkeys.**

Authors: Seaman MS, Xu L, Beaudry K, Martin KL, Beddall MH, Miura A, Sambor A, Chakrabarti BK, Huang Y, Bailer R, Koup RA, Mascola JR, Nabel GJ, Letvin NL

Journal: J Virol 2005 Mar;79(5):2956-63.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac239 gag-pol-nef *Type:* DNA *Route:* Intramuscular *Formulation:* SIVmac239 gag-pol-nef + Saline, PBS

Vaccine Name: HXBc2/BaL clade B env plasmid *Type:* DNA *Route:* Intramuscular *Formulation:* HXBc2/BaL clade B env plasmid + PBS

Vaccine Name: HXBc2/BaL clade C env plasmid *Type:* DNA *Route:* Intramuscular *Formulation:* HXBc2/BaL clade C env plasmid + PBS

Vaccine Name: HxBc2/BaL clade A env plasmid *Type:* DNA *Route:* Intramuscular *Formulation:* HxBc2/BaL clade A env plasmid + PBS

Vaccine Name: rAd expressing HxBc2/BaL clade B env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd expressing HxBc2/BaL clade B env + PBS

Vaccine Name: rAd expressing HxBc2/BaL clade c env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd expressing HxBc2/BaL clade c env + PBS

Vaccine Name: rAd expressing HxBc2/BaL clade A env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd expressing HxBc2/BaL clade A env + PBS

Vaccine Name: rAd5-SIVmac239 gag/pol *Type:* Recombinant Vector (virus/bacteria) *Route:*

Intramuscular *Formulation:* rAd5-SIVmac239 gag/pol + Saline, PBS

Challenge: SHIV89.6P *Route:* Intravenous

Main Findings:

- A study to examine the magnitude and breadth of envelope (Env)-specific T-lymphocyte and antibody responses generated by vaccines containing either a single or multiple genetically distant HIV-1 Env immunogens.
- Rhesus monkeys were immunized with DNA prime–recombinant adenovirus boost vaccines encoding a Gag-Pol-Nef polyprotein in combination with either a single Env or a mixture of clade-A, clade-B, and clade-C Envs.
- Monkeys receiving the multiclade Env immunization developed robust immune responses to all vaccine antigens and, importantly, a greater breadth of Env recognition than monkeys immunized with vaccines including a single Env immunogen.
- All groups of vaccinated monkeys demonstrated equivalent immune protection following challenge with the pathogenic simian-human immunodeficiency virus 89.6P.

NHP.435 (15858035) **Replication-defective adenovirus serotype 5 vectors elicit durable cellular and humoral immune responses in nonhuman primates.**

Authors: Santra S, Seaman MS, Xu L, Barouch DH, Lord CI, Lifton MA, Gorgone DA, Beaudry KR, Svehla K, Welcher B, Chakrabarti BK, Huang Y, Yang ZY, Mascola JR, Nabel GJ, Letvin NL

Journal: J Virol 2005 May;79(10):6516-22.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac239 gag-pol-nef *Type:* DNA *Route:* Intramuscular *Formulation:* SIVmac239 gag-pol-nef + Saline, PBS

Vaccine Name: rAd5-SIVmac239 gag/pol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd5-SIVmac239 gag/pol + Saline, PBS

Vaccine Name: gp145 DCFI 89.6P Env *Type:* DNA *Route:* Intramuscular *Formulation:* gp145 DCFI 89.6P Env + Saline, PBS

Vaccine Name: rAd5 89.6P Env (DCFI) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd5 89.6P Env (DCFI) + Saline, PBS

Main Findings:

- The durability of ADV and DNA/ADV vaccine responses was assessed.
- The findings suggest that ADV5 vaccines may be more useful as components of heterologous prime/boost regimens than as single-modality immunogens.
- The magnitudes of the total HIV- and SIV-specific PBMC SFC responses and the PBMC CTL epitope-specific tetramer and SFC responses were greater in the monkeys receiving plasmid DNA/ADV5 immunizations than in monkeys receiving ADV5-alone immunizations.
- The ADV5 alone-immunized monkeys developed CD8 T-lymphocyte biased responses.
- The plasmid DNA/ADV5-immunized monkeys developed both CD4 and CD8 T-lymphocyte responses.
- Finally, the data suggest that multiple immunizations with the same ADV5 vectors are likely to prove of limited utility, since durable, high-titer anti-ADV5 antibody responses are generated following even a single ADV5 administration that will neutralize the immunogenicity of subsequent inoculated ADV5 vaccine constructs.

NHP.436 (15731236) **A noninfectious simian/human immunodeficiency virus DNA vaccine that protects macaques against AIDS.**

Authors: Singh DK, Liu Z, Sheffer D, Mackay GA, Smith M, Dhillon S, Hegde R, Jia F, Adany I, Narayan O

Journal: J Virol 2005 Mar;79(6):3419-28.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Vaccine Name: SHIV(KU2)-delta RT *Type:* DNA *Route:* Intradermal *Formulation:* SHIV(KU2)-delta RT + PBS

Challenge: SHIV89.6P *Route:* Intrarectal

Main Findings:

- Reports deletion of the reverse transcriptase gene from SHIVKU2 and insertion of this DNA (DELTArtSHIVKU2) into a plasmid that was then used to test gene expression and immunogenicity.
- Four macaques were injected intradermally with 2 mg of the DNA at 0, 8, and 18 weeks.
- The animals developed neutralizing antibodies and low enzyme-linked immunospot assay (E-SPOT) titers against SHIVKU2.
- These four animals and two unvaccinated control animals were then challenged with heterologous SHIV89.6P administered into their rectums. The two control animals developed viral RNA titers exceeding 106 copies/ml of plasma, and these titers were accompanied by the loss of CD4+ T cells by 2 weeks after challenge. The two control animals died at weeks 8 and 16, respectively. All four of the immunized animals became infected with the challenge virus but developed lower titers of viral RNA in plasma than the control animals, and the titers decreased over time in three of the four macaques. The fourth animal remained viremic and died at week 47.
- Whereas the control animals failed to develop E-SPOT responses, all four of the immunized animals developed anamnestic E-SPOT responses after challenge.

NHP.437 (15725752) **Studies in macaques on cross-clade T cell responses elicited by a DNA/MVA AIDS vaccine, better conservation of CD8 than CD4 T cell responses.**

Authors: Smith JM, Amara RR, Wyatt LS, Ellenberger DL, Li B, Herndon JG, Patel M, Sharma S, Chennareddi L, Butera S, McNicholl J, McClure HM, Moss B, Robinson HL

Journal: AIDS Res Hum Retroviruses 2005 Feb;21(2):140-4.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pGA2/JS2-HIV-1.gag.pol.env *Type:* DNA *Route:* Intramuscular *Formulation:* pGA2/JS2-HIV-1.gag.pol.env + PBS

Vaccine Name: MVA/HIV 48 *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* MVA/HIV 48 + PBS

Main Findings:

- A macaque model was used to investigate the ability of our clade B vaccine that consists of DNA priming and modified vaccinia Ankara (MVA) virus boosting to elicit T cell responses that recognize an A/G recombinant of HIV-1.
- The ability of a HIV vaccine from one clade to protect against other clades may be more limited by the ability to provide CD4 T cell help than the ability to elicit CD8 effector functions.,

NHP.438 (15943571) **Comparison of whole gene and whole virus scrambled antigen approaches for DNA prime and fowlpox virus boost HIV type 1 vaccine regimens in macaques.**

Authors: Pamungkas J, De Rose R, Iskandriati D, Noviana R, Paramastri Y, Dale CJ, Shoobridge M, Medveczky CJ, Ramshaw IA, Thomson S, Kent SJ

Journal: AIDS Res Hum Retroviruses 2005 Apr;21(4):292-300.

Objectives: Immunogenicity.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Vaccine Name: rFPV-HIV gag/pol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rFPV-HIV gag/pol + PBS

Vaccine Name: pHIS-HIV-B *Type:* DNA *Route:* Intramuscular *Formulation:* pHIS-HIV-B + PBS

Vaccine Name: SAVINE (scrambled antigen vaccine) *Type:* DNA *Route:* *Formulation:* SAVINE (scrambled antigen vaccine) + PBS

Vaccine Name: rFPV-SAVINE *Type:* Recombinant Vector (virus/bacteria) *Route:* *Formulation:* rFPV-SAVINE + PBS

Main Findings:

- Three groups of seven pigtail macaques were immunized with sets of DNA and rFPV expressing Gag/Pol antigens only, the whole genome SAVINE antigens, or no HIV-1 antigens and T cell immunity was monitored by ELISpot and intracellular cytokine staining.
- High levels of cross-subtype HIV-specific T cell immunity to Gag were consistently induced in the seven macaques primed with DNA and rFPV vaccines expressing Gag/Pol as intact proteins. It was, however, difficult to repeatedly boost immunity with further rFPV immunizations, presumably reflecting high levels of anti-FPV immunity.

NHP.439 (15734067) **Subtype AE HIV-1 DNA and recombinant Fowlpoxvirus vaccines encoding five shared HIV-1 genes: safety and T cell immunogenicity in macaques.**

Authors: De Rose R, Chea S, Dale CJ, Reece J, Fernandez CS, Wilson KM, Thomson S, Ramshaw IA, Coupar BE, Boyle DB, Sullivan MT, Kent SJ

Journal: Vaccine 2005 Mar 14;23(16):1949-56.

Objectives: Immunogenicity.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Vaccine Name: pHis-HIV-AE *Type:* DNA *Route:* Intramuscular *Formulation:* pHis-HIV-AE + PBS

Vaccine Name: rFPV-HIV-AE *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rFPV-HIV-AE + PBS

Main Findings:

- This study evaluated the safety, immunogenicity and dose-response relationship of DNA and recombinant Fowlpoxvirus (rFPV) vaccines encoding five shared HIV subtype AE genes (Gag, Pol, Env, Tat, Rev) in pigtail macaques.
- Broadly reactive HIV-specific T cell immunity was stimulated by all doses of the vaccines administered, without significant differences between the high and low doses studied.
- The vaccines induced both CD4 and CD8 T cell responses to Gag, Pol, Env and Tat/Rev proteins, with CD4 T cell responses being greater in magnitude than CD8 T cell responses.

NHP.440 (15867489) **Loss of reactivity of vaccine-induced CD4 T cells in immunized monkeys after SIV/HIV challenge.**

Authors: Puaux AL, Delache B, Marconi S, Huerre M, Le Grand R, Riviere Y, Michel ML

Journal: AIDS 2005 May 20;19(8):757-65.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: BCG 1173P2 *Type:* Live Virus *Route:*

Vaccine Name: HBsAg/SHIV *Type:* DNA *Routes:* Intradermal, Intramuscular *Formulation:* HBsAg/SHIV + Water

Vaccine Name: rMVA-Gag/Pol/Env/Nef /Tat *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular *Formulation:* rMVA-Gag/Pol/Env/Nef /Tat + Water

Challenge: SHIV89.6P *Route:* Intrarectal

Main Findings:

- Rhesus monkeys (Macaca mulatta) were vaccinated by DNA priming followed by rMVA boost.
- After intrarectal challenge with SHIV 89.6P, immunized animals demonstrated early

control of viral replication and stable CD4 T-cell counts.

NHP.441 (15755586) **Protection by dendritic cells-based HIV synthetic peptide cocktail vaccine: preclinical studies in the SHIV-rhesus model.**

Authors: Nehete PN, Nehete BP, Manuri P, Hill L, Palmer JL, Sastry KJ

Journal: Vaccine 2005 Mar 18;23(17-18):2154-9.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: HIV-1 Env peptide cocktail *Type:* Synthetic Protein/Peptide *Routes:* Intravenous, Subcutaneous *Formulation:* HIV-1 Env peptide cocktail + IFA, autologous dendritic cells + Saline

Challenge: SHIV89.6P *Route:* Intravenous

Main Findings:

- Rhesus macaques were vaccinated with a multivalent vaccine comprised of highly conserved HIV envelope peptide cocktail focused on priming antigen-specific helper T cell and CTL responses.
- Vaccinated animals were protected against pathogenic SHIV89.6P challenge through priming cell-mediated immunity by prophylactic vaccination with the peptide-cocktail delivered by dendritic cells.
- Compared to monkeys mock-vaccinated or immunized with the peptide cocktail using IFA, vaccination with peptide cocktail-pulsed DC showed significant protection from AIDS-associated mortality and reduction in plasma viremia to undetectable levels.

NHP.442 (15795274) **Retroviral recombination in vivo: viral replication patterns and genetic structure of simian immunodeficiency virus (SIV) populations in rhesus macaques after simultaneous or sequential intravaginal inoculation with SIVmac239Deltavpx/Deltavpr and SIVmac239Deltanef.**

Authors: Kim EY, Busch M, Abel K, Fritts L, Bustamante P, Stanton J, Lu D, Wu S, Glowczwskie J, Rourke T, Bogdan D, Piatak M Jr, Lifson JD, Desrosiers RC, Wolinsky S, Miller CJ

Journal: J Virol 2005 Apr;79(8):4886-95.

Objectives: Challenge, Pathogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Challenge: SIVmac239 delta nef, SIVmac239 delta vpx/delta vpr *Route:* Vaginal or perivaginal

Main Findings:

- Rhesus macaques inoculated with attenuated deletion mutant viruses and challenged with wild-type or with attenuated viruses carrying different deletions, recombined to produce non-attenuated viruses. Recombination can occur readily after the intravaginal SIV inoculation of rhesus monkeys.

NHP.443 (15795244) **Vaccine-elicited memory cytotoxic T lymphocytes contribute to Mamu-A*01-associated control of simian/human immunodeficiency virus 89.6P replication in rhesus monkeys.**

Authors: Seaman MS, Santra S, Newberg MH, Philippon V, Manson K, Xu L, Gelman RS, Panicali D, Mascola JR, Nabel GJ, Letvin NL

Journal: J Virol 2005 Apr;79(8):4580-8.

Objectives: Challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: DNA vaccines expressing SIVmac239 Gag and HIV-1 89.6P Env *Type:* DNA *Route:* Intramuscular *Formulation:* DNA vaccines expressing SIVmac239 Gag and HIV-1 89.6P Env + IL-2/lg plasmid + PBS

Vaccine Name: SIVmac239 gag-pol-nef *Type:* DNA *Route:* Intramuscular *Formulation:* SIVmac239 gag-pol-

nef + Saline, PBS

Vaccine Name: Recombinant fowlpox (rFPV) SIVmac239 gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular *Formulation:* Recombinant fowlpox (rFPV) SIVmac239 gag + PBS

Vaccine Name: Recombinant MVA-SIVmac239 gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular *Formulation:* Recombinant MVA-SIVmac239 gag + PBS

Vaccine Name: Recombinant vaccinia virus (rVac).SIVmac239 gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular *Formulation:* Recombinant vaccinia virus (rVac).SIVmac239 gag + PBS

Vaccine Name: rAd-SIVmac239 gag/pol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd-SIVmac239 gag/pol + PBS

Vaccine Name: rMVA-HIV-1 89.6P env *Type:* DNA *Routes:* Intradermal, Intramuscular *Formulation:* rMVA-HIV-1 89.6P env + PBS

Vaccine Name: recombinant fowlpox vaccine expressing HIV-1 89.6 env *Type:* Live Virus *Routes:* Intradermal, Intramuscular *Formulation:* recombinant fowlpox vaccine expressing HIV-1 89.6 env + PBS

Vaccine Name: recombinant vaccinia virus expressing HIV-1 89.6P env *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular *Formulation:* recombinant vaccinia virus expressing HIV-1 89.6P env + PBS

Vaccine Name: HXBc2/BaL clade B env plasmid *Type:* DNA *Route:* Intramuscular *Formulation:* HXBc2/BaL clade B env plasmid + PBS

Vaccine Name: HXBc2/BaL clade C env plasmid *Type:* DNA *Route:* Intramuscular *Formulation:* HXBc2/BaL clade C env plasmid + PBS

Vaccine Name: HxBc2/BaL clade A env plasmid *Type:* DNA *Route:* Intramuscular *Formulation:* HxBc2/BaL clade A env plasmid + PBS

Vaccine Name: rAd expressing HxBc2/BaL clade B env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd expressing HxBc2/BaL clade B env + PBS

Vaccine Name: rAd expressing HxBc2/BaL clade c env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd expressing HxBc2/BaL clade c env + PBS

Vaccine Name: rAd expressing HxBc2/BaL clade A env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd expressing HxBc2/BaL clade A env + PBS

Vaccine Name: Mono-gp120H (89.6) *Type:* Recombinant Subunit Protein *Routes:* Intratracheal, Oral, Intramuscular, Intranasal *Formulation:* Mono-gp120H (89.6) + QS-21 + PBS

Challenge: SHIV89.6P *Route:* Intravenous

Main Findings:

- This study examined the impact of the MHC class I allele Mamu-A*01 on simian/human immunodeficiency virus 89.6P (SHIV-89.6P) infection in unvaccinated and vaccinated rhesus monkeys by exploring the contribution of dominant-epitope specific CTL in this setting. For each DNA immunization, monkeys received 5 mg of SIVmac239 gag plasmid and 5 mg of HIV-1 89.6P env plasmid (10 mg total). These monkeys also received 5 mg of IL-2/Ig plasmid on day 2 after DNA vaccination. Following SHIV-89.6P infection, robust cellular immune responses were observed for all monkeys that had previously received experimental vaccines. Interestingly, the peak Gag-specific cellular immune responses elicited in Mamu- A*01 and Mamu-A*01 monkeys following both the DNA prime and recombinant poxvirus or rAd boost immunizations were of similar frequencies. However, in the DNA prime/rAd boost-immunized monkeys, but not in the DNA prime/recombinant poxvirus-boosted monkeys, higher-frequency Gag-specific responses were detected in Mamu-A*01 than in Mamu- A*01 monkeys on the day of challenge, 16 weeks following the last immunization.

NHP.444 (15956591) **DNA vaccines expressing different forms of simian immunodeficiency virus antigens decrease viremia upon SIVmac251 challenge.**

Authors: Rosati M, von Gegerfelt A, Roth P, Alicea C, Valentin A, Robert-Guroff M, Venzon D, Montefiori DC, Markham P, Felber BK, Pavlakis GN

Journal: J Virol 2005 Jul;79(13):8480-92.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: HIV-1 env *Type:* DNA *Route:* Intramuscular *Formulation:* HIV-1 env + PBS

Vaccine Name: HIV-1 gag *Type:* DNA *Route:* Intramuscular *Formulation:* HIV-1 gag + PBS

Vaccine Name: MCP3-gag *Type:* DNA *Route:* Intramuscular *Formulation:* MCP3-gag + PBS

Vaccine Name: MCP3-env *Type:* DNA *Route:* Intramuscular *Formulation:* MCP3-env + PBS

Vaccine Name: CATE-env *Type:* DNA *Route:* Intramuscular *Formulation:* CATE-env + PBS

Vaccine Name: CATE-gag *Type:* DNA *Route:* Intramuscular *Formulation:* CATE-gag + PBS

Challenge: SIVmac251 *Route:* Intrarectal

Main Findings:

- This study found a significant negative correlation between virus load and cellular immune responses, since the animals having high responses in all groups had the lowest virus loads. The combinations of DNA vaccines producing native and modified forms of antigens elicit more balanced immune responses able to significantly reduce viremia for a long period (8 months) following pathogenic challenge with SIVmac251.

NHP.445 (15956564) **Enhanced potency of plasmid DNA microparticle human immunodeficiency virus vaccines in rhesus macaques by using a priming-boosting regimen with recombinant proteins.**

Authors: Otten GR, Schaefer M, Doe B, Liu H, Srivastava I, Megede J, Kazzaz J, Lian Y, Singh M, Ugozzoli M, Montefiori D, Lewis M, Driver DA, Dubensky T, Polo JM, Donnelly J, O'Hagan DT, Barnett S, Ulmer JB

Journal: J Virol 2005 Jul;79(13):8189-200.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SF162ΔV2 gp140 protein *Type:* Recombinant Subunit Protein *Routes:* Intradermal, Intramuscular *Formulation:* SF162ΔV2 gp140 protein + MF59 + PBS

Vaccine Name: p55gag-SF2 *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* p55gag-SF2 + PLG + PBS

Vaccine Name: pCMV-HIV-gag *Type:* DNA *Route:* Intramuscular *Formulation:* pCMV-HIV-gag + PLG + Saline

Vaccine Name: pSINCP-HIVgag *Type:* DNA *Route:* Intramuscular *Formulation:* pSINCP-HIVgag + PLG + Saline

Vaccine Name: pCMV-HIV-Env *Type:* DNA *Route:* Intramuscular *Formulation:* pCMV-HIV-Env + PLG + Saline

Vaccine Name: pSINCP-HIV-Env *Type:* DNA *Route:* Intramuscular *Formulation:* pSINCP-HIV-Env + PLG + Saline

Main Findings:

- This study demonstrated that two fundamentally different DNA vectors (pCMV, pSINCP) are effective in macaques. The potencies of both DNA vaccines were enhanced by delivery via PLG microparticles, and boosting with recombinant proteins further increased antibodies and T cells. The combined use of alternative DNA vectors, improved formulation and delivery systems, and adjunct technologies such as booster vaccines will likely be vital to effective use of DNA vaccines in humans.

NHP.446 (15671796) **Attenuated poxvirus-based simian immunodeficiency virus (SIV) vaccines given in infancy partially protect infant and juvenile macaques against repeated oral challenge with virulent SIV.**

Authors: Van Rompay KK, Abel K, Lawson JR, Singh RP, Schmidt KA, Evans T, Earl P, Harvey D, Franchini G, Tartaglia J, Montefiori D, Hattangadi S, Moss B, Marthas ML

Journal: J Acquir Immune Defic Syndr 2005 Feb 1;38(2):124-34.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: rMVA SIVmac239 gagpolenv *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intramuscular, Intranasal *Formulation:* rMVA SIVmac239 gagpolenv + PBS

Vaccine Name: vCP180 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Subcutaneous, Intramuscular *Formulation:* vCP180 + Kehole Limpet Hemocyanin, Tetanus toxoid (TT) + PBS

Challenge: SIVmac251 *Route:* Oral

Main Findings:

- After repeated daily oral inoculations with virulent SIVmac251 at 4 weeks of age, significantly fewer ALVAC-SIV– immunized infants were infected compared with unimmunized infants. Six ALVAC-SIV–immunized animals that were uninfected after the repeated low-dose SIV challenges at 4 weeks of age were reinoculated orally at 8 months of age with a relatively high dose of SIVmac251 (2 doses of 105 TCID50). All 6 animals became infected (plasma RNA level of .105 copies/mL at 1 week after challenge); thus, immunization with ALVAC-SIV shortly after birth did not protect against a highdose oral SIVexposure later in life.

NHP.447 (15802969) **Enhanced immunity and protective efficacy against SIVmac251 intrarectal challenge following ad-SIV priming by multiple mucosal routes and gp120 boosting in MPL-SE.**

Authors: Pinczewski J, Zhao J, Malkevitch N, Patterson LJ, Aldrich K, Alvord WG, Robert-Guroff M

Journal: Viral Immunol 2005;18(1):236-43.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Ad5hr-SIVmac239gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Oral, Intranasal *Formulation:* Ad5hr-SIVmac239gag + Saline, PBS

Vaccine Name: Ad5hr-SIVsmH4 env/rev *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Oral, Intranasal *Formulation:* Ad5hr-SIVsmH4 env/rev + PBS

Vaccine Name: SIVmac251-gp120 *Type:* Purified Viral Products *Routes:* Intrarectal, Intramuscular, Intranasal *Formulation:* SIVmac251-gp120 + MPL-SE, QS-21 + PBS

Challenge: SIVmac251 *Route:* Intrarectal

Main Findings:

- This study examines the effect of different vaccine regimens using MPL-SE and QS21 adjuvants on induced immunity associated with the different challenge outcomes. The MPL-SE study exhibited greater protective efficacy, increased levels of p11C and p54m tetramer positive cells and a trend toward enhanced interferon-gamma secreting cells in response to Env and Gag peptides, modestly enhanced serum neutralizing antibodies, and greater positivity in anti-gp120 rectal IgA and IgG antibodies. The QS21 study macaques exhibited greater positivity in salivary IgA anti-gp120 antibodies.

NHP.448 (15827187) **Rapid viral escape at an immunodominant simian-human immunodeficiency virus cytotoxic T-lymphocyte epitope exacts a dramatic fitness cost.**

Authors: Fernandez CS, Stratov I, De Rose R, Walsh K, Dale CJ, Smith MZ, Agy MB, Hu SL, Krebs K, Watkins DI, O'connor DH, Davenport MP, Kent SJ

Journal: J Virol 2005 May;79(9):5721-31.

Objectives: Challenge.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Challenge: SHIV-SF162P3, SHIV.229(mn) *Route:* Intrarectal, Vaginal or perivaginal

Main Findings:

- T-cell escape viral variants are retained following HIV-1 transmission between major histocompatibility complex (MHC)-matched individuals. However, reversion to wild type can occur following transmission to MHC-mismatched hosts in the absence of cytotoxic T-lymphocyte (CTL) pressure, due to the reduced fitness of the escape mutant virus. Both the strength of immune selection and the fitness cost of escape variants were estimated by studying the rates of T-cell escape and reversion in pigtail macaques. Near-complete replacement of wild-type with T-cell escape viral variants at an immunodominant simian immunodeficiency virus Gag epitope KP9 occurred rapidly (over 7 days) following infection of pigtail macaques with SHIVSF162P3. Another challenge virus, SHIVmn229, previously serially passaged through pigtail macaques, contained a KP9 escape mutation in 40/44 clones sequenced from the challenge stock. When six KP9-responding animals were infected with this virus, the escape mutation was maintained. By contrast, in animals not responding to KP9, rapid reversion of the K165R mutation occurred over 2 weeks after infection. Quantifying both the selection pressure exerted by CTL and the fitness costs of escape mutation has important implications for the development of CTL-based vaccine strategies.

NHP.449 (15843571) **Molecular and functional characterization of NKG2D, NKp80, and NKG2C triggering NK cell receptors in rhesus and cynomolgus macaques: monitoring of NK cell function during simian HIV infection.**

Authors: Biassoni R, Fogli M, Cantoni C, Costa P, Conte R, Koopman G, Cafaro A, Ensoli B, Moretta A, Moretta L, De Maria A

Journal: J Immunol. 2005 May 1;174(9):5695-705.

NHP.450 (15824066) **Novel simian immunodeficiency virus CTL epitopes restricted by MHC class I molecule Mamu-B*01 are highly conserved for long term in DNA/MVA-vaccinated, SHIV-challenged rhesus macaques.**

Authors: Su J, Luscher MA, Xiong Y, Rustam T, Amara RR, Rakasz E, Robinson HL, MacDonald KS

Journal: Int Immunol. 2005 May;17(5):637-48. Epub 2005 Apr 11.

NHP.451 (15994781) **Pathogenicity of simian-human immunodeficiency virus SHIV-89.6P and SIVmac is attenuated in cynomolgus macaques and associated with early T-lymphocyte responses.**

Authors: Reimann KA, Parker RA, Seaman MS, Beaudry K, Beddall M, Peterson L, Williams KC, Veazey RS, Montefiori DC, Mascola JR, Nabel GJ, Letvin NL

Journal: J Virol. 2005 Jul;79(14):8878-85.

Objectives: Immunogenicity, Pathogenicity.

Main Findings:

- Pathogenicity of both SHIV89.6P and SIV-MAC251 was lower for Chinese rhesus and cynomolgus macaques than for Indian rhesus macaques. Attenuated pathogenicity in cynomolgus monkeys was associated with early and strong virus-specific cellular immune responses.

NHP.452 (15564508) **A dominant role for CD8+-T-lymphocyte selection in simian immunodeficiency virus sequence variation.**

Authors: O'Connor DH, McDermott AB, Krebs KC, Dodds EJ, Miller JE, Gonzalez EJ, Jacoby TJ, Yant L, Piontkivska H, Pantophlet R, Burton DR, Rehrauer WM, Wilson N, Hughes AL, Watkins DI

Journal: J Virol. 2004 Dec;78(24):14012-22.

Species/Subspecies: -

Challenge: Mac239 *Route:* Intravenous

Main Findings:
- 35 Rhesus macaques infected with SIV-MAC239 between 1998 and 2001 were studied, and the range of survival was from 14 to 167 weeks after infection. Complete genome sequences of 26 viruses sampled at death, revealed that the majority of nonsynonymous mutations occurred in recognized CD8 T-cell epitopes.

NHP.453 (15994776) **A human T-cell leukemia virus type 1 regulatory element enhances the immunogenicity of human immunodeficiency virus type 1 DNA vaccines in mice and nonhuman primates.**

Authors: Barouch DH, Yang ZY, Kong WP, Korioth-Schmitz B, Sumida SM, Truitt DM, Kishko MG, Arthur JC, Miura A, Mascola JR, Letvin NL, Nabel GJ

Journal: J Virol. 2005 Jul;79(14):8828-34.

Objectives: Immunogenicity.

Main Findings:
- Plasmid DNA vaccines containing the cytomegalovirus immediate-early (CMV-IE) promoter plus or minus the HTLV-I R region (CMV or CMV-R), and Rouse Sarcoma Virus promoter plus or minus HTLV-I R (RSV or RSV-R) were used to express the gp145deltaCF1 envelope of HIV-1. The HTLV-I R region acted as an enhancer and more env was produced from plasmids containing the R region. Mice and Adult cynomolgus monkeys were injected intramuscularly. ELISPOT assays were done to determine CD8 T-cell responses in vaccinated animals.

NHP.454 (15919923) **Immunization of macaques with single-cycle simian immunodeficiency virus (SIV) stimulates diverse virus-specific immune responses and reduces viral loads after challenge with SIVmac239.**

Authors: Evans DT, Bricker JE, Sanford HB, Lang S, Carville A, Richardson BA, Piatak M Jr, Lifson JD, Mansfield KG, Desrosiers RC

Journal: J Virol. 2005 Jun;79(12):7707-20.

Objectives: Challenge, Immunogenicity. Use of single cycle SIV as vaccine approach

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: single cycle SIV *Type:* Live Attenuated Virus *Route:* Intravenous *Formulation:* single cycle SIV + PBS

Challenge: SIVmac239 *Route:* Intravenous

Main Findings:
- Genetically engineered simian immunodeficiency viruses (SIV) that is limited to a single cycle of infection was evaluated as a nonreplicating AIDS vaccine approach for rhesus macaques. Four Mamu-A*01(+) macaques were inoculated intravenously with three concentrated doses of single-cycle SIV (scSIV). Six weeks after the third dose, each animal was challenged intravenously with SIV(mac)239. All four animals became infected. However, three of the four scSIV-immunized animals exhibited 1 to 3 log reductions in acute-phase plasma viral loads relative to two Mamu-A*01(+) control animals. Given the extraordinary difficulty in protecting against SIV(mac)239, these results are encouraging and support further evaluation of lentiviruses that are limited to a single cycle of infection as a preclinical AIDS vaccine approach.

NHP.455 (16060834) **Priming with plasmid DNAs expressing interleukin-12 and simian immunodeficiency virus gag enhances the immunogenicity and efficacy of an experimental AIDS vaccine based on recombinant vesicular stomatitis virus.**

Authors: Egan MA, Chong SY, Megati S, Montefiori DC, Rose NF, Boyer JD, Sidhu MK, Quiroz J, Rosati M, Schadeck EB, Pavlakis GN, Weiner DB, Rose JK, Israel ZR, Udem SA, Eldridge JH

Journal: AIDS Res Hum Retroviruses. 2005 Jul;21(7):629-43.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: WLV-104 *Type:* DNA *Route:* Intramuscular *Formulation:* WLV-104 + PBS

Vaccine Name: WLV-102 *Type:* DNA *Route:* Intramuscular *Formulation:* WLV-102 + PBS

Vaccine Name: rVSV HIV1 envG *Type:* Recombinant Vector (virus/bacteria) *Route:* Intranasal *Formulation:* rVSV HIV1 envG + RPMI-1640

Vaccine Name: rVSV SIV gag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intranasal *Formulation:* rVSV SIV gag + RPMI-1640

Challenge: SHIV89.6P *Route:* Intravenous

Main Findings:

- This study was designed to assess whether a series of intramuscular priming immunizations with a plasmid DNA vaccine expressing SIVgag p39, in combination with plasmid expressed rhesus IL-12, could effectively enhance the immunogenicity and postchallenge efficacy of two intranasal doses of recombinant vesicular stomatitis virus (rVSV)-based vectors expressing HIV-1 env 89.6P gp160 and SIVmac239 gag p55 in rhesus macaques.
- In macaques receiving the combination plasmid DNA prime, rVSV boost vaccination regimen they observed significantly increased SIVgag-specific cell-mediated and humoral immune responses and significantly lower viral loads postintravenous SHIV89.6P challenge relative to macaques receiving only the rVSV vectored immunizations. In addition, the plasmid DNA prime, rVSV boost vaccination regimen also tended to increase the preservation of peripheral blood CD4(+) cells and reduce the morbidity and mortality associated with SHIV89.6P infection. An analysis of immune correlates of protection after SHIV89.61 challenge revealed that the prechallenge SHIV-specific IFN-gamma ELISpot response elicited by vaccination and the ability of the host to mount a virus-specific neutralizing antibody response postchallenge correlated with postchallenge clinical outcome.
- The correlation between vaccine-elicited cell-mediated immune responses and an improved clinical outcome after SHIV challenge provides strong justification for the continued development of a cytokine-enhanced plasmid DNA prime, rVSV vector boost immunization regimen for the prevention of HIV infection.

NHP.456 (16128921) **SIV DNA vaccine co-administered with IL-12 expression plasmid enhances CD8 SIV cellular immune responses in cynomolgus macaques.**

Authors: Boyer JD, Robinson TM, Kutzler MA, Parkinson R, Calarota SA, Sidhu MK, Muthumani K, Lewis M, Pavlakis G, Felber B, Weiner D

Journal: J Med Primatol. 2005 Oct;34(5-6):262-70.

NHP.457 (16128917) **Polyvalent DNA prime and envelope protein boost HIV-1 vaccine elicits humoral and cellular responses and controls plasma viremia in rhesus macaques following rectal challenge with an R5 SHIV isolate.**

Authors: Pal R, Wang S, Kalyanaraman VS, Nair BC, Whitney S, Keen T, Hocker L, Hudacik L, Rose N, Cristillo A, Mboudjeka I, Shen S, Wu-Chou TH, Montefiori D, Mascola J, Lu S, Markham P

Journal: J Med Primatol. 2005 Oct;34(5-6):226-36.

NHP.458 (15956558) **Effect of CD8+ lymphocyte depletion on virus containment after simian immunodeficiency virus SIVmac251 challenge of live attenuated SIVmac239delta3-vaccinated rhesus macaques.**

Authors: Schmitz JE, Johnson RP, McClure HM, Manson KH, Wyand MS, Kuroda MJ, Lifton MA, Khunkhun RS, McEvers KJ, Gillis J, Piatak M, Lifson JD, Grosschupff G, Racz P, Tenner-Racz K, Rieber EP, Kuus-Reichel K, Gelman RS, Letvin NL, Montefiori DC, Ruprecht RM, Desrosiers RC, Reimann KA

Journal: J Virol. 2005 Jul;79(13):8131-41.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac239Δ3+ *Type:* Live Attenuated Virus *Routes:* Intravenous, Other, Intramuscular *Formulation:* SIVmac239Δ3+ + Saline, PBS

Challenge: SIVmac251 *Route:* Intravenous

Main Findings:

- To test whether cellular immune responses mediated by CD8+ lymphocytes contribute to this vaccine-induced protection, we depleted rhesus macaques vaccinated with the live attenuated virus SIVmac239Delta3 of CD8+ lymphocytes and then challenged them with SIVmac251 by the intravenous route. While vaccination did not prevent infection with the pathogenic challenge virus, the postchallenge levels of virus in the plasmas of vaccinated control animals were significantly lower than those for unvaccinated animals. Interestingly, at the time of challenge, animals expressing the Mamu-A*01 major histocompatibility complex class I allele showed significantly higher frequencies of SIV-specific CD8+ T-cell responses and lower neutralizing antibody titers than those in Mamu-A*01- animals, suggesting that both humoral and cellular immune responses induced by live attenuated SIV vaccines can contribute to protection against a pathogenic challenge.

NHP.459 (15956548) **Enhanced breadth of CD4 T-cell immunity by DNA prime and adenovirus boost immunization to human immunodeficiency virus Env and Gag immunogens.**

Authors: Wu L, Kong WP, Nabel GJ

Journal: J Virol. 2005 Jul;79(13):8024-31.

NHP.460 (15994817) **CD8+ T-lymphocyte response to major immunodominant epitopes after vaginal exposure to simian immunodeficiency virus: too late and too little.**

Authors: Reynolds MR, Rakasz E, Skinner PJ, White C, Abel K, Ma ZM, Compton L, Napoe G, Wilson N, Miller CJ, Haase A, Watkins DI

Journal: J Virol. 2005 Jul;79(14):9228-35.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Challenge: SIVmac239, SIVmac251 *Route:* Vaginal or perivaginal

Main Findings:

- The study examined whether vaccination using a series of intramuscular priming immunizations with a plasmid DNA vaccine expressing SIVgag p39, in combination with plasmid expressed rhesus IL-12, could effectively enhance the immunogenicity and postchallenge efficacy of two intranasal doses of recombinant vesicular stomatitis virus (rVSV)-based vectors expressing HIV-1 env 89.6P gp160 and SIVmac239 gag p55 in rhesus macaques. In macaques receiving the combination plasmid DNA prime, rVSV boost vaccination regimen we observed significantly increased SIV- gag-specific cell-mediated and humoral immune responses and significantly lower viral loads postintravenous SHIV89.6P challenge relative to macaques receiving only the rVSV vectored immunizations. The correlation between vaccine-elicited cell-mediated immune responses and an improved clinical outcome after SHIV challenge provides strong justification for the continued development of a cytokine-enhanced plasmid DNA prime, rVSV vector boost immunization regimen for the prevention of HIV infection.

NHP.461 (15963361) **Efficacy of a SHIV 89.6 proviral DNA vaccine against mucosal SIVmac239 challenge.**

Authors: Busch M, Abel K, Li J, Piatak M Jr, Lifson JD, Miller CJ

Journal: Vaccine. 2005 Jul 1;23(31):4036-47. Epub 2005 Apr 9.

Objectives: Challenge.

Main Findings:

- Although monkeys inoculated with pMA SHIV-89.6 or SHIV 89.6 virus had similar plasma anti-SIV binding antibody titers and number of anti-SIV IFN- secreting cells on the day of mucosal SIVmac239 challenge, a smaller proportion of monkeys immunized with pMA SHIV-89.6 were protected from vaginal SIVmac239 challenge compared to monkeys immunized using SHIV 89.6 virus. Protected DNA immunized monkeys had stronger anti-SIV IFN- ELISPOT responses in the acute stage post-challenge than unprotected monkeys. Plasma anti-SIV binding antibody titers and PBMC cytokine responses in the acute stages post-challenge were similar in DNA vaccinated-protected and DNA vaccinated-unprotected monkeys. These results suggest that the delay in systemic infection resulting from delivery of SHIV 89.6 as a plasmid decreased the effectiveness of this live attenuated vaccine.

NHP.462 (16148092) **Vaccine-induced CD8+ central memory T cells in protection from simian AIDS.**

Authors: Vaccari M, Trindade CJ, Venzon D, Zanetti M, Franchini G

Journal: J Immunol. 2005 Sep 15;175(6):3502-7.

Objectives: Challenge, Immunogenicity, Immunotherapy.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: NYVAC-SIV-gag-pol-env (NYVAC-SIV-gpe) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* NYVAC-SIV-gag-pol-env (NYVAC-SIV-gpe) + PBS

Vaccine Name: CMV/kan-SIV-env *Type:* DNA *Routes:* Intradermal, Intramuscular *Formulation:* CMV/kan-SIV-env + PBS

Vaccine Name: CMV/kan-SIV-gag *Type:* DNA *Routes:* Intradermal, Intramuscular *Formulation:* CMV/kan-SIV-gag + PBS

Challenge: SIVmac251 *Route:* Intrarectal, Intravenous

Main Findings:

- This study demonstrates that virus-specific TCM (central memory T cells) correlated inversely with containment of viral replication in both preventive and therapeutic vaccine studies, suggesting that the goal of an effective vaccine for HIV should primarily be to elicit central memory cells rather than CTLs.

