Human Immunodeficiency Virus Type 1 gp120 Mimics a Hidden Monomorphic Epitope Borne by Class I Major Histocompatibility Complex Heavy Chains

By Fabio Grassi,* Raffaella Meneveri,* Martin Gullberg,† Lucia Lopalco,* Giovanni Battista Rossi,§ Paola Lanza,* Claudio De Santis,* Goran Brattsand,‡ Stefano Butto,* Enrico Ginelli,* Alberto Beretta,∥ and Antonio G. Siccardi*

From the *Dipartimento di Biologia e Geneticaper le Scienze Mediche, Università di Milano, 20133 Milano, Italy; the †Unit for Applied Cell and Molecular Biology, University of Umeå, 90187 Umeå, Sweden; the §Laboratorio di Virologia, Istituto Superiore di Sanità, 00161 Roma, Italy, and the ∥Dipartimentodi Biologia e Tecnologia, Istituto H S. Raffaele, 20132 Segrate, Italy

Summary

Murine monoclonal antibodies (mAbs) M38 and L31 define two epitopes of a surface protein of activated lymphocytes and monocytes. It has been shown that M38 also defines a crossreactive epitope of human immunodeficiency virus type 1 (HIV-1) gp120 (Beretta et al., 1987. *Eur. J. Immunol.* 17:1793). The mAb inhibits syncytia formation driven by HIV-1-infected cells. The surface protein was demonstrated to be a class I MHC α chain, by sequence analysis of the corresponding cDNA and by immunological means. The epitopes defined by mAbs M38 and L31 are monomorphic and hidden (i.e., inaccessible to antibodies) on native HLA molecules expressed by resting cells, but can be evidenced on denatured proteins by Western blot analysis. The two epitopes become accessible after activation processes have been implemented, likely reflecting a conformational alteration of α chains (such as that described by Schnabl et al. 1990. *J. Exp. Med.* 171:1431). Consistent with molecular data are the results of functional analysis, which indicate that the molecule recognized by M38 and L31 is a gate for pleiotropic negative signals, since the two mAbs were shown to inhibit monocyte antigen presentation and lymphocyte mitogenic proliferation, respectively.

HIV infection of susceptible cells starts with the interaction of viral gp120 with the CD4 molecule (1-3). Since CD4 belongs to the Ig superfamily, whose members are involved in regulatory interactions essential for the immune system function (4-6), the specificity of gp120 for this molecule could be central for the virus in evading the host immune response.

Beside the depletion of CD4+ cells due to HIV cytopathic effects, other gp120-related mechanisms for amplification of immune damage have been proposed: killing of bystander cells induced by soluble gp120 (7, 8), anti-CD4 autoantibodies induced by CD4-like idiotopes expressed within the env-specific repertoire (9), synergism between gp120 and anti-gp120 antibodies in blocking T cell activation (10), and blockade of the differentiation of CD4+CD8+ thymocytes into CD4+ CD8- T lymphocytes secondary to gp120 binding to CD4 (11, 12).

CD4 is a ligand of class II MHC and interacts with other proteins in the context of a multimolecular complex (13, 14). HIV might have evolved its specificity for CD4 by mimicry of a physiological ligand of CD4. Experimental evidence of serological crossreactivity between viral envelope and human epitopes have already appeared in two independent reports. One case is the identification of homologous regions in HIV-1 gp41 and human class II MHC (β-1 domain). A fraction (36%) of AIDS patient sera was shown to contain antibodies reacting with a class II-derived peptide and with native class II antigens (15). Further, a gp120-specific mAb, M38, was shown to crossreact with a surface protein of activated human monocytes endowed with negative signaling potentials (16).

The present work describes by biochemical, immunological, and genetic means the crossreactive human surface protein defined by mAb M38. Such a molecule resulted in being a class I MHC heavy chain, present on activated immuno-
cytes in a form that differs from that of HLA molecules on resting cells, likely corresponding to the conformational alteration of α chains (not associated with β3m) recently described by Schnabl et al. (17). We present evidence that such conformationally altered molecules might be involved in functional regulatory mechanisms.

