Reagents for HIV/SIV Vaccine Studies

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Since last year's edition of this section, a few new attenuated SIVs and SHIVs have been added to the collection. We have attempted to include all strains represented in the literature. If there are any that are not included, we would very much appreciate hearing about them; we will make sure they will be added in the next edition of the Compendium. 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. Suggestions to make this section more useful are welcome.

In Figures 1–3 we present an overview of the virus strains that are frequently used in these studies and their derivation. A distinction must be made between strains used for vaccination, which obviously must be non-pathogenic, and strains used for challenge, which tend to be pathogenic. Some strains have been used both as vaccine and as challenge strains. Pathogenicity is relative, and depends on the virus, the host species, and the individual host. For example, SIVsm is not pathogenic in its natural host, the sooty mangabey, but can be highly pathogenic to macaques.

SIVmac viruses are used most extensively in these studies. The SIVmac isolates 251 and 32H both have a less pathogenic counterpart, clones 1A11 and C8, respectively. These clones are genetically very similar to the quasispecies they were derived from, but they have one or more attenuating genetic deletions. Another important SIVmac isolate, 239, is a clonal isolate from rhesus monkey #239. SIVmac239 is pathogenic, but a long series of reduced- or non-pathogenic strains with varying number of deletions in the genome has been derived from it. These strains cover a spectrum of pathogenicity, ranging from highly pathogenic to apparently non-infectious (unable to replicate in the host) (Desrosiers *et al*. 1998). It has recently become apparent that monkeys infected with SIVmac239-Δ3, in the lower mid range of the pathogenicity spectrum, do develop AIDS after several years (Cohen 1997). Two macrophage-tropic variants have also been derived from SIVmac-239: SIVmac316 and 17E (see Figure 1a).

SIVsm isolates can be highly pathogenic to macaques. Pathogenic challenge stocks in this group are usually bulk (rather than clonal) isolates, passaged in one of several macaques. Genetic clones of this group (such as SIVsmH4) tend to be much less pathogenic. An important and highly pathogenic strain is SIVsmPBj14, which kills a majority of infected macaques at primary infection, within a few weeks; monkeys that survive primary infection usually die of an AIDS-like illness within two years. Other isolates that have been used as challenge stocks are B670 and E660. Derivation of commonly used isolates from this group is shown in Figure 1b.

In recent years the repertoire of non-pathogenic vaccine strains has been extended by the creation of artificially attenuated virus variants. This is usually done either by creating stop codons in non-vital sections, or deleting sections from the genome of a virulent strain. Figure 2 shows a schematic representation of attenuated SIV strains. The diagram shows where changes have been made or documented with respect to the wild type.

Figure 3 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.

Acknowledgments

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Fig. 1a Derivation of SIVmac isolates

