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Short Communication

Infection of macaques with simian immunodeficiency virus induces a species-specific antibody response to major histocompatibility complex class I and class II molecules

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Envelopes of retroviruses, including human immunodeficiency virus and simian immunodeficiency virus (SIV), contain host cell proteins that potentially represent novel targets for vaccine development. We show here that sera from rhesus macaques recognized simian major histocompatibility complex (MHC) molecules in response to infection with SIV. Antibodies from these animals did not cross-react with human MHC antigens on mitogen-activated peripheral blood mononuclear cells. The development of antibodies to MHC class I α-chain did not correlate with anti-SIV envelope antibody responses, suggesting that these antibodies did not arise through molecular mimicry. In contrast to the species-specific response in infected animals, sera from animals vaccinated with inactivated human cell-grown SIV reacted to both human and rhesus MHC class I and class II molecules.

Envelopes of immunodeficiency lentiviruses including human immunodeficiency virus (HIV) and simian immunodeficiency virus (SIV) contain, in addition to virus-encoded glycoproteins, host cell membrane proteins, particularly molecules encoded by the major histocompatibility complex (MHC) (reviewed in Tremblay *et al.*, 1998). MHC molecules are present in virions at levels exceeding gp120/gp41 (Henderson *et al.*, 1987; Arthur *et al.*, 1992) and are incorporated non-randomly (Hoxie *et al.*, 1987; Poon *et al.*, 2000; Nguyen & Hildreth, 2000). Furthermore, it has been shown that incorporation of HLA-DR by clinical isolates of HIV-1 expanded in primary human cells depends on the producing cell and the donor source (Cantin *et al.*, 2001).

The influence of immune responses to virus-incorporated host cell antigens was dramatically illustrated when vaccination with uninfected human T-cells was shown to protect a proportion of macaques against challenge with human cell-grown SIV (Stott, 1991). Furthermore, human cell-grown SIV and HIV inactivated virus vaccines conferred potent protection against systemic autologous and heterologous virus challenge and even against mucosal challenge (Cranage *et al.*, 1992a) but only when the challenge virus was grown in human cells. Critically, no vaccine-induced protection was seen against SIV that had been grown in simian cells (Cranage *et al.*, 1992b). This xeno-immunization effect was correlated with antibody responses to human MHC class I antigens (Chan *et al.*, 1992; Cranage *et al.*, 1993). A direct demonstration of the role of xeno-MHC molecules in this vaccine effect was the finding that a proportion of macaques were protected from challenge with human cell-grown SIV following immunization with purified human MHC class I (Chan *et al.*, 1995), class II (Arthur *et al.*, 1995) or L-cells transfected with HLA-DR4 (Stott *et al.*, 1994). In the latter case it was shown that protective immunity could be passively transferred to naïve macaques.

Much less is known about the biological significance of virion-incorporated allogeneic host cell molecules, i.e. the situation arising in nature, and immune responses directed against these proteins; however, it is reasonable to assume that virion-incorporated molecules may influence virus pathogenesis including early entry events and activation of the immune system. This is evidenced by studies indicating that these molecules may maintain function after incorporation into virions (Rossio *et al.*, 1995; Fortin *et al.*, 1997; Cantin *et al.*, 1997; Saifuddin *et al.*, 1994). Anti-lymphocyte antibodies have been associated with infection by HIV (Dorsett *et al.*, 1985; Müller *et al.*, 1994; Riera *et al.*, 1992; Daniel *et al.*, 1989; Ozturk *et al.*, 1987) and it has been suggested that immune responses to regions of MHC homology within virus-encoded proteins may be involved in HIV- and SIV-induced pathology (Habeshaw, 1994; Kion & Hoffmann, 1991; Grassi *et al.*, 1991). Antibodies to MHC molecules during infection may arise therefore through recognition of virion-acquired host proteins and/or through molecular mimicry.

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In this study we have investigated the specificity of anti-cell antibody responses arising during SIV infection in comparison to those induced by vaccination with inactivated-human cell-grown virus.