NHP.463 (16005121) **Vaccination of macaques with SIV immunogens delivered by Venezuelan equine encephalitis virus replicon particle vectors followed by a mucosal challenge with SIVsmE660.**

Authors: Johnston RE, Johnson PR, Connell MJ, Montefiori DC, West A, Collier ML, Cecil C, Swanstrom R, Frelinger JA, Davis NL

Journal: Vaccine. 2005 Oct 10;23(42):4969-79.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: VEE-SIVsm (SIV MA/CA-VRP and gp160-VRP) *Type:* DNA *Routes:* Intravenous, Subcutaneous *Formulation:* VEE-SIVsm (SIV MA/CA-VRP and gp160-VRP) + PBS

Challenge: SIVsmE660 *Route:* Intrarectal

Main Findings:

- VEE replicon particles (VRP), non-propagating vaccine vectors derived from Venezuelan equine encephalitis virus (VEE), were engineered to express immunogens from the cloned isolate SIVsmH-4, combined in a vaccine cocktail and inoculated subcutaneously to immunize rhesus macaques. A concentrated SIVsmE660 challenge dose was given intrarectally. The experiment was designed to test the efficacy of an SIV-VRP vaccine cocktail against a rigorous mucosal challenge with a nonhomologous virulent SIV. Several protective effects of vaccination were seen, both in the acute phase, at set point and at 41 weeks post-challenge, when the experiment was concluded.

NHP.464 (16051831) **Influence of glycosylation on the efficacy of an Env-based vaccine against simian immunodeficiency virus SIVmac239 in a macaque AIDS model.**

Authors: Mori K, Sugimoto C, Ohgimoto S, Nakayama EE, Shioda T, Kusagawa S, Takebe Y, Kano M, Matano T, Yuasa T, Kitaguchi D, Miyazawa M, Takahashi Y, Yasunami M, Kimura A, Yamamoto N, Suzuki Y, Nagai Y

Journal: J Virol. 2005 Aug;79(16):10386-96.

Objectives: Challenge, Immunogenicity, Pathogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pJWSU-mac239 *Type:* DNA *Route:* Intramuscular *Formulation:* pJWSU-mac239 + Saline

Vaccine Name: pJWSU-Delta5G *Type:* DNA *Route:* Intramuscular *Formulation:* pJWSU-Delta5G + Saline

Vaccine Name: WRvvENVmac239 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular *Formulation:* WRvvENVmac239 + PBS

Vaccine Name: WRvvENV-Delta5G *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular *Formulation:* WRvvENV-Delta5G + PBS

Challenge: SIVmac239 *Route:* Intravenous

Main Findings:

- The envelope glycoprotein (Env) of human immunodeficiency viruses (HIVs) and simian immunodeficiency viruses (SIVs) is heavily glycosylated, and this feature has been speculated to be a reason for the insufficient immune control of these viruses by their hosts. In a macaque AIDS model, we demonstrated that quintuple deglycosylation in Env altered a pathogenic virus, SIVmac239, into a novel attenuated mutant virus (delta5G). To examine the effect of deglycosylation, we constructed prime-boost vaccines consisting of Env from SIVmac239 and delta5G and compared their immunogenicities and vaccine efficacies by challenge infection with SIVmac239. Changes in glycosylation affected both cell-mediated and humoral immune responses and vaccine efficacy.

NHP.465 (16051813) **Replicating rather than nonreplicating adenovirus-human immunodeficiency virus recombinant vaccines are better at eliciting potent cellular immunity and priming high-titer antibodies.**

Authors: Peng B, Wang LR, Gomez-Roman VR, Davis-Warren A, Montefiori DC, Kalyanaraman VS, Venzon D, Zhao J, Kan E, Rowell TJ, Murthy KK, Srivastava I, Barnett SW, Robert-Guroff M

Journal: J Virol. 2005 Aug;79(16):10200-9.

Objectives: Immunogenicity.

Species/Subspecies: Pan Troglodytes (Chimpanzee)

Vaccine Name: Ad5-deltaE3/HIV-MN-env rev gp160 *Type:* Recombinant Vector (virus/bacteria) *Route:* Intranasal *Formulation:* Ad5-deltaE3/HIV-MN-env rev gp160 + PBS

Vaccine Name: Ad7-delta E3/HIV-MN-env/rev gp160 *Type:* Recombinant Vector (virus/bacteria) *Route:* Intranasal *Formulation:* Ad7-delta E3/HIV-MN-env/rev gp160 + PBS

Vaccine Name: Ad5- delta E1E3-HIV-MN-env/rev gp160 *Type:* Recombinant Vector (virus/bacteria) *Route:* Intranasal *Formulation:* Ad5- delta E1E3-HIV-MN-env/rev gp160 + PBS

Vaccine Name: Ad7-deltaE1E3-HIV-MN-env/rev gp160 *Type:* Recombinant Vector (virus/bacteria) *Route:* Intranasal *Formulation:* Ad7-deltaE1E3-HIV-MN-env/rev gp160 + PBS

Vaccine Name: Delta-V2 gp140 oligomeric *Type:* Recombinant Subunit Protein *Routes:* Intramuscular, Intranasal *Formulation:* Delta-V2 gp140 oligomeric + MF59, LTK63, LTK72 + PBS

Main Findings:

- The authors report the results of a preclinical trial using the chimpanzee model to investigate a combination vaccine strategy involving sequential priming immunizations with different serotypes of adenovirus (Ad)/HIV-1(MN)env/rev recombinants and boosting with an HIV envelope subunit protein, oligomeric HIV(SF162) gp140deltaV2. The immunogenicities of replicating and nonreplicating Ad/HIV-1(MN)env/rev recombinants were compared. Replicating Ad/HIV recombinants were better at eliciting

HIV-specific cellular immune responses and better at priming humoral immunity against HIV than nonreplicating Ad-HIV recombinants carrying the same gene insert.

NHP.466 (15907968) **Phenotypic and kinetic analysis of effective simian-human immunodeficiency virus-specific T cell responses in DNA--and fowlpox virus-vaccinated macaques.**

Authors: Stratov I, Dale CJ, Kent SJ

Journal: Virology. 2005 Jul 5;337(2):222-34.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Vaccine Name: pHis-SHIV B *Type:* DNA *Route:* Intramuscular *Formulation:* pHis-SHIV B + Saline, PBS

Vaccine Name: rFPV SIV gag/pol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rFPV SIV gag/pol + Saline, PBS

Vaccine Name: rFPV-HIV-AE (env) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rFPV-HIV-AE (env) + Saline, PBS

Vaccine Name: rFPV-SIV gag/pol-IFNgamma *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rFPV-SIV gag/pol-IFNgamma + Saline

Vaccine Name: pHis-HIV-AE *Type:* DNA *Route:* Intramuscular *Formulation:* pHis-HIV-AE + PBS

Vaccine Name: rFPV-HIV-AE *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rFPV-HIV-AE + PBS

Challenge: SHIV-SF162P3, SHIV.229(mn) *Route:* Intrarectal, Vaginal or perivaginal

Main Findings:

- A detailed kinetic and phenotypic study of T cell immunity induced by DNA/fowlpox vaccines prior to and following SHIV challenge was examined utilizing intracellular cytokine staining in pigtail macaques. Animals exhibited a coordinated induction of first Gag-specific CD4 T cell responses and then a week later Gag-specific CD8 T cell responses following the fowlpox virus boost. Overall, the magnitude and timing of the peak CD8 T cell responses following challenge was significantly associated with reductions in SHIV viremia following pathogenic challenge. After pathogenic lentiviral challenge, virus-specific effector memory T cells derived from animals controlling SHIV infection recognized a broad array of epitopes, expressed multiple effector cytokines and rapidly recognized virus-exposed cells ex vivo.

NHP.467 (15896883) **Systemic mobilization of antigen presenting cells, with a chimeric Flt-3 and G-CSF receptor agonist, during immunization of Macaca mulatta with HIV-1 antigens is insufficient to modulate immune responses or vaccine efficacy.**

Authors: Koopman G, Mortier D, Niphuis H, Farese AM, Kahn LE, Mann D, Wagner R, MacVittie TJ, Woulfe SL, Heeney JL

Journal: Vaccine. 2005 Jul 21;23(33):4195-202.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pcDNA synGagSIV *Type:* DNA *Routes:* Intradermal, Intramuscular *Formulation:* pcDNA synGagSIV + PBS

Vaccine Name: pcDNA synEnv gp140 89.6 *Type:* DNA *Routes:* Intradermal, Intramuscular *Formulation:* pcDNA synEnv gp140 89.6 + PBS

Vaccine Name: rMVA expressing Gag,Pol of SIVmac239 *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rMVA expressing Gag,Pol of SIVmac239 + PBS

Vaccine Name: rMVA expressing HIV-1 Env of SHIV89.6p (KB9) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rMVA expressing HIV-1 Env of SHIV89.6p (KB9) + PBS

Challenge: SHIV 89.6p *Route:* Intravenous

Main Findings:

- In order to improve the efficacy of current vaccine candidates against HIV/AIDS, chimeric Flt-3 and G-CSF receptor agonists (ProGP) were used to strengthen the induction of immune responses via simultaneous in vivo mobilization of dendritic cells. Administration of this Flt-3/G-CSF chimera elicited marked increases in numbers of both plasmacytoid and myeloid dendritic cells. However, there was no increase seen in T-cell responses either directly following the DNA immunization or after further boosting with MVA vectors expressing HIV-Env89.6p, SIV-Gag. After challenge with SHIV89.6p all animals became infected and no differences were seen between the ProGP treated versus the control group with regard to plasma virus load or CD4 T-cell count. Possibly, additional stimuli to induce dendritic cell maturation may be needed for avid boosting of antigen specific immune activation.

NHP.468 (16103206) **Reversion in vivo after inoculation of a molecular proviral DNA clone of simian immunodeficiency virus with a cytotoxic-T-lymphocyte escape mutation.**

Authors: Kobayashi M, Igarashi H, Takeda A, Kato M, Matano T

Journal: J Virol. 2005 Sep;79(17):11529-32.

Objectives: Challenge, Pathogenicity.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Challenge: SIVmac239 proviral DNA, SIVmac239Gag216S proviral DNA *Route:* Intramuscular

Main Findings:

- In a previous study, macaques vaccinated with a DNA prime/Gag-expressing Sendai viral boost controlled the replication of SIVmac239 in macaques. In the process of viral control, a mutant virus escaping from epitope-specific cytotoxic-T-lymphocyte (CTL) responses was rapidly selected and contained. In this study, the escape mutant virus was studied further. The escape virus reverted to wild-type virus following challenge and became predominant in the absence of the epitope-specific CTL after inoculation of naive macaques with a molecular clone DNA of the CTL escape mutant SIV. This is the first report describing reversion in vivo from an inoculated, molecular proviral DNA clone of immunodeficiency virus with a CTL escape mutation.

NHP.469 (16254351) **Immunogenicity of recombinant fiber-chimeric adenovirus serotype 35 vector-based vaccines in mice and rhesus monkeys.**

Authors: Nanda A, Lynch DM, Goudsmit J, Lemckert AA, Ewald BA, Sumida SM, Truitt DM, Abbink P, Kishko MG, Gorgone DA, Lifton MA, Shen L, Carville A, Mansfield KG, Havenga MJ, Barouch DH

Journal: J Virol. 2005 Nov;79(22):14161-8.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: rAd5-SIV gag and HIV-1 Env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd5-SIV gag and HIV-1 Env + PBS

Vaccine Name: rAd35k5-SIV gag HIV-1 Env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd35k5-SIV gag HIV-1 Env + PBS

Vaccine Name: rAd35-SIV Gag HIV-1 Env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd35-SIV Gag HIV-1 Env + PBS

Main Findings:

- In this study, the differences in immunogenicity between rAd5 and rAd35 vectors were explored to determine whether the fiber proteins of these viruses contributed to differential immune responses. Capsid chimeric rAd35 vectors containing the Ad5 fiber knob (rAd35k5) were constructed and compared to the immunogenicities of rAd5 and rAd35 vectors expressing simian immunodeficiency virus Gag and HIV-1 Env in mice and rhesus monkeys. In vitro studies demonstrated that rAd35k5 vectors utilized the Ad5

receptor CAR rather than the Ad35 receptor CD46. In vivo studies showed that rAd35k5 vectors were more immunogenic than rAd35 vectors in both mice and rhesus monkeys. These data suggest that the Ad5 fiber knob contributes substantially to the immunogenicity of rAd vectors. Moreover, these studies demonstrate that capsid chimeric rAd vectors can be constructed to combine beneficial immunologic and serologic properties of different Ad serotypes.

NHP.470 (16023165) **Comparative immunogenicity in rhesus monkeys of multi-protein HIV-1 (CRF02_AG) DNA/MVA vaccines expressing mature and immature VLPs.**

Authors: Ellenberger D, Wyatt L, Li B, Buge S, Lanier N, Rodriguez IV, Sariol CA, Martinez M, Monsour M, Vogt J, Smith J, Otten R, Montefiori D, Kraiselburd E, Moss B, Robinson H, McNicholl J, Butera S

Journal: Virology. 2005 Sep 15;340(1):21-32.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pGA1/IC1-90 (HIV-1 gag,pol,env) *Type:* DNA *Route:* Intramuscular *Formulation:* pGA1/IC1-90 (HIV-1 gag,pol,env) + PBS

Vaccine Name: pGA1/IC48 (HIV-1 gag,pol,env) *Type:* DNA *Route:* Intramuscular *Formulation:* pGA1/IC48 (HIV-1 gag,pol,env) + PBS

Vaccine Name: rMVA (gag,pol,env) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rMVA (gag,pol,env) + PBS

Main Findings:

- In this study, the immunogenicities of two DNA vaccine constructs, IC1-90 and IC48, based on HIV-1 subtype CRF02_AG were compared in rhesus monkeys using a DNA prime/rMVA boost regimen. IC1-90 produces primarily immature (core comprises unprocessed Pr55Gag) HIV-like particles (VLPs) and IC48 produces mature VLP with processed Pr55Gag, immature VLP, and intracellular protein aggregates. Both vaccines raised significant cellular responses for Gag, Pol, and Env. Approximate twofold higher ELISPOT responses to Gag and Env epitopes were observed for IC48 animals than for IC1-90 animals at the peak post-MVA effector ($P = 0.028$) and late memory ($P = 0.051$) phases, respectively. Greater breadth for IC48-primed animals was observed than for IC1-90-primed animals at peak response ($P = 0.03$). These results indicate that the vaccines elicited high frequency T cell responses and primed anti-Env antibody. They also suggest that expression of different forms of VLP has a significant effect on elicited cellular and humoral immunity.

NHP.471 (16095768) **Multi-envelope HIV-1 vaccine devoid of SIV components controls disease in macaques challenged with heterologous pathogenic SHIV.**

Authors: Zhan X, Martin LN, Slobod KS, Coleclough C, Lockey TD, Brown SA, Stambas J, Bonsignori M, Sealy RE, Blanchard JL, Hurwitz JL

Journal: Vaccine. 2005 Nov 16;23(46-47):5306-20. Epub 2005 Jul 20.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: HIV-1 multi-env cocktail *Type:* DNA *Route:* Intramuscular *Formulation:* HIV-1 multi-env cocktail + PBS

Vaccine Name: rVV-env cocktail *Type:* Recombinant Vector (virus/bacteria) *Route:* Subcutaneous *Formulation:* rVV-env cocktail + PBS

Vaccine Name: Env protein cocktail *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* Env protein cocktail + PBS

Challenge: SHIV89.6P *Route:* Intravenous

Main Findings:

- In this study, the efficacy of an HIV-1 envelope cocktail vaccine, delivered by successive immunizations with recombinant DNA, recombinant vaccinia virus and recombinant envelope proteins, was tested in six macaques. Following vaccination, animals developed a diversity of anti-envelope antibody binding and neutralizing activities toward proteins and viruses that were not represented by sequence in the vaccine. T-cells were also elicited, as measured by gamma-interferon production assays with envelope-derived peptide pools. Vaccinated and control animals were then challenged with the heterologous pathogenic SHIV, 89.6P. Vaccinated monkeys experienced significantly lower virus titers and better maintenance of CD4+ T-cells than unvaccinated controls. The B- and T-cell immune responses were far superior post-challenge in the vaccinated group.

NHP.472 (16194587) **Comparative evaluation of three different intramuscular delivery methods for DNA immunization in a nonhuman primate animal model.**

Authors: Rao SS, Gomez P, Mascola JR, Dang V, Krivulka GR, Yu F, Lord CI, Shen L, Bailer R, Nabel GJ, Letvin NL

Journal: Vaccine. 2006 Jan 16;24(3):367-73. Epub 2005 Aug 9.

Objectives: Immunogenicity.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: CMV/R gp145 (dCFI) *Type:* DNA *Route:* Intramuscular *Formulation:* CMV/R gp145 (dCFI) + PBS

Vaccine Name: CMV/R gp145 (delCFI) *Type:* DNA *Route:* Intramuscular *Formulation:* CMV/R gp145 (delCFI) + PBS

Vaccine Name: CMV/R R5 gp145 (delCFI) *Type:* DNA *Route:* Intramuscular *Formulation:* CMV/R R5 gp145 (delCFI) + PBS

Vaccine Name: CMV/R Gag, Pol, Nef *Type:* DNA *Route:* Intramuscular *Formulation:* CMV/R Gag, Pol, Nef + PBS

Main Findings:

- The immunogenicity of three different methods of intramuscular plasmid DNA administration was compared in cynomolgus monkeys: needle and syringe, Biojector (R) 2000, and Mini-Ject (TM).
- The needle-free approaches to vaccine administration do not significantly improve the immunogenicity of the plasmid DNA vaccine used in the study.

NHP.473 (16079886) **Prime-boost vaccination with plasmid DNA and a chimeric adenovirus type 5 vector with type 35 fiber induces protective immunity against HIV.**

Authors: Xin KQ, Jounai N, Someya K, Honma K, Mizuguchi H, Naganawa S, Kitamura K, Hayakawa T, Saha S, Takeshita F, Okuda K, Honda M, Klinman DM, Okuda K

Journal: Gene Ther. 2005 Dec;12(24):1769-77.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Ad5-luc *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* Ad5-luc + PBS

Vaccine Name: Ad5/35-Luc *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* Ad5/35-Luc + PBS

Vaccine Name: Ad5/35-HIV gp160 *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* Ad5/35-HIV gp160 + PBS

Main Findings:

- This study examines the safety and immunogenicity of a replication-defective chimeric Ad5 vector with the Ad35 fiber (Ad5/35) in BALB/c mice and rhesus monkeys. This novel Ad5/35 vector showed minimal hepatoxicity after intramuscular administration with

the novel Ad5/35 vector. An Ad5/35 vector expressing HIV Env gp160 protein (Ad5/35-HIV) generated strong HIV-specific immune responses in both animal models. The Ad5/35-HIV vector was significantly less susceptible to the pre-existing Ad5 immunity than a comparable Ad5 vector.

NHP.474 (16306626) **Cytotoxic T-lymphocyte escape does not always explain the transient control of simian immunodeficiency virus SIVmac239 viremia in adenovirus-boosted and DNA-primed Mamu-A*01-positive rhesus macaques.**

Authors: McDermott AB, O'Connor DH, Fuenger S, Piaskowski S, Martin S, Loffredo J, Reynolds M, Reed J, Furlott J, Jacoby T, Riek C, Dodds E, Krebs K, Davies ME, Schleif WA, Casimiro DR, Shiver JW, Watkins DI

Journal: J Virol. 2005 Dec;79(24):15556-66.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIV/gag/V1Jns *Type:* DNA *Route:* Intramuscular *Formulation:* SIV/gag/V1Jns + BAK, CRL1005 + PBS

Vaccine Name: Ad5/SIV gag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* Ad5/SIV gag + PBS

Challenge: SIVmac239/nef-open *Route:* Intrarectal

Main Findings:

- In this study, macaques were immunized with either a homologous Ad5-gag/Ad5-gag In (Ad5/Ad5) or a heterologous DNA-gag/Ad5-gag (DNA/Ad5) prime-boost regimen, and then challenged with SIVmac239. Macaques vaccinated with the DNA/Ad5 regimen experienced a brief viral load nadir of less than 10,000 viral copies per ml blood plasma that was not seen in Mamu-A*01-negative DNA/Ad5 vaccinees, Mamu-A*01-positive Ad5/Ad5 vaccinees, or vaccine-naive controls. To investigate the reasons underlying this short-lived vaccine effect, breadth of the T-cell response, immunogenetic background, and viral escape from CD8+ lymphocytes was investigated. These animals do not mount unusually broad cellular immune response, nor do they express unusual major histocompatibility complex class I alleles. Viral recrudescence occurred in four of the five Mamu-A*01-positive vaccinated macaques. However, only a single animal in this group demonstrated viral escape in the immunodominant Gag181-189 CM9 response.

NHP.475 (16306625) **Attenuation of simian immunodeficiency virus SIVmac239 infection by prophylactic immunization with dna and recombinant adenoviral vaccine vectors expressing Gag.**

Authors: Casimiro DR, Wang F, Schleif WA, Liang X, Zhang ZQ, Tobery TW, Davies ME, McDermott AB, O'Connor DH, Fridman A, Bagchi A, Tussey LG, Bett AJ, Finnefrock AC, Fu TM, Tang A, Wilson KA, Chen M, Perry HC, Heidecker GJ, Freed DC, Carella A, Punt KS, Sykes KJ, Huang L, Ausensi VI, Bachinsky M, Sadasivan-Nair U, Watkins DI, Emini EA

Journal: J Virol. 2005 Dec;79(24):15547-55.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIV/gag/V1Jns *Type:* DNA *Route:* Intramuscular *Formulation:* SIV/gag/V1Jns + BAK, CRL1005 + PBS

Vaccine Name: Ad5/SIV gag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* Ad5/SIV gag + PBS

Challenge: SIVmac239/nef-open *Route:* Intrarectal

Main Findings:

- The prophylactic efficacy of DNA and replication-incompetent adenovirus serotype 5 (Ad5) vaccine vectors expressing simian immunodeficiency virus (SIV) Gag was examined in rhesus macaques using an SIVmac239 challenge. Cohorts of either Mamu-A*01(+) or Mamu-A*01(-) macaques were immunized with a DNA prime-Ad5 boost

regimen; for comparison, a third cohort consisting of Mamu-A*01(+) monkeys was immunized using the Ad5 vector alone for both prime and boost. All animals, along with unvaccinated control cohorts of Mamu-A*01(+) and Mamu-A*01(-) macaques, were challenged intrarectally with SIVmac239. Only the DNA prime-Ad5-boosted Mamu-A*01(+) cohort exhibited a notable reduction in peak plasma viral load (sevenfold) as well as in early set-point viral burdens in both plasma and lymphoid tissues (10-fold) relative to those observed in the control monkeys sharing the same Mamu-A*01 allele. The degree of control in each animal correlated with the levels of Gag-specific immunity before virus challenge. However, virus control was short-lived, and indications of viral escape were evident as early as 6 months postinfection.

NHP.476 (16306607) **A combination DNA and attenuated simian immunodeficiency virus vaccine strategy provides enhanced protection from simian/human immunodeficiency virus-induced disease.**

Authors: Amara RR, Patel K, Niedziela G, Nigam P, Sharma S, Staprans SI, Montefiori DC, Chenareddi L, Herndon JG, Robinson HL, McClure HM, Novembre FJ

Journal: J Virol. 2005 Dec;79(24):15356-67.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pGA1-gag-pol DNA vaccine *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal *Formulation:* pGA1-gag-pol DNA vaccine + PBS

Vaccine Name: SIVmac239-Δnef *Type:* Live Attenuated Virus *Route:* Intravenous *Formulation:* SIVmac239-Δnef + PBS

Challenge: SHIV89.6P *Route:* Intravenous

Main Findings:

- To investigate if preimmunization would increase the level of protection afforded by live attenuated SIVmac239Deltanef (Deltanef), macaques were given two priming immunizations of DNA encoding SIV Gag and Pol proteins, with control macaques receiving vector DNA immunizations. In macaques receiving the SIV DNA inoculation, SIV-specific cellular but not humoral responses were readily detectable 2 weeks after the second DNA inoculation. Following boosting with live attenuated virus, control of Deltanef replication was superior in SIV-DNA-primed macaques versus vector-DNA-primed macaques and was correlated with higher levels of CD8+/gamma-interferon-positive and/or interleukin-2-positive cells. Challenge with an intravenous inoculation of simian/human immunodeficiency virus (SHIV) strain SHIV89.6p resulted in infection of all animals. However, macaques receiving SIV DNA as the priming immunizations had statistically lower viral loads than control animals and did not develop signs of disease, whereas three of seven macaques receiving vector DNA showed severe CD4+ T-cell decline, with development of AIDS in one of these animals. These results demonstrate that addition of a DNA prime to a live attenuated virus provided better protection from disease following challenge than live attenuated virus alone.

NHP.477 (16365439) **Effects of immunization with CCR5-based cycloimmunogen on simian/HIVSF162P3 challenge.**

Authors: Misumi S, Nakayama D, Kusaba M, Iiboshi T, Mukai R, Tachibana K, Nakasone T, Umeda M, Shibata H, Endo M, Takamune N, Shoji S

Journal: J Immunol. 2006 Jan 1;176(1):463-71.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: cDDR5-MAP *Type:* Synthetic Protein/Peptide *Routes:* Subcutaneous, Intraperitoneal *Formulation:* cDDR5-MAP + CFA, IFA + PBS

Challenge: SHIV-SF162P3 *Route:* Intravenous

Main Findings:

- A synthetic cycloimmunogen targeting the HIV-1 coreceptor CCR5 was evaluated for its capacity to induce CCR5-specific Abs with anti-HIV-1 activity in cynomolgus macaques. The immunization of cynomolgus macaques with the cDDR5-conjugated multiple-Ag peptide (cDDR5-MAP) induced anti-cDDR5 serum production for approximately 15 wk after the third immunization. The antisera raised against cDDR5-MAP reacted with both human and macaque CCR5s, and potently suppressed infection by 2 HiV and 1 SHIV isolates in vitro. To examine the prophylactic efficacy of anti-CCR5 serum Ab for acute HIV-1 infection, cynomolgus macaques were challenged with SHIV SF162P3. The cDDR5-MAP immunization attenuated the acute phase of SHIV SF162P3 replication. These results suggest that cDDR5-MAP immunization is an effective prophylactic vaccine strategy for the containment of HIV-1 replication subsequent to infection.

NHP.478 (16365424) **Immunodomination in the evolution of dominant epitope-specific CD8+ T lymphocyte responses in simian immunodeficiency virus-infected rhesus monkeys.**

Authors: Newberg MH, McEvers KJ, Gorgone DA, Lifton MA, Baumeister SH, Veazey RS, Schmitz JE, Letvin NL

Journal: J Immunol. 2006 Jan 1;176(1):319-28.

Objectives: Challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Challenge: SIVmac251 *Route:* Intravenous

Main Findings:

- Cohorts of rhesus monkeys that expressed the MHC class I molecules Mamu-A*01, Mamu-A*02, or both, were assessed for the evolution of their dominant epitope-specific CD8+ T lymphocyte responses (Gag p11C- and Tat TL8-specific in the Mamu-A*01+ and Nef p199RY-specific in the Mamu-A*02+ monkeys) following acute SIV infection. The Mamu-A*02+ monkeys that also expressed Mamu-A*01 exhibited a significant delay in the evolution of the CD8+ T lymphocyte responses specific for the dominant Mamu-A*02-restricted SIV epitope, Nef p199RY. This delay in kinetics was not due to differences in viral load kinetics or magnitude or in viral escape mutations, but was associated with the evolution of the Mamu-A*01-restricted CD8+ T lymphocyte responses to the highly dominant SIV epitopes Gag p11C and Tat TL8. Thus, the evolution of dominant epitope-specific CD8+ T lymphocyte responses can be suppressed by other dominant epitope-specific responses, and this immunodomination is important in determining the kinetics of dominant epitope-specific responses.

NHP.479 (16365399) **Improved vaccine protection from simian AIDS by the addition of nonstructural simian immunodeficiency virus genes.**

Authors: Hel Z, Tsai WP, Tryniszewska E, Nacsa J, Markham PD, Lewis MG, Pavlakis GN, Felber BK, Tartaglia J, Franchini G

Journal: J Immunol. 2006 Jan 1;176(1):85-96.

Objectives: Challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: NYVAC-SIV-gag-pol-env (NYVAC-SIV-gpe) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* NYVAC-SIV-gag-pol-env (NYVAC-SIV-gpe) + PBS

Vaccine Name: DNA-Retanef *Type:* DNA *Route:* Intradermal

Vaccine Name: NYVAC-Retanef *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name: DNA-SIV-gag, env *Type:* DNA *Route:* Intradermal

Challenge: SIVmac251 (561) *Route:* Intrarectal

Main Findings:

- Two control groups one unvaccinated and one mack vaccinated with empty NYVAC were compared to DNA-retanef prime plus NYVAC-retanef boost; DNAretanef plus DNA-gag-

env prime plus NYVAC-retanef plus NYVAC-gag-env boost; DNA-gag-env prime plus NYVAC-gag-env boost.
- The retanef plus gag-env animals had an average viral load after challenge, that was lower than either retanef alone or gag-env alone.
- Variations in set point viral load was as great between individual animals in a group, as it was between groups.
- Peak viremia correlated with set-point viral loads.

NHP.480 (16359235) **Timing of retroviral infection influences anamnestic immune response in vaccinated primates.**

Authors: Anderson DE, Singapuri A, Kang KH, Montefiori DC, Torres JV

Journal: Viral Immunol. 2005;18(4):689-94.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: HECs (hypervariable epitope constructs) - SIV Env gp130 *Type:* Recombinant Subunit Protein *Route:* *Formulation:* HECs (hypervariable epitope constructs) - SIV Env gp130 + MPL™ + PBS

Challenge: SIVmac251 *Route:* Intravenous

Main Findings:
- This study examined whether broadly reactive vaccine-induced humoral immunity would remain broadly reactive after viral challenge in a simian immunodeficiency virus (SIV) infection model of rhesus macaques. In addition, animals were challenged when predominately effector or memory lymphocyte populations were present to determine whether there would be significant differences in anamnestic antibody responses. Animals immunized over a prolonged period and challenged 11 months after vaccination mounted more broadly reactive and stronger humoral immunity than those rapidly vaccinated and challenged 2 weeks after their final vaccinations. These data suggest that vaccination schedule and the timing of virus challenge should be considered when evaluating future candidate HIV vaccines.

NHP.481 (16361426) **Broad cellular immunity with robust memory responses to simian immunodeficiency virus following serial vaccination with adenovirus 5- and 35-based vectors.**

Authors: Barratt-Boyes SM, Soloff AC, Gao W, Nwanegbo E, Liu X, Rajakumar PA, Brown KN, Robbins PD, Murphey-Corb M, Day RD, Gambotto A

Journal: J Gen Virol. 2006 Jan;87(Pt 1):139-49.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Ad5-p17 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular *Formulation:* Ad5-p17 + Saline

Vaccine Name: Ad5-p45 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular *Formulation:* Ad5-p45 + Saline

Vaccine Name: Ad35-p17 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular *Formulation:* Ad35-p17 + Saline

Vaccine Name: Ad35-p45 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular *Formulation:* Ad35-p45 + Saline

Challenge: SIVDeltaB670 *Route:* Intrarectal

Main Findings:
- The immunogenicity of a first-generation, replication-competent Ad35-based vaccine was tested in the simian immunodeficiency virus (SIV) rhesus macaque model by evaluating its capacity to boost immunity generated by Ad5-based vectors. A series of four immunizations with replication-defective Ad5 vectors expressing SIVmac239 gag induced

high-frequency responses mediated by both CD8(+) and CD4(+) T cells directed against several epitopes. Ad5-specific neutralizing antibody responses that did not neutralize Ad35 were rapidly induced but waned over time. Subsequent immunization with Ad5-based vectors was minimally effective, whereas immunization with Ad35-based vectors generated a strong increase in the frequency of Gag-specific T cells with specificities that were unchanged. Challenge with the distinct pathogenic isolate SIV/DeltaB670 generated robust and selective recall responses to Gag with similar specificities as induced by vaccination that were elevated for 25 weeks relative to controls.

NHP.482 (16325880) **Preclinical evaluation of cellular immune responses elicited by a polyvalent DNA prime/protein boost HIV-1 vaccine.**

Authors: Cristillo AD, Wang S, Caskey MS, Unangst T, Hocker L, He L, Hudacik L, Whitney S, Keen T, Chou TH, Shen S, Joshi S, Kalyanaraman VS, Nair B, Markham P, Lu S, Pal R

Journal: Virology. 2006 Mar 1;346(1):151-68. Epub 2005 Dec 2.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: polyvalent HIV-1 env/gag *Type:* DNA *Routes:* Intradermal, Intramuscular *Formulation:* polyvalent HIV-1 env/gag + PBS

Vaccine Name: HIV-1 Env/Gag *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* HIV-1 Env/Gag + QS-21 + PBS

Main Findings:

- A polyvalent DNA prime/protein boost vaccine, consisting of codon optimized HIV-1 env (A, B, C, E) and gag (C) and homologous gp120 proteins in QS-21, was evaluated in rhesus macaques and BALB/c mice. Humoral and cellular responses, detected following DNA immunization, were increased following protein boost in macaques and mice. Our study reveals that, in addition to augmenting humoral responses, protein boosting of DNA-primed animals augments cellular immune responses mediated by CD8+ CTL, CD4+ T-helper cells and Th1 cytokines.

NHP.483 (16128922) **Immune mechanisms associated with protection from vaginal SIV challenge in rhesus monkeys infected with virulence-attenuated SHIV 89.6.**

Authors: Miller CJ, Abel K

Journal: J Med Primatol. 2005 Oct;34(5-6):271-81.

NHP.484 (16616287) **Polyvalent HIV-1 Env vaccine formulations delivered by the DNA priming plus protein boosting approach are effective in generating neutralizing antibodies against primary human immunodeficiency virus type 1 isolates from subtypes A, B, C, D and E.**

Authors: Wang S, Pal R, Mascola JR, Chou TH, Mboudjeka I, Shen S, Liu Q, Whitney S, Keen T, Nair BC, Kalyanaraman VS, Markham P, Lu S

Journal: Virology. 2006 Jun 20;350(1):34-47. Epub 2006 Apr 17.

Objectives: Challenge.

NHP.485 (16359231) **Adjuvant action of murine IL-2/Ig plasmid after intramuscular immunization with Indian HIV-1 subtype C recombinant env.gp 120 construct.**

Authors: Aggarwal P, Kumar S, Vajpayee M, Seth P

Journal: Viral Immunol. 2005;18(4):649-56.

NHP.486 (16424209) **Induction of positive cellular and humoral immune responses by a prime-boost vaccine**

encoded with simian immunodeficiency virus gag/pol.

Authors: Someya K, Ami Y, Nakasone T, Izumi Y, Matsuo K, Horibata S, Xin KQ, Yamamoto H, Okuda K, Yamamoto N, Honda M

Journal: J Immunol. 2006 Feb 1;176(3):1784-95.

Objectives: Immunogenicity, Immunotherapy.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: SIV gag/pol *Type:* DNA *Route:* Intramuscular *Formulation:* SIV gag/pol + PBS

Vaccine Name: rDIs SIV gag/pol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rDIs SIV gag/pol + PBS

Challenge: SHIV-C2/1 *Route:* Intravenous

Main Findings:

- In this study, macaques were primed with plasmid DNA encoding SIV gag and pol genes (SIVgag/pol DNA) and then boosted with replication-deficient vaccinia virus DIs recombinant expressing the same genes (rDIsSIVgag/pol). This prime-boost regimen generated higher levels of Gag-specific CD4+ and CD8+ T cell responses than did either SIVgag/pol DNA or rDIsSIVgag/pol alone. When the macaques were i.v. challenged with pathogenic simian/HIV, the prime-boost group maintained high CD4+ T cell counts and reduced plasma viral loads up to 30 wk after viral challenge, whereas the rDIsSIVgag/pol group showed only a partial attenuation of the viral infection, and the group immunized with SIVgag/pol DNA alone showed none at all. These results demonstrate that a vaccine regimen that primes with DNA and then boosts with a replication-defective vaccinia virus DIs generates anti-SIV immunity.

NHP.487 (16814356) **Durable protection of rhesus macaques immunized with a replicating adenovirus-SIV multigene prime/protein boost vaccine regimen against a second SIV(mac251) rectal challenge: Role of SIV-specific CD8+ T cell responses.**

Authors: Malkevitch NV, Patterson LJ, Aldrich MK, Wu Y, Venzon D, Florese RH, Kalyanaraman VS, Pal R, Lee EM, Zhao J, Cristillo A, Robert-Guroff M

Journal: Virology. 2006 Sep 15;353(1):83-98. Epub 2006 Jun 30.

NHP.488 (16511428) **A randomized, placebo-controlled phase I trial of DNA prime, recombinant fowlpox virus boost prophylactic vaccine for HIV-1.**

Authors: Kelleher AD, Puls RL, Bebbington M, Boyle D, Ffrench R, Kent SJ, Kippax S, Purcell DF, Thomson S, Wand H, Cooper DA, Emery S

Journal: AIDS. 2006 Jan 9;20(2):294-7.

NHP.489 (16439550) **Involvement of multiple epitope-specific cytotoxic T-lymphocyte responses in vaccine-based control of simian immunodeficiency virus replication in rhesus macaques.**

Authors: Kawada M, Igarashi H, Takeda A, Tsukamoto T, Yamamoto H, Dohki S, Takiguchi M, Matano T

Journal: J Virol. 2006 Feb;80(4):1949-58.

Objectives: Challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- This is a follw-up of animals in trial NHP-382.
- During 2 years of follow-up, all the seven noncontrollers maintained high levels of plasma viremia, four of them developed AIDS and had to be euthanized.
- plasma viremia was undetectable and peripheral CD4 T-cell counts were maintained even after 2 years of infection in three (V4, V6, and V8) of five controllers. In the other two controllers (V5 and V3), however, plasma viremia reappeared and was detectable (more

than 400 RNA copies/ ml) at week 58 after challenge.

NHP.490 (16524647) **Delivery of the HIV-1 Tat protein to dendritic cells by the CyaA vector induces specific Th1 responses and high affinity neutralizing antibodies in non human primates.**

Authors: Mascarell L, Bauche C, Fayolle C, Diop OM, Dupuy M, Nougarede N, Perraut R, Ladant D, Leclerc C

Journal: Vaccine. 2006 Apr 24;24(17):3490-9. Epub 2006 Feb 21.

NHP.491 (16438642) **Short communication: characteristics of effective immune control of simian/human immunodeficiency virus in pigtail macaques.**

Authors: Stratov I, Dale CJ, Chea S, Montefiori DC, De Rose R, Reece JC, Kent SJ

Journal: AIDS Res Hum Retroviruses. 2006 Jan;22(1):27-32.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Vaccine Name: pHIS-SHIV-B *Type:* DNA *Route:* Intramuscular *Formulation:* pHIS-SHIV-B + Saline

Vaccine Name: rFPV-gag/pol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rFPV-gag/pol + Saline

Vaccine Name: rFPV-HIV env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rFPV-HIV env + Saline

Challenge: SHIV-SF162P3, SHIV.229(mn) *Route:* Intrarectal, Intravenous

Main Findings:

- T cell and nAb responses were studied in three pigtail macaques protected from chronic simian/human immunodeficiency virus (SHIV) viremia by DNA prime/fowlpoxvirus boost vaccine regimens. Immunity was studied both after an initial intrarectal SHIV challenge, as well as during CD8 T cell depletion and a subsequent intravenous SHIV rechallenge. Remarkably, SHIV-specific CD4 and CD8 T cells were detectable in the absence of viremia following an initial SHIV challenge in one animal, subsequent to recovery from CD8 T cell depletion in all three animals, and following control of heterologous SHIV rechallenge in two animals. Neutralizing antibodies were also enhanced following CD8 depletion without recrudescence of viremia in all three animals. These observations, although in a small subset of animals, suggest the hypothesis that combinations of primed T cell immunity and neutralizing antibodies can maintain control of chronic primate lentiviral infections.