Materials and Methods

Monoclonal Antibodies. mAbs OKT3, -4, -8, and -9 were purchased from Ortho Diagnostics Systems, Inc., (Raritan, NJ), and Leu-3a was from Becton Dickinson & Co. (Mountain View, CA). The anti-TAC DMS-1 (18) and the anti-CD3 UCHT-1 (19) were kindly provided by Drs. Smith and Beverly (ICRF, London), respectively. mAb 01.65 (20), specific for a common determinant of HLA-A, -B, -C molecules, and mAb RL30, specific for β3m (20), were kind gifts of Dr. Malavasi (Department of Genetics, University of Torino, Italy), mAb CR11.351, specific for a polymorphism determinant of HLA-A2 (21), was a kind gift of Dr. Russe (Columbia University, New York). M38, L31, and D28 were derived from the same fusion (16); D28 was used as a control of irrelevant specificity.

Cells. Human PBMC, isolated by Ficoll-Hypaque discontinuous gradient centrifugation were cultured after stimulation with OKT3 and rabbit anti–mouse Ig antibodies (22) or with 5 μg/ml Con A to obtain activated lymphocytes. Rer cells, a human T lymphoblastoid cell line, were a kind gift of Dr. Acuto (Department of Immunology, Pasteur Institute, Paris). 8E51 (LAV) cells, which harbor a single integrated copy of a pol mutant of HIV-1 (LAV) and produce defective, uninfected virions (23), were a kind gift of Dr. Folks (Center for Disease Control, Atlanta, GA). MOLT3 cells were a kind gift of Dr. De Rossi (Oncology Institute, University of Padova, Italy).

Cytotoxicity. Lymphocytes of 8E51 (LAV) cells were washed and resuspended in RPMI 1640 containing 20% normal human serum. Cells (106 cells/200 μl) were incubated on ice for 30 min with the appropriate dilution of mAb. After two washings in RPMI 1640, FITC-conjugated rabbit anti–mouse Iggs (Dakopatts a/s, Glostrup, Denmark) were added and cells were incubated on ice. Washed cells were fixed in 5% paraformaldehyde and applied to a Spectrum III flow cytometer (Ortho Diagnostics Systems, Inc.).

Results

Characterization of mAb L31. mAb L31 was derived from the same HIV-immunized mouse that yielded M38 (16). It
Reactivity pattern of mAbs M38 and L31. (A) Western blot of radioiodinated M38 (M) and L31 (L) on HIV-1, HIV-2, and HTLV-1 commercial strips (Sorin Biomedica and BioRad Laboratories). The reference AIDS serum (S) was revealed by 125I-Protein A. (B) SDS-PAGE of the materials immunoprecipitated by M38 (M), L31 (L), and UCTH-1 (L) from lysates of OKT3-stimulated lymphocytes, surface labeled by 125I (lactoperoxidase method).

Figure 1. Reactivity pattern of mAbs M38 and L31. (A) Western blot of radioiodinated M38 (M) and L31 (L) on HIV-1, HIV-2, and HTLV-1 commercial strips (Sorin Biomedica and BioRad Laboratories). The reference AIDS serum (S) was revealed by 125I-Protein A. (B) SDS-PAGE of the materials immunoprecipitated by M38 (M), L31 (L), and UCTH-1 (L) from lysates of OKT3-stimulated lymphocytes, surface labeled by 125I (lactoperoxidase method).

was selected for its strong reactivity in commercial HIV-ELISA and was shown to bind the surface of activated human PBMC by cell binding assays and by flow cytometry. Since these properties were similar to those described for M38, we compared the specificities of the two antibodies in Western blot and radioimmunoprecipitation assays.

The reactivity pattern of 125I-L31 and -M38 on HIV-1, HIV-2, and HTLV-1 Western blot strips (Fig. 1 A) proved to be similar, even though not identical: both antibodies reacted with a 45-kD protein band, while only M38 recognized the env product of HIV-1 (but not that of the other two retroviruses). Radioimmunoprecipitations of lysates from surface-labeled activated lymphocytes demonstrated that both L31 and M38 precipitate similar (likely identical) 45-kD bands and fainter 90-kD bands (Fig. 1 B).