Flow cytometry of concanavalin-A activated (10 μg ml^{-1}, 72 h) human and rhesus peripheral blood mononuclear cells (PBMC) revealed that sera from SIV-infected animals ($n=7$), taken at various times 3 to 18 weeks after infection, bound to rhesus but not to human cells (data not shown). In contrast, sera from animals vaccinated with human cell-grown SIV or HIV-1 ($n=12$) bound to cells from both species although preferentially to human cells, confirming previously reported results (Langlois *et al.*, 1992; Bergmeier *et al.*, 1994). Sera from neither infected nor vaccinated animals competed the binding of labelled monoclonal antibodies (W6/32 and CR3/43) against species cross-reactive monomorphic anti-MHC class I or class II antigens.

To determine directly the cell surface targets of the anti-cell antibodies and to investigate the molecular specificity of the differential antibody binding activity seen by flow cytometry, activated human and rhesus PBMC were surface labelled with biotin (Meier *et al.*, 1992) and serum reactivity was determined by immunoprecipitation (Fig. 1).

Sera from naïve animals or from animals infected with SIV were essentially unreactive with labelled membranes of human PBMC (Fig. 1a, tracks 1 and 2). Sera from vaccinated animals precipitated various proteins including species of 12, 32, 35 and 43 kDa (Fig. 1a, track 3) co-migrating with proteins precipitated by antibodies to MHC class II (32 and 35 kDa; β- and α-chains respectively) and to HLA class I (12 and 43 kDa; β- and α-chains respectively) (Fig. 1a, tracks 4 and 5 respectively). These results were consistent with those described previously, following immunoprecipitation of unlabelled cell lysates followed by Western blotting and probing with MHC-specific labelled antibodies (Cranage *et al.*, 1993). In addition, the previous study revealed that sera from vaccinated macaques precipitated an 86 kDa dimer of the class I heavy chain detectable under non-reducing conditions. A biotinylated species of 86 kDa was detected in the present study but was not precipitated by the anti-class I monoclonal antibody.

In contrast to the results with human PBMC, when surface-labelled rhesus PBMC were used, sera from SIV-infected macaques precipitated a range of proteins of relative molecular mass 47 to 25 kDa (Fig. 1b, track 2), corresponding to species precipitated by sera from vaccinated animals (Fig. 1b, track 3). In addition, sera from vaccinated animals precipitated proteins of 66, 60, 56 and 12 kDa. Sera from both infected and vaccinated macaques precipitated proteins that corresponded in migration to MHC class II and class I heavy chains (Fig. 1b, tracks 4 and 5 respectively).

Next, to confirm the specificity of sera for MHC molecules, non-labelled lysates of mitogen-activated PBMC were used in immunoprecipitation assays. Eluted products were separated by SDS-PAGE and the presence of MHC class I