NHP.492 (16460776) **Immunization of rhesus macaques with a polyvalent DNA prime/protein boost human immunodeficiency virus type 1 vaccine elicits protective antibody response against simian human immunodeficiency virus of R5 phenotype.**

Authors: Pal R, Kalyanaraman VS, Nair BC, Whitney S, Keen T, Hocker L, Hudacik L, Rose N, Mboudjeka I, Shen S, Wu-Chou TH, Montefiori D, Mascola J, Markham P, Lu S

Journal: Virology. 2006 May 10;348(2):341-53.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: polyvalent HIV-1 env *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal *Formulation:* polyvalent HIV-1 env + PBS

Vaccine Name: polyvalent gp120 proteins *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* polyvalent gp120 proteins + QS-21 + PBS

Vaccine Name: Gag p41 *Type:* Recombinant Subunit Protein *Route:* Intramuscular *Formulation:* Gag p41 + QS-21 + PBS

Challenge: Ba-L *Route:* Intrarectal

Main Findings:

- The immunogenicity of a polyvalent HIV-1 vaccine comprised of Env antigens from primary R5 isolates was evaluated in rhesus macaques. DNA vaccines encoding four Env antigens from multiple HIV-1 subtypes and HIV-1 Gag antigen from a single subtype elicited a persistent level of binding antibodies to gp120 from multiple HIV-1 isolates that were markedly enhanced following boosting with homologous gp120 proteins in QS-21 adjuvant irrespective of the route of DNA immunization. These sera neutralized homologous and, to a lesser degree, heterologous HIV-1 isolates. Four of the six immunized animals were completely protected following rectal challenge with a SHIV encoding Env from HIV-1Ba-L, whereas the virus load was reduced in the remaining animals compared to naïve controls. Hence priming with DNA encoding Env antigens from multiple HIV-1 clades followed by boosting with homologous Env proteins elicits anti-HIV-1 immune responses capable of protecting macaques against mucosal transmission of R5 tropic SHIV isolate.

NHP.493 (16274888) **Reduction of viral loads by multigenic DNA priming and adenovirus boosting in the SIVmac-macaque model.**

Authors: Suh YS, Park KS, Sauermann U, Franz M, Norley S, Wilfingseder D, Stoiber H, Fagrouch Z, Heeney J, Hunsmann G, Stahl-Hennig C, Sung YC

Journal: Vaccine. 2006 Mar 10;24(11):1811-20. Epub 2005 Oct 25.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: Gag/Env SIVmac239 *Type:* DNA *Route:* Intramuscular *Formulation:* Gag/Env SIVmac239 + hIL-12(N222L) + PBS

Vaccine Name: sPol-SIV *Type:* DNA *Route:* Intramuscular *Formulation:* sPol-SIV + hIL-12(N222L) + PBS

Vaccine Name: sVif-Nef SIVmac239 *Type:* DNA *Route:* Intramuscular *Formulation:* sVif-Nef SIVmac239 + hIL-12(N222L) + PBS

Vaccine Name: sTat-Vpx SIVmac239 *Type:* DNA *Route:* Intramuscular *Formulation:* sTat-Vpx SIVmac239 + hIL-12(N222L) + PBS

Vaccine Name: rAd5/gag-env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd5/gag-env + PBS

Vaccine Name: rAd5/sPol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd5/sPol + PBS

Vaccine Name: rAd5/sVif-Nef *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd5/sVif-Nef + PBS

Vaccine Name: rAd5/sTat-Vpx *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd5/sTat-Vpx + PBS

Challenge: SIVmac251 *Route:* Intrarectal

Main Findings:

- This study investigated the ability of a multigenic SIV DNA prime/replication-defective adenovirus serotype 5 (rAd/SIV) boost regimen to induce SIV-specific immune responses and protection against intrarectal challenge with SIVmac251 in rhesus macaques. Four rhesus macaques were immunized with SIV DNA vaccine and boosted once with rAd/SIV vaccine. While the SIV DNA vaccine included plasmids expressing a mutated human IL-12 gene (IL-12N222L) as well as SIVmac239 structural and regulatory genes, the rAd/SIV vaccine contained rAd vectors expressing SIVmac239 genes only. Immunization with SIV DNA vaccine alone induced SIV-specific IFN-gamma ELISPOT responses in only two of four vaccinated macaques, whereas all animals developed SIV-specific T-cell responses and Env- and Tat-specific antibody responses following the rAd/SIV vaccine boost. Upon intrarectal challenge with pathogenic SIVmac251, strong anamnestic Env-specific binding and neutralizing antibody responses were detected in the vaccinated macaques. Overall, the immunized macaques had lower peak and set-point viral loads

than control macaques, suggesting that the induced immune responses play a role in the control of viremia.

NHP.494 (16706622) **Expansion after epitope peptide exposure in vitro predicts cytotoxic T lymphocyte epitope dominance hierarchy in lymphocytes of vaccinated mamu-a*01+ rhesus monkeys.**

Authors: Subbramanian RA, Charini WA, Kuroda MJ, Seaman M, Chhay H, Lifton MA, Gorgone DA, Schmitz JE, Carville A, Letvin NL

Journal: AIDS Res Hum Retroviruses. 2006 May;22(5):445-52.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: rAd5-SIVmac239 gag/pol *Type:* Recombinant Vector (virus/bacteria) *Routes:* --, Intramuscular *Formulation:* rAd5-SIVmac239 gag/pol + Saline, PBS

Vaccine Name: CTL epitopes/p11C-deleted SIVmac239Gag *Type:* DNA *Route:* Intramuscular *Formulation:* CTL epitopes/p11C-deleted SIVmac239Gag + PBS

Vaccine Name: CTL epitopes/EGFP *Type:* DNA *Route:* Intramuscular *Formulation:* CTL epitopes/EGFP + PBS

Vaccine Name: CTL epitopes *Type:* DNA *Route:* Intramuscular *Formulation:* CTL epitopes + PBS

Vaccine Name: rVac SIVmac251 pol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rVac SIVmac251 pol + PBS

Vaccine Name: Ad5 HIV 89.6 env *Type:* Recombinant Vector (virus/bacteria) *Route:* -- *Formulation:* Ad5 HIV 89.6 env + PBS

Vaccine Name: rVac SIVmac251 gag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rVac SIVmac251 gag + PBS

Vaccine Name: rVac HIV-1 89.6 Env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rVac HIV-1 89.6 Env + PBS

Vaccine Name: MVA-SIV gag-pol and HIV-1 89.6 env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* MVA-SIV gag-pol and HIV-1 89.6 env + PBS

Main Findings:

- Cytotoxic T lymphocytes (CTL) have a propensity to focus recognition on a limited number of dominant epitopes. In studies of rhesus monkeys expressing the Mamu-A*01 MHC class I allele, variously configured multiepitope plasmid DNA vaccine constructs elicited CTL populations that do not show evidence of skewing recognition to dominant epitopes. Nevertheless, repeated boosting of these vaccinated monkeys with different live recombinant vaccine vectors uncovers and amplifies the usual CTL epitope dominance hierarchy. Importantly, in vitro peptide stimulation of peripheral blood mononuclear cells from monkeys that have received only a multiepitope plasmid DNA priming immunization uncovers this dominance hierarchy. Therefore, the dominance hierarchy of the vaccine-elicited epitope-specific CTL populations is inherent in the T lymphocytes of the monkeys after initial exposure to epitope peptides, and the ultimate breadth of epitope recognition cannot be modified thereafter. This finding underscores the enormous challenge associated with increasing the breadth of CTL recognition through vaccination.

NHP.495 (16735692) **Vaccination preserves CD4 memory T cells during acute simian immunodeficiency virus challenge.**

Authors: Mattapallil JJ, Douek DC, Buckler-White A, Montefiori D, Letvin NL, Nabel GJ, Roederer M

Journal: J Exp Med. 2006 Jun 12;203(6):1533-41. Epub 2006 May 30.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac239 gag/pol *Type:* DNA *Route:* Intradermal (Gene Gun DNA-coated gold beads) *Formulation:* SIVmac239 gag/pol + PBS

Vaccine Name: SIVmac239 Env *Type:* DNA *Route:* Intradermal (Gene Gun DNA-coated gold beads) *Formulation:* SIVmac239 Env + PBS

Vaccine Name: rAd5-SIVmac239 gag/pol *Type:* Recombinant Vector (virus/bacteria) *Routes:* --, Intramuscular *Formulation:* rAd5-SIVmac239 gag/pol + Saline, PBS

Vaccine Name: rAd5 SIVmac239 env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd5 SIVmac239 env + PBS

Challenge: SIVmac251 *Route:* Intravenous

Main Findings:

- These results demonstrate that prior vaccination reduces the destruction of CD4 memory cells during acute SIV Mac251 infection, leading to better survival and long-term outcome. Systemic vaccination with a DNA-prime recombinant adenovirus boost regimen preserved memory CD4 T cells throughout the body. The vaccine regimen induced broad CD4 and CD8 T cell responses in all tissues examined and, importantly, induced antibodies that neutralized the primary isolate of SIV used for challenge. The extent of preservation of the CD4 memory compartment during the acute phase is a strong predictor for subsequent progression to death. This data underscores the need for interventions that protect against early destruction of CD4 memory T cells during acute infection.

NHP.496 (16796533) **Comparative evaluation of simian, simian-human, and human immunodeficiency virus infections in the pigtail macaque (Macaca nemestrina) model.**

Authors: Batten CJ, De Rose R, Wilson KM, Agy MB, Chea S, Stratov I, Montefiori DC, Kent SJ

Journal: AIDS Res Hum Retroviruses. 2006 Jun;22(6):580-8.

Objectives: Challenge.

Species/Subspecies: Macaca nemestrina (pigtailed macaque)

Challenge: SHIV-SF162P3, LAI isolate K98227/W35, SHIV.229(mn), HIV-1.LAI, mac239 proviral DNA, SIVmac251 *Route:* Intrarectal, Intrarectal, Intravenous, Intravenous, Vaginal or perivaginal, Intradermal (Gene Gun DNA-coated gold beads), Intramuscular

Main Findings:

- The virologic and immunologic characteristics of HIV-1, SIV, and SHIV infection of naive pigtail macaques was compared across a series of preclinical HIV vaccine studies. SIVmac251 and SIVmac239 infection of naive pigtail macaques resulted in a gradual decline in peripheral CD4+ T cells in the setting of high levels of viremia, approximating most closely human infection of HIV-1. In contrast, the CXCR4-utilizing SHIVmn229 virus resulted in rapid depletion of CD4+ T cells and minimal generation of humoral or cellular immune responses, similar to that observed with SHIV89.6P infection of rhesus macaques. Infection with the CCR5-utilizing, rhesus macaque passaged, SHIVSF162P3 resulted in some overall CD4+ T cell decline, however, three of eight macaques naturally control SHIVSF162P3 viremia to very low levels in the setting of robust adaptive immunity. Despite attempts at infecting pigtail macaques with HIV-1 strains passaged in juvenile pigtail macaques in vivo or in PBMC isolated from pigtail macaques in vitro, only lower nonsustained levels of viral replication were observed. These results provide a series of virologic models with which to evaluate potential AIDS vaccines in pigtail macaques.

NHP.497 (16288822) **A dose sparing effect by plasmid encoded IL-12 adjuvant on a SIVgag-plasmid DNA vaccine in rhesus macaques.**

Authors: Schadeck EB, Sidhu M, Egan MA, Chong SY, Piacente P, Masood A, Garcia-Hand D, Cappello S, Roopchand V, Megati S, Quiroz J, Boyer JD, Felber BK, Pavlakis GN, Weiner DB, Eldridge JH, Israel ZR

Journal: Vaccine. 2006 May 22;24(21):4677-87. Epub 2005 Oct 26.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pSIV gag p39 *Type:* DNA *Route:* Intramuscular *Formulation:* pSIV gag p39 + IL-12 plasmid + PBS

Main Findings:

- An experimental pDNA vaccine adjuvant expressing IL-12 was evaluated for its ability to augment the humoral and cellular immune responses elicited by a SIVmac239 gag p39 expressing pDNA vaccine. Rhesus macaques were immunized with 1.5 mg or 5.0 mg of SIVmac239 gag pDNA, with or without co-immunization of IL-12 pDNA at 1.5 mg and 5.0 mg, respectively. Serum antibody responses and cellular immune responses to simian immunodeficiency virus (SIV) gag were significantly increased in macaques receiving IL-12 pDNA. There was no statistical difference between the immune responses elicited by the high and low dose of IL-12 pDNA, a finding which could allow a dose reduction of vaccine without the concomitant loss of imunogenicity. Furthermore, analysis of the breadth of the T-cell response during the vaccination schedule, using overlapping peptides to SIV gag, demonstrated a significant correlation between the magnitude and breadth of the immune responses in the vaccines.

NHP.498 (16181711) **Potent immunogenicity of an HIV-1 gag-pol fusion DNA vaccine delivered by in vivo electroporation.**

Authors: Otten GR, Schaefer M, Doe B, Liu H, Megede JZ, Donnelly J, Rabussay D, Barnett S, Ulmer JB

Journal: Vaccine. 2006 May 22;24(21):4503-9. Epub 2005 Aug 19.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- DNA immunization by in vivo intramuscular electroporation was effective for inducing high levels of Gag and Pol T-cell responses.

NHP.499 (16185790) **Rhesus macaques with high levels of vaccine induced IFN-gamma producing cells better control viral set-point following challenge with SIV239.**

Authors: Boyer JD, Maciag PC, Parkinson R, Wu L, Lewis MG, Weiner DB, Paterson Y

Journal: Vaccine. 2006 May 22;24(21):4498-502. Epub 2005 Aug 18.

Objectives: Challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pcSIVgag *Type:* DNA *Route:* Intramuscular

Vaccine Name: pCSIV-env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name: Lyseria monocyogenes SIV-gag *Type:* Recombinant Vector (virus/bacteria) *Route:* Oral

Vaccine Name: Lysteria monocytogenes SIV-env *Type:* Recombinant Vector (virus/bacteria) *Route:* Oral

Challenge: SIVmac239 *Route:* Intrarectal

Main Findings:

- The correlation between vaccine-induced immune response and viral load in infected challenged macaques was greatest early in infection.

NHP.500 (16571790) **Systemic immunization with an ALVAC-HIV-1/protein boost vaccine strategy protects rhesus macaques from CD4+ T-cell loss and reduces both systemic and mucosal simian-human immunodeficiency virus SHIVKU2 RNA levels.**

Authors: Pal R, Venzon D, Santra S, Kalyanaraman VS, Montefiori DC, Hocker L, Hudacik L, Rose N, Nacsa J, Edghill-Smith Y, Moniuszko M, Hel Z, Belyakov IM, Berzofsky JA, Parks RW, Markham PD, Letvin NL, Tartaglia J, Franchini G

Journal: J Virol. 2006 Apr;80(8):3732-42.

Objectives: Challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: o-gp140-US4 *Type:* Synthetic Protein/Peptide *Route:* Intramuscular *Formulation:* o-gp140-US4 + MF59

Vaccine Name: ALVAC- SIVmac251-gag-pol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* ALVAC- SIVmac251-gag-pol + Saline

Vaccine Name: ALVAC-HIV-1-IIIB-gag-pol-gp120-env vCP250 *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* ALVAC-HIV-1-IIIB-gag-pol-gp120-env vCP250 + Saline

Vaccine Name: ALVAC-HIV-1-IIIB-gag-pol-gp160-env vCP1420 *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* ALVAC-HIV-1-IIIB-gag-pol-gp160-env vCP1420 + Saline

Vaccine Name: gp120 *Type:* Purified Viral Products *Route:* Intramuscular

Challenge: SHIV-KU2 *Route:* Intrarectal

Main Findings:

- ALVAC-HIV-1 recombinant vaccine expressing Gag, Pol and gp120 along with an Env peptide boost reduced viral load in challenged macaques.
- Adding Tat peptides to the boost did not increase effectiveness.
- Mucosal site viral load as well as plasma viral load was decreased.
- Challenged animals were protected from peripheral CD4+ T-cell loss.

NHP.501 (16621178) **Oral delivery of replication-competent adenovirus vectors is well tolerated by SIV- and SHIV-infected rhesus macaques.**

Authors: Gomez-Roman VR, Grimes GJ Jr, Potti GK, Peng B, Demberg T, Gravlin L, Treece J, Pal R, Lee EM, Alvord WG, Markham PD, Robert-Guroff M

Journal: Vaccine. 2006 Jun 5;24(23):5064-72. Epub 2006 Mar 31.

Objectives: Immunotherapy.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- This paper assessed the safety of administering Adenovirus-based therapeutic vaccine to SIV or SHIV-infected rhesus macaques.
- The Ad5hr-delta-E3 virus was administered to uninfected macaques, and SIV and SHIV-infected macaques with no adverse events.

NHP.502 (16622001) **Preservation of functional virus-specific memory CD8+ T lymphocytes in vaccinated, simian human immunodeficiency virus-infected rhesus monkeys.**

Authors: Acierno PM, Schmitz JE, Gorgone DA, Sun Y, Santra S, Seaman MS, Newberg MH, Mascola JR, Nabel GJ, Panicali D, Letvin NL

Journal: J Immunol. 2006 May 1;176(9):5338-45.

Objectives: Challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: AD4-gp160(MN) *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intravenous, Intranasal *Formulation:* AD4-gp160(MN) + RPMI-1640

Vaccine Name: rMVA.SIVmac239gagpolHIVenv *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intranasal *Formulation:* rMVA.SIVmac239gagpolHIVenv + Saline

Vaccine Name: SIVmac239 gag-pol-nef *Type:* DNA *Route:* Intramuscular *Formulation:* SIVmac239 gag-pol-nef + Saline, PBS

Challenge: SHIV89.6P, SIVmac251 *Route:* Intravenous

Main Findings:

- Rhesus macaques vaccinated with either DNA/recombinant adenovirus, or DNA/recombinant poxvirus and challenged with SHIV-89.6P were followed up to 101 weeks post infection, to monitor CD4 count, viral load and CD8 functions.

NHP.503 (16373659) **Impact of vaccine-induced mucosal high-avidity CD8+ CTLs in delay of AIDS viral**

dissemination from mucosa.

Authors: Belyakov IM, Kuznetsov VA, Kelsall B, Klinman D, Moniuszko M, Lemon M, Markham PD, Pal R, Clements JD, Lewis MG, Strober W, Franchini G, Berzofsky JA

Journal: Blood. 2006 Apr 15;107(8):3258-64. Epub 2005 Dec 22.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: PCLUS3-CL10/PCLUS6.1-CL10/PCLUS3_POL_143/PCLUS3_GAG_372/PCLUS3_TAT2/PCLUS3_TAT3/PCLUS3_VIF *Type:* Synthetic Protein/Peptide *Route:* Intrarectal *Formulation:* PCLUS3-CL10/PCLUS6.1-CL10/PCLUS3_POL_143/PCLUS3_GAG_372/PCLUS3_TAT2/PCLUS3_TAT3/PCLUS3_VIF + MF59, Interleukin-12, CpG 2006, LT-R192G

Vaccine Name: NYVAC-SIVgagpol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intrarectal *Formulation:* NYVAC-SIVgagpol + MF59, Interleukin-12, CpG 2006, LT-R192G

Vaccine Name: NYVAC-IIIB-Env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intrarectal *Formulation:* NYVAC-IIIB-Env + MF59, Interleukin-12, CpG 2006, LT-R192G

Challenge: SHIV-KU2 *Route:* Intrarectal

Main Findings:

- In Indian rhesus macaques, priming with peptides followed by boosting with recombinant vaccinia Mac239 gag-pol and vaccinia HIV-1 env all by intrarectal mucosal delivery, was found to delay the spread of challenge virus from delivery site to systemic infection, although not to protect the animals from infection.
- peptides or vaccinia vaccines tested seperately, did not delay challenge virus spread in comparison to mock vaccination.
- Peptide priming plus NY-VAC boosting resulted in high avidity mucosal CTL activity.

NHP.504 (16616946) **Immunogenicity and efficacy of immunodeficiency virus-like particles pseudotyped with the G protein of vesicular stomatitis virus.**

Authors: Kuate S, Stahl-Hennig C, Stoiber H, Nchinda G, Floto A, Franz M, Sauermann U, Bredl S, Deml L, Ignatius R, Norley S, Racz P, Tenner-Racz K, Steinman RM, Wagner R, Uberla K

Journal: Virology. 2006 Jul 20;351(1):133-44. Epub 2006 Apr 17.

Objectives: Challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SX2-delta-frxn *Type:* DNA *Route:* Subcutaneous *Formulation:* SX2-delta-frxn + RPMI-1640

Vaccine Name: SCIV Single Cycle Immunodeficiency Virus with VSV-G pseudotyping *Type:* Virus-like Particle *Route:* Subcutaneous *Formulation:* SCIV Single Cycle Immunodeficiency Virus with VSV-G pseudotyping + RPMI-1640

Challenge: SIVmac239 *Route:* Oral

Main Findings:

- Incorporation of Vesicular Stomatitis Virus G protein (VSV-G) into noninfectious HIV-1 virus-like particles led ot hundred-fold higher antibody titers to HIV-1 Gag in mice.
- In this study VSV-G incorporated into a SIV-MAC239 vaccine was used.

NHP.505 (16439000) **DNA immunization in combination with effective antiretroviral drug therapy controls viral rebound and prevents simian AIDS after treatment is discontinued.**

Authors: Fuller DH, Rajakumar PA, Wu MS, McMahon CW, Shipley T, Fuller JT, Bazmi A, Trichel AM, Allen TM, Mothe B, Haynes JR, Watkins DI, Murphey-Corb M

Journal: Virology. 2006 Apr 25;348(1):200-15. Epub 2006 Jan 24.

Objectives: Challenge, Immunotherapy.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: HBcAg-CTL epitope expressing DNA *Type:* DNA *Route:* Intradermal (Gene Gun DNA-coated gold beads) *Formulation:* HBcAg-CTL epitope expressing DNA + Gold Particles

Vaccine Name: pcSIVgag *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intramuscular *Formulation:* pcSIVgag + Gold Particles

Vaccine Name: pcSIV-tat *Type:* DNA *Route:* Intradermal (Gene Gun DNA-coated gold beads) *Formulation:* pcSIV-tat + Gold Particles

Challenge: SIVDeltaB670 *Route:* Intravenous

Main Findings:

- Rhesus macaques infected with SIV-DeltaB670 and treated with PMPA (tenofovir, Gilead Sciences) from weeks 2 to 30 post-infection, were subsequently immunized at 6 and 12 months post-therapy with DNA vaccines expressing either SIV gag/tat or SIV gag/tat plus 19 CD8+ T-cell epitopes. Half of the animals in each group were also immunized pre-challenge.
- Only 60% of the animals (4 controls and 20 vaccinated) responded to PMPA.
- All 4 controls showed viral rebound after PMPA withdrawal, but 17 of 20 vaccinated animals supressed viral loads for more than 7 months after PMPA withdrawal.

NHP.506 (16085341) **DNA vaccination of macaques by a full-genome SHIV plasmid that has an IL-2 gene and produces non-infectious virus particles.**

Authors: Horiuchi R, Akahata W, Kuwata T, Enose Y, Ido E, Suzuki H, Miyake A, Saito N, Ibuki K, Goto T, Miura T, Hayami M

Journal: Vaccine. 2006 Apr 24;24(17):3677-85. Epub 2005 Jul 20.

Objectives: Challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pSHIV-ZF1-IL2 *Type:* Recombinant Live Attenuated Virus *Route:* Intramuscular *Formulation:* pSHIV-ZF1-IL2 + Saline

Challenge: SHIV-C2/1 *Route:* Intravenous

Main Findings:

- Four rhesus macaques vaccinated with a Nef-deleted IL-2 inserted SHIV DNA vaccine were challenged with SHIV-C2/1. One of the four was protected from CD4 T-cell loss.

NHP.507 (16636134) **Toll-like receptor agonists influence the magnitude and quality of memory T cell responses after prime-boost immunization in nonhuman primates.**

Authors: Wille-Reece U, Flynn BJ, Lore K, Koup RA, Miles AP, Saul A, Kedl RM, Mattapallil JJ, Weiss WR, Roederer M, Seder RA

Journal: J Exp Med. 2006 May 15;203(5):1249-58. Epub 2006 Apr 24.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: HIV Gag protein *Type:* Purified Viral Products *Route:* Subcutaneous

Vaccine Name: rAD Gag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAD Gag + Saline

Main Findings:

- Indian rhesus macaques immunized with HIV-1 Gag protein plus 2 mg of Cpg ODN or TLR7/8 agonist had a higher frequency of Th1 response than those immunized tiwh Gag protein alone.

NHP.508 (16699037) **Anti-V3 humanized antibody KD-247 effectively suppresses ex vivo generation of human immunodeficiency virus type 1 and affords sterile protection of monkeys against a heterologous simian/human immunodeficiency virus infection.**

Authors: Eda Y, Murakami T, Ami Y, Nakasone T, Takizawa M, Someya K, Kaizu M, Izumi Y, Yoshino N, Matsushita S, Higuchi H, Matsui H, Shinohara K, Takeuchi H, Koyanagi Y, Yamamoto N, Honda M

Journal: J Virol. 2006 Jun;80(11):5563-70.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: Mab KD-247 *Type:* Passive Antibody *Route:* Intravenous *Formulation:* Mab KD-247 + Saline

Challenge: SHIV-C2/1 *Route:* Intravenous

Main Findings:

- Cynomolgus macaques innodulated with 15, 30 or 45 mg per kg body weight of monoclonal antibody KD-247 specific for the V3 loop tip, were challenged 24 hours later with SHIV-C2/1.
- The 45 mg dose was protective.

NHP.509 (16775324) **Rapid virus dissemination in infant macaques after oral simian immunodeficiency virus exposure in the presence of local innate immune responses.**

Authors: Abel K, Pahar B, Van Rompay KK, Fritts L, Sin C, Schmidt K, Colon R, McChesney M, Marthas ML

Journal: J Virol. 2006 Jul;80(13):6357-67.

Objectives: Challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Challenge: SIVmac251 *Route:* Oral

Main Findings:

- Infant macaques infected orally with SIV-mac251.
- Animals sacrificed one week post-infection were studied to determine extent and pattern of virus dissemination.

NHP.510 (16725169) **HIV-1 DNA/MVA vaccination reduces the per exposure probability of infection during repeated mucosal SHIV challenges.**

Authors: Ellenberger D, Otten RA, Li B, Aidoo M, Rodriguez IV, Sariol CA, Martinez M, Monsour M, Wyatt L, Hudgens MG, Kraiselburd E, Moss B, Robinson H, Folks T, Butera S

Journal: Virology. 2006 Aug 15;352(1):216-25. Epub 2006 May 24.

Objectives: Challenge.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: pGA1/IC1-90 (HIV-1 gag,pol,env) *Type:* DNA *Route:* Intramuscular *Formulation:* pGA1/IC1-90 (HIV-1 gag,pol,env) + PBS

Vaccine Name: rMVA (gag,pol,env) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rMVA (gag,pol,env) + PBS

Challenge: SHIV-SF162P3 *Route:* Intrarectal

Main Findings:

- This trial used a HIV-1 CRF02_AG Gag-Pol-Tat-Rev-Vpu-Env prime, and a MVA HIV-1 CRF02_AG gag-pol-env boost.
- Challenge virus was SHIVSF162P3 with a SIV-Mac239 backbone and HIV-1 subtype B env.
- Challenge route was non-traumatic rectal exposure to low doses of challenge stock virus, to mimic human sexual exposure.
- Challenges were repeated up to 26 times, with naive control animals infected after less an average of 4.6 (range 1 to 14) exposures, while six of 16 vaccinated animals remained uninfected after 17 exposures.

NHP.511 (16625206) **Hexon-chimaeric adenovirus serotype 5 vectors circumvent pre-existing anti-vector immunity.**

Authors: Roberts DM, Nanda A, Havenga MJ, Abbink P, Lynch DM, Ewald BA, Liu J, Thorner AR, Swanson PE, Gorgone DA, Lifton MA, Lemckert AA, Holterman L, Chen B, Dilraj A, Carville A, Mansfield KG, Goudsmit J, Barouch DH

Journal: Nature. 2006 May 11;441(7090):239-43. Epub 2006 Apr 16.

Objectives: Immunogenicity.

Main Findings:
- Recombinant Adenovirus 5 expressing SIV-Gag were engineered to avoid pre-existing immuntity to Ad5, by replacing Ad5 hypervariable regions with the rare Ad8 hypervariable regions.
- Pre-existing immunity to Ad5 did not diminish the immune response to the recombinant vector.

NHP.512 (16912320) **Molecularly cloned SHIV-1157ipd3N4: a highly replication- competent, mucosally transmissible R5 simian-human immunodeficiency virus encoding HIV clade C Env.**

Authors: Song RJ, Chenine AL, Rasmussen RA, Ruprecht CR, Mirshahidi S, Grisson RD, Xu W, Whitney JB, Goins LM, Ong H, Li PL, Shai-Kobiler E, Wang T, McCann CM, Zhang H, Wood C, Kankasa C, Secor WE, McClure HM, Strobert E, Else JG, Ruprecht RM

Journal: J Virol. 2006 Sep;80(17):8729-38.

Objectives: Pathogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- This paper dexcribes the construction and pathogenicity testing (in Chinese Rhesus macaques, and in Indian Rhesus macaques) of a SHIV containing the HIV-1 subtype C envelope gene.
- SHIV-1157ipd3N4 was found to be pathogenic to both the Indian and the Chinese macaques.
- The original infectious clone was passaged through Indian macaques, and the ipd3 clone was taken during the disease stage from an infected macaque.
- GenBank accession DQ779174

NHP.513 (17014915) **Immunogenicity of a chimeric hepatitis A virus (HAV) carrying the HIV gp41 epitope 2F5.**

Authors: Kusov YY, Zamjatina NA, Poleschuk VF, Michailov MI, Morace G, Eberle J, Gauss-Muller V

Journal: Antiviral Res. 2006 Sep 5;.

Objectives: Immunogenicity.

Main Findings:
- The hepatitis A virus carrying an HIV-1 gp41 epitope was able to replicate in marmosets and cause an antibody response to the epitope.

NHP.514 (16763152) **Preserved CD4+ central memory T cells and survival in vaccinated SIV-challenged monkeys.**

Authors: Letvin NL, Mascola JR, Sun Y, Gorgone DA, Buzby AP, Xu L, Yang ZY, Chakrabarti B, Rao SS, Schmitz JE, Montefiori DC, Barker BR, Bookstein FL, Nabel GJ

Journal: Science. 2006 Jun 9;312(5779):1530-3.

Objectives: Challenge, Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac239 gag-pol-nef *Type:* DNA *Route:* Intramuscular *Formulation:* SIVmac239 gag-pol-nef + Saline, PBS

Vaccine Name: rAd5-SIVmac239 gag/pol *Type:* Recombinant Vector (virus/bacteria) *Routes:* --, Intramuscular *Formulation:* rAd5-SIVmac239 gag/pol + Saline, PBS

Vaccine Name: gp145 DCFI 89.6P Env *Type:* DNA *Route:* Intramuscular *Formulation:* gp145 DCFI 89.6P Env + Saline, PBS

Vaccine Name: rAd-HxB2/BaL Env DCFI *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* rAd-HxB2/BaL Env DCFI + Saline, PBS

Challenge: SIVmac251 *Route:* Intravenous

Main Findings:

- Vaccine-induced cellular immunity controls virus replication in simian immunodeficiency virus (SIV)-infected monkeys only transiently, leading to the question of whether such vaccines for AIDS will be effective. Rhesus monkeys were immunized with plasmid DNA and replication-defective adenoviral vectors encoding SIV proteins and then challenged them with pathogenic SIV. Although these monkeys demonstrated a reduction in viremia restricted to the early phase of SIV infection, they showed a prolonged survival. This survival was associated with preserved central memory CD4+ T lymphocytes and could be predicted by the magnitude of the vaccine-induced cellular immune response. These immune correlates of vaccine efficacy should guide the evaluation of AIDS vaccines in humans.

NHP.515 (12941922) **Magnitude and diversity of cytotoxic-T-lymphocyte responses elicited by multiepitope DNA vaccination in rhesus monkeys.**

Authors: Subbramanian RA, Kuroda MJ, Charini WA, Barouch DH, Costantino C, Santra S, Schmitz JE, Martin KL, Lifton MA, Gorgone DA, Shiver JW, Letvin NL

Journal: J Virol. 2003 Sep;77(18):10113-8.

Objectives: Immunogenicity.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: CTL epitopes/p11C-deleted SIVmac239Gag *Type:* DNA *Route:* Intramuscular *Formulation:* CTL epitopes/p11C-deleted SIVmac239Gag + PBS

Vaccine Name: CTL epitopes *Type:* DNA *Route:* Intramuscular *Formulation:* CTL epitopes + PBS

Vaccine Name: MVA-SIV gag-pol and HIV-1 89.6 env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular *Formulation:* MVA-SIV gag-pol and HIV-1 89.6 env + PBS

Main Findings:

- Two prototype multiepitope plasmid DNA vaccines in the SHIV/rhesus monkey model was examined to determine their efficiency in priming for high-frequency CTL responses with a specificity for diversity of viral epitopes. While a simple multiepitope vaccine construct demonstrated limited immunogenicity in monkeys, this same multiepitope genetic sequence inserted into an immunogenic simian immunodeficiency virus gag DNA vaccine elicited high-frequency CTL responses specific for all of the epitopes included in the vaccine. Both multiepitope vaccine prototypes primed for robust epitope-specific CTL responses that developed following boosting with recombinant modified vaccinia virus Ankara vaccines expressing complete viral proteins. These studies suggest that multiepitope plasmid DNA vaccine-based prime-boost regimens can efficiently prime for CTL responses of increased breadth and magnitude, although they do not overcome predicted hierarchies of immunodominance.

NHP.516 (16960778) **Repeated intravaginal inoculation with cell-associated simian immunodeficiency virus results in persistent infection of nonhuman primates.**

Authors: Kaizu M, Weiler AM, Weisgrau KL, Vielhuber KA, May G, Piaskowski SM, Furlott J, Maness NJ, Friedrich TC, Loffredo JT, Usborne A, Rakasz EG

Journal: J Infect Dis. 2006 Oct 1;194(7):912-6. Epub 2006 Aug 29.

Main Findings:

- Female cynomolgus macaques challenged with cell-associated SIV-Mac239 isolate.

III. VACCINES

This section contains a list of vaccines used in the studies compiled in the database. We devised a simple nomenclature to group the vaccines by type of vaccine. This includes (alphabetically) the following:

- Cell/Tissue
- DNA
- Live Attenuated Virus
- Live Virus
- Other
- Passive Antibody
- Purified Viral Products
- Recombinant Live Attenuated Virus
- Recombinant Subunit Protein
- Recombinant Vector (virus/bacteria)
- Synthetic Protein/Peptide
- Virus-like Particle
- Whole (killed) Inactivated Virus

In most cases the name and description of the vaccine, as provided by the authors of the paper, was retained. The virus (HIV, SIV or SHIV), the viral component (Gene or protein) and the subtype (for HIV or HIV fragment in SHIV) were also recorded. The database trial numbers (NHP number) where the vaccine was used are listed for reference.

Cell/Tissue Vaccines

Vaccine Name: **AT-2 inactivated SIV-loaded DC**
Description: AT-2 SIV (mac251) loaded dendritic cells suspended in RPMI 1640 medium
Virus: SIV *Strain:* SIVmac251 *Subtype:* -
Gene/Protein:
Trial(s): NHP.299

Vaccine Name: **SIVmac239Δ3 (cell-infected)**
Description: SIVmac239Δ3-infected peripheral blood mononuclear cells
Trial(s): NHP.305

DNA Vaccines

Vaccine Name: **bSIVgp120**
Description: Recombinant baculovirus expressing SIV gp120
Trial(s): NHP.33

Vaccine Name: **CHO-SIVgp120**
Description: Recombinant Chinese hamster cells expressing SIV gp120
Trial(s): NHP.33, NHP.156

Vaccine Name: **CMV SHIV dEN**
Description: CMV-SHIVdEN) was constructed from an env and nef deletion SHIV DNA (SIVGP1 DNA) by replacing the 5' long terminal repeat region with a cytomegalovirus promoter with an immediate-early enhancer and the 3' long terminal repeat region with simian virus 40 poly(A).
Virus: SHIV *Strain:* SIVGP1 DNA *Subtype:* B
Gene/Protein: gag, pol, Accessory (vif,vpx, vpr (partial))
Notes: lacking env and nef
Trial(s): NHP.326

Vaccine Name: **CMV/kan-SIV-env**
Description:
Trial(s): NHP.462

Vaccine Name: **CMV/kan-SIV-gag**

Description:
Trial(s): NHP.462

Vaccine Name: **CMV/R Gag, Pol, Nef**
Description: CMV/R Gag Clade B, CMV/R Pol (Clade B)/h, CMV/R Nef (delta Myr) (Clade B)
Trial(s): NHP.472

Vaccine Name: **CMV/R gp145 (dCFI)**
Description: h Clade A
Trial(s): NHP.472

Vaccine Name: **CMV/R gp145 (delCFI)**
Description: h Clade B
Trial(s): NHP.472

Vaccine Name: **CMV/R R5 gp145 (delCFI)**
Description: h Clade C
Trial(s): NHP.472

Vaccine Name: **CMVKm2-gp140TM**
Description: The sequence for the native subtype B HIV-1US4 envelope was modified to reflect the optimal codon usage in highly expressed human genes. Contained the oligomeric secreted membrane-bound gp140TM, which include the membrane-spanning domain of gp41 (residues1-691). The gene cassettes constructed synthetically using EcoR1 and Xba1 by the Midland Certified Reagent Company, and were cloned into plasmid vectors for DNA vaccination (pCMVKm2).
Virus: HIV-1 *Strain:* HIV-1.US4 *Subtype:* B
Gene/Protein: env
Trial(s): NHP.354

Vaccine Name: **CTL epitopes**
Description: Prototype multiepitope vaccine consisting of p199A, p41A, p68A, and p11c CTL epitopes separated by triple alanine spacers. The 5'-to-3' order of the epitopes in this vaccine construct was as follows: the control epitope p199A (RYPKTFGWL), HIV-Env p41A (YAPPITGQI), Pol p68A (STPPLVRLV), and Gag p11C (CTPYDINQM)
Trial(s): NHP.494, NHP.515

Vaccine Name: **CTL epitopes/EGFP**
Description: p11C, p68A, and p41A CTL epitopes fused together with no spacers in between, fused to EGFP
Trial(s): NHP.494

Vaccine Name: **CTL epitopes/p11C-deleted SIVmac239Gag**
Description: p199A, p41A, p68A, and p11c CTL epitopes separated be triple alanine spacers, fused to a full-length SIVmac239 gag gene with the internal Gag-derived p11C sequence deleted. The 5'-to-3' order of the epitopes in this vaccine construct was as follows: the control epitope p199A (RYPKTFGWL), HIV-Env p41A (YAPPITGQI), Pol p68A (STPPLVRLV), and Gag p11C (CTPYDINQM)
Trial(s): NHP.494, NHP.515

Vaccine Name: **d81**

Description: In this vaccine the SIVmac239 env-nef expression cassette was inserted into the TK gene of the HSV-1 genome. It has a deletion in the essential ICP27 gene in addition to the deletion in TK, rendering it replication defective in Vero cells. CMV, promoter/enhancer sequences of the CMV IE gene; PA, signal sequences for poly(A) addition. The SIV sequences are from the SphI site (nucleotide 6450) rightward in SIVmac239. These include rev exon 1, the entire env ORF, rev exon 2, and the nef open reading frame

Notes: Herpes simplex vector

Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein: env

Trial(s): NHP.54

Vaccine Name: **DermaVir**

Description: Full-length, but integration defective SHIV plasmid pSHIV(int-), expresses LTR, gag, pol and nef sequences from SIVmac239 and env, tat, and rev genes from HIV1

Trial(s): NHP.405, NHP.413

Vaccine Name: **DNA (pCMVKm2) gp140**

Description: Unmodified gp140. pCMVKm2 vector expressing the gp140 ectodomain form of the HIV envelope immunogen, with an intact gp120-gp41 cleavage site

Virus: HIV-1 *Strain:* SF162 *Subtype:* B

Gene/Protein:

Trial(s): NHP.22

Vaccine Name: **DNA Vaccine pNL432-ZF1***

Description: DNA vaccine derived from pNL432, an infectious molecular clone of HIV-1 in which the first two cysteine residues of the N-terminal zinc finger motif (Cys-X2-Cys-X4-His-X4-Cys) were replaced by serine residues

Virus: HIV-1 *Strain:* NL432 *Subtype:* B

Gene/Protein: All (Full genome (modified))

Notes: first two amino cysteine residues of the N-terminal zinc finger motif (Cys-X2-Cys-X4-His-X4-Cys) were replaced by serine residues

Trial(s): NHP.31, NHP.149.2

Vaccine Name: **DNA vaccines expressing SIVmac239 Gag and HIV-1 89.6P Env**

Description:

Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein: gag

Virus: HIV-1 *Strain:* HIV-1.89.6 *Subtype:* -

Gene/Protein: env

Trial(s): NHP.443

Vaccine Name: **DNA-gag,env**

Description: DNA vaccines encoding SIVmac239 Gag and HIV-1-89.6P Env

Notes: 2 constructs

Virus: HIV-1 *Strain:* HIV-1.89.6 *Subtype:* B

Gene/Protein: env
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag
Trial(s): NHP.23

Vaccine Name: **DNA-pCI-rev**
Description: Eukaryotic expression vector pCI (Promega, Charbonnieres, France) with HIV-1 primary isolate ACH320 2.1 rev cDNA. Expression checked in 293T cells.
Virus: HIV-1 *Strain:* ACH320 2.1 *Subtype:* B
Gene/Protein: rev
Trial(s): NHP.276

Vaccine Name: **DNA-pCI-tat**
Description: Eukaryotic expression vector pCI (Promega, Charbonniers, France) with tat cDNA cloned from primary isolate ACH320 2.1. Expression checked in 293T cells.
Virus: HIV-1 *Strain:* ACH320 2.1 *Subtype:* B
Gene/Protein: tat
Trial(s): NHP.276

Vaccine Name: **DNA-Retanef**
Description: Coding regions from Rev, Tat and Nef fused together to make a synthetic open readiong frame as shown in [Hel et al Vaccine 20:3171-86 (2002)]. DNA Retanef is inserted into a pVR1332 kanamycin-expressing plasmid (Vical Inc San Diego CA) under control of aCMV promoter.
Virus: SIV *Strain:* Mac251 *Subtype:* -
Gene/Protein: Accessory (epitopes from Rev, Tat and Nef)
Trial(s): NHP.479

Vaccine Name: **DNA-SIV**
Description: This vaccine consists of five plasmids expressing different combinations of SIV mac proteins. The 5 plasmids encoded for non-infectious SIVmac239 virus particle, envelope of SIVmac239 and SIVmac251, and a monocyte/macrophage tropic isolate of SIVmac316
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: All
Virus: SIV *Strain:* SIVmac251 *Subtype:* -
Gene/Protein: env
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: env
Virus: SIV *Strain:* SIVmac316 *Subtype:* -
Gene/Protein:
Trial(s): NHP.275, NHP.423

Vaccine Name: **DNA-SIV-gag, env**
Description: Not described in [Hel et al Vaccine 20:3171-86 (2002)] where it was uused as a control vaccine for comparison to another vaccine.
Virus: SIV *Strain:* *Subtype:* -
Gene/Protein: gag, env (gag and env)

Trial(s): NHP.479

Vaccine Name: **DNA.pND14-G1.SIVmac251.env**

Description: DNA vaccine; DNA vector using hCMV IE promoter and expressing SIVmac251 structural env gene

Virus: SIV *Strain:* SIVmac251 *Subtype:* -

Gene/Protein: env

Trial(s): NHP.58, NHP.406

Vaccine Name: **DNA.PTH.SIVmac.J5.gptnr**

Description: DNA vaccine; DNA vector using hCMV IE promoter expressing SIVmac251J5 structural (gag,pol) and regulatory (tat, nef and rev) genes

Virus: SIV *Strain:* SIVmac251.J5 *Subtype:* -

Gene/Protein: gag, pol

Trial(s): NHP.58, NHP.406

Vaccine Name: **DNA.SF162ΔV2 gp140**

Description: This is a DNA vector expressing the SF162ΔV2 gp140 envelope with an intact gp120-gp41 cleavage site. The DNA construct was codon optimized for high expression in mammalian cells

Virus: HIV-1 *Strain:* HIV-1.SF162 *Subtype:* B

Gene/Protein: env

Trial(s): NHP.62

Vaccine Name: **FMSIV**

Description: This is a chimeric simian-human immunodeficiency virus (SHIV) with ecotropic Friend murine leukemia virus (FMLV) env in place of SHIV env in combination with FMLV receptor , mCAT1, which is not normally expressed in primate cells. FMSIV DNA has SIV-derived LTR, gag, pol, vif, vpx and partial vpr sequences, HIV-1-derived partial vpr, tat, rev and partial env (containing the second exon of tat, the second exon of rev, and RRE) sequences and FMLV-derived env sequences.

Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein: LTR, gag, pol, Accessory (vif,vpx)

Virus: HIV-1 *Strain:* HIV-1DH12 *Subtype:* B

Gene/Protein: env, Accessory (vpr,tat,partial env (containing the second exon of tat, the second exon of rev, and RRE))

Trial(s): NHP.67, NHP.70, NHP.350, NHP.421

Vaccine Name: **Gag/Env SIVmac239**

Description: To generate pGX10-Gag-Env, the gag-protease (1193–3233) and rev/env (6695–9537) fragments of SIVmac239 proviral DNA were ligated and inserted into the pGX10 vector

Trial(s): NHP.493

Vaccine Name: **gp140 DCFI (HxB2/BaL) Env**

Description: The env gene region encoding aa 205 to 361 of HxB2 was replaced with the corresponding BaL gene sequence, CCR5 tropic clade B immunogen

Trial(s): NHP.381, NHP.418

Vaccine Name: **gp145 DCFI 89.6P Env**

Description: A synthetic 89.6P gp145DCFI Env gene was made by constructing overlapping oligos covering 1,950

DNA bp of the theoretical gene and using PCR. The sequence from nt 1501 (amino acids [aa] 501, R) to 1602 (aa 534, T) and nt 1771 (aa 591, M) to 1851 (aa 617,V) with respect to start codon ATG (A as nt 1) were deleted. A nucleotide deletion mutation at in the position of aa 713 resulted in a 25 aa extension, SCEDPDLLCLLVASHLLFAPPPCLP. The gp145DCFI gene was cloned into vector pVR1012.

Trial(s): NHP.381, NHP.418, NHP.514

Vaccine Name: **HBcAg-CTL epitope expressing DNA**

Description: Chimeric hepatitis B virus core antigen (HBcAg) carrier expression vector pHBc expresses HBcAg under the control of the cytomegalovirus (CMV) immediate-early promoter (PJV 7198). Contains a unique Bsp120I restriction site within the immunodominant loop ofHBcAg. Oligonucleotides encoding Bsp120I- or NotI-flanked, codon-optimized SIV CTL epitopes were annealed, and ligated into pHBc at the immunodominant region or carboxy terminus, respectively, of HBcAg.

Virus: SIV *Strain:* ? *Subtype:* -

Gene/Protein:

Trial(s): NHP.505

Vaccine Name: **HIV env MN**

Description: HIV-1 subtype B isolate MN, env gene cloned into pCDNA3 plasmid. See Wang,J.J. et al AIDS 9 S1: pp S159-S170 (1995) for details.

Virus: HIV-1 *Strain:* HIV-1.MN *Subtype:* B

Gene/Protein: env

Virus: HIV-1 *Strain:* MN *Subtype:* B

Gene/Protein: env

Trial(s): NHP.16.2

Vaccine Name: **HIV env_{MN}/rev(pCEnv)**

Description: Plasmid DNA containing HIV-1 env/rev

Virus: HIV-1 *Strain:* HIV-1.MN *Subtype:* B

Gene/Protein: env, Accessory (rev)

Trial(s): NHP.16.1, NHP.16.2, NHP.363

Vaccine Name: **HIV-1 89.6P Env gp140 (KB9) DNA**

Description: KB9 plasmid expressing HIV-1 89.6P

Virus: HIV-1 *Strain:* HIV-1.89.6P *Subtype:* B

Gene/Protein: env (gp140)

Trial(s): NHP.400

Vaccine Name: **HIV-1 multi-env cocktail**

Description: Env genes encoding 51 unique envelope proteins were cloned into a pVVkan vector encompassing a CMV promoter/enhancer/intron and polyA sequences

Trial(s): NHP.471

Vaccine Name: **HIV-1 p55 gag**

Description: HIV-1 pCMVkm p55 gag plasmid transformed into E. coli HB101 and fermented underdefined growth conditions

Trial(s): NHP.426

Vaccine Name: **HIV-1.89.6P env DNA**
Description:
Virus: HIV-1 *Strain:* HIV-1.89.6P *Subtype:* B
Gene/Protein: env
Trial(s): NHP.126

Vaccine Name: **HIV-1.89.6P env DNA**
Description:
Virus: SHIV *Strain:* SHIV89.6P *Subtype:* B
Gene/Protein: env
Trial(s): NHP.60.1, NHP.60.3, NHP.98

Vaccine Name: **HIV-2UC2.tat.nef.gag**
Description: A mixture of 3 plasmids constructs based on the gene sequences of the gp140 envelope, p55 Gag, Nef, and Tat proteins from the HIV-2UC2 isolate. The plasmid DNA was then resuspended to 2 mg/ml in 2x phosphate buffer saline for intramuscular and intradermalimmunizations or in water for intranasal immunizations and stored at -20^0C.
Virus: HIV-2 *Strain:* HIV-2UC2 *Subtype:* -
Gene/Protein: gag, Accessory (tat,nef,p55)
Trial(s): NHP.378

Vaccine Name: **HIV1-gag**
Description: HIV1-gag (HXB2) under the control of human CMV immediate early promoter
Trial(s): NHP.401

Vaccine Name: **HIV1-gp160**
Description: HIV1-gp160 (BRU) under the control of human CMV immediate early promoter
Trial(s): NHP.401

Vaccine Name: **HIV1-nef**
Description: HIV1-nef (HXB3) under the control of the human CMV immediate early promoter
Trial(s): NHP.401

Vaccine Name: **HIV1-rev**
Description: HIV1-rev under the control of human CMV immediate early promoter
Trial(s): NHP.401

Vaccine Name: **HIV1-RT**
Description: HIV1-RT under the control of human CMV immediate early promoter
Trial(s): NHP.401

Vaccine Name: **HIV1-tat**
Description: HIV1-tat under the control of human CMV immediate early promoter
Trial(s): NHP.401

Vaccine Name: **HxBc2/BaL clade A env plasmid**
Description:
Trial(s): NHP.443

Vaccine Name: **HXBc2/BaL clade B env plasmid**
Description:
Trial(s): NHP.443

Vaccine Name: **HXBc2/BaL clade C env plasmid**
Description:
Trial(s): NHP.443

Vaccine Name: **K81**
Description: This is a replication-competent HSV recombinant K81. The SIVmac239 env-nef expression cassette was inserted into the TK gene of the HSV-1 genome. CMV, promoter/enhancer sequences of the CMV IE gene; PA, signal sequences for poly(A) addition. The SIV sequences are from the SphI site (nucleotide 6450) rightward in SIVmac239. These include rev exon 1, the entire env ORF, rev exon 2, and the nef open reading frame
Notes: Herpes simplex vector
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: env
Trial(s): NHP.54

Vaccine Name: **MVA.HIVA**
Description: Same vaccine used in human trial in Oxford, UK and Nairoby, Kenya
Trial(s): NHP.118

Vaccine Name: **o-gp140**
Description: Oligomeric gp140DV2 was derived from the R5 primary isolate SF162 with a deletion in the V2 loop.
Trial(s): NHP.426

Vaccine Name: **p55gagSF2**
Description:
Virus: HIV-1 *Strain:* HIV-1.SF2 *Subtype:* B
Gene/Protein: gag
Trial(s): NHP.354

Vaccine Name: **pC-SIV17E-Fred (gagpolenv)**
Description: This is a plasmid DNA vaccine encoding the SIVmac17E-Fr (which is closely related to SIVmac239) gag-pol-env, including vif, vpx, vpr, tat, and rev, except that the 5' LTR is deleted and the 3' LTR is truncated by 360 bp. SIV nef was truncated atthe sequence for amino acid 93 by insertion of a stop codon
Virus: SIV *Strain:* SIVmac17E-Fr *Subtype:* -
Gene/Protein: gag, env
Trial(s): NHP.52

Vaccine Name: **pC-SIVrev**

Description: DNA vaccine; Contains pC-SIVnef-TPA and pC-SIVnef (both constructed based on pC-SIVmac17E-Fred)

Trial(s): NHP.52

Vaccine Name: **pc-synGag (SIVmac239)**

Description: Contains a codon-optimized gene, cloned under transcriptional control of the cytomegalovirus immediate-early promoter-enhancer unit in pcDNA 3.1 (Invitrogen). Protein expression is about four- to fivefold greater than that of the corresponding wild-type construct

Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein: gag

Trial(s): NHP.374

Vaccine Name: **pc-syngp120 (SHIV-189.6p)**

Description: Contains a codon-optimized gene, cloned under transcriptional control of the cytomegalovirus immediate-early promoter-enhancer unit in pcDNA 3.1 (Invitrogen). Protein expression is about four- to fivefold greater than that of the corresponding wild-type construct

Virus: SHIV *Strain:* SHIV-1.89.6P *Subtype:* B

Gene/Protein: env (gp120)

Trial(s): NHP.374

Vaccine Name: **pc-synTat (HIV-1IIIB)**

Description: contain a codon-optimized gene, cloned under transcriptional control of the cytomegalovirus immediate-early promoter-enhancer unit in pcDNA 3.1 (Invitrogen). Protein expression is about four- to fivefold greater than that of the corresponding wild-type construct

Virus: HIV-1 *Strain:* HIV-1IIIB *Subtype:* B

Gene/Protein: Accessory (tat)

Trial(s): NHP.374

Vaccine Name: **pcDNA synEnv gp140 89.6**

Description: Plasmid expresses the env gene of HIV189.6 under the control of the human cytomegaloviurs immediate-early (HCMV IE1) enhancer/promoter background of expression vector pNDi. All constructs also contain the human CMV intron A sequence 5' of the expressed gene in order to increase expression from the HCMV enhancer/promoter sequence, and the bovine growth hormone (BGH) poly A signal/terminator sequence.

Trial(s): NHP.467

Vaccine Name: **pcDNA synGagSIV**

Description: Plasmid expresses the gag gene of SIVmac239 under the control of the human cytomegaloviurs immediate-early (HCMV IE1) enhancer/promoter background of expression vector pNDi. All constructs also contain the human CMV intron A sequence 5' of the expressedgene in order to increase expression from the HCMV enhancer/promoter sequence, and the bovine growth hormone (BGH) poly A signal/terminator sequence.

Trial(s): NHP.467

Vaccine Name: **pcDNA3--tet.CCR5**

Description: This DNA vaccine encodes for CCR5 and tetanus genes.
Trial(s): NHP.68

Vaccine Name: **pcDNA3-CCR5**
Description:
Trial(s): NHP.68

Vaccine Name: **pCGag/Pol**
Description: DNA constructs expressing HIV-1-IIIB gag/pol protein
Virus: HIV-1 *Strain:* HIV-1.IIIB *Subtype:* -
Gene/Protein: gag, pol
Trial(s): NHP.71

Vaccine Name: **pCI-Nef plasmid**
Description: A mixture of six pCI-Nef plasmids expressing the nef epitopes from SIVmac251 primary isolate (BK28, SO4, SO5, SO8, SO9 and SO12)
Virus: SIV *Strain:* SIVmac251 (BK28) *Subtype:* -
Gene/Protein:
Virus: SIV *Strain:* SIVmac251 (SO4) *Subtype:* -
Gene/Protein:
Virus: SIV *Strain:* SIVmac251 (SO5) *Subtype:* -
Gene/Protein:
Virus: SIV *Strain:* SIVmac251 (SO8) *Subtype:* -
Gene/Protein:
Virus: SIV *Strain:* SIVmac251 (SO9) *Subtype:* -
Gene/Protein:
Virus: SIV *Strain:* SIVmac251 (SO12) *Subtype:* -
Gene/Protein:
Trial(s): NHP.12

Vaccine Name: **pCMN160 (HIV-1 MN env)**
Description: DNA constructs expressing HIV-1-MN env and rev proteins (pCMN160)
Virus: HIV-1 *Strain:* HIV-1.MN *Subtype:* B
Gene/Protein: env
Trial(s): NHP.71

Vaccine Name: **pCMN160 HIV-1.MN env-rev**
Description: A DNA vaccine (plasmid) expressing HIV-1 MN env and rev
Virus: HIV-1 *Strain:* HIV-1.MN *Subtype:* B
Gene/Protein: env
Trial(s): NHP.202

Vaccine Name: **pCMV-gag-mod**
Description: HIV-1SF2 p55 Gag modified to highly expressed human codons; regions with INS were inactivated. Produces a p55 Gag protein with three amino acid changes (Asn377Thr, Ile403Thr, and Lys405Arg). An

optimal initiation of translation (GCCACCAUGG) was employed. This 1,527 bp SF2-gag-mod sequence was cloned into the SalI and EcoRI sites of pCMVKm2(Chiron Corporation, Emeryville, Calif.).

Notes: zur Megede et al J Virol 74(6): 2628 (2000) PubMed ID 10684277

Virus: HIV-1 *Strain:* SF2 *Subtype:* B

Gene/Protein: gag

Trial(s): NHP.321, NHP.354

Vaccine Name: **pCMV-V3.S (HBV-HIV vaccine)**

Description: HIV-1 LAI V3 inserted within the frame of HBV envelope in pCV-S2.S

Virus: HIV-1 *Strain:* *Subtype:* B

Gene/Protein:

Virus: HIV-1 *Strain:* HIV-1.LAI *Subtype:* B

Gene/Protein:

Trial(s): NHP.10

Vaccine Name: **pCMV/nef**

Description: pCMV/nef plasmid vaccine comprises the PstI-StuI Nef-encoding fragment of clone BK28 inserted into pCMV5

Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein:

Trial(s): NHP.56

Vaccine Name: **pCMV/SIVsmH4/rev-gp160**

Description:

Virus: SIV *Strain:* SIVsmH4 *Subtype:* -

Gene/Protein: env, Accessory (rev)

Trial(s): NHP.371

Vaccine Name: **pCMVKm2-Delta-V2 gp140**

Description: Modified V2-deleted gp140. pCMVKm2 vector expressing the unmodified gp140 ectodomain form of the HIV envelope immunogen, with an intact gp120-gp41 cleavage site

Virus: HIV-1 *Strain:* SF162 *Subtype:* B

Gene/Protein:

Trial(s): NHP.22

Vaccine Name: **pCMVKm2-gp140mut**

Description: The sequence for the native subtype B HIV-1US4 envelope was modified to reflect the optimal codon usage in highly expressed human genes. Contained the oligomeric secreted gp140mut (uncleaved, containing a single R522S cleavage site mutation; includes residues 1-668). The gene cassettes constructed synthetically using EcoR1 and Xba1 by the Midland Certified Reagent Company, and were cloned into plasmid vectors for DNA vaccination (pCMVKm2).

Virus: HIV-1 *Strain:* HIV-1US4 *Subtype:* B

Gene/Protein: env

Trial(s): NHP.354

Vaccine Name: **pCMVmCAT1**

Description: constructed from pCMV (Clontech) by replacing the B-gal gene with a PCR fragment encoding mCAT1B (See Matano, 2000 for details)
Virus: HIV-1 *Strain:* *Subtype:* -
Gene/Protein:
Trial(s): NHP.350, NHP.421

Vaccine Name: **pCSGag/Pol.SIV**
Description: SIV gag/pol
Virus: SIV *Strain:* ND *Subtype:* -
Gene/Protein: gag, pol
Trial(s): NHP.16.1, NHP.16.2

Vaccine Name: **pcSIV-tat**
Description: SIV-MAC239 Tat expressed under control of CMV immediate-early promoter. ;Vogel et al J Virol. 77(24) 13348-13360 (2003).
Virus: SIV *Strain:* *Subtype:* -
Gene/Protein: Accessory (Tat protein coding region from SIV-MAC239)
Trial(s): NHP.505

Vaccine Name: **pcSIVgag**
Description: SIV-MAC239 gag p55 expressed under control of CMV immediate-early promoter. Vogel et al J Virol. 77(24) 13348-13360 (2003).
Virus: SIV *Strain:* MAC239 *Subtype:* -
Gene/Protein: gag (Gag p55)
Trial(s): NHP.499, NHP.505

Vaccine Name: **pCV-tat**
Description: DNA vaccine: the plasmid pCV-tat contains the cDNA of the HIV-1 tat gene (BH-10) under the transcriptional control of the adenovirus major late promoter and the vector pCV-0. Plasmids were purified on CsCl gradient and dialyzed for 48h against 300 volumesof sterile PBS without calcium and magnesium.
Virus: HIV-1 *Strain:* BH10 *Subtype:* B
Gene/Protein: Accessory (tat)
Trial(s): NHP.2, NHP.162, NHP.402

Vaccine Name: **pGA1-gag-pol DNA vaccine**
Description: The Gag-Pol (SIVmac239) insert was cloned into the pGA1 expression vector (GenBank accession no. AF425297)
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag, pol
Trial(s): NHP.89, NHP.476

Vaccine Name: **pGA1/IC1-90 (HIV-1 gag,pol,env)**
Description: Gag,pol,env PCRed from HIV-1 subtype AG (CRF02_AG); IC1-90 contains two substitutions in protease sequence, an Arg to Gly substitution at position 70 and Met to Leu substitution at position 90
Trial(s): NHP.470, NHP.510

Vaccine Name: **pGA1/IC48 (HIV-1 gag,pol,env)**

Description: IC48 contains point muations in gag NC zinc fingers and pol RT and a Gly to Val substitution at position 48

Trial(s): NHP.470

Vaccine Name: **pGA2/JS2-HIV-1.gag.pol.env**

Description: A vaccine derived from pGA1/JS1 after a series of safety measures (mutation and deletion) in the HIV-1 inserts. The vaccine uses pGA expression vectors that use the CMV immediate early promoter and the bovine growth hormone polyadenylation sequence to express RNAs.

Virus: HIV-1 *Strain:* HIV-1.BH10 *Subtype:* B

Gene/Protein: gag, pol, env, Accessory

Trial(s): NHP.384

Vaccine Name: **pGagpol/EnvRev SIV239 DNA**

Description: This is a DNA vaccine containing a plasmid backbone which takes advantages of a CMV promoter and a SV40 poly A signal to express SIV239 gagpol and EnvRev (in two recombinant plasmid constructs). The effect of the rev gene is thought to increase the expression of gagpolconstruct (in vitro assays)

Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein:

Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein: env

Trial(s): NHP.300

Vaccine Name: **pHis-HIV-AE**

Description: DNA vaccine encoded two thirds of AE subtype p93TH253 provirus derived from Thailand. Plasmid encodes sequences expressing modified Gag, modified RT, protease , modified mRNaseH, Rev, Tat, truncated Nef and Env containing a deletion in the middle one-third of the gene that included the CD4 binding region. Modified HIV genome was inserted into the plasmid DNA vaccine vector pHIS-64.

Trial(s): NHP.466

Vaccine Name: **pHIS-HIV-B**

Description: pHIS-HIV-B contains ~65% of the B subtype pNL(AD8) provirus, with sequences expressing modified Gag, modified RT, protease, Rev, Tat, Vpu, truncated Nef (first 31 aa) and truncated Env (first 275 aa). Modified HIV-1 genome was inserted into plasmid vector pHIS-64, which contained 14 primate-optimized CpG immunostimulatory sequences

Trial(s): NHP.415

Vaccine Name: **pHis-SHIV B**

Description: The DNA vaccine strain, pHIS-SHIV-B, encoded full-length unmutated SIVmac239 Gag and Pol, HIV-1AD8, Tat, Rev, and Vpu, and the 5' third of HIV-1AD8 Env. These genes were inserted into vector pHIS-64 behind the human cytomegalovirus immediate-early promoter. Plasmid vector pHIS-64 has kanamycin resistance, the bovine growth hormone poly(A) termination signal, and 64 CpG motifs in addition to those naturally present that are primate optimized.

Trial(s): NHP.466

Vaccine Name: **pHIS-SHIV-B**

Description: The DNA vaccine strain, pHIS-SHIV-B, encoded full-length unmutated SIVmac239 Gag and Pol, HIV-1AD8, Tat, Rev, and Vpu, and the 5' third of HIV-1AD8 Env. Genes were inserted into vector pHIS-64 (Coley Pharmaceutical Group, Wellesley, Mass.) behind the human cytomegalovirus immediate-early promoter.

Trial(s): NHP.491

Vaccine Name: **pJW4303/HXB-2.dpol**

Description: A DNA immunogen expressing the pol gene of SHIV-IIIB

Virus: SHIV *Strain:* SHIV-IIIB *Subtype:* B

Gene/Protein: pol

Trial(s): NHP.56

Vaccine Name: **pJW4303/HXB-2.gp120**

Description: Same as pHXB2gp120; This is a eukaryotic expression vector that uses enhancer and promoter elements, including intron A from the cytomegalovirus immediate-early promoter, and polyadenylation sequences from the bovine growth hormone pJW4303 supports Env expression in the absence of Rev. A stop codon introduced at the boundary of the surface (SU) and transmembrane (TM) subunits of Env followed by a BamHI site for cloning into the BamHI site in pJW4303

Virus: HIV-1 *Strain:* HIV1.HXB2 *Subtype:* B

Gene/Protein: env

Trial(s): NHP.56

Vaccine Name: **pJW4303/HXB-2.gp140**

Description: A recombinant plasmid constructed by cloning env fragments in frame with a synthetic tissue plasminogen activator-(tPA)- leader sequence in pJW4303. This is an eukaryotic expression vector that uses enhancer and promoter elements, including intron A fromthe cytomegalovirus immediate-early promoter, and polyadenylation sequences from the bovine growth hormone pJW4303 supports Env expression in the absence of Rev. Contain a stop codon immediately prior to the transmembrane domain of TM

Virus: HIV-1 *Strain:* HIV-1.HXB2 *Subtype:* B

Gene/Protein: env

Trial(s): NHP.56

Vaccine Name: **pJWSU-Delta5G**

Description: gp120/SU containing five mutations that remove asparagines at positions 79, 146, 171, 460, and 479 and cloned into eukaryotic expression vector pJW4303

Trial(s): NHP.464

Vaccine Name: **pJWSU-mac239**

Description: wt env gp120/SU from SIVmac239 was cloned into eukaryotic expression vector pJW4303

Trial(s): NHP.464

Vaccine Name: **pMA SHIV89.6**

Description:

Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein: Accessory, gag, LTR, pol (LTR, gag,pol,vpx,vpr,nef)

Virus: HIV-1 *Strain:* HIV89.6 *Subtype:* B

Gene/Protein: Accessory, env (tat,rev,vpu,env)
Trial(s): NHP.140

Vaccine Name: **polyvalent HIV-1 env**
Description: The polyvalent DNA vaccines encoded the env gene from four primary HIV-1 isolates: 92US715.6 (clade B), Ba-L (clade B), 96ZM651 (clade C), and 93TH976.17 (clade E) and the gag gene from a molecularly cloned virus NL4-3 (clade B). All DNA vaccines were constructed using the same vector pSW3891
Trial(s): NHP.492

Vaccine Name: **polyvalent HIV-1 env/gag**
Description: Plasmid contains codon optimized HIV-1 env genes (clades A, B, C, and E) and HIV-1 gag (Czm) under control of CMV promoter. The following 6 immunogens were used in DNA vaccine: gp120A (92UGO37.8, subtype A), gp120-B175 (92US715.6, subtype B),gp120-BaL (Ba-L, subtype B), gp120-C (96ZM651, subtype C), gp120-E (93TH976.17 subtype EA), and gag (96ZM651, subtype C)
Trial(s): NHP.482

Vaccine Name: **Pooled SIVgag/HIVtat.rev DNA vaccine**
Description: Mixture of 3 plasmids encoding SIVmac239gag (pSIVoptgag), HIV-1.NL4.3 tat and rev. Plasmid pCMVNLtat, encoding the HIV-1NL4- tat, was constructed from plasmid vector pEGFP-N1 by replacing the EGFP coding sequence with the SalI-BamHI restricted tat fragment from the cDNA clone pCR2-tat1. The expression of tat is under the control of the human cytomegalovirus (CMV) immediate- early promoter. HIV-1NL4.3 rev expression is under the control of the rous sarcoma virus promoter
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag
Virus: HIV-1 *Strain:* HIV-1.NL4.3 *Subtype:* B
Gene/Protein: Accessory (tat)
Virus: HIV-1 *Strain:* HIV-1.NL4.3 *Subtype:* B
Gene/Protein: Accessory (rev)
Trial(s): NHP.339

Vaccine Name: **pRS102 -SIVmac239 gag-pol proteins**
Description: The plasmid pRS102 expresses SIVmac239 Gag and Pol proteins. The vaccine insert for pRS102 comprised a Kozak sequence, the SIV239 gag-pol region (nucleotides 1309-5753) and the Mason-Pfizer Monkey virus cytoplasmic transport element. This insert was cloned into the HindIII and NheI sites of the eukaryotic expression vector pJW4303, and expression in transiently transfected COS cells was verified.
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag, pol
Trial(s): NHP.56

Vaccine Name: **pSabRV1-SIV**
Description: Polio virus vector expressing SIV gag, pol, env, nef, and tat in overlapping fragments
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: env, gag, pol
Trial(s): NHP.13

Vaccine Name: **pSabRV2-SIV**
Description: Polio virus vector expressing SIV gag, pol, env, nef, and tat in overlapping fragments

Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: env, gag, pol
Trial(s): NHP.13

Vaccine Name: **pSHIV-NM-3rn ZF1***
Description: the construct was based on the infectious molecular clone of SHIV-NM-3rn (Kuwata et al., 1995) from which the BamHI-PvuII fragment was subcloned between the BamHI/HincII sites of pUC119 and, using this plasmid as a template, site-directed mutagenesis ofthe zinc-finger motifs was performed by PCR. The plasmid pSHIV-NM-3rn ZF1* has mutations (Cys... Cys... His... CysSer... Ser... His... Cys) in an N-terminal zinc-finger motif of the NC protein in the gag region of SHIV-NM-3rn see paper for details)
Virus: HIV-1 *Strain:* HIV-1.NL432 *Subtype:* B
Gene/Protein: env, Accessory (vpr,tat,vpu,env,nef)
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: LTR, gag, pol, Accessory (vif,vpx)
Trial(s): NHP.322

Vaccine Name: **pSIV gag p39**
Description: Plasmid encodes a C-terminally truncated SIV mac 239 gag gene (p39) under control of the HCMV immediated early promoter and bovine growth hormone polyadenylation signal. p39 corresponds to the SIV gag p19 and p27 regions of the SIV gag protein. The p39gene was RNA optimized by introducing multiple silent point mutations to disrupt endogenous inhibitory sequences that impede nuclear transport
Trial(s): NHP.497

Vaccine Name: **pSIVNef-TPA**
Description: DNA vaccine; Constructed based on SIVmac17E-fred +nef
Trial(s): NHP.323

Vaccine Name: **pTH.HW DNA**
Description: A DNA vaccine contained an SIV gag-derived epitope, TPYDINQML, recognized by CTLs in rhesus macaques (Macaca mulatta) in the context of the Mamu-A*01 MHC class I molecule
Trial(s): NHP.57

Vaccine Name: **pTHr.HIVA DNA**
Description: Same vaccine used in human trial in Oxford, UK and Nairoby, Kenya
Trial(s): NHP.118

Vaccine Name: **pUCgp120SF2-gold particle**
Description: Vaccine based on a modification of pCMV6agp120SF2 which has been previously described. pUCgp120 expresses gp120 of HIV-1 SF2 by using the cytomegalovirus promoter-intron A, tissue plasminogen activator signal sequences, and bovine growth hormone termination sequences; Plasmid DNA was isolated by using plasmid purification columns and endotoxin-free buffers (Qiagen, Chatsworth, Calif.). DNA was bound to 2.6-µm-diameter gold particles to a concentration of 2 µg of DNA/mg of gold
Virus: HIV-1 *Strain:* HIV-1.SF2 *Subtype:* B
Gene/Protein: env
Trial(s): NHP.75

Vaccine Name: **pV1P-HIV-1.89.6P env**

Description: Plasmid DNA expressing HIV-1 89.6P env
Virus: HIV-1 *Strain:* HIV-1.89.6P *Subtype:* B
Gene/Protein: env
Trial(s): NHP.24.1

Vaccine Name: **pV1P-SIVmac239 gag**
Description: Plasmid DNA expressing SIVmac239
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag
Trial(s): NHP.24.1

Vaccine Name: **pV1R-SIVmac239-gag**
Description: A plasmid DNA constructed by annealing a series of overlapping oligonucleotides.
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag
Trial(s): NHP.306.1, NHP.306.2

Vaccine Name: **pVacc1 DNA**
Description: pVacc1 includes a full SIVmac239 genome with multiple mutations in the NC basic domain and the functional domains of RT and INT, under the control of the CMV promoter. A 3.1-kb SphI-NcoI fragment that includes the env gene from pSHIV-KB9-3' replaced the corresponding SphI-SnaBI fragment of pVacc1 that includes the SIV env of SIVmac239. In addition, a stop codon replaced the initiation codon of the vpr gene.
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: All
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: All
Trial(s): NHP.61

Vaccine Name: **pVacc4 DNA**
Description: The DNA plasmid pVacc4 used in the vaccination is a derivative of pVacc1; It includes a full SIVmac239 genome with multiple mutations in the NC basic domain and the functional domains of RT and INT, under the control of the CMV promoter. A 3.1-kb SphI-NcoI fragment that includes the env gene from pSHIV-KB9-3' replaced the corresponding SphI-SnaBI fragment of pVacc1 that includes the SIV env of SIVmac239. In addition, a stop codon replaced the initiation codon of the vpr gene.
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: All
Trial(s): NHP.366

Vaccine Name: **rFPV**
Description: Designed to express the gag, pol, env and nef genes of SHIV-IIIb
Virus: SHIV *Strain:* SHIV.IIIB *Subtype:* B
Gene/Protein: gag
Trial(s): NHP.56

Vaccine Name: **rMVA-HIV-1 89.6P env**

Description:
Trial(s): NHP.443

Vaccine Name: **SFV-SIVmac**
Description: Semliki forest virus (SFV) vaccine expressing (SIV)macJ5 env, gag-pol, nef, rev, and tat genes
Trial(s): NHP.406

Vaccine Name: **SIV Diected GLV**
Description: SIV GLV of PC-derived, directed inserts in the UB vector
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein:
Trial(s): NHP.120

Vaccine Name: **SIV gag/pol**
Description: pcDNA3.1(–) was digested with XhoI and EcoRI and ligated to SIVgag and pol genes that were amplified from SHIV-C2/1 DNA (GenBank no. AF217181) with the primers 5'-AACTCGAGAAGATAGAGTGGGAGATGGG and AAGAATTCAGGCTATGCCACCTCTCTA-3'. gag/pol genes were derived from the molecular clone SIVmac239.
Trial(s): NHP.486

Vaccine Name: **SIV mac239 Gag DNA**
Description: pV1R plasmid expressing SIVmac239 gag.
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag (gag)
Trial(s): NHP.400

Vaccine Name: **SIV Random-GLV**
Description: SIV GLV comprised of random genomic-DNA inserts expressed in the UB and tPA vectors (Random-GLV)
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein:
Trial(s): NHP.120

Vaccine Name: **SIV-HIV89.6 DNA vaccine**
Description: SHIV-89.6 sequences cloned into the vector pGA2; This cloning deleted both LTRs and nef; SHIV sequence is internally mutated for a 12bp region encoding the first four amino acids of the 2nd zinc finger in nucleocapsid which renders it noninfectious
Virus: HIV-1 *Strain:* HIV-1.89.6 *Subtype:* B
Gene/Protein: env, Accessory (tat,rev)
Virus: SIV *Strain:* *Subtype:* -
Gene/Protein: gag, pol, Accessory (vpr, vpx)
Notes: No LTR
Trial(s): NHP.19, NHP.132, NHP.325, NHP.349

Vaccine Name: **SIV-MAC251 plasmid DNA cocktail**

Description: Single plasmid DNAs (pDNA) expressing SIV-Gag (EVA2023.1, pTH.UbgagPK), -Pol (EVA2023.2, pTH.UbpolPK), -Tat (EVA2023.5, pTH.tat), -Rev (EVA2023.4, pTH.rev), -Nef (EVA2023.3, pTH.UbnefPK) and -Env (EVA2024, pND14-G4) proteins of SIVmac251/32H/J5 (SIVmacJ5) (Rud et al., J Gen Virol 75, 529–543. 1994) were pooled.
Virus: SIV *Strain:* MAC251 *Subtype:* -
Gene/Protein:
Trial(s): NHP.403

Vaccine Name: **SIV-pcDNA3gag/pol**
Description:
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag, pol
Trial(s): NHP.9.2

Vaccine Name: **SIV-Run-Cyt. GLV**
Description: An SIV random library from sheared proviral DNA plus plasmids encoding IL-2 and GMCSF
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein:
Trial(s): NHP.120

Vaccine Name: **SIV/17E-Fr gag-pol-env**
Description: SIV strain 17E-Fr (SIV/17E-Fr) gag sequences isolated using StuI and BamHI sites and cloned into pCMV-BGHpA/AMP. pol-env sequences isolated from SIV/17E-Fr and were ligated into WRG7132 by using BsiEI and DraIII sites to generate vaccine plasmid WRG7135 carrying SIV/17E-Fr gag-pol-env. Cloning fully deleted the 5' LTR and truncated the 3' LTR by 360 bp. SIV nef truncated at amino acid 93 by the insertion of a stop codon
Virus: SIV *Strain:* SIV17E-Fr *Subtype:* -
Gene/Protein: env, gag, pol
Trial(s): NHP.63

Vaccine Name: **SIV/gag/V1Jns**
Description: Expression under the control of the human cytomegalovirus (hCMV) promoter with intron A and a bovine growth hormone polyadenylation sequence
Trial(s): NHP.474, NHP.475

Vaccine Name: **SIVmac17E-Fr Nef**
Description: DNA vaccine
Virus: SIV *Strain:* SIVmac17E-Fr *Subtype:* -
Gene/Protein:
Trial(s): NHP.52

Vaccine Name: **SIVmac239 Env**
Description:
Trial(s): NHP.495

Vaccine Name: **SIVmac239 gag DNA**

Description:
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag
Trial(s): NHP.126

Vaccine Name: **SIVmac239 gag DNA**
Description:
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag
Trial(s): NHP.60.1, NHP.60.3, NHP.98

Vaccine Name: **SIVmac239 gag-pol-nef**
Description: Protein sequences of Gag, Pol, and Nef from SIVmac239 were reverse translated with codons typically utilized in human cells. Oligos covering 5169 DNA bp of the theoretical gene with 5' SalI and 3' BamHI sites and a consensus Kozak sequence were synthesized from multiple fragments, each 75 bp long with 25 nt of overlap. The codon-modified gag-pol-nef was assembled by PCR. The full-length synthetic gag-pol-nef gene was cloned into the mammalian expression vector, pVR1012, and confirmed by sequencing.
Trial(s): NHP.381, NHP.418, NHP.443, NHP.502, NHP.514

Vaccine Name: **SIVmac239 gag/pol**
Description: Protein sequences from gag and pol were reverse translated using codons typically utilized in human cells. Oligonucleotides covering the genes were synthesized from multiple fragments and assembled by PCR. The full-length clone was cloned into the mammalian expression vector pVR1012
Trial(s): NHP.495

Vaccine Name: **SIVmac239 sbbvΔ3 DNA**
Description: Contains the full genome of mac239 with a 105-bp (35-amino-acid) deletion in the 3' nef/LTR, analogous to the common deletion observed in HIV-1 strains isolated from the Sydney Blood Bank Cohort (SBBC)
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein:
Trial(s): NHP.66

Vaccine Name: **SIVmac239 sbbvΔ3Delta5 DNA**
Description: Contains the full genome of mac239 with a 105-bp (35-amino-acid) deletion in the 3' nef/LTR, analogous to the common deletion observed in HIV-1 strains isolated from the Sydney Blood Bank Cohort (SBBC) and additional deletion at the 5'LTR
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein:
Trial(s): NHP.66

Vaccine Name: **sPol-SIV**
Description: To construct pGX10-sPol, the hepatitis C virus (HCV) E2t gene of pTV2-gDsE2t [30] was replaced with the SIV reverse transcriptase (rt) and integrase (int) (3107–5670) gene, and the insert was then transferred into the pGX10 vector. A part of the integrase gene encoding Asp116 and Asn117 in pGX10-sPol was deleted (5130–5132, Asp116) and modified (5133–5135, Asn 117 to Ser 117) to increase vaccine safety.
Trial(s): NHP.493

Vaccine Name: **sTat-Vpx SIVmac239**

Description: To generate pGX10-sTat-Vpx, SIVmac239 tat exon 1 (6561–6815) and vpx (6068–6406) genes were ligated and used to replace the vif-nef gene of pGX10-sVif-Nef.