The number of antibody binding sites on the lymphocyte surface was found to increase 10-40-fold after polyclonal lymphocyte stimulation by OKT3 (Fig. 2 A). The affinity of the interaction (Kd = 5 nM) was deduced by Scatchard plot analysis after subtraction of nonsaturable binding, as detected in the presence of 100-fold molar excess of unlabeled L31. (B) L31-cytofluorimetry and Western blots on whole cell lymphocyte lysates at day 0 and at day 3 after OKT3 stimulation.

Figure 2. Differential reactivity of mAb L31 on live cells and on denatured proteins. (A) Binding of L31 to a cell surface antigen of activated lymphocytes. PBMC were cultured after stimulation with OKT3 and rabbit anti–mouse Ig antibodies. The number of 125I-L31 binding sites was determined by Scatchard plot analysis after subtraction of nonsaturable binding, as detected in the presence of 100-fold molar excess of unlabeled L31. (B) L31-cytofluorimetry and Western blots on whole cell lymphocyte lysates at day 0 and day 3 after OKT3 stimulation.

The hypothesis that M38 and L31 recognize two epitopes of the same cell protein, lysates from activated lymphocytes were adsorbed onto four immunoaffinity columns bearing L31, M38, and two control irrelevant isotype-matched mAbs, respectively. Either eluents or SDS-released eluates were analyzed by immunoblotting with 125I-M38 (Fig. 3 A) or 125I-L31 (Fig. 3 B). The L31 column (but not those bearing control antibodies) caused a major immunodepletion in the effluent (Fig. 3, lanes a) and an almost quantitative recovery of the 45-kD band in the eluate (lanes b). The protein band was decorated equally well by either antibody. Similar results were obtained with the M38 column, although this antibody was less efficient than L31 in retaining the 45-kD protein. These results indicate that the cell protein defined by M38 is identical to that recognized by L31.

Fine Specificity of M38 and L31. The interaction of M38 with the cellular antigen on the surface of activated lymphocytes (measured by flow cytometry) could be significantly reduced by soluble recombinant gp160; in the same conditions, the binding of mAb 01.65 (20), specific for a common determinant of HLA-A, -B, -C molecules was unaffected (Fig. 4). Also unaffected was the binding of L31 (data not shown).

To further analyze the specificities of M38 and L31 with respect to HIV-1, the two antibodies were used in gp120-related assays on living cells. 8E51(LAV) cells and MOLT3 cells, sedimented together in V-shaped wells and incubated as a pellet, form large syncytia. The assay can be inhibited by anti-CD4 mAbs and by patients sera containing neutralizing antibodies. The addition of mAb M38 resulted in a marked inhibitory effect (Fig. 5 A), while L31 and a number of mAbs (specific for HIV antigens or of irrelevant specificity) had no effect at all. These data, together with the cytofluorimetry findings on 8E51(LAV) cells, labeled by M38 and by other anti-gp120 mAbs, while not by L31 (Fig. 5 B), confirm the differential anti-gp120 specificity of M38.

M38 and L31 React with the Same Cell Protein. To confirm
Immunoselection of Recombinant Phages and Sequence Analysis of the cDNA of the Cellular Protein Defined by M38 and L31. To identify the cell protein defined by the two antibodies, 125I-L31 was used to screen a commercial XGT11 cDNA expression library from PHA-activated human PBL. Positive plaques were counter-screened with 125I-M38 and with an irrelevant radioiodinated mAb. A clone, reactive with both L31 and M38 and showing no binding with the isotype-matched control antibody, was selected. The reactivity of phage recombinant β-galactosidase was confirmed by Western blot analysis of IPTG-induced phage lysates (data not shown).

The insert (1,549 bp) was subcloned into the vector pUC8, and the recombinant plasmid (PL208) was then sequenced. The insert sequence contained an open reading frame (between nucleotide residues 10 and 1108) (Fig. 6) coding for a protein of 366 amino acids. A data bank comparison of the nucleotide sequence revealed a high degree of homology with the class I MHC gene family. The sequence is not identical to any of the already sequenced alleles, while maximal homology was found with the alleles of the C locus.