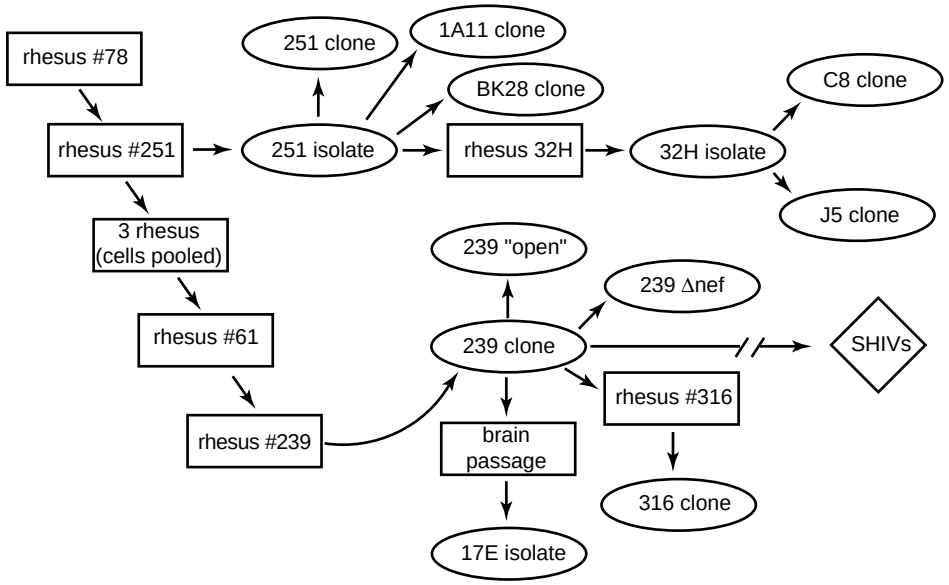


Fig. 1b Derivation of SIVsm isolates

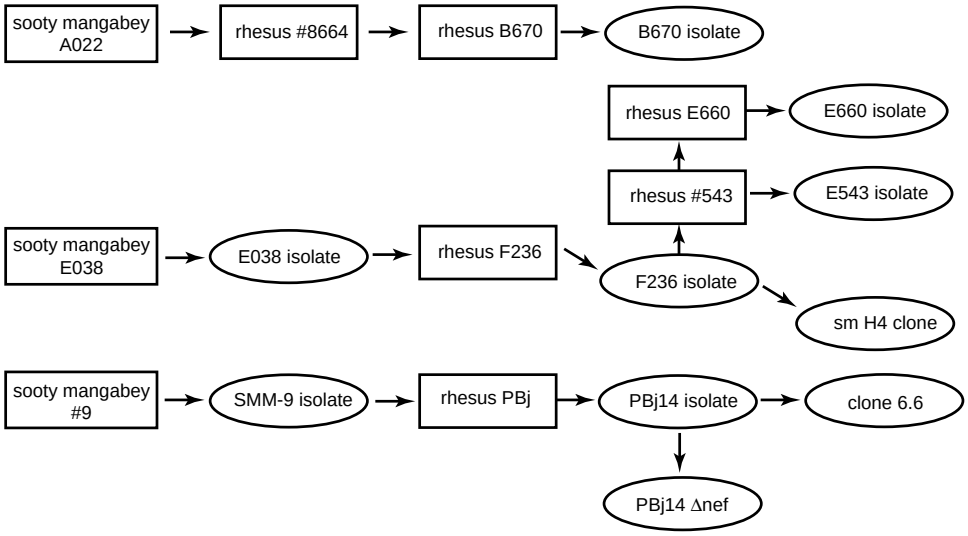
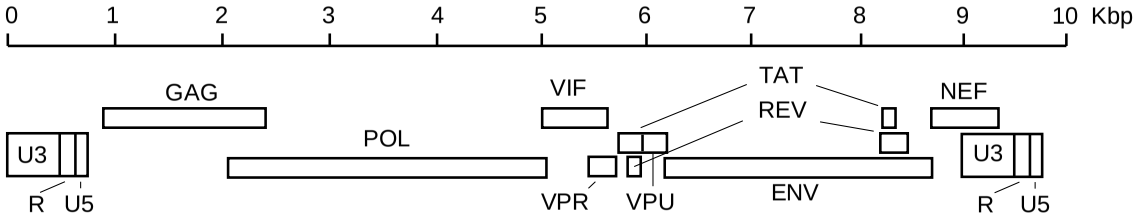


Figure 1a, b. *An overview of derivation of SIVmac (a) and SIVsm (b) strains. Rectangles indicate passages in a rhesus macaque, ovals indicate isolates or clones derived from these. Figure updated from Schultz & Hu (1993). References: SIVmac (Figure1a): 251/BK8 (Kornfeld et al., 1987); 1A11 (Marthas et al., 1990); 32H-C8 (Rud et al., 1992); 32H-J5 (Rud et al., 1992); 239 (Kestler et al., 1990); 239 derivatives (Desrosiers et al., 1998); 17E (Anderson et al., 1993); 316 (Mori et al., 1992).*
SIVsm (Figure 1b): B670 (Conway et al., 1991); H4 (Novembre et al., 1993); PBj14 (Dewhurst et al., 1990); PBj14-Δnef (Novembre et al., 1996); E543 (Hirsch et al., 1997).