Trial(s): NHP.493

Vaccine Name: **sVif-Nef SIVmac239**

Description: To generate pGX10-sVif-Nef, the vif (5599–6237) and nef (9336–10128) genes of SIVmac239 were ligated and replaced with the HCV structural gene (?ST) of pGX10-s?ST

Trial(s): NHP.493

Vaccine Name: **SX2-delta-frxn**

Description: SX2-delta-frxn is a plasmid containing the SIV-MAC239 proviral genome with deletions in vir, vpr, vpx and nef gene regions, and mutations in the Lys-tRNA primer binding site to render viral particles non-replicative.

Virus: SIV *Strain:* MAC239 *Subtype:* -

Gene/Protein: gag, pol, env

Trial(s): NHP.504

Vaccine Name: **V1R-SIV gag**

Description: pUC-based vector that utilizes the human cytomegalovirus immediate-early promoter with intron A and bovine growth hormone transcription terminator/polyadenylation signal as expression regulatory elements and expresses full-length SIV gag. The SIV gag openreading frame is homologous to that of SIVmac239 and was synthesized using optimal codons for human gene expression.

Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein: gag

Trial(s): NHP.59

Vaccine Name: **VEE-SIVsm (SIV MA/CA-VRP and gp160-VRP)**

Description: VEE replicon plasmid pVR2 with SIVgag (Gly to Ala change in codon 2 ablate myristylation signal; entire env ORF (gp160; base 6587 to 9244); env lacking 3' region encoding membrane-spanning domain and cytoplasmic tail (gp140; base 6587 to 8626)

Notes: gag encoding matrix-capsid (MA/CA; nucleotides 1049 to 2143, numbering from the 5' end of the SIVsm H-4i genome)

Virus: SIV *Strain:* SIVsm H-4i *Subtype:* -

Gene/Protein: gag

Virus: SIV *Strain:* SIVsm H-4i *Subtype:* -

Gene/Protein: env

Virus: SIV *Strain:* SIVsm H-4i *Subtype:* -

Gene/Protein:

Trial(s): NHP.27, NHP.463

Vaccine Name: **vSIVgp160**

Description: Recombinant vaccinia virus expressing SIV gp160

Trial(s): NHP.33

Vaccine Name: **vvrgp140**

Description: Vaccinia expressing SIVmac251 env gp140
Virus: SIV *Strain:* SIVmac251 *Subtype:* -
Gene/Protein: env
Trial(s): NHP.73

Vaccine Name: **WLV-102**
Description: SIV-Mac-239 gag gene (p39) under control of a human cytomegalovirus immediate-early promoter. The gag gene sequence was RNA optimized for expression.
Virus: SIV *Strain:* MAC239 *Subtype:* -
Gene/Protein: gag
Trial(s): NHP.455

Vaccine Name: **WLV-104**
Description: Rhesus macaque IL12 p35 and p40 genes expresed from a dual-promoter plasmid.
Trial(s): NHP.455

Live Attenuated Virus Vaccines

Vaccine Name: **AT-2 rx HIV-1.DH12**
Description: Aldrithiol-2 (AT-2)-inactivated HIV-1.DH12
Trial(s): NHP.303

Vaccine Name: **AT-2 rx SIVmac239**
Description: Aldrithiol-2 (AT-2)-inactivated SIVmac239
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein:
Trial(s): NHP.303

Vaccine Name: **DeltavpuDeltaNefSHIV-4**
Description:
Trial(s): NHP.107, NHP.112

Vaccine Name: **DeltavpuSHIV-ppc**
Description:
Trial(s): NHP.107, NHP.112

Vaccine Name: **S8-NCΔZF2**
Description: This construct is based on the pCEP4 mammalian expression vector from Invitrogen Corp. (Carlsbad, Calif.); contains the complete coding region of SIV(Mne), including the nef gene. The 5' portion of the U3 region in the 5' long terminal repeat (LTR) and host genomic sequences upstream from the StyI site were removed. In addition, the R and U5 regions of the 3' LTR were also deleted and replaced with the simian

virus 40 (SV40) poly(A)
Virus: SIV *Strain:* SIV.Mne *Subtype:* -
Gene/Protein:
Trial(s): NHP.64, NHP.65.2, NHP.265

Vaccine Name: **SHIV-4 (Deltavpu-Deltanef)-I**
Description:
Notes: T-cell tropic
Virus: SHIV *Strain:* SHIV-4 *Subtype:* B
Gene/Protein:
Trial(s): NHP.17

Vaccine Name: **SHIV-dn**
Description: Live attenuated SHIV lacking the nef gene. The deletion is at the 5'-portion including the initial codon of the nef gene.
Virus: SIV *Strain:* mac239 *Subtype:* -
Gene/Protein: gag, LTR (LTR, gag, pol, vif and/or vpx)
Virus: HIV-1 *Strain:* NL432 *Subtype:* B
Gene/Protein: pol (env, tat, rev and vpu)
Trial(s): NHP.35, NHP.131

Vaccine Name: **SHIV-drn**
Description: Live attenuated SHIV lacking the nef gene. The deletion is at the 5'-portion including the initial codon of the nef anf vpr genes. The splicing of vpr was modified so that it does not function..
Virus: SIV *Strain:* mac239 *Subtype:* -
Gene/Protein: gag, LTR (LTR, gag, pol, vif and/or vpx)
Virus: HIV-1 *Strain:* NL432 *Subtype:* B
Gene/Protein: pol (env, tat, rev and vpu)
Trial(s): NHP.28, NHP.35

Vaccine Name: **SHIV-dxrn**
Description: Live attenuated SHIV lacking the nef gene. The deletion is at the 5'-portion including the initial codon of the nef, vpr gene and the 3' portion of vpx. The initial codon of vpx was modified to a non-sense codon.
Virus: SIV *Strain:* mac239 *Subtype:* -
Gene/Protein: gag, LTR (LTR, gag, pol, vif and/or vpx)
Virus: HIV-1 *Strain:* NL432 *Subtype:* B
Gene/Protein: pol (env, tat, rev and vpu)
Trial(s): NHP.28, NHP.35

Vaccine Name: **SHIV-NM3n**
Description:
Trial(s): NHP.114

Vaccine Name: **SHIV-PPC (Deltavpu)**
Description:

Notes: This vaccine is dual tropic and was administered orally
Virus: SHIV *Strain:* SHIV-PPC *Subtype:* -
Gene/Protein:
Trial(s): NHP.17

Vaccine Name: **SIMmac239Δ2**
Description: Contains 182bp deletion in nef and a 172bp deletion upstream of U3 of LTR.
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein:
Trial(s): NHP.207

Vaccine Name: **single cycle SIV**
Description: Genetically engineered SIV that is limited to a single cycle of infection, dose consisted of equivalent amounts of scSIV strains expressing the SIVmac239 and SIVmac316 envelope glycoproteins with mutations in nef that prevent MHC class I downregulation
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: env
Virus: HIV-1 *Strain:* SIVmac316 *Subtype:* -
Gene/Protein: env
Trial(s): NHP.454

Vaccine Name: **SIV(Mne)NCΔZF2 DNA**
Description: A live attenuated SIVMne. It consists of a 12-nucleotide deletion in the gene coding for the NC protein [nucleotide positions 1772 to 1783 of the SIV(Mne) sequence (GenBank accession no. M32741) were deleted]. Also known as ΔCys 33-Cys 36 or pRB130.
Virus: SIV *Strain:* SIVMne *Subtype:* -
Gene/Protein:
Trial(s): NHP.64, NHP.65.1, NHP.65.2, NHP.265

Vaccine Name: **SIV-IFN**
Description: This is a clone of SIVmac239 (SIVΔNU) for which a total of 513bp in the nef and U3 region has been replaced with the coding region of IFN
Trial(s): NHP.309

Vaccine Name: **SIV-IL4**
Description: This is a clone of SIVmac239 (SIVΔNU) for which a total of 513bp in the nef and U3 region has been replaced with the coding region of IL-4.
Trial(s): NHP.309

Vaccine Name: **SIV-PBJ6.6Δnef**
Description:
Trial(s): NHP.34

Vaccine Name: **SIV.GX2**
Description: SIVgx2 is a nef-disrupted molecular clone. EcoRI-NdeI fragment of an SIVmacJ5 proviral clone was replaced with a PCR product that was amplified from proviral DNA isolated from an SIVmacJ5-infected

macaque. This resulted in a 66 bp deletion in nef, removing the coding sequence for aa 62-83.

Virus: SIV *Strain:* SIV.GX2 *Subtype:* -

Gene/Protein: All (nef disrupted)

Notes: Nef gene disrupted

Trial(s): NHP.397

Vaccine Name: **SIVDeltaNU**

Description: SIVDeltaNef is a nef deleted mac239

Trial(s): NHP.327.1, NHP.327.2

Vaccine Name: **SIVhu**

Description: A pathogenic virus isolated from a lab. worker infected accidentally with biological materials from rhesus macaque infected with SIVsmB670; it has 97.9% genetic homology with parental SIVsmB670; 4 base deletion in nef gene causing a frame shift in nef

Virus: SIV *Strain:* SIV.hu/SIVsmB670 *Subtype:* -

Gene/Protein:

Trial(s): NHP.36, NHP.72

Vaccine Name: **SIVmac1A11**

Description: The SIVmac1A11 is a live attenuated virus. The virus stock was grown on stimulated CD4-enriched rhesus macaque peripheral blood mononuclear cells (PBMC) and had a titer of 10^5 50% tissue culture infectious doses (TCID50)/ml.

Virus: SIV *Strain:* SIVmac1A11 *Subtype:* -

Gene/Protein:

Trial(s): NHP.240, NHP.294

Vaccine Name: **SIVmac239Δ3**

Description: Contains 182bp deletion in nef and a 172bp deletion upstream of U3 of LTR. It has an additional 101-bp deletion in vpr. This is is a derivatives of SIVmac239. It lacks the nef, vpr and U5 sequences.

Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein: LTR, gag, pol, env (Lacks nef, vrp and US)

Trial(s): NHP.37, NHP.150.2, NHP.207, NHP.305

Vaccine Name: **SIVmac239Δ3**

Description: Produced by transfection of cloned DNA into CEMx174 cells; SIVmac239Δ3 is missing unique nef, vpr, and nef sequences that overlap U3. Described by Gibbs et al ARHR 10(5): 607-616 (1994).

Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein: All (All but nef, vpr and the U3 region overlapping with nef)

Trial(s): NHP.32, NHP.323

Vaccine Name: **SIVmac239Δ3+**

Description: Produced by infection of rhesus macaquest with cloned SIVmac239Δ3 DNA. SIVmac239Δ3 is missing unique nef, vpr, and nef sequences that overlap U3. A pathogenic variant named SIVmac239Δ3+ was selected and cloned. Described byGibbs et al ARHR 10(5): 607-616 (1994).

Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein: All (all but vpr, nef and LTR/U3 regions.)

Trial(s): NHP.323, NHP.458

Vaccine Name: **SIVmac239Δ3x**

Description: Produced by transfection of cloned DNA into CEMx174 cells; SIVmac239Δ3X is missing nef, vpx,and US sequences.

Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein: All but nef, vpx and U

Trial(s): NHP.32

Vaccine Name: **SIVmac239Δ4**

Description: Produced by transfection of cloned DNA into CEMx174 cells; SIVmac239Δ4 is missing nef, vpr, vpx, and US.

Virus: SIV *Strain:* Mac239 *Subtype:* -

Gene/Protein: All but nef, vpr, vpx, and US

Trial(s): NHP.32

Vaccine Name: **SIVmac239ΔNef**

Description: SIV-Mac239 with a deletion in nef as described in Daniel et al Science 258: 1938-1941 (1992) PMID 1470917

Virus: SIV *Strain:* *Subtype:* -

Gene/Protein: All

Notes: Lacking nef

Trial(s): NHP.148, NHP.416

Vaccine Name: **SIVmac239-Δnef**

Description: Constructed by deleting a 186-base pair fragment of the nef coding sequences of SIV mac239

Notes: dkdkd

Trial(s): NHP.33, NHP.34, NHP.109, NHP.476

Vaccine Name: **SIVmac239Delta5G**

Description: created by mutagenesis of the parental infectious DNA clone so that the asparagine residues for N-glycosylation at positions 79, 146, 171, 460, and 479 were converted to glutamine residues

Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein: All

Trial(s): NHP.39

Vaccine Name: **SIVmac251ΔNef**

Description: derived from the SIVmac251 BK28 clone by three modifications: (i) the premature stop codon at position 8785 in the env gene was mutated to restore a complete env ORF, (ii) the nef initiator codon ATG was mutated to ACG (cont'd, see notes)

Notes: at position 9059, and (iii) nucleotides 9225 to 9401 in the nef region, which do not overlap either the 3' end of env or the U3 part of the LTR, were deleted

Trial(s): NHP.38, NHP.101, NHP.416

Vaccine Name: **SIVmac251Δnef**

Description:

Trial(s): NHP.108

Vaccine Name: **SIVmac251, 32H, (C8)**

Description: grown in the human C8166 cell line. The nef coding region contains an in-frame deletion of four amino acids in pC8 and two conservative amino acid changes

Virus: SIV *Strain:* SIVmac251 *Subtype:* -

Gene/Protein: All

Trial(s): NHP.40, NHP.194.1, NHP.194.2, NHP.422

Live Virus Vaccines

Vaccine Name: **HIV-1LAI**

Description: HIV-1 M group subtype B isolate LAI (also known as IIIB see accession number K03455). Used as a "vaccine" for superinfection study in chimpanzees.

Trial(s): NHP.416

Vaccine Name: **HIV-2 SBL6669**

Description: Isolated from the PBMCs of a patient from Gambia by cocultivation with the T cells of the neoplastic cell line HUT-78.

Notes: under Franchini 30-JAN-1989 in sequence database.

Virus: HIV-2 *Strain:* HIV-2 SBL6669 *Subtype:* -

Gene/Protein: All

Trial(s): NHP.4

Vaccine Name: **recombinant fowlpox vaccine expressing HIV-1 89.6 env**

Description:

Virus: HIV-1 *Strain:* 89.6 *Subtype:* -

Gene/Protein: env

Trial(s): NHP.443

Vaccine Name: **rSFV-cocktail**

Description: Recombinant Semliki Forest virus (rSFV) (Tubulekas et al., Alphavirus expression vectors and their use as recombinant vaccines: a minireview. Gene 190, 191–195. 1997) constructs, expressing SIV proteins (EVA2108.2, SFVSIVmacJ5 TMGag; EVA2108.3, SFV-SIVmacJ5 Pol; EVA2108.6, SFV-SIVmacJ5 Tat; EVA2108.5, SFV-SIVmacJ5 Rev; EVA2108.4, SFV-SIVmacJ5 Nef; EVA2108.1, SFV-SIVmacJ5 Env),

Virus: SIV *Strain:* J5 derived from Mac251 *Subtype:* -

Gene/Protein:

Trial(s): NHP.403

Vaccine Name: **RT-SHIV**

Description: The chimeric simian/human immunodeficiency virus (SHIV) containing the HIV-1 HXBc2 gene for reverse transcriptase (RT) in the genomic background of SIVmac239 (RT-SHIV)
Virus: HIV-1 *Strain:* HXB2 *Subtype:* B
Gene/Protein: pol
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: All
Trial(s): NHP.111

Vaccine Name: **SFV- Pr56gag VLP-type II**
Description: Components: Pr56-wt; gp120-TM
Trial(s): NHP.77

Vaccine Name: **SHIV-4**
Description: The chimeric SHIV-4 contains the gag, pol, vif, vpx, vpr and nef genes of SIVmac239 and the env, tat and rev genes of HIV-1IIIB
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag, pol, Accessory (vif,vpx,vpr)
Virus: HIV-1 *Strain:* HIV-1.IIIB *Subtype:* B
Gene/Protein: env, Accessory (tat,rev)
Trial(s): NHP.93

Vaccine Name: **SHIV89.6**
Description: This is a chimeric virus containing HIV-1.89.6 env in the the SIV backbone
Virus: HIV-1 *Strain:* HIV-189.6 *Subtype:* B
Gene/Protein: env (Env,tat,rev,vpu)
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: Accessory, gag, LTR, pol (gag,pol,LTR,vpx,vpr,nef)
Trial(s): NHP.24.1, NHP.29.1, NHP.140, NHP.411

Vaccine Name: **SHIV89.6P**
Description:
Virus: HIV-1 *Strain:* HIV-1.89.6 *Subtype:* B
Gene/Protein: env
Virus: SIV *Strain:* SIVmac *Subtype:* -
Gene/Protein: LTR
Trial(s): NHP.24.1

Vaccine Name: **SHIVIIIBc2**
Description:
Virus: HIV-1 *Strain:* HIVIIIBc2 *Subtype:* B
Gene/Protein:
Virus: SIV *Strain:* ??? *Subtype:* -
Gene/Protein:
Trial(s): NHP.24.1

Vaccine Name: **SIV-Mac-32H**
Description: Live SIV-Mac-32H virus propagated on MT-2 cells
Virus: SIV *Strain:* MAC-32H *Subtype:* -
Gene/Protein: All (All, complete genome)
Trial(s): NHP.320

Vaccine Name: **SIV-Mac-MPBMC**
Description: Not described by authors.
Virus: SIV *Strain:* MAC-MPBMC *Subtype:* -
Gene/Protein: All (all, complete genome)
Trial(s): NHP.320

Vaccine Name: **SIVmac251**
Description:
Virus: SIV *Strain:* SIVmac251 *Subtype:* -
Gene/Protein: All
Trial(s): NHP.41, NHP.194.2, NHP.345

Vaccine Name: **SIVsmE660**
Description:
Virus: SIV *Strain:* SIVsmE660 *Subtype:* -
Gene/Protein: All
Trial(s): NHP.18, NHP.41, NHP.198

Other Vaccines

Vaccine Name: **CD4 Immunoadhesin (CD4-IgG)**
Description: A chimeric consisting of the N-terminal two immunoglobulin-like regions of CD4 joined to the Fc region of human IgG1. This is used as a CD4 analogue because it has a half life longer than CD4. In human, the complex results in 25 folds increase of concentration of CD4-IgG in the blood compared with recombinant CD4.
Trial(s): NHP.156

Vaccine Name: **Crosslinked gp120-CD4**
Description: HIV-1 IIIB gp120 and CD4 chemically crosslinked with 0.5 mM bis(sulfosuccinimidyl)suberate (BS3, Sigma)
Virus: HIV-1 *Strain:* HIV-1.IIIB *Subtype:* B
Gene/Protein:
Trial(s): NHP.53

Vaccine Name: **Crosslinked gp140-CD4**

Description: HIV-1 IIIB gp140 and CD4 chemically crosslinked with 0.5 mM bis(sulfosuccinimidyl)suberate (BS3, Sigma)
Virus: HIV-1 *Strain:* HIV-1.IIIB *Subtype:* B
Gene/Protein:
Trial(s): NHP.53

Vaccine Name: **HIV-1 HXBc2 Tat Toxoid**
Description: Contact authors
Virus: HIV-1 *Strain:* HXBc2 *Subtype:* -
Gene/Protein: Accessory (tat)
Trial(s): NHP.121

Vaccine Name: **inactivated Tat toxoid**
Description:
Trial(s): NHP.78

Vaccine Name: **SHIV89.6P tat toxoid**
Description: Contact authors
Virus: SHIV *Strain:* SHIV89.6P *Subtype:* B
Gene/Protein: Accessory (tat)
Trial(s): NHP.121

Passive Antibody Vaccines

Vaccine Name: **Anti-HIV-1 ch1206**
Description: Anti-HIV-1 antibodies obtained from chimpanzees infected with HIV-1DH12. The chimpanzee was infected for 2.8 years prior to sample collection
Trial(s): NHP.86.1, NHP.86.2

Vaccine Name: **Anti-HIV-1 ch4750**
Description: Anti-HIV-1 antibodies obtained from chimpanzees infected with HIV-1DH12, HIV-1DH20 and HIV-1DH20. The chimpanzee was infected for 3 years prior to sample collection
Trial(s): NHP.86.1

Vaccine Name: **Anti-HIV-1 ch911**
Description: Anti-HIV-1 antibodies obtained from chimpanzees infected with HIV-1 IIIB. The chimpanzee was infected for 9.9 years prior to sample collection
Trial(s): NHP.86.1

Vaccine Name: **Anti-HIV-2**
Description: Antibody obtained from a Cynomolgous macaque inoculated with HIV-2 (SBL-6669) in a whole

inactivated form. The monkey has subsequently shown to be protected from an autologous challenge.

Virus: HIV-2 *Strain:* HIV-2 SBL6669) *Subtype:* -

Gene/Protein: All

Trial(s): NHP.149.1, NHP.149.2

Vaccine Name: **Anti-SHIV Plasma**

Description: Pool of antiSHIV plasma from macaques infected with non-pathogenic SHIV-4. This pool consists mainly of polyclonal IgG

Trial(s): NHP.87

Vaccine Name: **Anti-SIVmac251**

Description: Antibodies generated by the immunization of pregnant macaques with whole-inactivated SIVmac251 plus montanide ISA 51 adjuvant.

Virus: SIV *Strain:* SIVmac251 *Subtype:* -

Gene/Protein: All

Trial(s): NHP.294

Vaccine Name: **Anti-SIVmacC8**

Description: Pool of antibodies collected from 4 cynomolgous macaques (L103, L106) inoculated with 10^4 TCID50 of 9/90 live attenuated virus SIVmacC8, prepared in C8166 cell. all macaques were shown to be infected and were subsequencently challenged with SIVmacJ5M and SHIV-4. The challenge did not induce superinfection. Serum collected from the 4 monkeys was stored at -70^{o}C and used as reagent.

Trial(s): NHP.215

Vaccine Name: **Cβ1 anti-V3**

Description: This is a mouse-human IgG1 chimeric monoclonal antibody. It contains the intact variable region of the murine 0.5 β monoclonal antibody which is directed to the V3 loop of HIV-1 IIIB variant gp120 and has potent in vitro IIIB-specific virus-neutralizing activity.

Virus: HIV-1 *Strain:* HIV-1.IIIB *Subtype:* B

Gene/Protein: env (V3)

Trial(s): NHP.152.1, NHP.152.2

Vaccine Name: **Chimp anti-HIV IgG**

Description: Antibodies were obtained from chimpanzees that were infected with a variety of HIV-1 isolates and subsequently developed high-titer neutralizing antibodies

Trial(s): NHP.249

Vaccine Name: **Chimp-anti-HIV-IgG**

Description: The authors [Nishimura et al J Virol 76(5): 2123-30 (2002)] state that the IgG was harvested in 2000, from chimpanzee 4750 which had been infected in 1993 with 3 different HIV-1 strains including HIV-1 strain DH12.

Trial(s): NHP.354, NHP.394

Vaccine Name: **F105/2G12/2F5 mab**

Description: Cocktail of 3 monoclonal antibodies (F105, 2G12 and 2F5)

Trial(s): NHP.85, NHP.117

Vaccine Name: **HIVIG**

Description: Anti-HIV-1 immunoglubulin obtained by plasmapheresis from HIV-1 infected individuals. The neutralising antibody titer was above or equal to 1:128. Virus-sterilized coagulation factors by application of solvents and detergents were used to inactivate thevirus in the plasma.

Notes: derived from the pooled plasma of several HIV-1 positive donors

Virus: HIV-1 *Strain:* HIV-1.IIIB *Subtype:* B

Gene/Protein: All

Trial(s): NHP.8, NHP.82.1, NHP.82.2, NHP.361

Vaccine Name: **IgG1 b12**

Description: Human antibody (IgG1,) recognizing an epitope overlapping the CD4 binding site of gp120 , contained <1 IU of endotoxin/ml

Trial(s): NHP.6, NHP.15, NHP.304

Vaccine Name: **mAb B4**

Description: This is a monoclonal antibody directed against HIV receptor complex;Broad neutralizing activity against HIV; Provides postexposure prophylaxis to hu-peripheral blood leukocyte (PBL)-severe combined immunodeficient mice and chimpanzees;Recognized a complexreceptor site for HIV on the T cell surface including CD4;Preferentially neutralizes primary HIV-1 isolates compared with T cell line-adapted strains, including SI and NSI-inducing phenotypes, representatives from HIV-1 subtypes A-G, HIV-2, SIV, and SHIV

Trial(s): NHP.84

Vaccine Name: **Mab KD-247**

Description: Monoclonal antibody KD-247 is a humanized Mab directed against the tip of the V3 loop of subtype B HIV-1 envelope (Pro-Gly-Arg).

Trial(s): NHP.508

Vaccine Name: **Monoclonal antibody 2F5**

Description:

Notes: 2F5 is an subclass IgG1. recognizes the gp41 sequence ELDKWA that is conserved among many HIV-1 strains

Trial(s): NHP.8, NHP.15, NHP.82.1, NHP.82.2, NHP.304

Vaccine Name: **Monoclonal antibody 2G12**

Description: 2G12 is a subclass IgG1. Binds to a conformationally sensitive epitope in the C3-V4 region of gp120

Trial(s): NHP.8, NHP.15, NHP.82.1, NHP.82.2, NHP.304

Vaccine Name: **Monoclonal antibody 4E10**

Description: This is a human monoclonal antibody that recognizes the conserved HIV-1 gp41 epitope NWEDIT

Trial(s): NHP.304

Vaccine Name: **Monoclonal antibody F105**

Description: obtained by fusion of antibody- producing EBV-transformed cells with the HMMA2.11TG/O cell line; This is a IgG1 kappa antibody that binds to the surfaces of cells infected with all HIV-1 strains tested: MN, RF, IIIB, and SF2, but not uninfected cells

Trial(s): NHP.15

Vaccine Name: **SIVIG**

Description: Approximately 16 g of IgG purified from 1.5 liters of plasma obtained by plasmapheresis from a single long-term nonprogressing Macaca mulatta macaque, infected with the F236 isolate of SIVsm and remaining clinically healthy for more than 6 years

Virus: SIV *Strain:* SIVsmF236 *Subtype:* -

Gene/Protein: All

Trial(s): NHP.377

Vaccine Name: **SIVIG-1**

Description: Antibody preparation from pooled plasma from SIVmac251-infected macaques. The preparation contains 15 mg/ml of purified IgG, a titer of 68,000 gp120; 31,00 anti-p27 and 1.15 ug/ml 50% neutralization titer

Trial(s): NHP.83

Vaccine Name: **SIVIG-2**

Description: Antibody preparation from pooled plasma from SIVmac251-infected macaques. The preparation contains 16 mg/ml of purified IgG, a titer of 170,000 gp120; 30,00 anti-p27 and 0.6 ug/ml 50% neutralization titer

Trial(s): NHP.83, NHP.363

Purified Viral Products Vaccines

Vaccine Name: **biologically active Tat protein**

Description:

Trial(s): NHP.78

Vaccine Name: **gp120**

Description: gp120 purified from supernatant of Hut-78 cells infected with HXB2/IIIB virus

Virus: HIV-1 *Strain:* IIIB/HXB2 *Subtype:* B

Gene/Protein: env

Trial(s): NHP.500

Vaccine Name: **gp160/BSC-40**

Description: This is a gp160 protein produced in BSC-40 cells infected with recombinant vaccinia virus

Trial(s): NHP.269

Vaccine Name: **HIV Gag protein**

Description: Details not specified in paper, contact authors for details.

Trial(s): NHP.507

Vaccine Name: **HIV-1 gp160**

Description: subunit consisting of oligomeric gp160 purified from tissue culture fluid of cells productively infected with HIV-1 IIIB
Virus: HIV-1 *Strain:* HIV-1.IIIB *Subtype:* -
Gene/Protein:
Trial(s): NHP.47

Vaccine Name: **HIV-1 HXBc2 Tat**
Description: Contact authors
Virus: HIV-1 *Strain:* HIVHXBc2 *Subtype:* B
Gene/Protein: Accessory (tat)
Trial(s): NHP.121

Vaccine Name: **HIV-1 IIIB gp120**
Description: HIV-1 isolate LAI/IIIB gp120 purified by sequential affinity chromatographic steps. Amino acid sequence analysis of gp120 showed the loss of the signal peptide.
Virus: HIV-1 *Strain:* LAI/IIIB *Subtype:* B
Gene/Protein: env
Trial(s): NHP.53, NHP.247, NHP.371

Vaccine Name: **HIV-1 IIIB gp140**
Description: gp140 protein was purified by lentil lectin chromatography from the serum-free medium of cells infected with the recombinant viruses, then further purified by chromatography on Superdex-200; Virtually all of the gp140 was oligomeric; Contained gp41
Virus: HIV-1 *Strain:* IIIB *Subtype:* B
Gene/Protein: env
Trial(s): NHP.14, NHP.53

Vaccine Name: **HIV-2 gp160**
Description: subunit consisting of oligomeric gp160 purified from tissue culture fluid of cells productively infected with HIV-2.NIHZ
Virus: HIV-2 *Strain:* HIV-2.NIHZ *Subtype:* -
Gene/Protein:
Trial(s): NHP.47

Vaccine Name: **HIV-2 native gp125**
Description: purified native HIV-2 gp125 protein
Virus: HIV-2 *Strain:* HIV-2 SBL6669 *Subtype:* -
Gene/Protein: env (gp125)
Trial(s): NHP.4

Vaccine Name: **MVA(SIVsmH-4)gag-pol-env**
Description: Viral components from SIVsmH-4 env. Selected after transfection of transfer plasmid pMC03gag-pol into CEF infected with MVA-env recombinant
Virus: SIV *Strain:* SIVsmH4 *Subtype:* -
Gene/Protein: gag, pol

Trial(s): NHP.45

Vaccine Name: **Native SIV gp120**

Description: Purified by sequential affinity chromatographic steps using a monoclonal antibody to HIV-1 gp41 and an anti-HIV-1-positive human serum; heavily glycosylated and contain complex carbohydrates

Virus: SIV *Strain:* SIVsmH4 *Subtype:* -

Gene/Protein: env (gp120)

Trial(s): NHP.5, NHP.205.1, NHP.205.3

Vaccine Name: **Native SIV gp148 env**

Description: The glycoproteins were purified by a one-step procedure to a high level of purity by using Galanthus nivalis agglutinin (GNA).

Virus: SIV *Strain:* SIVsm *Subtype:* -

Gene/Protein: env

Trial(s): NHP.125

Vaccine Name: **p55Gag**

Description: p55Gag (source virus not specified, but presumed to be HIV-1 subtypeB) produced in yeast.

Trial(s): NHP.321

Vaccine Name: **Prt-env gp160**

Description: full- length, unmutated Env of HIV-1-IIIb. The IIIb Env had an apparent molecular weight of 160 kDa with gp120 and gp41 covalently attached

Virus: HIV-1 *Strain:* HIV-1.IIIB *Subtype:* B

Gene/Protein: env

Trial(s): NHP.56

Vaccine Name: **SHIV89.6P tat**

Description: Contact authors

Virus: SHIV *Strain:* SHIV89.6P *Subtype:* -

Gene/Protein: Accessory (tat)

Trial(s): NHP.121

Vaccine Name: **SIVmac251 p27**

Description:

Virus: SIV *Strain:* SIVmac251 *Subtype:* -

Gene/Protein:

Trial(s): NHP.125

Vaccine Name: **SIVmac251-gp120**

Description: The SIV gp120 was purified from the serum-free culture supernatant of SIVmac251 chronically infected Hut 78 cells by immunoaffinity column chromatography using anti-gp120 Ab

Virus: SIV *Strain:* SIVmac251 *Subtype:* -

Gene/Protein:

Trial(s): NHP.30, NHP.328, NHP.363

Vaccine Name: **soluble gp160**
Description: HIV-1 MN strain from Pasteur Merieux Connaught, Paris)
Trial(s): NHP.78

Recombinant Live Attenuated Virus Vaccines

Vaccine Name: **pSHIV-ZF1-IL2**
Description: pSHIV-ZF1-IL2 is derived from pSHIV-nm-3rn-ZF1 and pSHIV-IL-2 by replacing nef in the former with IL-2 from the latter.
Trial(s): NHP.506

Vaccine Name: **SIV 17E-CL**
Description: SIV/17E-CL is a recombinant molecular clone that contains gp120 and part of gp41 from SIV/17E-Br (a macrophage-tropic strain obtained by passage of SIVmac239 in rhesus macaques, Sharma et al., J. Infect. Dis. 66:3550, 1992) into the SIVmac239 molecular clone.
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: Accessory, gag, pol
Virus: SIV *Strain:* SIV/17E-Br *Subtype:* -
Gene/Protein: env (gp120, gp41)
Trial(s): NHP.100

Recombinant Subunit Protein Vaccines

Vaccine Name: **CHO cell-expressed HIV-1SF2 gp120**
Description:
Virus: HIV-1 *Strain:* HIV-1.SF2 *Subtype:* B
Gene/Protein: env (gp120)
Trial(s): NHP.141, NHP.193

Vaccine Name: **Delta-V2 gp140 oligomeric**
Description: Purified oligomeric lacking the V2 region of gp140
Virus: HIV-1 *Strain:* HIV-1.SF162 *Subtype:* B
Gene/Protein:
Trial(s): NHP.22, NHP.426, NHP.465

Vaccine Name: **Env protein cocktail**

Description: CHO cells were transformed with two HIV envelope proteins (UG92005 and 1007) and immortalized cell lines were selected and cloned. Envelope proteins were purified and combined with envelope proteins MN and CM (Protein Sciences Corp.) for a total of fourEnv proteins

Trial(s): NHP.471

Vaccine Name: **Gag p41**

Description: Gag gene obtained from a molecularly cloned virus NL4-3 (clade B). Recombinant protein was produced in either 293 or CHO cells stably transfected with Gag expression plasmid.

Trial(s): NHP.492

Vaccine Name: **Gag-Pol particles**

Description:

Trial(s): NHP.65.1

Vaccine Name: **gp140 oligomeric**

Description: Purified gp140 oligomeric

Virus: HIV-1 *Strain:* HIVSF162 *Subtype:* -

Gene/Protein:

Trial(s): NHP.22

Vaccine Name: **HECs (hypervariable epitope constructs) - SIV Env gp130**

Description: Cocktail of eight peptides representing the invivo variability see throughout envelope glycoprotein of SIV SIV-based HECs conjugated to SIVmac239 gp130 at a 100:1 molar ratio

Trial(s): NHP.480

Vaccine Name: **HIV BH10-tat protein**

Description:

Virus: HIV-1 *Strain:* BH10 *Subtype:* B

Gene/Protein: Accessory (tat)

Trial(s): NHP.2

Vaccine Name: **HIV-1 Env/Gag**

Description: The following 6 immunogens were used in recombinant gp120 protein vaccine: gp120A (92UGO37.8, subtype A), gp120-B175 (92US715.6, subtype B), gp120-BaL (Ba-L, subtype B), gp120-C (96ZM651, subtype C), gp120-E (93TH976.17 subtype EA), and gag (96ZM651, subtype C)

Trial(s): NHP.482

Vaccine Name: **HIV-1 W6.1D gp120**

Description: recombinant gp120 of HIV-1W6.1D from an infectious molecular clone

Virus: HIV-1 *Strain:* HIV-1 W6.1D *Subtype:* B

Gene/Protein:

Trial(s): NHP.21

Vaccine Name: **HIV-1.MN.rgp120**

Description:
Virus: HIV-1 *Strain:* HIV-1.MN *Subtype:* B
Gene/Protein: env (gp120)
Trial(s): NHP.198

Vaccine Name: **HIV-1.SF2 gp120/p24 Recombinant**
Description: Monomeric recombinant gp120 and p24 of HIV-1.SF2
Virus: HIV-1 *Strain:* HIV-1.F2 *Subtype:* B
Gene/Protein: gag, env (gp120, p24)
Trial(s): NHP.164

Vaccine Name: **HIV-189.6 Env gp140-ISCOM**
Description: 200 µl of ISCOM matrix mixed overnight at 4°C with 25 µg of HIV-189.6 Env gp140 (produced in human 293T cells, containing gp120 and the gp41 ectodomain, and purified by lectin chromatography [University of Pennsylvania, Philadelphia]) in 250 µl of PBS.
Virus: HIV-1 *Strain:* HIV-1.89.6P *Subtype:* B
Gene/Protein: env
Trial(s): NHP.374

Vaccine Name: **HIV-1SF2 rgp120**
Description: Recombinant protein produced in Chinese hamster ovary cells
Virus: HIV-1 *Strain:* HIV-1.SF2 *Subtype:* B
Gene/Protein: env
Trial(s): NHP.75

Vaccine Name: **HIV-2 gp160**
Description:
Virus: HIV-2 *Strain:* ND *Subtype:* -
Gene/Protein: env
Trial(s): NHP.174

Vaccine Name: **HSP70-Baculovirus-infected cells.gp120-pGEX-3X.p27**
Description: Recombinant SIVmac251 gp120 was expressed in Baculovirus-infected cells and recombinant SIV p27 was generated in pGEX-3X as a glutathione S-transferase fusion protein. With both preparations 100µg was covalently linked to HSP70 by 0.0025% glutaraldehyde (Sigma Fine Chemicals Ltd.) and 200 µg was mixed with equal concentration of HSP70; thus, a total of 400µg of HSP70 and 200µg (3
Virus: SIV *Strain:* SIVmac251 *Subtype:* -
Gene/Protein: gag, env (gp120, p27)
Trial(s): NHP.395

Vaccine Name: **Mono-gp120H (89.6)**
Description: Recombinant protein purified from plasmid expressing gp120 of HIV 89.6 strain; the proteins were tagged with histidine to facilitate their purification
Virus: HIV-1 *Strain:* HIV-1 89.6 *Subtype:* -
Gene/Protein:

Trial(s): NHP.11, NHP.363, NHP.443

Vaccine Name: **Mono-gp120H (DH12)**

Description: Recombinant protein purified from plasmid expressing gp120 of HIV DH12 strain; the proteins were tagged with histidine to facilitate their purification

Virus: HIV-1 *Strain:* HIV-1 DH12 *Subtype:* -

Gene/Protein:

Trial(s): NHP.11

Vaccine Name: **Monomeric rgp120**

Description: Monomeric rgp120 of the LAI isolate of HIV-1 was commercially produced by Intracel (Rockville, MD) by expressing HIV-1LAI gp120 DNA in CHO cells.The expression product was characterized by Western blot assay using sheep antibody to HIV-1 gp20 and sequencing. Purity of the recombinant product was >98%

Trial(s): NHP.79, NHP.423

Vaccine Name: **Nef-Tat**

Description: Nef-Tat is a full-length fusion protein of the two viral proteins. Antigens were expressed in the yeast Pichia pastoris as His-tagged proteins. The HIV-1 nef gene derived from the clone Bru/Lai, SIV nef was derived from the cloneSIVmac239 without a premature stop codon, and the HIV-1 tat gene derived from the clone BH10

Trial(s): NHP.296

Vaccine Name: **Oligomeric HIV-1.89.6 gp140**

Description: The 89.6 gp140 was produced from BS-C-1 cells infected with recombinant vaccinia virus vBD1 and purified by lentil lectin and Superdex 200 chromatography

Virus: HIV-1 *Strain:* HIV-1.89.6 *Subtype:* -

Gene/Protein: env

Trial(s): NHP.90.1, NHP.90.2

Vaccine Name: **p24 gag**

Description: p24 gag obtained from Chiron manufacturing division, soluble in PBS

Trial(s): NHP.426

Vaccine Name: **p55gag-SF2**

Description: Yeast-derived recombinant protein obtained from Chiron manufacturing division

Trial(s): NHP.426

Vaccine Name: **Poly-gp120H**

Description: Recombinant protein purified from plasmid expressing gp120 of HIV AD8, Bal, Lai, RF, 89.6 and DH12 strains; the proteins were tagged with histidine to facilitate their purification

Virus: HIV-1 *Strain:* HIV-1 DH12 *Subtype:* B

Gene/Protein:

Virus: HIV-1 *Strain:* HIV-1 AD8 *Subtype:* B

Gene/Protein:

Virus: HIV-1 *Strain:* HIV-1 BAL *Subtype:* B

Gene/Protein:
Virus: HIV-1 *Strain:* HIV-1 LAI *Subtype:* B
Gene/Protein:
Virus: HIV-1 *Strain:* HIV-1 RF *Subtype:* B
Gene/Protein:
Virus: HIV-1 *Strain:* HIV-1 89.6 *Subtype:* B
Gene/Protein:
Trial(s): NHP.11

Vaccine Name: **Poly-gp120H (-DH12)**
Description: Recombinant protein purified from plasmid expressing gp120 of HIV AD8, Bal, Lai, RF and 89.6 strains; ; the proteins were tagged with histidine to facilitate their purification
Virus: HIV-1 *Strain:* HIV-1 AD8 *Subtype:* B
Gene/Protein:
Virus: HIV-1 *Strain:* HIV-1 BAL *Subtype:* B
Gene/Protein:
Virus: HIV-1 *Strain:* HIV-1 LAI *Subtype:* B
Gene/Protein:
Virus: HIV-1 *Strain:* HIV-1 RF *Subtype:* B
Gene/Protein:
Virus: HIV-1 *Strain:* HIV-1 89.6 *Subtype:* B
Gene/Protein:
Trial(s): NHP.11

Vaccine Name: **polyvalent gp120 proteins**
Description: The polyvalent protein vaccines encoded the env gene from four primary HIV-1 isolates: 92US715.6 (clade B), Ba-L (clade B), 96ZM651 (clade C), and 93TH976.17 (clade E). Recombinant proteinswere produced in either 293 or CHO cells stably transfected with gp120 expression plasmids
Trial(s): NHP.492

Vaccine Name: **Recombinant gagpol particles**
Description:
Virus: SIV *Strain:* SIVmne *Subtype:* -
Gene/Protein: gag, pol
Trial(s): NHP.134

Vaccine Name: **Recombinant gagpolenv particles**
Description:
Virus: SIV *Strain:* SIVmne *Subtype:* -
Gene/Protein:
Trial(s): NHP.134

Vaccine Name: **Recombinant gp120**
Description: Antigen derived from the Dutch clinical HIV isolate ACH320, expressed in CHO cells
Virus: HIV-1 *Strain:* HIV-1.ACH320 *Subtype:* -

Gene/Protein:
Trial(s): NHP.296

Vaccine Name: **Recombinant gp130**
Description: Recombinant subunit protein produced by African green monkey kidney (BSC-40) cells infected with recombinant vaccinia virus expressing the gp130 glycoprotein under the control of the late vaccinia virus 11K promoter
Virus: SIV *Strain:* SIVmne *Subtype:* -
Gene/Protein:
Trial(s): NHP.134

Vaccine Name: **Recombinant HIV-1 env gp160 antigen**
Description: This is a recombinant protein (HIV-1 gp160 antigen) expressed in pMB1790
Virus: HIV-1 *Strain:* HIV-1.IIIB *Subtype:* B
Gene/Protein: env
Trial(s): NHP.204

Vaccine Name: **Recombinant HIV-1 gag core (p24,p15) antigen**
Description: This is a recombinant protein (HIV-1 p24 and p15 antigen) expressed in pCO1
Virus: HIV-1 *Strain:* HIV-1.IIIB *Subtype:* -
Gene/Protein: gag
Trial(s): NHP.204, NHP.328

Vaccine Name: **Recombinant p27**
Description: rSIVp27 was expressed in pGEX3X as a glutathione-S-transferase fusion protein
Virus: SIV *Strain:* SIVmac251 *Subtype:* -
Gene/Protein:
Trial(s): NHP.106, NHP.185.1, NHP.185.2, NHP.201.1, NHP.201.2

Vaccine Name: **rgp120**
Description: This protein was purified from cell culture medium containing 1%- -vo/vol- fetal calf serum) conditioned by the growth of the gD-env-trunc cell line
Trial(s): NHP.242, NHP.267

Vaccine Name: **rgp120W6.1D**
Description: recombinant gp120W6.1D antigen derived from HIV-1 clone 320.3 isolated from a Dutch AIDS patient
Trial(s): NHP.80

Vaccine Name: **rgp140-env (HIV-1.89.6)**
Description:
Virus: HIV-1 *Strain:* 89.6 *Subtype:* B
Gene/Protein: env (gp140)
Trial(s): NHP.348.1, NHP.348.2

Vaccine Name: **rgp160**

Description: Recombinant subunit protein produced by African green monkey kidney (BSC-40) cells infected with recombinant vaccinia virus expressing the gp160 glycoprotein under the control of the late vaccinia virus 11K promoter

Virus: SIV *Strain:* SIVmne *Subtype:* -

Gene/Protein:

Trial(s): NHP.134

Vaccine Name: **rgp160**

Description: See Mannhalter et al, 1991; ARHR, Vol. 7 (5) 485-493.