A direct comparison to all the available C alleles amino acid sequences (27, 28) is seen in Fig. 7. A 96% homology was found with allele Cb-1. The protein contains the characteristic six domains of class I MHC heavy chains (leader peptide, α 1, α 2, α 3, transmembrane, and cytoplasmic domains) and the three C-specific residues (val-52, glu-183, and glu-268). The five cysteine residues and the glycosylation site (gln-87) are conserved. Moreover, all but two variations from the consensus are in residues that show the same amino acid substitution in at least one other sequenced C allele; the two variations unique to this sequence are trp-14 and glu-49. These data strongly suggest that the sequenced polypeptide is a product of an allele of the HLA-C locus.

M38 and L31 Recognize "Hidden" Epitopes of Class I MHC α Chains. An immunological approach to confirm that the protein defined by M38 and L31 is a class I MHC heavy chain was based upon immunoprecipitations from detergent lysates of Rex cells (reactive with both M38 and L31) using either mAb 01.65 (20), specific for a common determinant of HLA-A, -B, -C molecules, or mAb R1.30, specific for βm (20). mAb OKT4 was included as a control. Both precipitates and supernatants were analyzed by immunoblotting with 125I-L31. As can be seen in Fig. 8, both antibodies precipitated...
L31-reactive material. However, mAb 01.65 precipitated most of the material, while only a fraction was bound by mAb R1.30. The control experiments with mAb OKT4 displayed all the L31-reactive material confined to the supernatant. M38 and L31 did react with the activated lymphocytes of 20 unrelated HLA-typed individuals. Further, SDS-denatured molecules immunoprecipitated from resting lymphocyte lysates by mAb CR11.351 (21), specific for HLA-A2 molecules, displayed similar reactivity when challenged with the two antibodies. As a consequence of these findings, the two epi-

---

**Figure 6.** Nucleotide sequence of the insert of a recombinant phage immunoselected by the mAbs. The insert (1,549 bp) was subcloned into the vector pUC8, and the recombinant plasmid (PL208) was then sequenced. The insert sequence contains an open reading frame (between nucleotide residues 10 and 1108) coding for 366 amino acids bearing high homology to HLA-C alleles. The first and last codons of the open reading frame are underlined. The boundaries of the six domains characteristic of class I MHC heavy chains are indicated. These sequence data are available from EMBL/Gen-Bank/DDBJ under accession number X58536.
The expression of class I MHC α chains in two different conformations. The conformation coprecipitable with β2m and inaccessible to M38 and L31 is identical to that of resting cells, while the second one is not coprecipitable with β2m and bears the "hidden" epitopes now accessible to antibodies.

The above reported findings (and their interpretation) are very similar to those of Schnabl et al. (17), who demonstrated that activated T lymphocytes express class I MHC heavy chains...
not associated with β2m. This was inferred on the basis of the reactivity of mAb LA45 with SDS-denatured, but not associated with β2m, heavy chains and with heavy chains expressed on the surface of activated (but not resting) lymphocytes.

The epitopes recognized by M38 and L31 seem to be similar to that recognized by LA45; indeed, neither our antibodies (Fig. 1 B), nor LA45, coprecipitated β2m. Conversely, the anti-β2m antibody R1.30 immunoprecipitated only a fraction of the L31-reactive material (Fig. 8), in close analogy with the observation by Schnabl et al. (17) with mAb W6/32, which immunoprecipitates only β2m-associated heavy chains.

Functional Consequences of the Interaction of M38 and L31 with Immunocytes. Schnabl et al. (17) have suggested that the conformational alteration of class I proteins upon T cell activation might have some important functional implications. In light of our previous finding of antigen presentation inhibited by M38 (16), we investigated the functional effects elicited by interaction of the two antibodies with immunocytes. Indeed, several mAbs reactive with class I monomorphic determinants were reported to influence lymphocyte proliferation in different experimental models (20, 29-31).