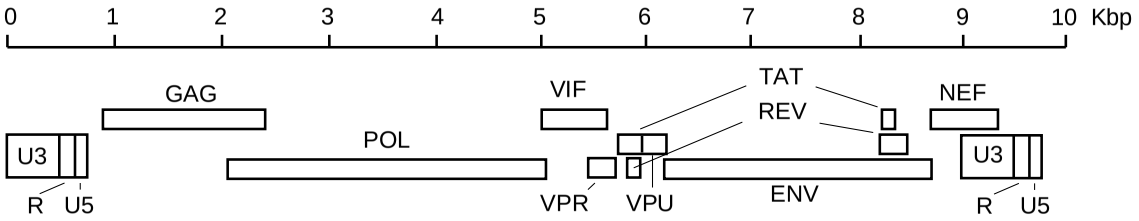
Figure 2. Chimeric SIV/HIV Strains



Name	Construct	Reference
$SHIV_{3'pCHN19-1}$	CHN19	Chen, *JVI* **74**:6501 (2000)
$SHIV_{3'pCHN19-2}$	SHIV33 CHN19	Chen, *JVI* **74**:6501 (2000)
$SHIV_{3'pCHN19-3}$	CHN19 SHIV33	Chen, *JVI* **74**:6501 (2000)
$SHIV_{3'pCHN19-4}$	SHIV33 CHN19 SHIV33	Chen, *JVI* **74**:6501 (2000)
$SHIV_{3'pCHN19-5}$	SHIV33 CHN19 SHIV33	Chen, *JVI* **74**:6501 (2000)
SHIV-E-CAR	* CAR402 SF33 CAR402	Himathongkham, *JVI* **74**:7851 (2000)
$SHIV_{KU-1bMC17}$	HXBc2	Narayan, *Virol*. **256**:54 (1999)
$SHIV_{DH12}$	DH12	Shibata, *Nat. Med.* **5**:204 (1999)
MA239/316	MAC316	Chen, *JGV* **79**:741 (1998)
NM-3m/JRFL	SF13 JRFL SF13	Chen, *JGV* **79**:741 (1998)
SHIV-KB9	HXBc2 89.6 HXBc2	Etemad-Moghadam, *JVI* **72**:8437 (1998)
$SHIV_{9466}$	9466	Klinger, *AIDS* **12**:849 (1998)
$SHIV_{9466-33}$	SF33 9466 SF33	Klinger, *AIDS* **12**:849 (1998)
SHIVppc	PPC	Stephens, *JVI* **72**:5207 (1998)
SHIVppcPBJ14	PPC PBJ14	Stephens, *JVI* **72**:5207 (1998)

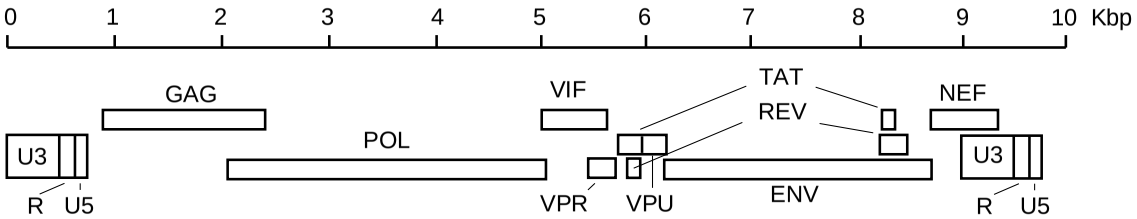
* mutation to correct stop codon in vpu in SHIV33

Figure 2. (cont.) Chimeric SIV/HIV Strains



Name	Construct	Reference
$SHIV_{W61D}$	ACH320	Ranjbar, *ARHR* **13**:797 (1997)
$SHIV_{HAN-2}$	ACH320	Ranjbar, *ARHR* **13**:797 (1997)
$SHIV_{MD1}$	NL43 / NL43 / DH12 / NL43	Shibata, *JVI* **71**:8141 (1997)
$SHIV_{sbg}$	LAI	Dunn, *Virol* **223**:351 (1996)
$SHIV_{Han-2}$	NL43 / Han-2 / NL43	Kuwata, *AIDS* **10**:1331 (1996)
$SHIVSF_2$	SF2	Kuwata, *AIDS* **10**:1331 (1996)
$SHIV_{SF13}$	SF13	Kuwata, *AIDS* **10**:1331 (1996)
NM-3rn	NL43	Kuwata, *AIDS* **10**:1331 (1996)
SHIV-89.6	HXBc2 / 89.6 / HXBc2	Reimann, *JVI* **70**:3198 (1996)
$SHIV_{SF33}$	SF33	Luciw, *PNAS USA* **92**:7490 (1995)
$SHIV_{SF162}$	SF162	Luciw, *PNAS USA* **92**:7490 (1995)
SHIV-4	HXBc2	Li, *J AIDS* **5**:639 (1992)
NM-10	NL43	Shibata, *ARHR* **8**:403 (1992)
NS-1	MAC251 / NL43 / MAC251	Shibata, *ARHR* **8**:403 (1992)
NS-3	MAC251 / NL43 / MAC251	Shibata, *ARHR* **8**:403 (1992)
NS-6	NL43 / MAC251 / MAC251	Shibata, *ARHR* **8**:403 (1992)
NS-7	NL43 / MAC251 / NL43	Shibata, *ARHR* **8**:403 (1992)