Virus: HIV-1 *Strain:* HIV-1 IIIB *Subtype:* B

Gene/Protein: env (gp160)

Trial(s): NHP.362

Vaccine Name: **rsgp160**

Description: Glycosylated This protein was produced in CHO under the transcriptional control of the SV40 early promoter. It differ from the wild type gp160 at the N terminus. The signal signal sequence and 12 amino acids of the wild type gp160 have been replaced with the signal sequence and 9 amino acids from the mature N-terminus of herpes simplex virus type 1 glycoprotein D

Trial(s): NHP.267

Vaccine Name: **rSIV-gp120 protein**

Description: Recombinant SIVmac251 gp120 was expressed in Baculovirusinfected cells

Virus: SIV *Strain:* SIVmac251 *Subtype:* -

Gene/Protein:

Trial(s): NHP.106, NHP.185.1, NHP.185.2, NHP.201.1, NHP.201.2

Vaccine Name: **rTat**

Description: GST-Tat plasmid encoding 86 aa Tat protein used for expression in E. coli

Trial(s): NHP.414

Vaccine Name: **SF162ΔV2 gp140 protein**

Description: gp140 lacking the V2 region

Virus: HIV-1 *Strain:* HIV-1.SF162 *Subtype:* B

Gene/Protein: env

Trial(s): NHP.62

Vaccine Name: **SIV Nef**

Description:

Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein:

Trial(s): NHP.296

Vaccine Name: **SIV(Mne) gp160Env protein**

Description:

Trial(s): NHP.65.1

Vaccine Name: **SIVenv-Bgal peptides**

Description: This is a cocktail of 4 SIVenv epitopes (2 from gp120 and 2 from gp32). These epitopes appear to be homologous in sequence and location to the highly conserved HIV-env epitopes as well as being hydrophilic in nature. The oligonucleotides coding for these peptides were prepared and inserted at the 5' end of the gene under the trp expression element of E. coli. The four recombinant SIVenv-B-galactosidase polypeptides were expresed in bacteria and purified by HPLC.

Virus: SIV *Strain:* SIVmac *Subtype:* -

Gene/Protein: env (gp32, gp120)

Trial(s): NHP.94, NHP.154

Vaccine Name: **SIVmac239 Gag-Pol-ISCOM**

Description: 25 µl SCOM matrix (Isconova, Uppsala, Sweden) mixed overnight at 4°C with either 25 µg SIVmac239 Gag-Pol in 250 µl of PBS

Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein: gag, pol

Trial(s): NHP.374

Vaccine Name: **Soluble 89.6 gp120 protein**

Description: Produced by infection of BS-C-1 cells with recombinant vaccinia virus, vBD2,13 at a multiplicity of infection of 5 plaque-forming units (pfu) per cell. Protein was purified from the media by lectin and Superdex-200 chromatography

Virus: HIV-1 *Strain:* HIV-1.89.6 *Subtype:* B

Gene/Protein: env (gp120)

Trial(s): NHP.349

Vaccine Name: **tat protein**

Description: HIV-1 Tat (IIIB) expressed in Eschericia coli, purified to homogeneity by heparin-affinity chromatography and high-performance liquid chromatography and stored lyophilized at -80 °C. Purified Tat had full biological activity in several assays. Tat wasresuspended in degassed buffer before use in vitro or in saline containing 20% of autologous serum for monkey injection.

Virus: HIV-1 *Strain:* HIV-1.IIIB *Subtype:* B

Gene/Protein: Accessory (tat)

Trial(s): NHP.374, NHP.402

Vaccine Name: **Tat-ISCOM**

Description: Immune stimulating complex

Trial(s): NHP.402

Recombinant Vector (virus/bacteria) Vaccines

Vaccine Name: **Ad35-p17**

Description: E3-deleted replication competent Ad35-p17 was constructed using the loxP recombination method
Trial(s): NHP.481

Vaccine Name: **Ad35-p45**
Description: E3-deleted replication competent Ad35-p45 was constructed using the loxP recombination method
Trial(s): NHP.481

Vaccine Name: **AD4-gp160(MN)**
Description:
Virus: HIV-1 *Strain:* HIV-1.MN *Subtype:* B
Gene/Protein: env
Trial(s): NHP.141, NHP.502

Vaccine Name: **Ad5 HIV 89.6 env**
Description:
Trial(s): NHP.494

Vaccine Name: **Ad5- delta E1E3-HIV-MN-env/rev gp160**
Description: Virus is nonreplicative-delta E1E3
Trial(s): NHP.465

Vaccine Name: **Ad5-deltaE3/HIV-MN-env rev gp160**
Description: Virus is capable of replication (delta E3)
Trial(s): NHP.465

Vaccine Name: **Ad5-luc**
Description: Luciferase-expressing Ad5 vector was constructed by an improved in vitro ligation method. Briefly, pCMVL1, in which the luciferase gene derived from pGL3-Control (Promega, Madison, WI) was inserted into the shuttle plasmid pHMCMV6 (Mizuguchi and Kay,1999), resulting in pAdHM34-L2. To generate the virus, PacI-digested pAdHM34-L2 was transfected into 293 cells plated in a 60 mm dish with SuperFect (Qiagen, Inc., Valencia, CA) and virus was prepared.
Trial(s): NHP.473

Vaccine Name: **Ad5-p17**
Description: E1/E3 deleted Ad5-p17 expressing codon-optimized fragment of SIVmac239 gag were constructed
Trial(s): NHP.481

Vaccine Name: **Ad5-p45**
Description: E1/E3 deleted Ad5-p45 expressing codon-optimized fragments of SIVmac239 gag were constructed
Trial(s): NHP.481

Vaccine Name: **Ad5-SIVgag**
Description: This vaccine was constructed using the adenovirus as the vector. The adenovirus vector was based on the serotype 5 that has been rendered incompetent to replicate by the deletion of E1 and E3 viral genes. The adenoviral vector, pHCMVIBGHpA1 contains Ad5nucleotides 1-341 and 3,534-5,798 and an expression cassette containing the human cytomegalovirus promoter with intron and the bovine growth hormone poly

adenylation signal (see paper for more information)

Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein: gag

Trial(s): NHP.306.1, NHP.306.2

Vaccine Name: **Ad5/35-HIV gp160**

Description: The gene fragment containing CAG promoter-HIVIIIB rev/env gp160-poly A was cloned into pLHSP plasmid. The plasmid was linearized and transfected with E1, E3-deletion chimeric Ad5/35 genome, which contains the Ad type 35 fiber in the Ad5 vector

Trial(s): NHP.473

Vaccine Name: **Ad5/35-Luc**

Description: Luciferase-expressing Ad5/35 vector, which contains the Ad type 35 fiber, was constructed by an improved in vitro ligation method. Briefly, pCMVL1, in which the luciferase gene derived from pGL3-Control (Promega, Madison, WI) was inserted into the shuttleplasmid pHMCMV6 (Mizuguchi and Kay, 1999), resulting in pAdHM34-L2. To generate the virus, PacI-digested pAdHM34-L2 was transfected into 293 cells plated in a 60 mm dish with SuperFect (Qiagen, Inc., Valencia, CA) and virus was prepared.

Trial(s): NHP.473

Vaccine Name: **Ad5/SIV gag**

Description:

Trial(s): NHP.474, NHP.475

Vaccine Name: **Ad5hr-SIVenv**

Description: E3-deleted Ad5hr vector containing the SIVsmH4 (also known as F236, accession number X14307)envelope gene

Notes: An E3-deleted Ad5hr vector containing the SIVsmH4 envelope gene

Virus: SIV *Strain:* SIVsmH4 *Subtype:* -

Gene/Protein: env

Notes: The H4 (F236) isolate of SIV-SMM is not related to the MAC251/MAC239 lineage.

Trial(s): NHP.5, NHP.205.1, NHP.205.3, NHP.324.1, NHP.328

Vaccine Name: **Ad5hr-SIVmac239gag**

Description: Adenovirus Ad5hr with a codon-optimized Gag cDNA derived from Mac239, with silent mutations to optimize expression and eliminate the inhibitory sequences.

Virus: SIV *Strain:* Mac239 *Subtype:* -

Gene/Protein: gag (Gag)

Trial(s): NHP.324.1, NHP.328, NHP.363

Vaccine Name: **Ad5hr-SIVnefδ1-13**

Description:

Virus: SIV *Strain:* Mac239 *Subtype:* -

Gene/Protein: Nef

Trial(s): NHP.328, NHP.363

Vaccine Name: **Ad5hr-SIVsmH4 env/rev**

Description: Ad5hr-SIVsmH4 env/rev, a replication-competent Ad5hr-SIV recombinant carrying the SIVsmH4env and rev genes in the deleted E3 region and expressing the entire SIV envelope and Rev proteins
Virus: SIV *Strain:* *Subtype:* -
Gene/Protein: env, Accessory (rev)
Trial(s): NHP.363, NHP.371

Vaccine Name: **Ad7-delta E3/HIV-MN-env/rev gp160**
Description: Virus is capable of replication - delta E3
Trial(s): NHP.465

Vaccine Name: **Ad7-deltaE1E3-HIV-MN-env/rev gp160**
Description: virus is non-replicative-delta E1E3
Trial(s): NHP.465

Vaccine Name: **ALVAC- SIVmac251-gag-pol**
Description: vCP172 is an ALVAC pox-derived virus carrying SIV-MAC251 gag-pol region.
Virus: SIV *Strain:* MAC251 *Subtype:* -
Gene/Protein:
Trial(s): NHP.500

Vaccine Name: **ALVAC-HIV-1-IIIB-gag-pol-gp120-env vCP250**
Description: HIV-1 subtype B isolate IIIB/HXB2 gag, pol and env
Virus: HIV-1 *Strain:* HXB2 *Subtype:* B
Gene/Protein: gag, pol, env
Trial(s): NHP.500

Vaccine Name: **ALVAC-HIV-1-IIIB-gag-pol-gp160-env vCP1420**
Description: ALVAC with HIV-1 subtype B gag, pol and gp160
Virus: HIV-1 *Strain:* HXB2 *Subtype:* B
Gene/Protein: gag, pol, env
Trial(s): NHP.500

Vaccine Name: **ALVAC-HIV-2 (gag,pol,gp125)**
Description: Recombinant canarypox virus expressing HIV-2 env, gag and pol genes
Virus: HIV-2 *Strain:* HIV-2 SBL6669 *Subtype:* -
Gene/Protein: gag, pol
Virus: HIV-2 *Strain:* HIV-2 SBL6669 *Subtype:* -
Gene/Protein: env (gp125)
Trial(s): NHP.4

Vaccine Name: **ALVAC-SIV-gp**
Description: Recombinant SIV vaccine composed of a live, weakened canarypox virus (ALVAC™) into which parts of SIV genes (gag and pol) were inserted. When ALVAC infects a human cell, the inserted SIV genes direct the cell to make SIV proteins. These proteinsare packaged into SIV-like particles that bud from the cell membrane. The particles are not infectious, fool the immune system and mount immune response to SIV.

As a safety precaution, ALVAC can infect but not grow in human or macaques cells.

Virus: SIV *Strain:* ? *Subtype:* -

Gene/Protein: pol

Trial(s): NHP.345

Vaccine Name: **ALVAC-SIV-gpe (vcp180)**

Description: The ALVAC-SIV-gpe (vcp180) was engineered to express the gag, pol, and env genes of SIVmac251(K6W)

Virus: SIV *Strain:* SIVmac251 *Subtype:* -

Gene/Protein: env, gag, pol

Trial(s): NHP.30, NHP.123, NHP.274

Vaccine Name: **ALVAC/vCP153 HIV-2 gag,pol,env**

Description:

Virus: HIV-2 *Strain:* ND *Subtype:* -

Gene/Protein: env, gag, pol

Trial(s): NHP.174

Vaccine Name: **F(+)SeV-gag**

Description: This is a replication-competent Gag-expressing Sendai virus (SeV is a nonsegmented negative-strand RNA virus considered nonpathogenic for humans and nonhuman primates)

Virus: SIV *Strain:* ND *Subtype:* -

Gene/Protein: gag

Trial(s): NHP.69, NHP.70, NHP.326, NHP.421

Vaccine Name: **F(+)SeV-Tat**

Description: Recombinant Sendai virus expressing Tat, replication competent

Trial(s): NHP.421

Vaccine Name: **F(-)SeV-Gag**

Description: Replication-incompetent Sendai virus expressing Gag

Trial(s): NHP.421

Vaccine Name: **FP-SIV-gp (FP74)**

Description:

Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein: gag, pol

Trial(s): NHP.9.2, NHP.345

Vaccine Name: **FPV.HIV-1.gag/pol**

Description: recombinant fowlpoxvirus (rFPV) vaccines expressing HIV-1 antigens gag and pol. The HIV-1gag/pol genes of ARV-2/SF2 strain were inserted into the FPV genome (FPV M3 strain) along with the E. coli Beta-gal and/orgpt selection and marker genes.

Virus: HIV-1 *Strain:* HIV-1.ARV-2/SF2 *Subtype:* B

Gene/Protein: gag, pol

Trial(s): NHP.48

Vaccine Name: **FPV.HIV-1.gag/pol-IFNgamma**

Description: recombinant fowlpoxvirus (rFPV) vaccines expressing both HIV-1 antigens and interferon-gamma. The HIV-1gag/pol genes of ARV-2/SF2 strain with the human IFNgamma gene were inserted into the FPV genome (FPV M3 strain) along with the E. coli Beta-gal and/orgpt selection and marker genes.

Virus: HIV-1 *Strain:* ARV-2/SF2 *Subtype:* B

Gene/Protein: gag, pol

Trial(s): NHP.48

Vaccine Name: **Lyseria monocyogenes SIV-gag**

Description: Lysteria monocytogenes expressing SIV gag from a plasmid.

Trial(s): NHP.499

Vaccine Name: **Lysteria monocytogenes SIV-env**

Description: Lysteria monocytogenes expressing SIV env from a plasmid

Trial(s): NHP.499

Vaccine Name: **MVA SIVsmH4 gag-pol**

Description:

Virus: SIV *Strain:* SIVsmH4 *Subtype:* -

Gene/Protein: gag, pol

Trial(s): NHP.3, NHP.45, NHP.46

Vaccine Name: **MVA-mac(J5)**

Description: MVA constructs expressing env, gag-pol, nef, rev and tat genes of SIVmacJ5

Virus: SIV *Strain:* SIVmacJ5 *Subtype:* -

Gene/Protein: gag, pol, env

Trial(s): NHP.51

Vaccine Name: **MVA-rev**

Description: Modified Vaccinia Anlkara expressing HIV-1 subtype B isolate IIIB rev cDNA.

Virus: HIV-1 *Strain:* IIIB *Subtype:* B

Gene/Protein: rev

Trial(s): NHP.276

Vaccine Name: **MVA-SIV gag-pol and HIV-1 89.6 env**

Description: MVA vectors (pLW-9 and pLW-17) expressing SIV gag-pol and HIV-1 89.6 env

Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein: gag, pol

Virus: HIV-1 *Strain:* HIV-1.89.6 *Subtype:* B

Gene/Protein: env

Trial(s): NHP.24.2, NHP.494, NHP.515

Vaccine Name: **MVA-SIV239tat**

Description: This vector encodes the full-length SIVmac239 Tat
Trial(s): NHP.88

Vaccine Name: **MVA-SIV251 32H tat**
Description: This vector encodes the full-length SIVmac251 32H Tat (clone J5)
Virus: SIV *Strain:* SIVmac251.32H *Subtype:* -
Gene/Protein:
Trial(s): NHP.88

Vaccine Name: **MVA-SIVgag**
Description: This MVA-SIV gag vaccine was constructed by cloning the SIV gag gene into the pSC59 shuttle vector. This plasmid was designed to insert the transgene fragment into a viral thymidine kinase region and to drive the transgene from a synthetic early/late promoter. The recombinant plasmid was inserted into the MVA for immunization of monkeys.
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag
Trial(s): NHP.306.1, NHP.306.2

Vaccine Name: **MVA-SIVmac239gag**
Description: Recombinant MVA virus vT338 contains the gag gene from SIVmac239 inserted into the deletion III region of the MVA genome under the control of the vaccinia virus 40K (H5R) promoter. The virus also contains the Escherichia coli lacZ gene under the control of the fowlpox C1 promoter for use as a colorimetric screen for recombinant viruses
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag
Trial(s): NHP.308

Vaccine Name: **MVA-SIVmacJ5 (gag-pol)**
Description: MVA constructs expressing gag-pol genes of SIVmac251 32H (pJ5) under the transcriptional control of the natural vaccinia virus early/late promoter P7.5
Notes: poorly immunogenic
Trial(s): NHP.3, NHP.401

Vaccine Name: **MVA-SIVSL8-tat28-35**
Description: This vector encodes a single Mamu-A*01-restricted CTL epitope Tat-SL8(positions 28-35)(STPESANL) inserted within the immunodominant region of hepatitis B core antigen
Virus: SIV *Strain:* SIVSL8 *Subtype:* -
Gene/Protein:
Trial(s): NHP.88

Vaccine Name: **MVA-SIVsmH-4 -env**
Description: MVA recombinants expressing the SIVsmH-4 env (MVA-env)
Virus: SIV *Strain:* SIVsmH-4 *Subtype:* -
Gene/Protein: env
Trial(s): NHP.45

Vaccine Name: **MVA-tat**
Description: Modified Vaccinia Ankara expressing HIV-1 IIIB strain tat cDNA
Virus: HIV-1 *Strain:* IIIB *Subtype:* B
Gene/Protein: tat
Trial(s): NHP.276

Vaccine Name: **MVA.HW**
Description: This is a recombinant MVA.HW expressing an MVA and SIV gag-derived epitope, TPYDINQML, recognized by CTLs in rhesus macaques (Macaca mulatta) in the context of the Mamu-A*01 MHC class I molecule
Virus: SIV *Strain:* ND *Subtype:* -
Gene/Protein: gag
Trial(s): NHP.57

Vaccine Name: **MVA.pUCII.SIVmac.J5**
Description: MVA vaccine expressing SIV structural (gag,pol) and regulatory genes (tat,nef and rev)
Virus: SIV *Strain:* SIVmac.J5 *Subtype:* -
Gene/Protein: gag, pol
Trial(s): NHP.58

Vaccine Name: **MVA/HIV 48**
Description: MVA/HIV 48 is an rMVA expressing HIV-1 clade B Gag, protease, RT, and Env constructed by homologous recombination in chick embryo fibroblasts. Contains HXB2 gag and BH10 pol. The pol sequences contained three safety mutations in RT and a truncated integrase. The env from CCR5-tropic HIV-1.ADA contained silent mutations to eliminate two copies of a TTTTTNT sequence that acts as a poxvirus transcription termination signal (See LINDA S. WYATT, et al. 2004)
Virus: HIV-1 *Strain:* HIV-1.BH10 *Subtype:* B
Gene/Protein: pol
Virus: HIV-1 *Strain:* HIV-1.HXB2 *Subtype:* B
Gene/Protein: gag
Virus: HIV-1 *Strain:* HIV-1.ADA *Subtype:* B
Gene/Protein: env
Trial(s): NHP.384

Vaccine Name: **MVAgagpol**
Description: The SIVsmH4 gag pol ORF (1049-5397) cloned into pMC03, then the product transfected into chicken embryo fibroblasts that had been infected with MVA. Plaques that stained blue upon addition of X-Gluc (CLONTECH) were purified
Virus: SIV *Strain:* SIVsmH4 *Subtype:* -
Gene/Protein: gag, pol
Trial(s): NHP.44

Vaccine Name: **MVAmacJ5-nef**
Description: A highly immunogenic vector construct with high anti-CTL response; associated with protection
Notes: zzz
Virus: SIV *Strain:* SIVmac251 32H (pJ5) *Subtype:* -

Gene/Protein: Accessory (nef)
Trial(s): NHP.3

Vaccine Name: **MVApIII-sp.SIVmac.J5.env**
Description: Recombinant MVA vaccine expressing SIVmac.J5 env gene
Virus: SIV *Strain:* SIVmac.J5 *Subtype:* -
Gene/Protein: env
Trial(s): NHP.58

Vaccine Name: **NYVAC-IIIB-Env**
Description: NYVAC with HIV-1 subtype B clone HXB2 envelope by Dr. James Tartaglia of Sanofi-Pasteur, Toronto, Ontario, Canada.
Virus: HIV-1 *Strain:* HXB2 *Subtype:* B
Gene/Protein: env
Trial(s): NHP.503

Vaccine Name: **NYVAC-Retanef**
Description: Synthetic open reading frame encoding epitopes of SIV-MAC-251 Rev, Tat and Nef proteins fused together. Inserted into NYVAC vaccinia vector.
Virus: SIV *Strain:* Mac251 *Subtype:* -
Gene/Protein: Accessory (Rev Tat and Nef epitopes)
Trial(s): NHP.479

Vaccine Name: **NYVAC-SIV-gag-pol-env (NYVAC-SIV-gpe)**
Description: A highly attenuated poxvirus NYVAC-SIV-gag-pol-env (NYVAC-SIV-gpe); Induce both CD4+ and CD8+ t cell responses in rhesus macaques and demonstrate effectiveness as a preventive vaccine candidate.
Notes: vaccinia
Virus: SIV *Strain:* Mac251 *Subtype:* -
Gene/Protein:
Notes: Described by Benson et al. J Virol. 1998 May;72(5):4170-82. PMID: 9557706
Virus: SIV *Strain:* Mac251 *Subtype:* -
Gene/Protein: env expression cassette under control of vaccinia H6 promoter and gag-pol with I3L promoter.
Notes: Described by Benson et al. J Virol. 1998 May;72(5):4170-82. PMID: 9557706
Trial(s): NHP.9.1, NHP.274, NHP.462, NHP.479

Vaccine Name: **NYVAC-SIVgagpol**
Description: NYVAC with SIV-Mac239 Gag and SIV-Mac239 Pol by Dr. James Tartaglia of Sanofi-Pasteur, Toronto, Ontario, Canada.
Virus: SIV *Strain:* MAC239 *Subtype:* -
Gene/Protein: gag, pol
Trial(s): NHP.503

Vaccine Name: **pCSIV-env**
Description: plasmid expression SIV envelope

Trial(s): NHP.499

Vaccine Name: **Polio (Sabin 1) - HIV-1.gag/env (2)**
Description:
Virus: HIV-1 *Strain:* IIIB?LAI (HXB2) *Subtype:* -
Gene/Protein: gag, env (gp120,gp140 (lacking signal sequece) gp120+gp140 ectodomain, p55 fused with VP4)
Virus: HIV-1 *Strain:* 92TH021 *Subtype:* D
Gene/Protein: env (gp120)
Virus: HIV-1 *Strain:* 92TH022 *Subtype:* CRF01_AE
Gene/Protein: env (gp120)
Virus: HIV-1 *Strain:* 92RW020 *Subtype:* A
Gene/Protein: env (gp120)
Virus: HIV-1 *Strain:* 92BR025 *Subtype:* C
Gene/Protein: env (gp120)
Trial(s): NHP.348.1

Vaccine Name: **Polio (Sabin 1) -HIV-1.gag/env (1)**
Description:
Virus: HIV-1 *Strain:* 92RW020 *Subtype:* A
Gene/Protein: env (GP120)
Virus: HIV-1 *Strain:* 92TH022 *Subtype:* CRF01_AE
Gene/Protein: env (gp120)
Virus: HIV-1 *Strain:* 92UG021 *Subtype:* D
Gene/Protein: env (gp120)
Virus: HIV-1 *Strain:* IIIB/LAI (HXB2) *Subtype:* B
Gene/Protein: gag, env (gp120,gp140 (lacking signal sequence), gp120+gp41 ectodomain, p55 fused with VP4)
Trial(s): NHP.348.1

Vaccine Name: **Polio (Sabin 2) - HIV-1.gag/env (3)**
Description:
Virus: HIV-1 *Strain:* IIIB/LAI (HXB2) *Subtype:* B
Gene/Protein: gag, env (gp120,gp140 (lacking signal sequence), gp120+gp41 ectodomain, p55 fused with VP4)
Virus: HIV-1 *Strain:* 92UG021 *Subtype:* D
Gene/Protein: env (gp120)
Virus: HIV-1 *Strain:* 92RW09 *Subtype:* A
Gene/Protein: env (gp120)
Virus: HIV-1 *Strain:* 92TH026 *Subtype:* CRF01_AE
Gene/Protein: env (gp120)
Trial(s): NHP.348.1

Vaccine Name: **Polio (Sabin 2) - HIV-1.gag/env (4)**
Description:
Virus: HIV-1 *Strain:* IIIB/LAI(HXB2) *Subtype:* B
Gene/Protein: gag, env (gp120,gp140 (lacking signal sequence), gp120+gp41 ectodomain, p55 fused with VP4)

Trial(s): NHP.348.1

Vaccine Name: **Polio- SIVmac239gag**
Description:
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag
Trial(s): NHP.348.2

Vaccine Name: **Polio-LAI/IIIB-Env**
Description:
Virus: HIV-1 *Strain:* IIIB/LAI *Subtype:* B
Gene/Protein: env (gp120)
Trial(s): NHP.348.2

Vaccine Name: **rAd expressing HxBc2/BaL clade A env**
Description:
Trial(s): NHP.443

Vaccine Name: **rAd expressing HxBc2/BaL clade B env**
Description:
Trial(s): NHP.443

Vaccine Name: **rAd expressing HxBc2/BaL clade c env**
Description:
Trial(s): NHP.443

Vaccine Name: **rAD Gag**
Description: replication-defective adenovirus expressing HIV-1 Gag, details not supplied, contact authors.
Trial(s): NHP.507

Vaccine Name: **rAd-HxB2/BaL Env DCFI**
Description: The env gene region encoding aa 205 to 361 of HxB2 was replaced with the corresponding BaL gene sequence, CCR5 tropic clade B immunogen. The vector encoding Env were modified in the cleavage, furin, and interhelical domain (?CFI) sites involving deletionof aa 515-546 and aa 608-625. The gp140 ?CFI contains a single nucleotide base insertion at position 632 resulted in a frameshift of the COOH-terminal 60 amino acids.
Trial(s): NHP.381, NHP.418, NHP.514

Vaccine Name: **rAd-SIVmac239 gag/pol**
Description:
Trial(s): NHP.443

Vaccine Name: **rAd35-SIV Gag HIV-1 Env**
Description: replication-incompetent
Trial(s): NHP.469

Vaccine Name: **rAd35k5-SIV gag HIV-1 Env**
Description: Replication-incompetent capsid chimeric rAd35 vector containing the Ad5 fiber knot
Trial(s): NHP.469

Vaccine Name: **rAd5 89.6P Env (DCFI)**
Description: DCFI mutations in cleavage site, fusion and interhelical domains of Env from HIV-1 89.6P
Trial(s): NHP.381, NHP.418

Vaccine Name: **rAd5 SIVmac239 env**
Description:
Trial(s): NHP.495

Vaccine Name: **rAd5-SIV gag and HIV-1 Env**
Description: replication-incompetent
Trial(s): NHP.469

Vaccine Name: **rAd5-SIVmac239 gag/pol**
Description: Synthetic SIVmac239 gag-pol was cut with SalI, blunted, and then digested with BamHI, after which it was subcloned into the blunted EcoRV and BamHI sites of the shuttle plasmid pAdAdaptCMVmcs. Virus was amplified in 293T cells.
Trial(s): NHP.381, NHP.418, NHP.494, NHP.495, NHP.514

Vaccine Name: **rAd5/gag-env**
Description: Gag/Env was cloned into the pShuttle-CMV (Qbiogene) and then inserted into pAdEasy-1 (E1/E3-deleted human adenovirus serotype five viral DNA, Qbiogene) by homologous recombination. Each adenoviral vector was transfected into QBI-293A cells (Qbiogene) to produce recombinant adenoviruses expressing each SIV gene.
Trial(s): NHP.493

Vaccine Name: **rAd5/sPol**
Description: sPol was cloned into the pShuttle-CMV (Qbiogene) and then inserted into pAdEasy-1 (E1/E3-deleted human adenovirus serotype five viral DNA, Qbiogene) by homologous recombination. Each adenoviral vector was transfected into QBI-293A cells (Qbiogene) to produce recombinant adenoviruses expressing each SIV gene.
Trial(s): NHP.493

Vaccine Name: **rAd5/sTat-Vpx**
Description: sTat-Vpx was cloned into the pShuttle-CMV (Qbiogene) and then inserted into pAdEasy-1 (E1/E3-deleted human adenovirus serotype five viral DNA, Qbiogene) by homologous recombination. Each adenoviral vector was transfected into QBI-293A cells (Qbiogene) toproduce recombinant adenoviruses expressing each SIV gene.
Trial(s): NHP.493

Vaccine Name: **rAd5/sVif-Nef**
Description: sVif-Nef was cloned into the pShuttle-CMV (Qbiogene) and then inserted into pAdEasy-1 (E1/E3-deleted human adenovirus serotype five viral DNA, Qbiogene) by homologous recombination. Each adenoviral

vector was transfected into QBI-293A cells (Qbiogene) toproduce recombinant adenoviruses expressing each SIV gene.

Trial(s): NHP.493

Vaccine Name: **rBCG-Env V3**

Description: Recombinant Mycobacterium bovis bacillus Calmette-Guerin secretes a chimeric protein consisting of the V3-neutralizing epitope of HIV-1 and alpha antigen. Plasmid used for insertion contains a mycobacterial codon-optimized DNA fragment encoding 10 aminoacids of the Japanese HIV-1 V3 consensus sequence (NTRKSIHIGPGRAFYATGS) which has a neutralization sequence identical to that f HIV-1(MN)

Trial(s): NHP.408

Vaccine Name: **rBCG-SIV^3**

Description: A mixture of 3 transformed strains of Mycobacterium bovis BCG expressing the SIV-MAC-251 gag, nef and env genes.

Virus: SIV *Strain:* MAC251 *Subtype:* -

Gene/Protein: Accessory, env, gag (nef, gag, env)

Trial(s): NHP.353

Vaccine Name: **rDIs SIV gag/pol**

Description: DIs is a restrictive host range mutant of vaccinia virus strain DIE that grows well only in chick embryo fibroblast cells. The SIVgag/pol gene was first amplified from SHIVNM-3rN DNA and then subcloned into the pUCvvp7.5H vector. A HindIII fragment encoding SIVgag/pol and the p7.5H promoter region were inserted into the HindIII site of a pUC/DIs transfer vector. rDIsSIVgag/pol was generated by homologous recombination and propagated in chicken embryo fibroblasts (CEF).

Trial(s): NHP.486

Vaccine Name: **Recombinant fowlpox (rFPV) SIVmac239 gag**

Description: Recombinant fowlpox virus expressing SIVmac239 gag. The SIV gene was inserted in the BamJHI region of POXVAC-TC (Schering-Plough) strain of FPV

Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein: gag

Trial(s): NHP.400, NHP.443

Vaccine Name: **Recombinant fowlpox (rFPV).SHIV89.6P env**

Description: Recombinant fowlpox virus expressing SHIV89.6P env. The SHIV gene was inserted in the BamJHI region of POXVAC-TC (Schering-Plough) strain of FPV.

Virus: SHIV *Strain:* SHIV89.6P *Subtype:* B

Gene/Protein: env

Trial(s): NHP.400

Vaccine Name: **Recombinant MVA-SHIV89.6P env**

Description: Recombinant MVA expressing SHIV89.6P gp140 (env). The SHIV gene was inserting in the deletion III region of a plaque-purified isolate of the replication-defective strain of vaccinia virus designated MVA. The env gene was under the control of the vacciniavirus 40K(H5R) promoter.

Virus: SHIV *Strain:* SHIV89.6P *Subtype:* B

Gene/Protein: env

Trial(s): NHP.400

Vaccine Name: **Recombinant MVA-SIVmac239 gag**

Description: Recombinant MVA expressing SIVmac239 gag. The SIVmac239 gene was inserting in the deletion III region of a plaque-purified isolate of the replication-defective strain of vaccinia virus designated MVA. The gag gene was under the control of the vacciniavirus 40K(H5R) promoter.

Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein: gag

Trial(s): NHP.400, NHP.443

Vaccine Name: **Recombinant vaccinia gagpol (v-SG11)**

Description:

Virus: SIV *Strain:* SIVmne *Subtype:* -

Gene/Protein: gag, pol

Trial(s): NHP.134

Vaccine Name: **Recombinant vaccinia gagpolenv (v-SGE14)**

Description:

Virus: SIV *Strain:* SIVmne *Subtype:* -

Gene/Protein: env, gag, pol

Trial(s): NHP.134

Vaccine Name: **Recombinant vaccinia gp130 (v-SE6)**

Description:

Virus: SIV *Strain:* SIVmne *Subtype:* -

Gene/Protein:

Trial(s): NHP.134

Vaccine Name: **Recombinant vaccinia virus (rVac).SHIV89.6P Env**

Description: Recombinant vaccinia virus expressing SHIV89.6P env, constructed by inserting the SHIV env gene in the HindIII M region of TBC-Wy Therion strain of vaccinia (see Mazzara, G. P., Destree, A.&Mahr, A. (1993) Methods Enzymol. 217, 557-581).

Virus: SHIV *Strain:* SHIV89.6P *Subtype:* B

Gene/Protein: env

Trial(s): NHP.400

Vaccine Name: **Recombinant vaccinia virus (rVac).SIVmac239 gag**

Description: Recombinant vaccinia virus expressing SIVmac239 gag, constructed by inserting the SIV gag gene in the HindIII M region of TBC-Wy Therion strain of vaccinia (see Mazzara, G. P., Destree, A.&Mahr, A. (1993) Methods Enzymol. 217, 557-581).

Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein: gag

Trial(s): NHP.400, NHP.443

Vaccine Name: **recombinant vaccinia virus expressing HIV-1 89.6P env**

Description:

Trial(s): NHP.443

Vaccine Name: **Recombinant vaccinia virus vac-gp160 (v-SE5)**

Description: Recombinant vaccinia virus vac-gp160 (v-SE5) contains the coding sequence of the full-length gp160 of SIVmne molecular clone 8 (GenBank accession number M32741) in a New York City Board of Health strain (v-NY) of vaccinia virus (16, 17). v-SE5 was plaque-purified and propagated on African green monkey kidney cells (BSC-40)

Virus: SIV *Strain:* SIVmne *Subtype:* -

Gene/Protein: env

Trial(s): NHP.134, NHP.269

Vaccine Name: **Recombinant vaccinia virus-HIVgp160 (cocktail)**

Description: Recombinant vaccinia virus expressing gp160 of HIV-1 isolates Bal, LAI, RF (vCB43, vCB41, and vCB36, respectively), 89.6 (vBD3), DH12, and AD8 (vvDHenv and vvADenv, respectively).

Virus: HIV-1 *Strain:* HIV-1 BAL *Subtype:* B

Gene/Protein: env

Virus: HIV-1 *Strain:* HIV-1 LAI *Subtype:* B

Gene/Protein: env

Virus: HIV-1 *Strain:* HIV-1 RF *Subtype:* B

Gene/Protein: env

Trial(s): NHP.11

Vaccine Name: **rFPV SIV gag/pol**

Description: FPVgag/pol, expressing SIV Gag and Pol, was constructed by inserting the promoter-SIV gag/pol PCR amplicon into pKG10a for insertion into FPV-M3 at the F6,7,9 site. PCR primers for the fowlpox virus early/late promoter and an early transcription terminator were used for insertion into fowlpox virus vector FPV-M3.