Inhibition of antigen presentation by M38 and lack of inhibition by L31 and controls. Tetanus toxoid presentation experiments were performed as described in Materials and Methods. (B) Inhibition of mitogenic proliferation by L31 and lack of inhibition by M38 and controls. PBMC were stimulated by crosslinked OKT3. [3H]Thymidine incorporation was evaluated at day 4. Antibodies were used as 1:200 ascites. (C) IL-2 production by human PBMC, cultured for 18 h after stimulation by crosslinked OKT3 in the presence of L31 or OKT9 (as a control).

Discussion

The interaction of CD4 to class II MHC and to HIV-1 gp120 has been recently reported as involving different domains of the molecule (12, 32). However, the finding that soluble gp120 can inhibit CD4-class II MHC binding raises the possibility that the CD4 binding sites for the two ligands may be overlapping.

To verify the hypothesis that HIV could mimic a physiological ligand of CD4, we analyzed a panel of murine mAbs raised against HIV-1 looking for crossreactivities between env products and activated human PBMC. The expectation to find a crossreactivity with class II MHC molecules was not fulfilled: instead, we characterized mAb M38, which defines an epitope shared by HIV-1 gp120 and by class I MHC heavy chains. Such a determinant proved to be monomorphic, common to HLAA, -B, -C molecules and accessible to the antibody on activated, but not resting, immunocytes.

We had earlier reported that the anti-gp120 specificity of mAb M38 was shared with an “activation protein” present on human monocytes (16). We then provided a tentative definition of the human target molecule as an “80 kD protein”, which was the most prominent band in radioimmunoprecipitation from metabolically labeled cells. The 45-kD minor band was also present, but was at the time interpreted as a nonspecific signal and overlooked. The findings obtained by several analytical approaches confidently demonstrate that the reactive protein has a molecular mass of 45 kD. The previous conclusions are likely to be referable to incomplete sample reduction: dimerization of HLA molecules in tissue extracts (33) and molecular masses of 90/45 kD under nonreducing conditions have been reported for HLA molecules (17).

Here, we report the results obtained from the analysis of L31, a mAb derived from the same fusion yielding M38. L31 proved to be specific for the same cell protein recognized...
by M38 (Fig. 3), even though lacking the crossreactivity with HIV-1 gp120. The anti-gp120 specificity of M38 was documented by western blot analysis on SDS-denatured proteins (Fig. 1) and by assays on live HIV-infected cells (i.e., inhibition of syncytia formation and cytotoxicity) (Fig. 5). M38 inhibited syncytia formation between 8E5(1LAV) and MOLT3 cells, a CD4-dependent reaction, although it did not inhibit the infectivity of free virus, as already reported (16). This finding confirms that virus penetration and syncytia formation are distinct, discrete reactions, although with common steps.

The cellular protein defined by M38 and L31 could be included among the products of class I MHC. This was inferred by sequence analysis of the cDNA (Figs. 6 and 7) from a recombinant phage expressing the epitopes recognized by the two antibodies and by immunoblotting with L31, the precipitates of mAb 01.65 (anti-HLA-A, -B, -C), of mAb R1.30 (anti-β2m) (Fig. 8), and of mAb CR11.351 (anti-HLA-A2) (20, 21). The two epitopes defined by L31 and M38 could be classified as monomorphic and common determinants of HLA-A, -B, and -C molecules. These findings explain the presence of the M38- and L31-defined protein in the retrovirus preparations used for Western blots (Fig. 1); as demonstrated by Gelderblom et al. (34), HLA proteins are present in retroviral virions.

The class I molecule recognized by the two mAbs on the surface of activated immunocytes could not be assimilated to conventional HLA molecules, since the corresponding epitopes appear to be hidden in HLA molecules present on the surface of resting immunocytes. A strikingly similar situation has recently been reported by Schnabl et al. (17). They demonstrated the reactivity of mAb LA45 with SDS-denatured (but not with β2m-associated) α chains and with α chains expressed on the surface of activated (but not resting) lymphocytes. By differential immunoprecipitations and “independent capping” experiments, they concluded that activated T lymphocytes express class I MHC heavy chains not associated with β2m, together with “conventional” β2m-associated HLA molecules. Analogous results and conclusions were reached by Smith and Barber in the mouse system (35).

