HIV Helper T-cell Epitopes

gp41 Helper Epitope Map

AVGMLGAMFLGFLGAAGSTMGAASMTLTQARLLLSSGIVQQQNLLRAIE 50

AQQHLFELETVGWIKQLQARVLAVERYLKDQQLLGIWGCGLICICTTTPW 100

NASWSNRSQDYIWNMTWMEWEINNYTGLIYNLIESQNOQEKNEQEL 150

LELDKWASLWTWFDISNWLWYIKIFIMIVGGVIILGRLIVFTVLSIVNVRQ 200

GYSPSFQTHLPAPRGRPDPEGIEEEGERDRDGRSGRLVDFLTLIWDL 250

RSLCLFLYHRLIDLLLLIAKRIVELLGRRGWEALKYCWNLLQYWSQELKNS 300
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AVSLNATAI AVAEGDRVIEIVQRTAILHIPIRRIRQGERALL
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References


[Berzofsky et al.(1988)] J. A. Berzofsky, A. Bensussan, K. B. Cease, J. F. Bourge, R. Cheynier, Z. Lurhama, J.-J. Salaun, R. C. Gallo, G. M. Shearer, & D. Zagury. Antigenic peptides recognized by T lymphocytes from AIDS viral envelope-immune humans. *Nature* **334**:706–708, 1988. OTE: (Medline: 88318926) Test of response to synthetic peptides of lymphocytes from 14 healthy human volunteers who had been immunized with a recombinant vaccinia virus containing HIV gp160, then boosted with a recombinant fragment containing the carboxy-terminal 40% of gp120. 8/14 showed a proliferative response to T1; 4/14 to T2. A reduced response to T2 in terms of both magnitude and frequency may have been because of the boost containing the region covering T1, but not T2, and because of the timing of sampling relative to immunization. Some HLA typing was done but no conclusive MHC restriction patterns were determined. Env epitopes: T1: KQIINMWQEVGLAMY A and T2: HEDIISLWDQSLK.


[Callahan et al.(1990)] K. M. Callahan, M. M. Fort, E. A. Obah, E. L. Reinherz, & R. F. Siliciano. Genetic variability in HIV-1 gp120 affects interactions with HLA molecules and T-cell receptor. *J Immunol* **144**:3341–3346, 1990. OTE: (Medline: 90229719) Synthetic peptides representing a defined CD4+ human T-cell epitope in gp120 were used to survey gp120 molecules from various HIV-1 strains for the capacity to be recognized in the context of a single human MHC molecule, DR4. gp120 epitope: GSDTITLPCRIKQFINMWQE.

[Cease et al.(1987)] K. B. Cease, H. Margalit, J. L. Cornette, S. D. Putney, W. G. Robey, C. Ouyang, H. Z. Streicher, P. J. Fischinger, R. C. Gallo, C. DeLisi, & J. J. Berzofsky. Helper T-cell antigenic site identification in the acquired immunodeficiency syndrome virus gp120 envelope protein and induction of immunity in mice to the native protein using a 16-residue synthetic peptide. *Proc Natl Acad Sci USA* **84**:4249–4253, 1987. OTE: (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: KQIINMWQEVGLAMY A.


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[Goodman-Snitkoff et al.(1990)] G. Goodman-Snitkoff, L. E. Eisele, E. P. Heimer, A. M. Felix, T. T. Andersen, T. R. Fuerst, & R. J. Mannino. Defining minimal requirements for antibody production to peptide antigens. *Vaccine* **8**:257–262, 1990. OTE: (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.


HIV Helper T-cell Epitopes

[Klinman et al.(1995)] D. M. Klinman, B. F. Haynes, & J. Conover. Activation of interleukin 4- and interleukin 6-secreting cells by HIV-specific synthetic peptides. *AIDS Res Hum Retroviruses* **11**:97–105, 1995. OTE: (AIDSLINE: 95251942) Immunized mice activate IL-4 and IL-6 producing cells in a dose dependent manner. The V3 region epitope as well as the T1 epitope is able to activate cytokine-producing cells. The order of immunization of T1-SP10 peptides influences the magnitude and cross-reactivity of the response, where the SP10, V3 portion of the immunogen is varied.