Trial(s): NHP.466

Vaccine Name: **rFPV-gag/pol**

Description: FPVgag/pol, expressing SIV Gag and Pol, was constructed by inserting the promoter-SIV gag/pol PCR amplicon into pKG10a for insertion into FPV-M3 at the F6,7,9 site. PCR primers for the fowlpox virus early/late promoter and an early transcription terminator were used for insertion into fowlpox virus vector FPV-M3.

Trial(s): NHP.491

Vaccine Name: **rFPV-HIV env**

Description: HIV-193TH254 env (mutated to remove the middle third) was amplified with fowlpox virus promoter and terminator sequences and inserted into the plasmid vector pCH34 for construction of a recombinant fowlpox virus with HIV Env expressed from the REV insertion site.

Trial(s): NHP.491

Vaccine Name: **rFPV-HIV gag/pol**

Description: rFPV expressing mutated gag/pol was constructed from pHIS-HIV-B , Pol antigens in the vaccines are expressed via a frameshift mutation. The FPV early/late promoter and an early transcription terminator were added by PCR. The promoter gag/pol PCR productwas cloned into pKG10.

Trial(s): NHP.415

Vaccine Name: **rFPV-HIV gag/pol/IFNg**

Description: human IFNg was inserted into rFPV expressing mutated Gag/Pol from pHIS-HIV-B, under the control of the early/late promoter downstream of FPV TK gene

Trial(s): NHP.415

Vaccine Name: **rFPV-HIV gag/pol/IL-12**

Description: Human IL-12 was inserted into rFPV expressing mutated Gag/Pol from pHIS-HIV-B, under the control of the early/late promoter immediately downstream of the FPV TK gene.

Trial(s): NHP.415

Vaccine Name: **rFPV-HIV-AE**

Description: Vaccine encodes identical sequences for the HIV-1 AE Gag, Pol, Env, Tat and Rev antigens, driven off the early/late FPV promoter at three separate insertion sites.

Trial(s): NHP.466

Vaccine Name: **rFPV-HIV-AE (env)**

Description: HIV-1 (93TH254) env (mutated to remove the middle third) was amplified with fowlpox virus promoter and terminator sequences and inserted into the plasmid vector pCH34 for construction of a recombinant fowlpox virus with HIV Env expressed from the REV insertion site.

Trial(s): NHP.466

Vaccine Name: **rFPV-SIV gag/pol-IFNgamma**

Description: Human IFN- was inserted into FPV-SIVgag/pol under the control of the fowlpox virus early/late promoter immediately downstream of the fowlpox virus thymidine kinase gene to construct vaccine FPV-SIVgag/pol-IFN-, coexpressing human IFN-.

Trial(s): NHP.466

Vaccine Name: **rMVA (gag,pol,env)**

Description: Gag, pol, env genes derived from HIV-1 subtype AG (CRF02_AG) strain IC0928; constructed with gag-pol inserted into deletion III and a truncated env into del II

Trial(s): NHP.470, NHP.510

Vaccine Name: **rMVA (SIVsm) gagpolenv**

Description: The rMVA-SIVsm co-expresses the gag-pol and env of SIVsmmH4. gag-pol was under the transcriptional control of the vaccinia early-late promoter P7·5. Env was expressed using a strong synthetic vaccinia virus early-late promoter. MVA-SIVsmwas amplified on primary chicken embryo fibroblasts and purified by ultracentrifugation. Purified viruses were reconstituted in PBS and titrated by end-point dilution in CEF to obtain the TCID50, aliquotted and stored at -70 °C.

Virus: SIV *Strain:* SIVsmmH4 *Subtype:* -

Gene/Protein: gag, pol, env

Trial(s): NHP.125

Vaccine Name: **rMVA 89.6**

Description: The MVA double recombinant virus expressed both the HIV 89.6 Env and the SIV 239 Gag-Pol, which were inserted into deletion II and deletion III of MVA, respectively . The 89.6 Env protein was truncated for the COOH-terminal 115 amino acids of gp41

Notes: The modified H5 promoter controlled the expression of both foreign genes
Virus: HIV-1 *Strain:* HIV-1.89.6 *Subtype:* B
Gene/Protein: env
Virus: SIV *Strain:* SIVmac329 *Subtype:* -
Gene/Protein: gag, pol
Trial(s): NHP.19, NHP.132, NHP.325, NHP.349

Vaccine Name: **rMVA expressing Gag,Pol of SIVmac239**
Description: Expression under control of modified H5 vaccinia virus promoter
Trial(s): NHP.467

Vaccine Name: **rMVA expressing HIV-1 Env of SHIV89.6p (KB9)**
Description: Expression under control of modified H5 vaccinia virus promoter
Trial(s): NHP.467

Vaccine Name: **rMVA SIV239 gag-pol**
Description: this recombinant MVA expresses SIV239 Gag-Pol
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag, pol
Trial(s): NHP.89

Vaccine Name: **rMVA SIVmac239 gagpolenv**
Description: For construction of MVA-SIVgpe, chicken embryo fibroblast cells were incubated simultaneously with five infectious units each of MVA/SIV239gagpol and MVA/SH4wt. The latter virus expresses the SIVmac239 env gene, truncated after amino acid 733, under the control of the moderate-strength vaccinia virus promoter p7.5. A virus isolate expressing all three genes was clonally purified and amplified.
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: env, gag, pol
Trial(s): NHP.294

Vaccine Name: **rMVA-SIVmac251 32H**
Description: Recombinant MVA expressing SIVmac251 genes (gag,pol,tat,rev or nef, separately) under the transcriptional control of vaccinia virus early and late promoters P7.5 and sP
Virus: SIV *Strain:* SIVmac251 *Subtype:* -
Gene/Protein: gag, pol
Trial(s): NHP.52, NHP.406

Vaccine Name: **rMVA-tat,rev,nef**
Description: HIV-1 LAI nef, tat, and rev were inserted into the MVA plasmid pUCII LZdel P7.5 to be placed under transcriptional control of the vaccinia virus early late promoter P7.5.
Trial(s): NHP.401

Vaccine Name: **rMVA.SIVmac239gagpolHIVenv**
Description:
Virus: SIV *Strain:* SIVmac239 *Subtype:* -

Gene/Protein: gag, pol
Virus: HIV-1 *Strain:* Unknown *Subtype:* -
Gene/Protein: env
Trial(s): NHP.366, NHP.502

Vaccine Name: **rMVA.SIVmac32H.tat.rev**
Description: Recombinant MVA expressing SIVmac32H tat and rev genes
Virus: SIV *Strain:* SIVmac32H *Subtype:* -
Gene/Protein: Accessory (tat,rev)
Trial(s): NHP.49

Vaccine Name: **rMVASIV239gagpol.HIV89.6env**
Description: A recombinant virus expressing the SIVmac239gagpol gene was constructed by insertion of the entire open reading frame from plasmid p239SpSp5' into a plasmid transfer vector, pLW-9 (Wyatt et al., 1996). The rMVA, MVA/SIV239gagpol, was selected by immunostaining with serum from an SIV-infected macaque. For construction of the double recombinant virus, CEF were incubated simultaneously with 5 infectious units each of MVA/SIV239gagpol and MVA/89.6T
Virus: HIV-1 *Strain:* HIV-1.89.6 *Subtype:* -
Gene/Protein: env
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag, pol
Trial(s): NHP.24.1, NHP.90.1, NHP.90.2

Vaccine Name: **rSalmonella typhi-SIVgag**
Description: Salmonella typhi expressing SIV gag
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag
Trial(s): NHP.308

Vaccine Name: **rSalmonella typhimurium-SIVgag**
Description: Salmonella typhimurium expressing SIV gag
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag
Trial(s): NHP.308

Vaccine Name: **rSFV-SIVmac32H.rev.tat**
Description: Recombinant Semliki Forest Virus encoding SIVmac32H rev and tat genes.
Virus: SIV *Strain:* *Subtype:* -
Gene/Protein: Accessory (rev, tat)
Trial(s): NHP.49

Vaccine Name: **rVac HIV-1 89.6 Env**
Description:
Trial(s): NHP.494

Vaccine Name: **rVac SIVmac251 gag**
Description:
Trial(s): NHP.494

Vaccine Name: **rVac SIVmac251 pol**
Description:
Trial(s): NHP.494

Vaccine Name: **rVac-HIV1gp120**
Description: Vaccinia HIV1 BRU gp120 65.0 was constructed by Osterhaus and Goudsmit
Trial(s): NHP.401

Vaccine Name: **rVaccinia-gp160**
Description: Recombinant vaccinia virus expressing HIV-1 HXB2 gp160
Virus: HIV-1 *Strain:* HIV-1 HXB2 *Subtype:* B
Gene/Protein: env
Trial(s): NHP.78

Vaccine Name: **rVaccinia-SIVmac-env.gagpol**
Description: Recombinant vaccinia virus containing both SIVmac env and SIVmac gag-pol (vAbT386.6.1)
Virus: SIV *Strain:* SIVmac *Subtype:* -
Gene/Protein: env, pol
Trial(s): NHP.76

Vaccine Name: **RVG dG-89.6P env**
Description: Rhabdovirus expressing the SHIV89.6P Env ectodomain fused to intracellular domain of the G glycoprotein
Trial(s): NHP.424

Vaccine Name: **rVSV G(I)-HIV env and SIV gag**
Description: rVSV expressed exxtracellular and transmembrane domains of HIV-1 89.6 gp160 fused to cytoplamsic domain of VSV G protein and other rVSV expressed the SIVmac239 gag p55 precursor protein; Indiana G protein serotype
Trial(s): NHP.409

Vaccine Name: **rVSV HIV1 envG**
Description: Encodes the extracellular and transmembrane domains of HIV-1 89.6P gp160 fused to the cytoplasmic domain of the VSV G protein
Trial(s): NHP.455

Vaccine Name: **rVSV SIV gag**

Description: Encodes the SIVmac239 gag p55 precursor protein
Trial(s): NHP.455

Vaccine Name: **rVV-env cocktail**
Description: pSC11 vector cloned with 21 envelope proteins to make recombinant vaccinia
Trial(s): NHP.471

Vaccine Name: **rVV-HIV-1.DH12env**
Description: Recombinant vaccinia virus expressing HIV-1 DH12 gp160 (env) protein.
Virus: HIV-1 *Strain:* HIV-1.DH12 *Subtype:* B
Gene/Protein: env
Trial(s): NHP.303

Vaccine Name: **rVV-SIVmacgag/pol**
Description: This is a recombinant vaccinia virus expressing SIV gag and pol (for additional information on this vaccine please contact Dr M. Cho directly)
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag, pol
Trial(s): NHP.303

Vaccine Name: **rVZV-SIVenv**
Description: Replication-competent recombinant AIDS vaccine based on attenuated varicella-zoster virus vaccine VZV-Oka. Cassette containing the gp160, env, rev genes from SIV strain smH4 was inserted into VZV cosmid MstIIA.
Trial(s): NHP.407

Vaccine Name: **SFV-rev**
Description: Semliki Forest Virus from pSFV (Invitrogen, Cergy-Pontoise, France) with rev cDNA from HIV-1 primary isolate ACH320 2.1 first subcloned in pCI (Promega, Charbonnieres, France) expression vector and then re-cloned into pSFV. Recombinant SFV-rev stocks prepared on BHK-21 cells.
Virus: HIV-1 *Strain:* ACH320 2.1 *Subtype:* B
Gene/Protein: rev
Trial(s): NHP.276

Vaccine Name: **SFV-tat**
Description: Semliki Forest Virus from pSFV (Invitrogen, Cergy-Pontoise, France) containing tat cDNA from HIV-1 subtype B primary isolate ACH320 2.1 first subcloned into pCI expression vector before re-cloning into pSFV.
Virus: HIV-1 *Strain:* ACH320 2.1 *Subtype:* B
Gene/Protein: tat
Trial(s): NHP.276

Vaccine Name: **SFVpSFVI.SIVmac.J5.gpetnr**
Description: A recombinant semliki forest virus expressing SIVmac clone J5 structural (gag,pol) and regulatory (tat, nef and rev) genes
Virus: SIV *Strain:* SIVmacJ5 *Subtype:* -

Gene/Protein: env, gag
Trial(s): NHP.58

Vaccine Name: **vAbT394**
Description: Recombinant vaccinia (NYCBH) expressing SIV_{MAC251} Gag-Pol.
Virus: SIV *Strain:* MAC251 *Subtype:* -
Gene/Protein: Gag-Pol
Trial(s): NHP.319

Vaccine Name: **Vaccinia-rDIsSIVgag**
Description: A recombinant vaccinia virus DIs expressing SIV Gag. Contains a full-length gag gene of SIVmac239 in the vector construct. rDIs expressing SIVmac239 Gag (rDIsSIVGag)
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag
Trial(s): NHP.365

Vaccine Name: **vCP180**
Description: vCP180 is ALVAC canarypox vector that contains sequences for SIVmac142 gag,pol,env. The vaccinia H6 promoter was used for env and the vaccinia I3L promoter was inserted for gag/pol
Trial(s): NHP.404

Vaccine Name: **vP1047, NYVAC HIV-2.SBL-ISY gp160.gag-pol**
Description: To generate the NYVAC-recombinant viruses, plasmids encoding sequences for HIV-2.SBL-ISY gp160 plus gag-pol were used by invitro recombination, using the NYVAC vector vP866 as rescue virus
Virus: HIV-2 *Strain:* HIV-2.SBL-ISY *Subtype:* -
Gene/Protein: gag, pol
Trial(s): NHP.47

Vaccine Name: **vP991, NYVAC HIV-1IIIB gp120.gag-pol**
Description: To generate the NYVAC-recombinant viruses, plasmids encoding sequences for HIV-1 IIIB gp120 (aa residues 1-511) plus gag-pol were used by invitro recombination, using the NYVAC vector vP866 as rescue virus
Virus: HIV-1 *Strain:* HIV-1.IIIB *Subtype:* B
Gene/Protein:
Trial(s): NHP.47

Vaccine Name: **vSIVgp120**
Description: Recombinant vaccinia virus expressing SIV gp120
Trial(s): NHP.33

Vaccine Name: **VSV(GCh)-Env+Gag**
Description: Recombinant vesicular stomatitis virus (VSV) encoding HIV-1.89.6 env gene and SIV gag. The VSV G protein (Indiana serotype, GI) was substituted with the VSV Chandipura glycoprotein (GCh)
Virus: HIV-1 *Strain:* HIV-1.89.6 *Subtype:* B
Gene/Protein: env

Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag
Trial(s): NHP.55, NHP.409

Vaccine Name: **VSV(GNJ)-Env+Gag**
Description: Recombinant vesicular stomatitis virus (VSV) expressing HIV-1.89.6 env and SIVmac239 gag. The VSV G protein (Indiana serotype, GI) was replaced with the G protein of the VSV New Jersey serotype (GNJ)
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag
Virus: HIV-1 *Strain:* HIV-1.89.6 *Subtype:* B
Gene/Protein: env
Trial(s): NHP.55, NHP.409

Vaccine Name: **VSV-(GI)-Env**
Description: Recombinant vesicular stomatitis virus (VSV) vector encoding HIV-1 env gene
Virus: HIV-1 *Strain:* HIV-1.89.6 *Subtype:* B
Gene/Protein: env
Trial(s): NHP.55

Vaccine Name: **vT107**
Description: Recombinant vaccinia (NYCBH)expressing HIV-1 89.6 Env
Virus: HIV-1 *Strain:* 89.6 *Subtype:* B
Gene/Protein: env (Env)
Trial(s): NHP.319

Vaccine Name: **WRvvENV-Delta5G**
Description: Env gp160 from delta 5G mutant of SIVmac 239 (contains mutations at asparagines 79, 146, 171, 460, and 479) introduced into vaccinia virus WR strain
Trial(s): NHP.464

Vaccine Name: **WRvvENVmac239**
Description: Env gp160 of SIVmac239 was introduced into vaccinia virus WR strain
Trial(s): NHP.464

Synthetic Protein/Peptide Vaccines

Vaccine Name: **C4/89.6-V3**
Description: Peptides were synthesized by SynPep Corporation (Dublin, Calif.) and purified by reverse-phase high-pressure liquid chromatography (HPLC). Peptides were >95% purified as determined by HPLC and mass spectrometry. SHIV-89.6 and SHIV-KB9 V3 loop peptideswere synthesized C-terminal to a T-helper determinant located in the C4 region of gp120 for enhanced immunogenicity

Notes: Two additional peptides are available (89.6-V3 and 89.6P-V3) consisted of the V3 loop portions of the C4/89.6-V3 and C4/89.6P-V3 peptides lacking C4.

Virus: SHIV *Strain:* 89.6 *Subtype:* B

Gene/Protein: env (C4)

Notes: Subtype is for the HIV-1 component

Virus: SHIV *Strain:* 89.6 *Subtype:* B

Gene/Protein: env (V3)

Notes: Subtype is for the HIV-1 component

Trial(s): NHP.7

Vaccine Name: **C4/89.6P-V3**

Description: Peptides were synthesized by SynPep Corporation (Dublin, Calif.) and purified by reverse-phase high-pressure liquid chromatography (HPLC). Peptides were >95% purified as determined by HPLC and mass spectrometry. SHIV-89.6 and SHIV-KB9 V3 loop peptideswere synthesized C-terminal to a T-helper determinant located in the C4 region of gp120 for enhanced immunogenicity

Virus: SHIV *Strain:* 89.6P *Subtype:* B

Gene/Protein: env (C4)

Notes: Subtype is for the HIV-1 component

Virus: SHIV *Strain:* 89.6P *Subtype:* B

Gene/Protein: env (V3)

Notes: Subtype is for the HIV-1 component

Trial(s): NHP.7

Vaccine Name: **CCR5 peptides**

Description: N-terminus human CCR5 N1 MDYQVSSPIYDINYYTSEPC; N-terminus human CCR5 N1/N2 MDYQVSSPIYDINYYTSEPCQKINVKQIAA; 1st extracellular loop human CCR5 X1 HYLAAQWDFGNTMC;2nd extracellular loop human CCR5 X2.2 YTCSSHFPYSQYQFWKNFQT

Trial(s): NHP.68

Vaccine Name: **cDDR5-MAP**

Description: cDDR5 mimicks the conformation-specific domain of human CCR5, in which the Gly-Glu dipeptide links the amino and carboxy termini of the decapeptidyl linear chain (Arg168 to Thr177) derived from the undecapeptidyl arch (Arg168 to Cys178) of extracellular loop-2 in CCR5. MAP is composed of a 2 fold bifurcating polylysine core developed as a carrier of a peptide Ag

Trial(s): NHP.477

Vaccine Name: **gp120/gp41 mimotopes**

Description: This is a cocktail of 5 synthetic peptides (p195: KSSGKLISL, p217: CNGRLYCGP, p197: GTKLVCFAA, p287: CAGGLTCSV, p335: SGRLYDKP). p195, p217 and p197 display similarity with some discrete regions of HIV-1 in V1, C2 and gp41, respectively. Peptides p287andp335 have no obvious sequence homology with HIV protein domains.

Trial(s): NHP.81

Vaccine Name: **o-gp140-US4**

Description: Oligomeric gp140US4 (o-gp140US4) was purified and characterized by immunoblot, antigen capture enzyme-linked immunosorbent assay (ELISA), CD4 binding and glycosylation profile. After the purification, o-gp140US4 was stored in citrate buffer (10 mmol/l sodium citrate, 500 mmol/l sodium

chloride) at a concentration of 0.2 mg/ml for immunizations.

Virus: HIV-1 *Strain:* HIV-1 *Subtype:* B

Gene/Protein: env (gp140)

Trial(s): NHP.354, NHP.500

Vaccine Name: **oligomeric gp130**

Description: gp130 oligomer s of Mac-32H

Virus: SIV *Strain:* MAC-32H *Subtype:* -

Gene/Protein: env gp130

Trial(s): NHP.320

Vaccine Name: **P3CSS CTL**

Description: The "P3CSS CTL epitopes" were a mixture of 4 lipopeptides. The sequences are taken from the SIVmac32H consensus sequences published or provided by Neil Almond et al (AIDS Research and Human Retroviruses, 8, 77 (1992)) and used for the basis of the overlapping peptides provided by the AIDS Reagent Repository at the NIBSC, UK

Virus: SIV *Strain:* SIVmac251-32H *Subtype:* -

Gene/Protein: gag

Notes: sequence: VWAANELDRFGLAESLLENKEGCQK

Virus: SIV *Strain:* SIVmac251-32H *Subtype:* -

Gene/Protein: gag

Notes: Sequence VPGFQALSEGCTPYDINQMLNCVGD

Virus: SIV *Strain:* SIVmac251-32H *Subtype:* -

Gene/Protein:

Notes: Sequence: LRTMSYKLAIDMSHFI

Virus: SIV *Strain:* SIVmac251-32H *Subtype:* -

Gene/Protein:

Notes: Sequence: DWQDYTSGPGIRYPKTFGWLWKLV

Trial(s): NHP.119

Vaccine Name: **PCLUS3-CL10/PCLUS6.1-CL10/PCLUS3_POL_143/PCLUS3_GAG_372**

Description: Cocktail of 4 peptides each containing 1 CTL and 1 helper epitope

Notes: This vaccine is a cocktail of 4 synthetic chimeric peptides containing T helper and CTL epitopes in HIV (env) and SIV(gag and pol), repectively.

Virus: SIV *Strain:* MM239 *Subtype:* -

Gene/Protein: gag

Notes: LOCATION-SIVmac239: (amino acids) Gag 181 - 190 = Capsid(p27) 46 - 55

Virus: HIV-1 *Strain:* IIIB *Subtype:* B

Gene/Protein: env

Notes: LOCATION: (amino acids) Env 421 - 444

Virus: HIV-1 *Strain:* IIIB *Subtype:* B

Gene/Protein: env

Virus: SIV *Strain:* MM239 *Subtype:* -

Gene/Protein: pol

Virus: SIV *Strain:* MM239 *Subtype:* -

Gene/Protein: gag
Trial(s): NHP.1

Vaccine Name: **PCLUS3-CL10/PCLUS6.1-CL10/PCLUS3_POL_143/PCLUS3_GAG_372/PCLUS3_TAT2/PCLUS3_TAT3/PCLUS3_VIF**
Description: Coctail of 7 peptides each containing a CTL and T-helper region. The CTL epitopes are: 3-CL10 = CTPYDINQML; 6.1-CL10 = CTPYDINQML; POL_143 = LGPHYTPKIV; GAG_372 = LAPVPIPFA; TAT2 = KHPGSQPKTA; TAT3 = VDPRLEPW; VIF = QVPSLQYLA.
Trial(s): NHP.503

Vaccine Name: **Peptomer SIVmac251 (gp120: 435-452)**
Description: The SIV peptomer was constructed with an 18 amino acid peptide polymer, is representative of part of the putative CD4 binding region in SIVmac251 gp120 (amino acids435-452: HIRQIINTWHKVGKNVYL)),
Virus: SIV *Strain:* SIVmac251 *Subtype:* -
Gene/Protein: env (gp120)
Trial(s): NHP.5

Vaccine Name: **Synthetic tat**
Description: CVDPNLEPWKHPGS (tat HXB2: 3-16), CRQRRRAPDSSQNHQ(TatHXB2: 52-66) conjugated to diphtheria toxoid
Trial(s): NHP.268.1

Vaccine Name: **Tat 1-61**
Description:
Virus: HIV-1 *Strain:* BRU *Subtype:* B
Gene/Protein: Tat
Trial(s): NHP.330, NHP.414

Vaccine Name: **Tat 19-53**
Description:
Notes: two amino acids different from HXB2 peptide
Virus: HIV-1 *Strain:* BRU *Subtype:* B
Gene/Protein: Tat
Trial(s): NHP.330

Vaccine Name: **Tat 19-53m**
Description:
Virus: HIV-1 *Strain:* BRU *Subtype:* B
Gene/Protein: Tat
Trial(s): NHP.330

Vaccine Name: **Tat 44-61**
Description:
Virus: HIV-1 *Strain:* *Subtype:* -
Gene/Protein: Tat

Trial(s): NHP.330, NHP.414

Vaccine Name: **Tat1-20**
Description: HXB2 Tat peptide amino acids 1-20 synthesized on ABI433A
Virus: HIV-1 *Strain:* HXB2 *Subtype:* B
Gene/Protein: Tat
Trial(s): NHP.330, NHP.414

Vaccine Name: **Tat8-53**
Description:
Notes: 2 amino acids different from same region of HXB2 peptide
Virus: HIV-1 *Strain:* BRU *Subtype:* B
Gene/Protein: Tat
Trial(s): NHP.330

Vaccine Name: **V2-MAP**
Description: The V2 fragment is a gp130 at positions 168-190: KFNMTGLKRDKTKEYNET; MAP: multiple antigen peptides (branched peptide)
Virus: SIV *Strain:* SIVmac *Subtype:* -
Gene/Protein:
Trial(s): NHP.119

Vaccine Name: **V2-P3CSS**
Description: The V2 fragment is a gp130 at positions 168-190: KFNMTGLKRDKTKEYNET
Virus: SIV *Strain:* SIVmac *Subtype:* -
Gene/Protein:
Trial(s): NHP.119

Vaccine Name: **V2.V3.HIV-1.SF2 Synth.peptides**
Description:
Virus: HIV-1 *Strain:* HIV-1.SF2 *Subtype:* B
Gene/Protein: env (V2)
Virus: HIV-1 *Strain:* HIV-1.SF2 *Subtype:* B
Gene/Protein: env (V3)
Trial(s): NHP.164

Vaccine Name: **V4.32-MAP**
Description: The V4 fragment is a gp130; MAP: multiple antigen peptides (branched peptide); gp130410-430 (V4.32), VEDRDVTNQRPKERHRRNYVP; gp130410-430 (V4.32H), VEDRNTTNQKPKEQHKRNYVP (Torres et al., 1993
Virus: SIV *Strain:* SIVmac *Subtype:* -
Gene/Protein:
Trial(s): NHP.119

Virus-like Particle Vaccines

Vaccine Name: **HIV-IIIB-p55gag-VLP**
Description: HIV-1 isolate LAI/IIIB p55 gag protein in virus-like particle
Virus: HIV-1 *Strain:* HXB2 *Subtype:* B
Gene/Protein: gag
Trial(s): NHP.321

Vaccine Name: **HPV/SHIV-VLP**
Description: This is a recombinant human papillona virus -like particle encoding HIV-1 tat and rev and SIV p27.
Virus: HIV-1 *Strain:* HIV-1.AD8 *Subtype:* B
Gene/Protein: Accessory (tat)
Virus: HIV-1 *Strain:* HIV-1.NL4.3 *Subtype:* B
Gene/Protein: Accessory (rev)
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein: gag (gag p27)
Trial(s): NHP.339

Vaccine Name: **SCIV Single Cycle Immunodeficiency Virus with VSV-G pseudotyping**
Description: A SIV-MAC239 with deletions in vif, vpr, vpx and nef, and an altered Lys-tRNA primer site, cotransfected with a Vesicular Stomatitis virus G protein expression vector produces single-cylle infectious but nonreplicating virus-like particles that contain the VSV G glycoprotein on their surface.
Trial(s): NHP.504

Vaccine Name: **SFV-SIV Pr56gag VLP-type I**
Description: Components: Pr56-V3, CD4BR,gp41
Trial(s): NHP.77

Vaccine Name: **SIV Pr56gag VLP-type II**
Description: This is a pseudovirion. The gp41 transmembrane domain of the Gp160 wild-type HIV-1 glycoprotein was replaced by a heterologous Epstein-Barr virus derived type I transmembrane region, consisting of a 22 amino acid spanning transmembrane domain and a shortcytoplasmic domain, which was covalently linked to the C-terminus of gp120 by a flexible -S-G-S-G-A-G- hinge region (gp120-TM). Components: Pr56-wt; gp120-TM
Trial(s): NHP.77

Whole (killed) Inactivated Virus Vaccines

Vaccine Name: **AT-2-Inactivated SHIV89.6**
Description: Aldritiol-2 (AT-2) inactivated $SHIV_{89.6}$
Trial(s): NHP.319

Vaccine Name: **Fixed inactivated SIVmac251 infected cells**
Description: The vaccine was prepared from SIVmac251 recovered from infected a rhesus monkey, and was mixed with withC8166 cells and fixed in 0.2% of β-propiolactone
Virus: SIV *Strain:* SIVmac251 *Subtype:* -
Gene/Protein: All
Trial(s): NHP.157.1, NHP.157.2, NHP.157.3

Vaccine Name: **HIV-1 GB8**
Description: Whole/killed inactivated HIV-1. A subtype B virus, GB8 was the first (October 1986) of a series of five sequential viral isolates isolated from a single British AIDS patient during his last 18 months of life.
Trial(s): NHP.203

Vaccine Name: **SIV/$Delta_{B670}$**
Description: Whole killed inactivated virus harvested from H9 cells . HPLC analysis revealed that complete virus particle was represented with 2-3% of the total protein consisting of the external glycoprotein gp110 and both full length and truncated glycoprotein gp41 and gp 35, respectively, along with the predicted stoichiometric amounts of the remaining viral core proteins (p61/61, p26, p17,p14 and p9). The harvested virion was formalin inactivated.
Virus: SIV *Strain:* SIVB670 *Subtype:* -
Gene/Protein: All
Trial(s): NHP.248

Vaccine Name: **SIVmac HUT-78 ((Psoralem-UV)**
Description: SIVmacgrown in HUT-78 T-cell culture, inactivated with Psoralem and UV light
Virus: SIV *Strain:* SIVmac *Subtype:* -
Gene/Protein: All
Trial(s): NHP.239

Vaccine Name: **SIVmac251 (encapsulated)**
Description: Gradient-purified SIVmac251 treated with formalin, encapsulated with emulsion-based process to produce 1-10ul microphere
Virus: SIV *Strain:* SIVmac251 *Subtype:* -
Gene/Protein: All
Trial(s): NHP.200

Vaccine Name: **SIVmac251, 32H, (C8)**
Description: Inactivated, partially purified SIVmac251 32H grown in C8166 cell line.
Virus: SIV *Strain:* SIVmac251 *Subtype:* -
Gene/Protein:
Trial(s): NHP.203

Vaccine Name: **SIVmac251.whole inactivated**
Description: Gradient-purifie d SIVmac251 grown in HuT-78 cells was treated with formalin before encapsulation by an emulsion-based process to produce 1- to 10-mm microspheres
Virus: SIV *Strain:* SIVmac251 *Subtype:* -
Gene/Protein:
Trial(s): NHP.73

Vaccine Name: **SIVmac251/32H (Tween/Ether)**
Description: The virus was obtained from in-vitro passage of SIVmac251 and the product was designated SIVmac251/32H. SIVmac251/32H was then grown in C81-66 cells, then purified by column chromatography. After TE extraction, , about 6 mg of the virus were dissolved in 4 ml PBS and 0.25% Tween. 4 ml of diethyl ether was added... (for details see Stahl-Hennig et al, 1992; Virology 186: 588-596)
Virus: SIV *Strain:* SIVmac251/32H *Subtype:* -
Gene/Protein: All
Trial(s): NHP.97, NHP.99.2, NHP.151

Vaccine Name: **Whole inactivated HIV-1 IIIB**
Description: A sucrose-gradient purified HIV-1 IIIB, inactivated by various methods including formaldehyde.
Virus: HIV-1 *Strain:* HIV-1 IIIB *Subtype:* B
Gene/Protein:
Trial(s): NHP.204

Vaccine Name: **Whole inactivated SIVmac239 (encapsulated)**
Description: This is a HuT-78 grown in sucrose gradient purified, formalin-inactivated and encapsulated in poly(DL-lactide-co-glycolide) microspheres. The median size of the resulting particle was 3 um
Virus: SIV *Strain:* SIVmac239 *Subtype:* -
Gene/Protein:
Trial(s): NHP.74

Vaccine Name: **Whole inactivated SIVmac251**
Description:
Virus: SIV *Strain:* SIVmac251 *Subtype:* -
Gene/Protein:
Trial(s): NHP.201.1, NHP.201.2, NHP.245.1, NHP.245.2, NHP.245.3

IV. CHALLENGES

This section contains a list of challenge viruses used in the studies compiled in the database. Challenge viruses are grouped into the following categories:

- SHIV
- SIV
- HIV-1
- HIV-2

In most cases, the name and description of challenge viruses were retained as provided by the authors in the paper reporting the trial. For HIV-1, HIV-2 and simian/human synthetic recombinant viruses, the subtype of the HIV-1 or HIV-2 portion(s) of the genome has been recorded. In addition, the studies in which each challenge virus was used are also shown for each challenge virus.

Viruses used in primate models of AIDS and vaccine studies are tremendously variable in infectivity, sequence diversity, and pathogenicity. For example, the SHIV89.6P virus is much more rapidly lethal to Rhesus macaques than the SHIV-89.6 virus from which it was derived [1,2]. The SHIV89.6P acutely patho\-genic virus has mutations which alter the carboxy terminus of the env gp41 protein and also alter the Nef protein [3]. Similarly, some of the PBJ isolates are far more acutely lethal than the SMM9 stock from which they were derived [4,5].

The database contains links to genetic sequences of challenge viruses whenever such sequences are available. Caution should be used in interpreting such links because the sequence may not be 100\% identical to the challenge virus. Even with an infectious molecular clone of a virus, the challenge dose is often created by culturing the clone though several amplification passages which could result in an accumulation of mutations.

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SHIV Challenges

Strain: **Ba-L**

Description: SHIV-BaL is an R5 isolate shown to transmit efficiently via the mucosal routewithout any decline in CD4+ T cell counts

Trial(s): NHP.492

Strain: **SHIV 89.6p**

Description: Contains the genes tat, rev, vpu, and env of HIV-1 subtype B isolate 89.6 in the genomic background of SIV mac239. This pathogenic variant was isolated after serial in vivo passage of the original SHIV 89.6 from rhesus macaques

HIV Subtype: B

Trial(s): NHP.467

Strain: **SHIV-4**

Description: Expresses SIVmac239 gag,pol,vif,vpx,vpr,nef and HIV-1 LAI env,tat,rev

Trial(s): NHP.401

Strain: **SHIV-4.vpu+**

Description: Contains gag, pol, vif and nef ORF of SIVmac239 (open nef) and tat, rev, vpu and env genes of HIVHXBc2, with defective start codon of vpu (ACG in HXB2) corrected. Obtained from Virus Research Institute, Cambridge MA, USA. Described in Li et al JAIDS 5:639-646 (1992) and J Virol 69(11):7061-7 (1995) PubMed ID 7474126

HIV Subtype: B

Notes: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=1613662

Trial(s): NHP.77

Strain: **SHIV-BX08**

Description: The SHIV-BX08 construct is a chimeric virus derived from SIV-MAC239 (gag, pol, vif, vpx and nef genes), HIV-1 isolate BX08 (env gp120), and HIV-1 isolate LAI (env gp41, tat and rev). Although SHIV-BX08m has been used in numerous studies, no DNA sequencesare available for the BX08 virus.

HIV Subtype: B

Trial(s): NHP.276

Strain: **SHIV-C2/1**

Description: SHIV-C2/1 is an SHIV-89.6 variant isolated by passaging the peak of initial plasma viremia from an infected cynomologus macaque as described in J Gen Virol 80(5):1231-40 (1999) by Shinohara et al. The original pSHIV, containing the SHIV-89.6P (and not the 89.6 as implied by Shinohara in J Gen Virol) was kindly provided by Y. Lu at the Harvard AIDS Institute (Boston, Mass. yichenlu@hsph.harvard.edu).

HIV Subtype: B

Notes: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10355770

Trial(s): NHP.365, NHP.486, NHP.506, NHP.508

Strain: **SHIV-DH12clone7**

Description: Infectious molecular clone derived from SHIV-DH12R-PS1 which in turn was derived from HIV-MD14YE [Igarashi et al PNASU 96(24): 14049-14054 (1999)].

HIV Subtype: B

Trial(s): NHP.386

Strain: **SHIV-DH12clone8**

Description: Infectious molecular clone derived from SHIV-DH12R-PS1 which in turn was derived from HIV-MD14YE [Igarashi et al PNASU 96(24): 14049-14054 (1999)].

HIV Subtype: B

Trial(s): NHP.386

Strain: **SHIV-IIIB/HXB2**

Description: Also known as SHIV-4, Described in J AIDS 5: 639-646 (1992) by Li et al. SIV-Mac239 virus with HIV-1 HXB2 env inserted. Described in J Virol 70(5):3198-3206 (1996) only as the arent plasmid from which SHIV-89.6 was created by replacing part of HXB2 gp160 with the same region for another HIV-1 subtype B virus with different tropism.

HIV Subtype: B

Notes: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=1613662

Trial(s): NHP.14, NHP.16.1, NHP.16.2, NHP.47, NHP.56

Strain: **SHIV-KU2**

Description: SHIV-Ku2 is a chimeric virus containing the HIV-1 IIIB strain (HXBc2) envelope gene and SIVmac239 gag and pol genes, and is pathogenic in rhesus macaque

HIV Subtype: B

Trial(s): NHP.1, NHP.79, NHP.107, NHP.500, NHP.503

Strain: **SHIV-MD14YE (DH12)**

Description: Derived from SHIV-1DH12, but with the HIV-1 nef gene replaced by SIV-Mac239 nef with two mutations R17Y and Q17E. The SIV nef R17Y mutation is known to create virus that depletes macaque T-cells self-activates T-cells such that the virus can replicate innon-stimulated PBMCs. R17Y creates SH2 binding ITAM motif YXXLXXXXXXXYXXL.

HIV Subtype: B

Notes: The tat, rev and env genes and the remainder of the vpr gene were derived mostly from HIV-1DH12, except for a small segment (145 bp) at the SIV/HIV-1 junction in vpr) that is of HIV-1NL4-3 origin.

Trial(s): NHP.86.1, NHP.86.2, NHP.387, NHP.389

Strain: **SHIV-MN**

Description: Strain contains V3 sequences homologous to rBCG Env V3 (Someya et al. 2005, J. Virol. 79: 1452)

Trial(s): NHP.408

Strain: **SHIV-NM-3rN**

Description:

HIV Subtype: B

Notes: The subtype relates to the HIV component only

Trial(s): NHP.28, NHP.31, NHP.35, NHP.322

Strain: **SHIV-SF162P3**

Description: Moderately pathogen CCR5-utilizing challenge virus. The SHIV-SF162 viruses have PC, P3, P4 etc appended to indicate passages in cells or animals after the infectious molecular clone was constructed. The SHIV-SF162P3 challenge can be obtained from the NIH AIDS Reference Reagent Repository where it has catalog number 6526.

HIV Subtype: B

Trial(s): NHP.466, NHP.477, NHP.491, NHP.496, NHP.510

Strain: **SHIV-vpu+**

Description: Described in Li et al J Virol 69(11):7061-7 (1995) PubMed ID 7474126. SHIV-4 modified by site-directed mutagenesis to correct defective vpu. HIV-1 subtype B clone HXB2 has a defective vpu gene due to an ATG to ACG mutation in the vpu start codon. ThisSHIV has a corrected start codon, plus a P5Q mutation in vpu.

HIV Subtype: B

Trial(s): NHP.15, NHP.85, NHP.117

Strain: **SHIV.229(mn)**

Description: The SHIV229(mn) is based on $SHIV_{IIIB}$ encoding HIV-1_{HXBc2}tat, rev and env on a SIV_{mac239} backbone, passaged through M. nemestrina in vivo to become pathogenic. The challenge stock was generated by expanding the SHIV229(mn) on PHA-activated M. nemestrina PBMC.

HIV Subtype: B

Trial(s): NHP.339, NHP.466, NHP.491, NHP.496

Strain: **SHIV.DH12 (MD1)**

Description: This chimeric simian-human immunodeficiency virus (SHIVs) carries envelope glycoproteins from a T cell-macrophage dual-tropic primary isolate (human immunodeficiency virus type 1 [HIV-1] strain DH12) in the SIVmac239 backbone. DH12 is also known as MD1.MD14 is derived from MD1 by replacing the DH12 nef with Mac239 nef.