The “hidden” epitopes recognized by our mAbs M38 and L31 seem to be, in all their properties, similar to that recognized by LA45 and, indeed, none of the three antibodies coprecipitated β2m. Immunohistochemistry analysis of M38 and L31 reactivity indicates that the tissue distribution is completely different from that of mAbs specific for monomorphic HLA-A, HLA-B, or for determinants common to HLA-A, -B, -C products (P. G. Natali, personal communication).

Schnabl et al. (17) hypothesize that the loss of β2m and the conformational alteration of class I MHC proteins upon T cell activation might have some important functional implications. Indeed, this issue has been already addressed in our previous work, where we showed that M38 inhibited antigen presentation (16). We have now expanded that initial observation by studying the functional consequence of the interaction of the two antibodies in lymphocyte proliferation assays. The results indicate that L31 treatment is associated with significant inhibitory effects, which are paralleled by a marked reduction of IL-2 production (Fig. 8). It is noteworthy that the interactions of the two antibodies with the target epitopes had distinct and independent effects.

The eventual relevance of the crossreactivity between HIV-1 gp120 and β2m-less class I proteins is still obscure, but two of the findings reported herein make it, in our opinion, a worthwhile field of further research. These are: (a) the involvement of the M38-defined gp120 epitope in syncytia formation; and (b) the involvement of β2m-less class I proteins in regulatory mechanisms related to fundamental immunocyte functions. Furthermore, it is known that lymphocyte activation is required to make the cell susceptible to HIV-1 infection; this could depend upon the requirement for activation products such as β2m-less class I proteins.

We thank M. Pelagi for handling the mAbs and F. Ciccomascolo for helping in the lymphocyte functional assays. We thank A. De Rossi for substantial help in setting up the syncytia formation assay, Sorin Biomedica for the generous gift of reagents, and Transgene and Pasteur Mérieux for kindly supplying recombinant gp160. We are grateful to F. Malavasi for critical reading of the manuscript and constructive suggestions. The secretarial assistance of S. Zanotta is gratefully acknowledged.

This work was supported by grants of Ministero della Sanità “Progetto AIDS 1988” and “Progetto AIDS 1989”, and by grants of Prodotti Genetici Srl., Milano.

F. Grassi, L. Lopalco and P. Lanza have fellowships from Fondazione Anna Villa Rusconi, Byk Gulden Italia, and Prodotti Genetici Srl., respectively.

Address correspondence to Antonio G. Siccardi, Dipartimento di Biologia e Genetica per le Scienze Mediche, Università di Milano, Via G. B. Viotti 3/5, I-20133 Milano, Italy.