Figure 2. (cont.) Chimeric SIV/HIV Strains



Name	Construct	Reference
NM-8	NL43	Shibata, *ARHR* **8**:403 (1992)
NM-9	NL43 NL43	Shibata, *ARHR* **8**:403 (1992)
NM-1	NL43 5925 8053 NL43	Shibata, *JVI* **65**:3514 (1991)
NM-2	NL43 NL43	Shibata, *JVI* **65**:3514 (1991)
NM-3	NL43	Shibata, *JVI* **65**:3514 (1991)
NM-4	NL43 NL43	Shibata, *JVI* **65**:3514 (1991)
NM-5	NL43 NL43	Shibata, *JVI* **65**:3514 (1991)
SHIVMD-14	NL43 DH12	Shibata, *JID* **176**:362 (1991)
$SHIV_{SF33A2}$	SF33	Harouse, *JAIDS* **27**:222 (2001)

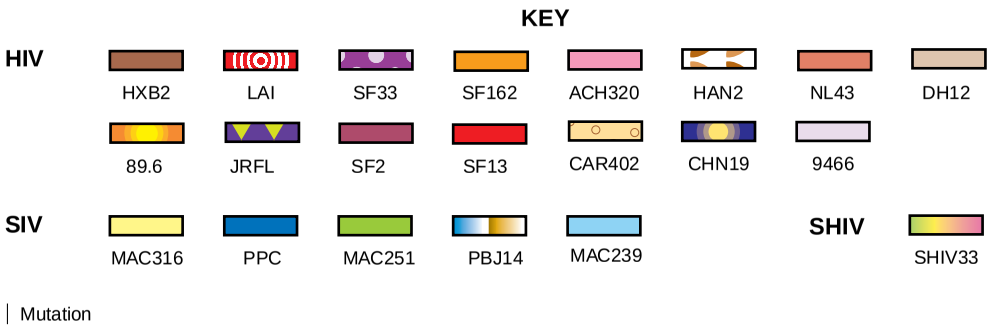
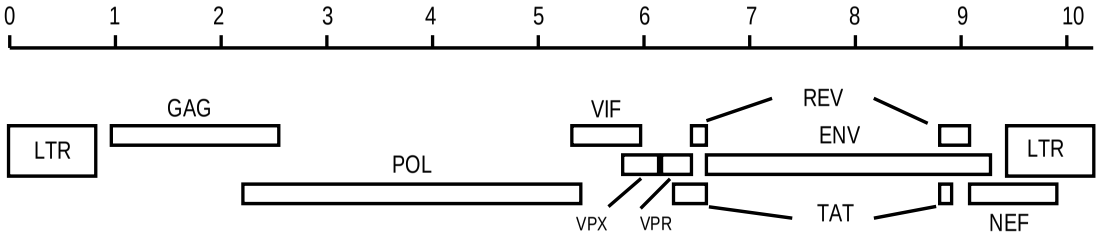


Figure 3. Attenuated SIV Strains



Name	Construct	Reference
Pathogenic SIV/HIV Strains		
$SHIV_{c2/1}$	89.6	Shinohara, *JGV* **80**:1231 (1999)
$SHIV_{KU-2MC4}$	HXBc2	Liu, *Virol.* **260**:295 (1999)
Other Strains		
SIVmac239-Δvpx	MAC239	Desrosiers, *JVI* **72**:1431 (1998)
SIVmac239-ΔvpxΔvpr		Desrosiers, *JVI* **72**:1431 (1998)
SIVmac239-Δvif		Desrosiers, *JVI* **72**:1431 (1998)
SIVmac239-Δ3x		Desrosiers, *JVI* **72**:1431 (1998)
SIVmac239-Δ5		Desrosiers, *JVI* **72**:1431 (1998)
ΔvpuΔnef SHIV-4	HXBc2	Joag, *JVI* **72**:9069 (1998)
ΔvpuΔnef SHIV-4	PPC	Joag, *JVI* **72**:9069 (1998)
SHIVdrn	NL43	Igarashi, *Micro. Immunol.* **42**:71 (1998)
SHIVdxrn		Igarashi, *Micro. Immunol.* **42**:71 (1998)
SIVagm3-Δnef	AGM	Beer, *PNAS USA* **94**:4062 (1997)
SIVmac251-Δnef	MAC251	Chakrabarti, *Virol* **213**:535 (1995)

