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NOTE: (Medline: 97265565) 23 overlapping 15 mers peptides from Gag p24 were used to pulse dendritic cells to identify epitopes by stimulating primary proliferative responses *in vitro* from PBMC from healthy HIV-negative donors. Novel responses were detected.

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NOTE: (Medline: 87231983) An algorithm based on a model of immunodominant helper T-cell sites forming amphipathic helices was used to identify for the first time two T-cell sites, env T1 and env T2. These two peptides were shown to stimulate proliferation of T-cells in mice immunized with a fragment of the env protein. Also, mice immunized with T1 were able to induce immunity to env gp120. Multiple haplotypes were responsive. Env epitopes: T2: HEDIISLWDQSLK and T1: KQIINMWQEVGKAMYA.

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NOTE: (Medline: 92259993) Cell-mediated immune response to HIV-1 can be detected in the absence of a humoral immune response in individuals recently exposed to HIV-1. gp160 epitopes: T1, T2, TH4.1, P18-IIIb, P18-MN.

[Clerici et al.(1991a)] M. Clerici, C. R. Lucey, R. A. Zajac, R. N. Boswell, H. M. Gebel, H. Takahashi, J. A. Berzofsky, & G. M. Shearer. Detection of cytotoxic T lymphocytes specific for synthetic peptides of gp160 in HIV-seropositive individuals. *J Immunol* **146**:2214–2219, 1991a.

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[Clerici et al.(1991b)] M. Clerici, C. O. Tacket, C. S. Via, D. R. Lucey, S. C. Muluk, R. A. Zajac, R. N. Boswell, J. A. Berzofsky, & G. M. Shearer. Immunization with subunit human immunodeficiency virus vaccine generates stronger T helper cell immunity than natural infection. *Eur J Immunol* **21**:1345–1349, 1991b.

NOTE: (Medline: 91257138) Immunization of uninfected individuals with an HIV subunit vaccine results in stronger Th cell immunity than does natural

infection. Boosting enhances helper function. Env epitopes: T1, T2, TH4.1, P18.

[De Berardinis et al.(1997)] P. De Berardinis, J. Guardiola, & F. Manca. Epitope context and reshaping of activated T helper cell repertoire. *Hum Immunol* **54**:189–93, 1997.

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NOTE: (AIDSLINE: 92227948) Helper T-cell epitopes in nef were investigated using five synthetic peptides selected for their amphipathic and α helix properties. One of the peptides, 45-59 was very immunogenic, and could induce functional T-cell help *in vivo*.

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NOTE: (Medline: 90302545) In this study, mice were immunized with multivalent peptides anchored in a phospholipid complex; these peptides were able to stimulate a potent antibody response. That a functional T-helper cell epitope is present within the peptide is inferred by the ability of B-cells to respond to these constructs. Using this system, adjuvant could be bypassed.

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[Haas et al.(1991)] G. Haas, R. David, R. Frank, H. Gausepohl, C. Devaux, J.-M. Claverie, & M. Pierres. Identification of a major human immunodeficiency virus-1 reverse transcriptase epitope recognized by mouse CD4+ T lymphocytes. *Eur J Immunol* **21**:1371–1377, 1991.

NOTE: (Medline: 91257142) RT peptides were recognized by several of the T-helper lines established from RT-primed mice. Further, T-cells from peptide-primed mice could be restimulated by native RT. RT epitope: KEKVYLAWVPAHKGIG.

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NOTE: (Medline: 91207940) Six helper T multideterminant regions of the HIV envelope protein are recognized by mice of either three or all four murine MHC types.

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NOTE: (Medline: 91132039) Induction of T-cell help in rhesus monkeys *Macaca mulatta* by priming with peptides T2 or TH4.1 enhances antibody response to a subsequent suboptimal gp160 immunization. T1 alone failed to elicit a response in these experiments. Env epitopes: T1, T2, TH4.1.

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NOTE: (Medline: 95308197) *In vitro* priming with peptides often induced CD4+ T-cells that did not recognize whole protein. Priming with protein did not always induce T-cells that could be recognized in the context of the virus.

[Manca et al.(1996)] F. Manca, P. D. P., D. Fenoglio, M. N. Ombra, G. Li Pira, D. Saverino, M. Autiero, L. Lozzi, L. Bracci, & J. Guardiola. Antigenicity of HIV-derived T helper determinants in the context of carrier recombinant proteins: effect on T helper cell repertoire selection. *Eur J Immunol* **26**:2461–9, 1996.