Received for publication 26 October 1990 and in revised form 1 April 1991.
Reference
1. Klatzman, D., E. Champagne, S. Chambert, J. Gruest, D. Guettard, T. Hecq, J.C. Gluckman, and L. Motagami. 1984. P-lymphocyte T4 molecule behaves as the receptor for human retrovirus LAV. Nature (London). 312:767.
2. Dalgleish, A.G., P.C. Beverley, P.R. Clapham, D.H. Crawford, M.Y. Greaves, and R.A. Weiss. 1984. The CD4 (T4) antigen is an essential component of the receptor for the AIDS retrovirus. Nature (London). 312:763.
3. McDougal, J.S., M.S. Kennedy, J.M. Sligh, S.P. Cort, A. Mawle, and J.K.A. Nicholson. 1986. Binding of HTLV-III/LAV to T4+ T cells by a complex of the 110K viral protein and the T4 molecule. Science (Wash. DC). 231:382.
4. Biddison, W.E., P.E. Rao, M.A. Talle, G. Goldstein, and S. Shaw. 1982. Possible involvement of the OKT4 molecule in T cell recognition of class II HLA antigens. J. Exp. Med. 156:1065.
5. Marrack, P., R. Endres, R. Shimonkevitz, A. Zlotnik, D. D'alyanas, F. Fitch, and J. Kappler. 1983. The Major histocompatibility complex-restricted antigen receptor on T cells. II. Role of the LYT4 product. J. Exp. Med. 158:1077.
6. Sleckman, B.P., A. Peterson, W.K. Jones, J.A. Foran, J.L. Greenstein, B. Seed, and S.J. Burakoff. 1987. Expression and function of CD4 in a murine T-cell hybridoma. Nature (London). 328:351.
7. Siliciano, R.F., T. Lawton, C. Knall, R.W. Karr, P. Berman, T. Gregory, and E.L. Reinherz. 1988. Analysis of host-virus interactions in AIDS with anti-gp120 T cell clones: effect of HIV sequence variation and a mechanism for CD4+ cell depletion. Cell. 54:561.
8. Lanzavecchia, A., E. Roosnek, T. Gregory, P. Berman, and S. Aigrignani. 1988. T cells can present antigens such as HIV gp120 targeted to their own surface molecules. Nature (London). 334:550.
9. Chanh, T.C., G.R. Dressman, and R.C. Kennedy. 1987. Monoclonal anti-idiotypic antibody mimics the CD4 receptor and binds human immunodeficiency virus. Proc. Natl. Acad. Sci. USA. 84:3891.
10. Mittler, R.S., and M.K. Hoffmann. 1989. Synergism between HIV gp120 and gp120-specific antibody in blocking human T cell activation. Science (Wash. DC). 245:1380.
11. Kruisbeek, A.M., J.J. Mond, B.J. Fowlkes, J.A. Carmen, S. Bridges, and D.L. Longo. 1985. Absence of the LYT-2+, LYT4+ lineages of T cells in mice treated neonatally with anti-LA correlates with absence of intrathymic LYT-bearing antigen-presenting cell function. J. Exp. Med. 161:1029.
12. Clayton, L.K., M. Sieh, D.A. Fous, and E.L. Reinherz. 1989. Identification of human CD4 residues affecting class II MHC versus HIV-1 gp120 binding. Nature (London). 339:348.
13. Kupfer, A., S.J. Singer, C.A. Janeway, and S.L. Swain. 1987. Cooclustering of CD4 (LYT4) molecule with the T-cell receptor is induced by specific direct interaction of helper T cells and antigen-presenting cells. Proc. Natl. Acad. Sci. USA. 84:5888.
14. Gay, D., P. Maddon, R. Sekaly, M.A. Talle, M. Godfrey, E. Long, G. Goldstein, L. Chess, R. Axel, J. Kappler, and P. Marrack. 1987. Functional interaction between human T-cell protein CD4 and the major histocompatibility complex HLA-DR antigen. Nature (London). 328:626.
15. Golding, H., F.A. Robey, E.T. Gates III, W. Linder, P.R. Beining, T. Hoffman, and B. Golding. 1988. Identification of homologous regions in human immunodeficiency virus I gp41 and human MHC class II B I domain. J. Exp. Med. 167:914.
16. Beretta, A., F. Grassi, M. Pelagi, A. Clivio, C. Parravicini, G. Giovinazzo, F. Andronico, L. Lopalo, P. Verani, S. Buttò, F. Titi, G.B. Rossi, G. Viale, E. Ginelli, and A.G. Siccardi. 1987. HIV env glycoprotein shares a cross-reacting epitope with a surface protein present an activated human monocytes and involved in antigen presentation. Eur. J. Immunol. 17:1793.