Figure 3. (cont.) Attenuated SIV Strains

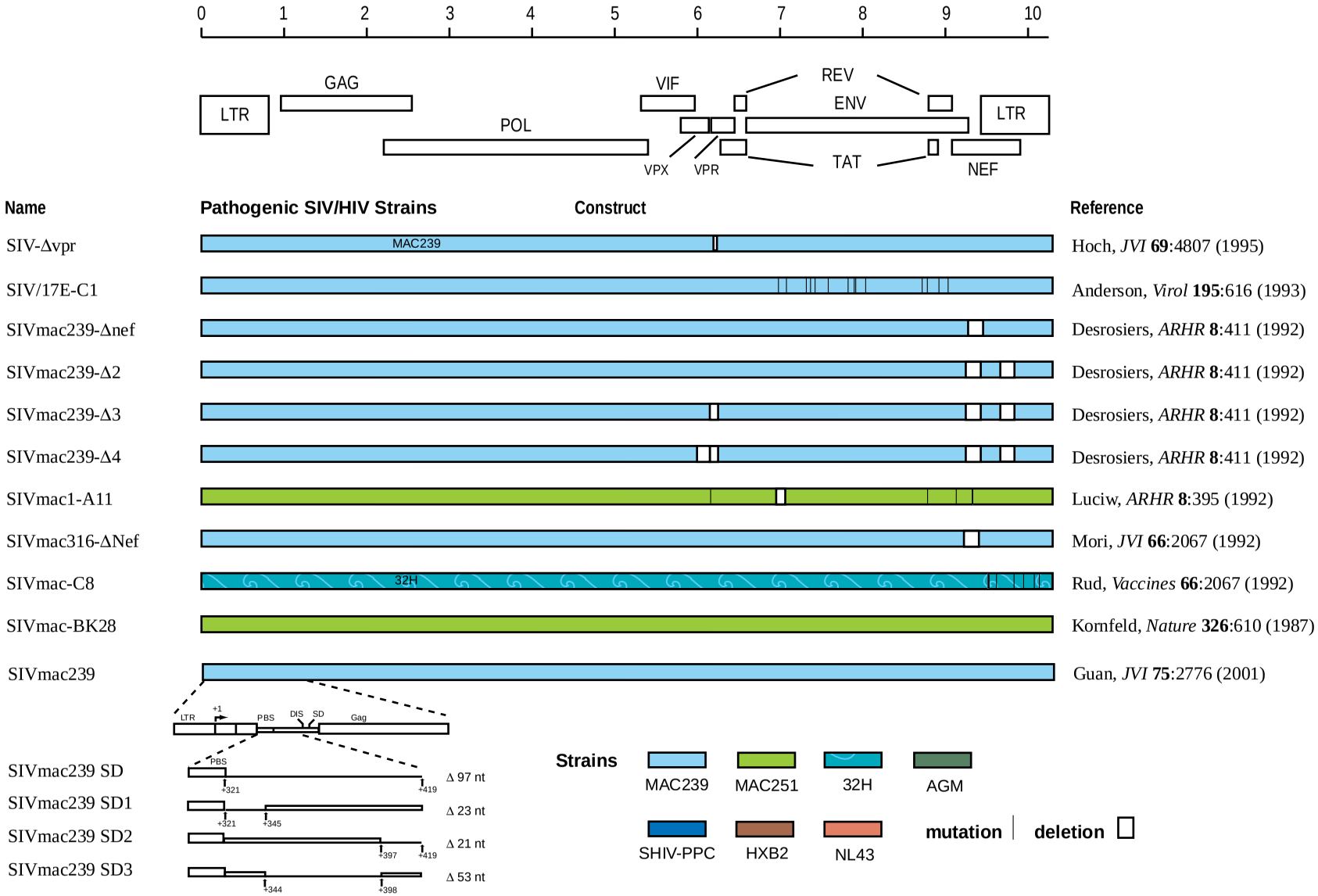


Figure 3. *Schematic representation of common attenuated SIV strains used in vaccine research. Deletions are indicated in white, mutations are shown as black lines. Mutations may include insertion or deletion of a stop codon.*
Notes: SIVmac239, a frequently used pathogenic strain, contains a stop codon (TAA) in nef. BK28 is a clone from the SIVmac251 bulk isolate; it is the only sequence available from SIVmac251. SHIV KU1 and KU2 are passages of SHIV-4. SHIV 98.6P and KB9 are passages of SHIV89.6. SF33A is a passage of SF33.

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