HIV Subtype: B

Trial(s): NHP.11

Strain: **SHIV.DH12R-PS1**

Description: This SHIV was obtained from the nonpathogenic SHIVDH12 (SHIVMD1) (Shibata, JID 176:362-73 1997). This highly pathogenic SHIVDH12R was isolated at week 68 from rhesus monkey 565Z (Igarashi et al PNASU 96(24):14049-14054 1999). Virus isolated at week 52 from animal 565Z also induced an irreversible and extremely rapiddepletion of CD4+ T lymphocytes following its inoculation into rhesus monkey PS1 and was designated SHIVDH12R-PS1.

HIV Subtype: B

Notes: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10570196

Trial(s): NHP.157.3, NHP.303, NHP.391

Strain: **SHIV.KU1**

Description: SHIV.KU1 was described in ARHR 13(8): 635-645 (1997) PMID: 9168232 and J Virol 73(2):976-84 (1999) PMID: 9882298. It is derived from SHIV-P3 by passage in donor PBMCs from a normal macaque.

HIV Subtype: B

Notes: This is an extremely virulent chimeric virus. Has an open vpu in addition to numerous mutations in the env and nef. Replicates efficiently in macrophage cultures and at extremely high titers in monkeys, with loss of CD4+ T cells and AIDS

Trial(s): NHP.87, NHP.112

Strain: **SHIV.MD1**

Description: It carries a portion of the U3 LTR, the R-U5 LTR, gag, pol, vif, and vpx, and approximately 20% of vpr from SIVmac239. The remainder of vpr, tat, rev, env, and nef and a portion of the U3 LTR are derived from HIV-1; most of the HIV-1 sequences came from aT-cell/macrophage dual-tropic primary isolate HIV-1DH12 except for small segments at SIV-HIV-1 junctions (145 bp in vpr; 27 bp in nef) that were derived from HIV-1NL43. NRE, negative regulatory element. Shibata et al. J Inf Dis 176:362 (1997)

HIV Subtype: B

Notes: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9237701

Trial(s): NHP.207, NHP.389, NHP.394

Strain: **SHIV.SF13**

Description: Described in AIDS 10(12): 1331-7 (1996) PubMed ID 8902061. This SHIV is a SIV-Mac239 LTR-Gag-Pol and Nef with HIV-1 subtype B clone SF13 Tat-Rev-Vpu-Env. The SF13 clone is from the same patient as the HIV-1 SF2 clone.

HIV Subtype: B

Trial(s): NHP.80, NHP.164

Strain: **SHIV.W6.1D**

Description: $SIV_{W6.1d}$ was constructred by replacing an NheI-to-AvrII fragment encompasing Env gp160, of SHIV-4 with the W6.1D cloned Env from HIV-1 subtype B isolate 320.3 which is a dual-tropic virus from a Dutch AIDS patient.

HIV Subtype: B

Trial(s): NHP.80

Strain: **SHIV162P4**

Description:

HIV Subtype: B

Trial(s): NHP.6, NHP.62

Strain: **SHIV33**

Description: This SHIV contains the tat, rev, vpu, and env genes of HIV-1 subtype B isolate SF33. The SHIV-SF33 construct was then passaged in Rhesus macaque to generate SHIV-SF33A. See also the entry with accession number AF401229, from this same SHIV construct.

HIV Subtype: B

Trial(s): NHP.268.1

Strain: **SHIV33A**

Description: This SHIV contains the tat, rev, vpu, and env genes of HIV-1 subtype B isolate SF33. The SHIV-SF33 construct was then passaged in Rhesus macaque to generate SHIV-SF33A. See also the entry with accession number AF401229, from this same SHIV construct.

HIV Subtype: B
Trial(s): NHP.268.1

Strain: **SHIV89.6**
Description:
HIV Subtype: B
Trial(s): NHP.7, NHP.15, NHP.90.1, NHP.114, NHP.126, NHP.319

Strain: **SHIV89.6P**
Description: Parental SHIV was SHIV-4 (also known as SHIV-IIIB/HXB2) from which env of HXB2 was replaced by env of 89.6 (also HIV-1 subtype B but different tropism). Described in J Virol 70(5): 3198-3206 (1996) by Reimann et al. Passaged to gain pathogenicity as described in J Virol 71(6): 4218-25 (1997) by Karlsson et al.
HIV Subtype: B
Notes: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed&cmd=Retrieve&list_uids=9151808&dopt=Citation
Trial(s): NHP.2, NHP.7, NHP.16.2, NHP.17, NHP.19, NHP.23, NHP.24.2, NHP.28, NHP.36, NHP.37, NHP.55, NHP.56, NHP.60.1, NHP.60.3, NHP.79, NHP.80, NHP.89, NHP.90.2, NHP.107, NHP.117, NHP.121, NHP.126, NHP.131, NHP.132, NHP.304, NHP.306.1, NHP.306.2, NHP.325, NHP.348.2, NHP.349, NHP.366, NHP.374, NHP.381, NHP.400, NHP.402, NHP.418, NHP.424, NHP.443, NHP.455, NHP.471, NHP.476, NHP.502

Strain: **SHIV89.6PD**
Description:
HIV Subtype: B
Trial(s): NHP.8, NHP.34, NHP.70, NHP.72, NHP.78, NHP.81, NHP.82.1, NHP.82.2, NHP.326, NHP.398, NHP.408, NHP.409, NHP.421

Strain: **SHIV89.6v**
Description: This is a stock virus from the SHIV89.6 after passage in rhesus macaques through intra vaginal inoculation and brief culture in rhesus PBMC. The stock concentration was determined as 10^3 TCID50/ml by culture on CEMx174 cells and p27 production
HIV Subtype: B
Trial(s): NHP.20

Strain: **$SHIV_{SF162\text{-}PC}$**
Description: $SHIV_{SF162\text{-}PC}$ is derived from $SHIV_{SF162}$ by replacing env V1-V5 with env V1-V5 from a passaged $SHIV_{SF162}$ that was more infectious and pathogenic ($SHIV_{SF162\text{-}P3}$).
HIV Subtype: B
Trial(s): NHP.312

Strain: **SHIVHan2**
Description: Described in AIDS 10(12): 1331-7 (1996) PubMed ID 8902061. This SHIV is a SIV-Mac239 LTR-Gag-Pol and Nef with HIV-1 subtype B clone pNL43 Tat-Rev-Vpu-Env, from which the SacII-HindIII region (most of env) was replaced by HIV-1 subtype B isolate Han2.
HIV Subtype: B
Trial(s): NHP.80

Strain: **SHIVsbg0.1**
Description:
Trial(s): NHP.10

SIV Challenges

Strain: **Mac239**
Description:
Trial(s): NHP.452

Strain: **mac239 proviral DNA**
Description: Plasmid was constructed from two clones, p239SpSp5' and p239pE3' encoding the 5' and 3' SIV halves, respectively
Trial(s): NHP.496

Strain: **SIV mac251 (European) stock 5**
Description: prepared by passaging the European SIVmac251-32H 11/88 challenge virus once through rhesus PBMC
Trial(s): NHP.119

Strain: **SIV(Mne) Cell-free**
Description:
Trial(s): NHP.269

Strain: **SIV(Mne) clone E11S**
Description:
Trial(s): NHP.64, NHP.65.1, NHP.65.2, NHP.94, NHP.134, NHP.154, NHP.265, NHP.269

Strain: **SIV8980**
Description: SIV8980 was derived from SIVB670 by 4 subsequent in vivo passages of late-stage disease virus. SIV8980 was cultivated on PBMCs from the fourth passaged macaque (8980), which developed end-stage AIDS within one month of infection
Trial(s): NHP.425

Strain: **SIVDeltaB670**
Description: The virus was described by Mickey Corb in a paper published by Gormus et. al. in the Journal of Infectious Diseases, Vol 160, No 3, Sept 1989. The virus came from mangabey A022 (naturally infected with SIV), was passed to rhesus macaque 8664, then passed to B670. Sooty mangabey A022 came from Yerkes to Tulane and appears to have been born at Yerkes.
Trial(s): NHP.63, NHP.248, NHP.481, NHP.505

Strain: **SIVmac (not determined)**
Description:
Trial(s): NHP.239, NHP.240

Strain: **SIVmac220**
Description:
Notes: Viral challenge (SIVmac 220) which is a cell-free virus stock prepared from the spleen of a rhesus monkey infected with the J5 molecular clone of SIVmac 251 (32H)
Trial(s): NHP.106, NHP.397

Strain: **SIVmac239**
Description:
Trial(s): NHP.16.2, NHP.18, NHP.39, NHP.54, NHP.61, NHP.67, NHP.69, NHP.88, NHP.148, NHP.308, NHP.411, NHP.454, NHP.460, NHP.464, NHP.499, NHP.504

Strain: **SIVmac239 delta nef**
Description:
Trial(s): NHP.425

Strain: **SIVmac239 proviral DNA**
Description: Proviral DNA clone of wild-type SIVmac239 (pBRmac239)
Trial(s): NHP.468

Strain: **SIVmac239/nef-open**
Description:
Trial(s): NHP.52, NHP.309, NHP.474, NHP.475

Strain: **SIVmac239Gag216S proviral DNA**
Description: Proviral DNA of SIVmac239Gag216S (pBRmac239Gag216S)
Trial(s): NHP.468

Strain: **SIVmac251**
Description:
Trial(s): NHP.9.1, NHP.13, NHP.32, NHP.33, NHP.38, NHP.51, NHP.57, NHP.66, NHP.73, NHP.74, NHP.108, NHP.109, NHP.120, NHP.123, NHP.148, NHP.157.1, NHP.157.2, NHP.200, NHP.201.2, NHP.205.1, NHP.205.2, NHP.205.3, NHP.245.1, NHP.245.2, NHP.245.3, NHP.294, NHP.300, NHP.324.1, NHP.327.1, NHP.327.2, NHP.353, NHP.363, NHP.406, NHP.413, NHP.419, NHP.458, NHP.460, NHP.462, NHP.478, NHP.480, NHP.493, NHP.495, NHP.496, NHP.502, NHP.509, NHP.514

Strain: **SIVmac251 (561)**
Description: This challenge stock was prepared by culturing PHA-activated peripheral blood mononuclear cells (PBMC) from a Mamu-A*01-positive infected macaque (561L) exposed to SIVmac251 by the vaginal route. The SIVmac251 (561) was titered in vivo in rhesus macaquesby inoculating 6 animals with different dilutions of virus stock via the rectal route. 6/6 animals inoculated with the virus (0.5 ml diluted to 1.5 ml with RPMI medium) became infected, evidenced by high plasma viremia and a drop in CD4 counts.

Trial(s): NHP.30, NHP.274, NHP.479

Strain: **SIVmac251 (J5)**
Description:
Trial(s): NHP.126, NHP.185.2

Strain: **SIVmac251(32H)**
Description:
Trial(s): NHP.5, NHP.41, NHP.49, NHP.97, NHP.99.2, NHP.116, NHP.151, NHP.152.1, NHP.152.2, NHP.185.1, NHP.194.1, NHP.203, NHP.205.2

Strain: **SIVmac251,32H.spl**
Description:
Notes: virus stock was prepared from a spleen homogenate of a rhesus monkey inoculated with SIVmac251, 32H and titrated in vitro in human T cells and in vivo in rhesus monkeys
Trial(s): NHP.40

Strain: **SIVmac251-BK28-delta nef**
Description: contains attenuating deletion in nef
Trial(s): NHP.425

Strain: **SIVmac251BK28**
Description:
Notes: molecular clone grown in monkey PBMCs
Trial(s): NHP.40

Strain: **SIVmac32H.IXc**
Description: Pathogenic cell-associated SIV from primary, uncultured rhesus monkey PBMC
Trial(s): NHP.58

Strain: **SIVmac8980**
Description: SIVmac 8980 grown in rhesus monkey PBMC and analyzed for CCR5 coreceptor binding using the "Ghost system" (see Trkola A et al., J Virol 1998;72:1876-85).
Trial(s): NHP.395, NHP.416

Strain: **SIVmacJ5M**
Description: Described in J Gen Virol. 1994 Mar;75 (Pt 3):529-43 and J Gen Virol. 2001 Sep;82(Pt 9):2225-34. SIVmac32H(pJ5) is "wild type" and the complete genome is sequenced with accession number D01065.
Notes: A "wild type" SIV-mac-251 re-isolate 32H infectious molecular clone.
Trial(s): NHP.215, NHP.422

Strain: **SIVmacR71**
Description:
Trial(s): NHP.107

Strain: **SIVmne clone A2-clone 5**
Description:
Trial(s): NHP.41

Strain: **SIVsm**
Description: SIV-sm described by Fultz et al Proc Nat Acad Sci 83(14):5286-90 (1986) PubMed ID 3014542 from an infected macaque at Yerkes. This SIV-sm is from the same animal from which the SIV-SMM9 virus was obtained. J. Virol. 66(1); 414-9 (1992) PubMed ID 1727495cites Fultz (1986) as the source of SMM9.
Trial(s): NHP.4, NHP.68, NHP.93, NHP.125, NHP.194.2

Strain: **SIVsmB670**
Description:
Trial(s): NHP.36, NHP.203

Strain: **SIVsmE660**
Description:
Trial(s): NHP.18, NHP.27, NHP.37, NHP.44, NHP.45, NHP.59, NHP.377, NHP.407, NHP.463

HIV-1 Challenges

Strain: **HIV-1 Han2**
Description: Isolate HAN was isolated from a 39 year old homosexual German patient with AIDS related complex, in 1986. This patient died from complications of AIDS in 1987. HAN was highly cytopathic in MT-2 T cell line, it was able to productively infect MT-4, H9 or Jurkatcell lines. Genomic DNA from infected MT-2 cells was used to prepare a lambda phage genomic library. Two full-length clones, HAN/2 and HAN/3 were purified. HAN/3 was used for DNA sequencing, but has a defective env gene.
HIV Subtype: B
Trial(s): NHP.21, NHP.416, NHP.425

Strain: **HIV-1 IIIB**
Description:
HIV Subtype: B
Trial(s): NHP.71, NHP.202, NHP.242, NHP.247, NHP.267, NHP.361

Strain: **HIV-1.5016**
Description:
HIV Subtype: B
Trial(s): NHP.141

Strain: **HIV-1.DH12**

Description:
HIV Subtype: B
Trial(s): NHP.84, NHP.392

Strain: **HIV-1.LAI**
Description:
HIV Subtype: B
Trial(s): NHP.48, NHP.204, NHP.425, NHP.496

Strain: **HIV-1.SF2**
Description:
HIV Subtype: B
Trial(s): NHP.141, NHP.193

Strain: **LAI isolate K98227/W35**
Description: This isolate was selected from an infected neonatal macaque with detectable HIV-1 RNA in the plasma 35 wks post infection
Trial(s): NHP.415, NHP.496

Strain: **LAV-1 or NY5**
Description:
HIV Subtype: B
Trial(s): NHP.249

HIV-2 Challenges

Strain: **HIV-2 (UC2-10568)**
Description: HIV-2 group A isolate UC2 was isolated from a woman originally from Burkina Faso but who was living in Cote d'Ivoire. She had developed AIDS and was co-infected with HIV-1. The isolate was cocultured in PBMC with then passaged through a baboons 9429, 12281 and 10568.
HIV Subtype: A
Trial(s): NHP.310

Strain: **HIV-2 (UC2-11966)**
Description: HIV-2 group A isolate UC2 was isolated from a woman originally from Burkina Faso but who was living in Cote d'Ivoire. She had developed AIDS and was co-infected with HIV-1. The isolate was cocultured in PBMC with then serially passaged through a baboons9429, 12281, 10568, 11999 and 11966.
HIV Subtype: A
Trial(s): NHP.310

Strain: **HIV-2 (UC2-11999)**

Description: HIV-2 group A isolate UC2 was isolated from a woman originally from Burkina Faso but who was living in Cote d'Ivoire. She had developed AIDS and was co-infected with HIV-1. The isolate was cocultured in PBMC with then serially passaged through a baboons9429, 12281, 10568 and 11999.

HIV Subtype: A

Trial(s): NHP.310

Strain: **HIV-2 (UC2-12281)**

Description: HIV-2 group A isolate UC2 was isolated from a woman originally from Burkina Faso but who was living in Cote d'Ivoire. She had developed AIDS and was co-infected with HIV-1. The isolate was cocultured in PBMC with then passaged through a baboons 9429 and12281.

HIV Subtype: A

Trial(s): NHP.310

Strain: **HIV-2 (UC2-12741)**

Description: HIV-2 group A isolate UC2 was isolated from a woman originally from Burkina Faso but who was living in Cote d'Ivoire. She had developed AIDS and was co-infected with HIV-1. The isolate was cocultured in PBMC with then serially passaged through a baboons9429, 12281, 10568, 11999, 11966 and 12741.

HIV Subtype: A

Trial(s): NHP.310

Strain: **HIV-2 (UC2-9429)**

Description: HIV-2 group A isolate UC2 was isolated from a woman originally from Burkina Faso but who was living in Cote d'Ivoire. She had developed AIDS and was co-infected with HIV-1. The isolate was cocultured in PBMC with then passaged through a baboon 9429.

HIV Subtype: A

Trial(s): NHP.310, NHP.378

Strain: **HIV-2.SBL6669**

Description:

HIV Subtype: A

Trial(s): NHP.47, NHP.149.1, NHP.174

V. ADJUVANTS AND STIMULANTS

As part of the vaccines database, we developed a separate and general database table and search interface for adjuvants and stimulants. The majority of the data on adjuvants was obtained from the National Institute of Allergy and Infectious diseases. We are indebted to Dr. Carl Alving for making the adjuvant data available. In this Vaccine compendium, we have listed only the adjuvants which were used in the Nonhuman Primate HIV/SIV Vaccine Trials Database. For information about other adjuvants and stimulants, the reader is advised to use the Adjuvant/Stimulant search form:

http://www.hiv.lanl.gov/content/vaccine/adjuvants-stimulants.html

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Name: **Adju-Phos**

Other Names: Aluminum phosphate gel

Description: Amorphous aluminum hydroxyphosphate. A schematic of the unit layer of amorphous aluminum bydroxyphosphate showing the surface hydroxyl, water, and phosphate groups. Key: Al, small closed circle; OH, large closed circle; H_20, open circle; $P0_4$, hatched circle. Obtained by precipitation. The degree of substitution of phosphate for hydroxyl depends on the concentration of reactants and precipitation conditions. White gelatinous precipitate in aqueous suspension.

Trial(s): NHP.330

Name: **Adjumer™**

Other Names: PCPP salt; polyphosphazene; polyidi (carboxylatophenoxy) lphosphazene

Description: Synthetic Solid: beige to off white powder. Aqueous solution: clear, colorless liquid

Trial(s): NHP.72, NHP.78

Name: **Alum**

Other Names: Alhydrogel; Aluminum hydroxide gel;

Description: Crystalline aluminum oxyhydroxide AIOOH, known mineralogically as boehmite. The structure consists of corrugated sheets of aluminum octahedra. Obtained by precipitation of aluminum hydroxide under alkaline conditions. White gelatinous precipitate in aqueous suspension.

Trial(s): NHP.97, NHP.99.2, NHP.151, NHP.162, NHP.185.1, NHP.185.2, NHP.198, NHP.205.3, NHP.248, NHP.349, NHP.362, NHP.402

Name: **AS-2 adjuvant**

Trial(s): NHP.21

Name: **B7-2**

Description: The gene product encoded by B7-2 is a co-stimulatory molecule for GM-CSF. The genes had been cloned by PCR from baboon peripheral blood mononuclear cells (PBMC) and were sequenced, then sub-cloned into the mammalian expression vector, pND-14.

Trial(s): NHP.378

Name: **BAK**

Other Names: benzalkonium chloride - cationic detergent

Trial(s): NHP.474, NHP.475

Name: **Bupivacaine**

Trial(s): NHP.2, NHP.16.1, NHP.202, NHP.322, NHP.402

Name: **Bupivacaine-HCl**

Trial(s): NHP.300

Name: **BWZL**

Trial(s): NHP.204

Name: **CCR5 peptides**

Description: N-terminal (aa 1-20): Met-Asp-Tyr-Gln-Val-Ser-Ser-Pro-ILe-Tyr-Asp-ILe-Asp-Tyr-Tyr-Thr-Ser-Glu-Pro-Cys First loop (aa 89-102): His-Tyr-Ala-Ala-Ala-Gln-Trp-Asp-Phe-Gly-Asn-Thr-Met-Cys-Gln Second loop (aa 178-197): Cys-Ser-Ser-His-Phe-Pro-Tyr-Ser-Gln-Tyr-Gln-Phe-Trp-Lys-Asn-Phe-Gln-Thr-Leu-Lys Neosystem Laboratories (Strasbourg, France)

Trial(s): NHP.395

Name: **CFA**

Other Names: complete Freud's adjuvant

Trial(s): NHP.477

Name: **CpG 2006**

Description: Eurogentec, Seraing, Belgium

Trial(s): NHP.330, NHP.503

Name: **CRL1005**

Other Names: Block Copolymer P1205

Description: ABA block polymer with mean values of x = 8 and y = 205. SOURCE: Linear chain polymers are synthesized by condensation of propylene oxide and ethylene glycol initiator in the presence of a cesium salt catalyst to form polyoxypropylene chain, followed by condensation of ethylene oxide on either end of the chain.

Individual polymeric species of triblock nonionic block copolymers result from controlled synthesis of chains with pre-determined length. Clear, colorless to slightly yellow, viscous liquid.

Trial(s): NHP.306.1, NHP.306.2, NHP.474, NHP.475

Name: **Diphtheria toxoid**

Trial(s): NHP.268.1

Name: **DL-PGL**

Other Names: Polyester poly (DL-lactide-co-glycolide)

Trial(s): NHP.200

Name: **Freund′s Complete Adjuvant**

Other Names: Complete Freund′s adjuvant; CIA; FCA

Description: Mixture of mineral oil (Marco 52) and emulsifier (Arlacel A [mannide monooleate]) as an emulsion of 85% mineral oil and 15% emulsifier with 500 µg heat-killed and dried Mycobacterium tuberculosis per mL of emulsifier mixture. M. tuberculosis grown and adjuvant is manufactured at the Statens Seruminstitut, Copenhagen, Denmark. Thick viscous liquid without color.

Trial(s): NHP.79, NHP.94, NHP.154, NHP.268.1

Name: **GM-CSF**

Other Names: Granulocyte-macrophage colony stimulating factor; Sargramostim (yeast-derived rh-GM-CSF)

STRUCTURE: GM-CSF is a glycoprotein of 127 amino acids. Recombinant human GM-CSF is produced in yeast and it differs from the natural human GM-CSF by substitution of Leu for Arg at position 23. <> Walter, M. R., et al., 1992, Three-dimensional structure of recombinant human granulocyte-macrophage colony stimulating factor, J. Mol. Biol. 224: 1075-1085.

Description: Sequence of recombinant human GM-CSF (Sargramostin):

APARSPSPSTQPWEHVNAIQEALRLLNLSRDTAAEMNETVEVISEMFDLQEPTC
LQTRLELYKQGLRGSLTKLKGPLTMMASHYKQHCPPTPETSCATQIITFESFKE
NLKDFLLVIPFDCWEPVQE Recombinant protein produced in yeast (S. cerevisiae). White, lyophilized powder (before reconstitution), or a clear colorless solution (after reconstitution).

Trial(s): NHP.68, NHP.106, NHP.401

Name: **hIL-12(N222L)**

Description: The murine IL-12N220L gene (mIL-12N220L) of pGX10-mIL-12N220L was replaced with the human IL-12N222L gene (hIL-12N222L) [22] to generate pGX10-hIL-12N222L. This is a N-glycosylation mutant of IL-12 that showed enhanced ability for long-term DNA vaccine-induced CD8+ T cell responses in mice

Trial(s): NHP.493

Name: **IFA**

Other Names: incomplete Freund's adjuvant

Trial(s): NHP.477

Name: **IFN-gamma in pCDNA3**

Trial(s): NHP.16.1

Name: **IL-12 DNA**

Description: The rhesus macaque IL-12 expression plasmid was derived from the plasmid pSFG.hIL12.p40.Lp35, which expresses human IL-12, by substituting the sequences encoding the human p40 and p35 subunits with the corresponding rhesus macaque sequences, positioned in the same configuration to produce plasmid pRM.IL-12.p40-p35. In this plasmid, the IL-12 p40 and -30 subunits are produced as a fusion protein in which the p35 subunit, deleted of its leader sequence, is fused to the p40 subunit by a Gly6Ser linker. IL-12 production by rmIL-12.p40.Lp35 was tested in 293T transfection supernatant by ELISA.

Trial(s): NHP.366

Name: **IL-12 plasmid**

Description: Rhesus IL-12 p35 subunit is expressed under control of the HCMV immediate early promoter and SV40 polyadenylation signal, while the rhesus IL-12 p40 subunit is expressed under control of the simian CMV promoter (SCMV) and BGH polyadenylation signal.

Trial(s): NHP.497

Name: **IL-12/GMCSF plasmid (Sykes)**

Description: Plasmids expressing the human cytokine IL-12 and GMCSF. Constructed by amplifying the cDNA coding sequences from pED and pXM vectors. EcoRI and SalI sites were incorporated into the end of the cDNAs encoding GMCSF and IL-12 subunit p35 by PCR (for more information contact authors) Sykes et al

Trial(s): NHP.120

Name: **IL-2 in pCDNA3**

Trial(s): NHP.16.1

Name: **IL-2/lg plasmid**

Trial(s): NHP.23, NHP.60.1, NHP.60.3, NHP.98, NHP.126, NHP.366, NHP.400, NHP.443

Name: **IL-2/lg protein**

Trial(s): NHP.24.1, NHP.60.1, NHP.98, NHP.126

Name: **IL-4**

Trial(s): NHP.106, NHP.309

Name: **IL-4 in pCDNA3**

Trial(s): NHP.16.1

Name: **Interferon-γ**

Other Names: Actimmune® (rhIFN-gamma, Genentech, Inc.); immune interferon; IFN-γ gamma-interferon

Description: Noncovalent dimer. Low resolution crystal structure available. Monomer consists of 140 amino acids, no glycosylation or cysteines in human form. Murine form is a covalent dimer (one cysteine per monomer). <> Ealick, S. E. et al., 1991, Three-dimensional structure of recombinant human interferon-g , Science, 252: 698-702. Sequence of human interferon-gamma:
QDPYVKEAENLKKYFNAGHSDVADNGTLFLGILKNWKEESDRKIMQSQIVSFYFKLFKNFKDDQSI
QKSVETIKEDMNVKFFNSNKKKRDDFEKLTNYSVTDLNVQRKAIHELIQVMAELSPAAKTGKRKRS
QMLFRGRRASQ Both human (rhIFN-gamma) and murine (rmuIFN-gamma) forms are expressed in Escherichia coli and distributed in a completely pure state. Clear aqueous solution.

Trial(s): NHP.309

Name: **Interleukin-12**

Other Names: IL-12; natural killer cell stimulatory factor (NKSF); cytotoxic lymphocyte maturation factor (CLMF)

Description: IL-12 is a heterodimeric protein composed of two disulfide-bonded glycoprotein subunits approximately 35 and 40 kDa in size. The two subunits represent two separate, unrelated gene products that have to be coexpressed to yield the secreted, bioactive, heterodimeric lymphokine. <> Gubler, U., et al., 1991, Coexpression of two distinct genes is required to generate secreted, bioactive cytotoxic lymphocyte maturation factor, Proc. Natl. Acad. Sci. USA 88: 4143-4147. <> Wolf, S. R, et al., 1991, Cloning of cDNA for natural killer cell stimulatory factor, a heterodimeric cytokine with multiple biologic effects on T and natural killer cells, J. Immunol. 146: 3074-3081. <> Schoenhaut, D. S., et al., 1992, Cloning and expression of murine IL-12, J. Immunol. 148: 3433-3440.

Sequence of 40-kDa subunit of human IL-12:
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKT
LTIQVKEFGDAGQYTCHKGGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKT
FLRCEAKNYSGRFrCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKP
DPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKD
RVFrDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

Sequence of 35-kDa subunit of human IL-12:
RNLPVATPDPGMFPCLHHSQNLLRAVSNMLQKARQTLEFYPCTSEEIDHEDITK
DKTSTVEACLPLELTKNESCLNSRETSFITNGSCLASRKTSFMMALCLSSIYEDL
KMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSETVPQKSSL
EEPDFYKTKIKLCILLHAFRIRAVTIDRVTSYLNAS Recombinant protein purified from the medium of cultures of CHO cells transfected with IL-12 cDNAs. Natural sources of the protein include activated monocyte/ macrophages and B lymphocytes. ISCOMs form a clear product in solution.

Trial(s): NHP.503

Name: **Interleukin-2**

Other Names: IL-2; T-cell growth factor; aldesleukin (des-alanyl-1, serine-125 human interleukin 2); Proleukin®;

Teceleukin®

Native human IL-2 contains 133 amino acids (see below); aldesleukin contains 132 amino acids. IL-2 exists as six alpha helical domains, termed A to F. Glycosylation not essential for function. <> Rosenberg, S. A. et al., 1983, Biological activity of recombinant human interleukin-2 produced in Escherichia coli, Science, 223: 1412-14. <> Brandhuber, B. J. et al., 1987, Three dimensional structure of interleukin-2, Science, 238: 1707-09. <> Ju, G. et al., 1987, Structure function analysis of human interleukin-2: Identification of amino acid residues required for biological activity. J. Biol. Chem., 262: 5723-31.

Description:

Sequence of human IL-2:

APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEELKPLE
EVLNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT
Recombinant protein expressed in E. coli. Lyophilized, white to off-white colored solid, Reconstituted with water for injection to give a clear, colorless solution.

Trial(s): NHP.106, NHP.126, NHP.245.3

Name: **ISCOM(s)™**

Other Names: Immune stimulating complexes

Description: ISCOMs are a complex composed of typically 0.5% Quillaja saponins, 0.1% cholesterol, 0.1% phospholipid, and antigen in phosphate-buffered saline (PBS). Occasionally, surfactants are used t are ISCOMs (such as Mega 10) but are removed from the final formulation before use. The adjuvant-active components of ISCOMs are derived by aqueous extraction of the bark of Quillaja saponaria and are further purified by chromatography. Quil A is a purified form of this. Further chromatographic purification provides components with high adjuvant activity and ISCOM-forming properties (see Iscoprep 7.0.3 TM). ISCOMs form a clear product in solution.

Trial(s): NHP.75, NHP.125, NHP.164, NHP.374

Name: **Kehole Limpet Hemocyanin**

Description: Unknown. Used in J Virol 71: 9475-9481 (1997) Jurkiewicz et al.

Trial(s): NHP.320, NHP.404

Name: **Lipid-based Adjuvant**

Other Names: LBA

Description: Data not available Mannhalter et al, 1991

Trial(s): NHP.362

Name: **Liposomes**

Other Names: Liposomes (L) containing protein or Th-cell and/ or B-cell peptides, or microbes with or without co-entrapped interieukin-2, BisHOP or DOTMA (see below). A, [L (Antigen)]; B, [L (IL-2 or DOTMA or BisHOP + Antigen)]; C, [L (Antigen)-mannose]; D, [L (Th-cel

Description: A: Multilamellar liposornes prepared by the dehydration-rehydration method (average diameter 600-800 nm) composed of egg phosphatidy1choline (PC) or distearoyl phosphatidylcholine (DSPQ and equimolar cholesterol and containing antigens such as tetanus toxoid and synthetic Th-cell peptides. 13: As in A with IL-2 (10^3 - 10^4 Cetus units) co-entrapped with the antigen in the aqueous phase or with 1,2-bis (hexadecylcycloxy)-3-trimethylaminopropane-HCL (BisHOP) or N-(2,3-dioleyloxy)-NNN-

triethylammonium (DOTMA) incorporated into the lipid phase of liposomes (0.8: 1.0: 0.2 molar ratio for PC or DSPC, cholesterol and DOTMA or BisHOP). C, as in A with marmosylated albumin covalently coupled to the surface of antigen-containing liposomes. D: As in A with Th-cell and B-cell peptides co-entrapped in the aqueous phase. E: Giant liposornes (average diameter 5-9 μm) prepared as in A or by a solvent-spherule evaporation method, composed of PC or DSPC, cholesterol, triolein (TO), and phosphatidylglycerol (PG) (4: 4: 1: 2 molar ratio) and containing killed or live Bacillus subtilis or killed Bacille Calmette-Guérin (BCG) with or without co-entrapped tetanus toxoid. PC, DSPC, and PG in pure forin from Lipid Products, Nuthill, Surrey, U. K.; TO in pure form from Sigma Chemical Co., Poole, Dorset, U. K.; recombinant interieukin-2 (des-Ala1-Ser125 mutein; 3 x 10 6 Cetus units/ mg) obtained from Cetus Corporation, Emeryville, CA; BisHOP and DOTMA obtained from Syntex Research, Palo Alto, CA. White, opalescent colloidal suspensions (A-E).

Trial(s): NHP.61, NHP.94

Name: **LT(R192G)**

Other Names: mutant heat-labile E. coli enterotoxin

Description: heat-labile enterotoxin with R-192-G mutation, eliminating trypsin cleavage site required for enterotoxin activation. Dickinson and Clements Infect. Immunol. 63: 1617-1623 (1995)

Trial(s): NHP.319

Name: **LT-R192G**

Trial(s): NHP.1, NHP.503

Name: **LTK63**

Other Names: mutated E. coli heat-labile enterotoxin

Description: mutated E. coli heat-labile enterotoxin which eliminates toxicity while retaining adjuvant activity. Pizza et al. Int. J. Med. Microbiol. 290: 455-461 (2000)

Trial(s): NHP.321, NHP.426

Name: **LTK72**

Other Names: mutant of E. coli heat-labile toxin LT that has minimal ADP-ribosylating activity

Description: Vajdy et.al. AIDS Research and Human Retroviruses 20: 1269 (2004)

Trial(s): NHP.426

Name: **MF59**

Other Names: None

Description: Squalene/ water emulsion. Composition: 43 mg/ mL squalene, 2.5 mg/ mL polyoxyethylene sorbitan monooleate (Polysorbate 80), 2.4 mg/ mL sorbitan trioleate (Span 85). Chiron Corporation, Emeryville, CA. White liquid.

Trial(s): NHP.22, NHP.23, NHP.62, NHP.75, NHP.141, NHP.193, NHP.354, NHP.426, NHP.503

Name: **MONTANIDE ISA 51**

Other Names: Purified IFA; Incomplete Freund′s adjuvant

Description: Mannide oleate (mostly mannide monooleate, esters of mannitol and oleic acids -an example shown below) (MONTANIDE 80) in mineral oil solution (DRAKEOL 6VR). Manufactured by SEPPIC. Limpid clear yellow liquid.

Trial(s): NHP.1, NHP.119

Name: **MONTANIDE ISA 720**

Other Names: metabolizable oil adjuvant

Description: A highly refined emulsifier from the mannide monooleate family (an example of mannide monooleate shown below) in a natural metabolizable oil solution. The exact nature of the emulsifier and the metabolizable in MONTANIDE ISA 720 is proprietary, but can be disclosed under specific agreement with SEPPIC. manufactured by SEPPIC. Yellow, odorless liquid

Trial(s): NHP.330

Name: **MPL™**

Other Names: 3-Q-desacyl-4

Description: MPL™ is composed of a series of 4'-monophosphoryl lipid A species that vary in the extent and position of fatty acid substitution. The hexaacyl structure shown below is the most highly acylated and most abundant component in MPLO. Species with five and four fatty acids are also present. All structures contribute to the adjuvant activity of MPLO. Derived from the lipopolysaccharide (LPS) of Salmonella minnesota R595. Obtained by treatment of LPS with mild acid and base hydrolytic conditions, and chromatographic purification of the resulting 3D-MLA. Colorless, odorless white powder.

Trial(s): NHP.306.1, NHP.480

Name: **MPL-SE**

Other Names: MPL-SE (monophosphoryl A-stable emulsion)

Description: Wyeth-Lederle Vaccines

Trial(s): NHP.328, NHP.363

Name: **MTP-PE**

Other Names: N-acetyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1,2-dipalmitoyl-sn-glycero-3-(hydroxy-phosphoryloxy)) ethylamide, mono sodium salt.

Description: Chemical synthesis by Ciba-Geigy Ltd., Basel, Switzerland. White powder.

Trial(s): NHP.141

Name: **nCT native Cholera Toxin**

Description: Yoshino et al J Immunol. 2004 Dec 1;173(11):6850-7. PMID: 15557179

Trial(s): NHP.423

Name: **non-toxic mutant E112K of Cholera Toxin mCT-E112K**

Other Names: mCT

Description: Yoshino et al Immunol. 2004 Dec 1;173(11):6850-7. PMID: 15557179

Trial(s): NHP.423

Name: **p-Hydroxybenzoique acid methyl ester**

Trial(s): NHP.2, NHP.402

Name: **pCIL-10**

Trial(s): NHP.71

Name: **pCIL12**

Trial(s): NHP.71, NHP.276

Name: **pCMVmCAT1**

Trial(s): NHP.67, NHP.70

Name: **pCMVN**

Trial(s): NHP.70

Name: **Peptomer-NP**

Trial(s): NHP.5

Name: **PLG**

Other Names: polyactide coglycolide

Trial(s): NHP.321, NHP.426

Name: **QS-21**

Other Names: Stimulon™ QS-21 Adjuvant.

Description: Natural product of the bark of the Quillaja saponaria Molina tree (species native to Chile and Argentina). Extracted from the bark by aqueous extraction. Purified by normal phase and reverse phase chromatography. <> Kensil, C. R. et al., 1991, Separation and characterization of saponins with adjuvant activity from Quillaja saponaria Molina cortex. J. Immunol., 146: 431-437. Solid: white odorless powder. Aqueous solution: clear, colorless solution.

Trial(s): NHP.11, NHP.14, NHP.53, NHP.81, NHP.303, NHP.371, NHP.482, NHP.492

Name: **Quil-A**

Other Names: Quil-A saponin, Quillaja saponin

Description: A complex but purified mixture of Quillaja saponins which are glycosides of Quillaic acid and carbohydrates. The Higuchi formula of Quil A is shown below. Purified extract from the bark of the South American tree Quillaja saponaria Molina. Lyophilized powder. Color is light brownish, almost white.

Trial(s): NHP.157.1, NHP.157.2

Name: **Rehydragel HPA**

Other Names: High Protein Adsorbency Aluminum Hydroxide Gel; alum

Description: Crystalline aluminum oxyhydroxide AlOOH, known minerologically as boehmite. the structure consists of corrugated sheets of aluminum octahedra. Synthetic oxyhydroxide of aluminum (aluminum hydroxide) prepared by acid-base precipitation. Translucent, thixotropic, colloidal aqueous gel supplied sterile.

Trial(s): NHP.47, NHP.174, NHP.201.1, NHP.201.2, NHP.203, NHP.204, NHP.242, NHP.306.1

Name: **RIBI**

Trial(s): NHP.94, NHP.119, NHP.162, NHP.320, NHP.402

Name: **Ribilike adjuvant system (MPL, TMD,CWS)**

Trial(s): NHP.68

Name: **SAF-1**

Other Names: SAF-m; Syntex Adjuvant Formulation

Description: Composed of threonyl-MDP (0.05-1%) in an emulsion vehicle [5% squalane, 2.5% Pluronic® L121, 0.2% Polysorbate 80 and phosphate buffered saline (pH 7.4)]. See individual components. White, fluid, oil-in-water emulsion.

Trial(s): NHP.203, NHP.205.1, NHP.245.2, NHP.245.3

Name: **Squalene 2**

Other Names: Spinacene; Supraene; 2,6,10,15,19, 23-hexamethyl-2,6,10,14,18,22 tetracosahexaene

Description: Found in shark liver oil and some vegetable oils. Intermediate in the biosynthesis of cholesterol. Clear oil, colorless. Faint, agreeable odor.

Trial(s): NHP.245.1

Name: **Tetanus toxoid (TT)**

Trial(s): NHP.404

Name: **Threonyl muramyl dipeptide (TMDP)**

Other Names: Termurtide™; [thr^{l}]-MDP; N-acetyl muramyl-L-threonyl-D-isoglutamine

Description: Synthetic. <> G. J. Jones, et al, Novel immunological adjuvant compounds and methods of preparation thereof. Syntex, U. S. A., U. S. Patent # 4,082,735. White to off-white, odorless powder.

Trial(s): NHP.239, NHP.245.2, NHP.248

VI. REFERENCES

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