17. Schnabl, E., H. Stockinger, O. Majdic, H. Gauditsch, I.J.D. Lindley, D. Maurer, A. Hajek-Rosennay, and W. Knapp. 1990. Activated human T lymphocytes express MHC class I heavy chains not associated with β2-microglobulin. J. Exp. Med. 171:1431.
18. Smith, K.A., M.F. Favata, and S. Oroszlan. 1983. Production and characterization of monoclonal antibodies to human intercellulin 2: strategy and tactics. J. Immunol. 131:1808.
19. Beverly, P.C.L., and R.E. Callard. 1981. Distinctive functional characteristics of human T lymphocytes defined by B rosetting or a monoclonal anti-T cell antibody. Eur. J. Immunol. 11:329.
20. Spagnoli, G.C., C.M. Ausiello, A. Cassone, C.U. Casciani, G. Bellone, and F. Malavasi. 1987. Inhibitory effects of anti-HLA- A, B, C heavy chain and anti-β2 microglobulin monoclonal antibodies on alloantigen and microbial antigen-induced immune responses in vitro. J. Immunol. 25:555.
21. Russo, C., A.K. Ng, M.A. Pellegrini, and S. Ferrone. 1987. The monoclonal antibody CR 11.351 discriminates HLA-A2 variants identified by T cells. Immunogenetics. 18:23.
22. Friedrich, B., M. Lundstrom, and M. Gullberg. 1986. Interleukin 2 versus phorbol-ester-induced cellular events in normal T lymphocytes. Med. Oncol. Tumor Pharmacother 3:237.
23. Folks, T.M., D. Powell, M. Lightfoote, S. Koenig, A.S. Fauci, S. Benn, A. Rabson, D. Daugherty, H.E. Gendelman, M.D. Hoggan, S. Venkatesan, and M.A. Martin. 1986. Biological and biochemical characterization of a cloned leu-3+ cell surviving infection with the acquired immune deficiency syndrome retrovirus. J. Exp. Med. 164:280.
24. Young, R.A., and R.W. Davis. 1983. Effcient isolation of genes by using antibody probes. Proc. Natl. Acad. Sci. USA. 80:1194.
25. Sanger, F., S. Nicklen, and A.R. Coulslon. 1977. DNA sequencing with chain-terminating inhibitors. Proc. Natl. Acad. Sci. USA. 74:5463.
26. Gillis, S., M.M. Ferm, W. Ou, and K.A. Smith. 1978. T cell growth factor: parameters of production and a quantitative microassay for activity. J. Immunol. 120:2027.
27. Titenesky, D., R. DeMars, E.W. Holowachuk, and T.L. Delovitch. 1989. Sequence and gene transfer analysis of HLA-CWBL18 (HLA-C blank) and HLA-CW5 genes. J. Immunol. 143:349.
28. Takiguchi, M., I. Nishimura, H. Hayashi, S. Karaki, A. Kariyone, and K. Kano. 1989. The structure and expression of genes encoding serologically undetected HL-A-C locus antigens. J. Immunol. 143:1372.
29. Sterkers, G., Y. Henin, J. Kalil, M. Bagot, and J.P. Levy. 1983. Influence of HLA class I- and class II-specific monoclonal antibodies on DR-restricted lymphoproliferative responses. J. Immunol. 131:2735.
30. Choushi, S., K. Wèle, and B. Dupont. 1985. Differential effect of anti-β2-microglobulin on IL-2 production and IL-2 receptor expression in the primary mixed lymphocyte culture reaction. J. Immunol. 134:940.
31. Turco, M.C., M. De Felice, L. Corbo, G. Morrone, R. Mertelmann, S. Ferrone, and S. Venuta. 1985. Regulatory role
of a monomorphic determinant of HLA Class I antigens in T cell proliferation. J. Immunol. 135:2268.
32. Lamarre, D., A. Ashkenazi, S. Fleury, D.H. Smith, R.P. Sekaly, and D.J. Capon. 1989. The MHC-binding and gp120-binding functions of CD4 are separable. Science (Wash. DC).N 245:743.
33. Snary, D., P. Goodfellow, W.F. Bodmer, and M.J. Crumpton. 1975. Evidence against a dimeric structure for membrane-bound HLA antigens. Nature (Lond.). 258:240.
34. Gelderblom, H.R., M. Ozel, and G. Pauli. 1989. Morphogenesis and morphology of HIV. Structure-function relations. Arch. Virol. 106:1.
35. Smith, M.H., and B.H. Barber. 1990. The conformational flexibility of class I H-2 molecules as revealed by anti-peptide antibodies specific for intracytoplasmic determinants: differential reactivity of β2-microglobulin “bound” and “free” H-2Kb heavy chains. Mol. Immunol. 27:169.