[Manca et al.(1993)] F. Manca, E. Seravalli, M. T. Valle, D. Fenoglio, A. Kunkl, G. L. Pira, S. Zolla-Pazner, & A. J. Kingsman. Induction of HIV-specific immune responses in primates: fine specificity of antibody and helper T-cell recognition of the HIV p24 protein. *Vaccines* **90**:213–218, 1990. OTE: Four cynomolgous macaques were immunized with 3 doses of p24 TY virus-like particles and their immune response was followed. Three 15 mer peptides stimulated CD4 T-cells proliferation and IL-2 production. Two of these responses were verified at the clonal level. B-cell responses were also studied in this paper.

[Mutch et al.(1994)] D. Mutch, J. Underwood, M. Geczy, & S. Rodda. Comprehensive T-Cell epitope mapping of HIV-1 env antigens reveals many areas recognized by HIV-1-seropositive and by low-risk HIV-1-seronegative individuals. *J. of Acquired Immune Deficiency Syndromes* **7**:879–890, 1994. OTE: (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 individually tested 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.

[Palker et al.(1989)] T. J. Palker, T. J. Matthews, A. Langlois, M. E. Tanner, M. E. Martin, R. M. Scearce, J. E. Kim, J. A. Berzofsky, D. P. Bolognesi, & B. F. Haynes. Polyvalent human immunodeficiency virus synthetic immunogen comprised of envelope gp120 T helper cell sites and B-cell neutralization epitopes. *J Immunol* **142**:3612–3619, 1989. OTE: (Medline: 89235170) Synthetic peptides containing type-specific neutralizing determinants of the V3 loop of gp120 were coupled to a 16 amino acid T-cell epitope (T1) of HIV-IIIB and used to immunize goats. The helper T-cell epitope T1 could induce both a proliferative response and a B-cell antibody response. Conversely, the B-cell epitope in the V3 region, SP10 was found to stimulate proliferative T-cell responses.


HIV Helper T-cell Epitopes

[Sarobe et al.(1994)] P. Sarobe, J.-J. Lasarte, I. Prieto, A. Gullon, M.-J. Soto, P. Labarga, J. Prieto, & F. Borras-Cuesta. Induction of neutralizing antibodies against human immunodeficiency virus type 1 using synthetic peptide constructs containing an immunodominant T-helper cell determinant from vpr. *J AIDS* 7:635–640, 1994. OTE: (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.

[Sastry & Arlinghaus(1991)] K. J. Sastry & R. B. Arlinghaus. Identification of T-cell epitopes without B-cell activity in the first and second conserved regions of the HIV Env protein. *AIDS* 5:699–707, 1991. OTE: (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\(^d\)) and B6C3 F1 (H-2\(^{sxd}\)).

[Schrier et al.(1989)] R. D. Schrier, J. W. Gnann Jr., R. Landes, C. Lockshin, D. Richman, A. McCutchan, C. Kennedy, M. B. A. Oldstone, & J. A. Nelson. T-cell recognition of HIV synthetic peptides in a natural infection. *J Immunol* 142:1166–1176, 1989. OTE: (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.


[Takeshita et al.(1995)] T. Takeshita, H. Takahashi, S. Kozlowski, J. D. Ahlers, C. D. Pendleton, R. L. Moore, Y. Nakagawa, K. Yokomuro, B. S. Fox, D. H. Margulies, & J. A. Berzofsky. Molecular analysis of the same HIV peptide functionally binding to both a class I and a class II MHC molecule. *J Immunol* 154:1973–1986, 1995. OTE: (AIDSLINE: 95138543) Of RGPGRAFVTI, the upper case iGPgRaFvTI are critical for for binding, consistent with the H-2D\(d\) motif XGPX(RKH)XXX(X)(LIF). Stimulation of the HLA class II I-A\(^d\) required a longer peptide, IQRGPGRAFVTI or RIQRGPGRAFVTI, and riqrgPgaFvtI were essential for binding to the Class II molecule.

[Vaslin et al.(1994)] B. Vaslin, J.-M. Claverie, O. Benveniste, F. C. Barre-Sinoussi, & D. Dormont. Nef and gag synthetic peptide priming of antibody responses to HIV type 1 antigens in mice and primates. *AIDS Res Hum Retroviruses* 10:1241–1250, 1994. OTE: (AIDSLINE: 95151361) Four Gag peptides, when that 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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