NOTE: (Medline: 97054664) A given Th epitope was recognized by a specific T cell clone only when it was inserted in a particular position of the carrier, and the permissive position was not the same for all epitopes.

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[Mazzoli et al.(1997)] S. Mazzoli, D. Trabattoni, S. Lo Caputo, S. Piconi, C. Ble, F. Meacci, S. Ruzzante, A. Salvi, F. Semplici, R. Longhi, M. L. Fusi, N. Tofani, M. Biasin, M. L. Villa, F. Mazzotta, & M. Clerici. HIV-specific mucosal and cellular immunity in HIV-seronegative partners of HIV-seropositive individuals [see comments]. *Nat Med* **3**:1250–7, 1997.

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NOTE: (Medline: 94328220) The proliferative T-cell response to pools of overlapping 17 mer peptides spanning Env were tested in both seronegative and low risk seropositive people. The pool that gave the greatest number of responders was pool 25, located in gp41. The 17 mer peptides used in this pool were tested individually for their ability to stimulate T-cell proliferation, and the most critical regions were found to be GIWGCSGKLIC and PWNASWSN. Mutch et al. suggest that the proliferative response in HIV-1 seronegative individuals is more likely due to cross-reactive, non-HIV induced memory cells than naive T-cells.

[Nakamura et al.(1997)] Y. Nakamura, M. Kameoka, M. Tobiume, M. Kaya, K. Ohki, T. Yamada, & K. Ikuta. A chain section containing epitopes for cytotoxic T, B and helper T cells within a highly conserved region found in the human immunodeficiency virus type 1 Gag protein. *Vaccine* **15**:489–96, 1997.

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NOTE: (AIDSLINE: 94267704) A vpr peptide was shown to stimulate a T-cell proliferative response in 37% of HIV+ individuals. This peptide was coupled with B-cell epitopes, and immunized mice were capable of antibody production.

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NOTE: (Medline: 91354553) Seven out of 19 peptides induced good T-cell proliferative response in mice representing four major histocompatibility complex haplotypes, without eliciting an Ab response. Eleven peptides were able to induce T-cells that could proliferate in response to recombinant gp160 (greater than or equal to 3 fold relative to unrelated peptides). Peptides were modified to generate polymers with disulfide bonds or micelles with palmitic acid residues attached to the amino-terminal lysine; in these configurations peptides were immunogenic without being coupled to a carrier molecule. F1 hybrid mice were used: ASW x BALBc F1 (H-2^{kxb}) and B6C3 F1 (H-2^{sxd}).

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NOTE: (Medline: 89124356) The ability of 21 peptides to stimulate T-cell proliferation was tested in 30 HIV-infected donors in different clinical stages. T-cells from 27/30 donors were able to respond to at least one peptide. Two of the peptides were able to stimulate proliferation in 48% of the donors. Schrier et al. did not write down the peptide sequences they used, but only provided the numbering of the boundaries on a reference sequence (LAI, Wain-Hobson et al., Cell 40:9-17 (1985)). In our experience, such numbering is often imprecise, so the peptide assignments in this database may be off by several residues. Two epitopes that Schrier et al. mistakenly labeled as p24 peptides are instead p15 peptides.

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NOTE: (Medline: 90155121) This same epitope can be recognized in the context of a class I MHC D^d, by CD4- CD8+ CTL, and in the context of a class II MHC A^d by CD4+ CD8- T-helper cells.

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NOTE: (AIDSLINE: 95138543) Of RGPGRAFVTI, the upper case iGPgRaFvtI are critical for for binding, consistent with the H-2Dd motif XGPX(RKH)XXX(X)(LIF). Stimulation of the HLA class II I-A^d required a longer peptide, IQRGPGRAFVTI or RIQRGPGRAFVTI, and riqrgPgRaFvti were essential for binding to the Class II molecule.

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NOTE: (AIDSLINE: 95151361) Four Gag peptides, that when pooled are able to prime for subsequent antibody response to HIV in mice, were studied. These peptides were also able to prime *in vitro* immunoproliferative responses. The two peptides of the four that were able to prime humoral responses to inactivated HIV-1 are included in the table (G2 and G4) – the other two are not included (G1 and G3). Three proposed nef helper T-cell epitopes are also not included in the table, but may be of interest. These nef peptides could prime the humoral response in mice, but not *in vitro* proliferation. Priming was also observed in baboons, using the pool of four Gag peptides.

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NOTE: (Medline: 97334261) Only three out of seven children with rapidly progressing disease had detectable CTL activity, and CTL activity was correlated with a normal Th1 response. Children that did not have a strong CTL response had an increased proportion of Th2 cells relative to Th1.

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