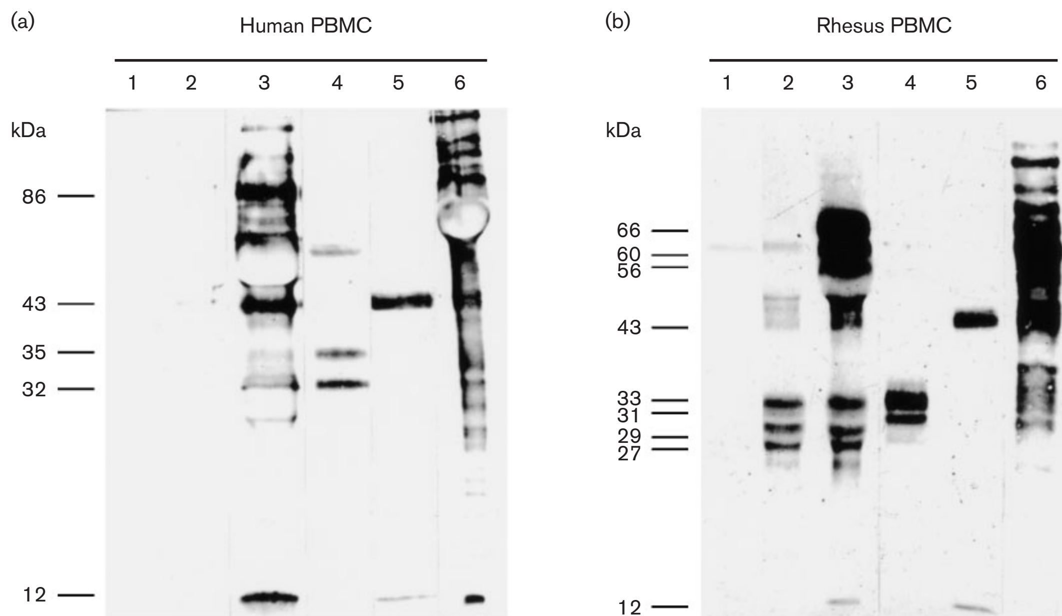

Fig. 1. Antibodies in SIV-infected macaques precipitate proteins from surface-labelled rhesus PBMC that co-migrate with MHC molecules. Lysates of surface-biotinylated human PBMC (a) or rhesus PBMC (b) were immune-precipitated with macaque serum taken pre-inoculation (1); from SIV-infected macaques (2); from SIV-vaccinated animals (3) or with monoclonal anti-MHC class II (4) or monoclonal anti-MHC class I (5). Track 6 shows total lysates. Representative results are shown for a SIV-infected and a SIV-vaccinated macaque.

and class II antigens was determined on Western blots essentially as described previously (Cranage *et al.*, 1993). When blots of products eluted from human and rhesus PBMC were probed with anti-MHC class I antibody (HC10), sera from vaccinates were found to precipitate class I α-chain from either species, although the strongest signal was obtained with human antigen (Fig. 2a and b, track 4). In contrast, sera from SIV-infected animals precipitated MHC class I α-chain only from rhesus PBMC lysates (Fig. 2a, b, track 3). Similar results were obtained for β_2-microglobulin and confirmed by ELISA (data not shown). The MHC class I α-chain was usually detected as a doublet of relative molecular mass 43/45 kDa in both human and rhesus preparations. Similarly, when immunoprecipitated products were probed with anti-MHC class II (CR3/43) (Fig. 2c, d), sera from vaccinates precipitated both human and rhesus class II (track 4) but sera from SIV-infected animals precipitated only rhesus MHC class II (track 3). Interestingly, vaccinate sera precipitated only the 31 kDa class II band. Sera from SIV-infected macaques precipitated both the 33 and 31 kDa class II band, although the relative intensity of the two bands was quite variable in different experiments.

Thus, in contrast to the cross-reactive antibody response induced by vaccination with inactivated virus, SIV-infected macaques had antibodies that specifically recognized macaque MHC but failed to recognize human MHC. We believe this to be the first report of a species-specific anti-MHC antibody response in SIV infection. Anti-lymphocyte antibody responses have been reported in virus infections including infection with HIV-1 but little is known about why they arise and their specificity. The species specificity of the reactivity shown here by flow cytometry and immunoprecipitation of surface labelled PBMC was surprising and was, at least in part, linked to recognition of MHC molecules. Anti-HLA antibodies arising in infection with HIV-1 have been attributed to molecular mimicry. Specifically, antibodies to the immunodominant C5 region of HIV-1 gp120 have been shown to cross-react with HLA class I on activated cells (De Santis *et al.*, 1994). Antibodies that cross-react with HIV-1 gp120 and HLA α-chains have been induced in persons vaccinated with experimental HIV-1 envelope vaccines (De Santis *et al.*, 1993) and antibodies to MHC class II have been described in patients with AIDS (De La Barrera *et al.*, 1987). A common epitope between HIV-1 gp41 and HLA class II has been described and one third of sera tested from HIV-1 infected individuals at different stages of disease were found to react with gp41 and HLA class II-derived peptides as well as with native HLA class II molecules (Golding *et al.*, 1989).

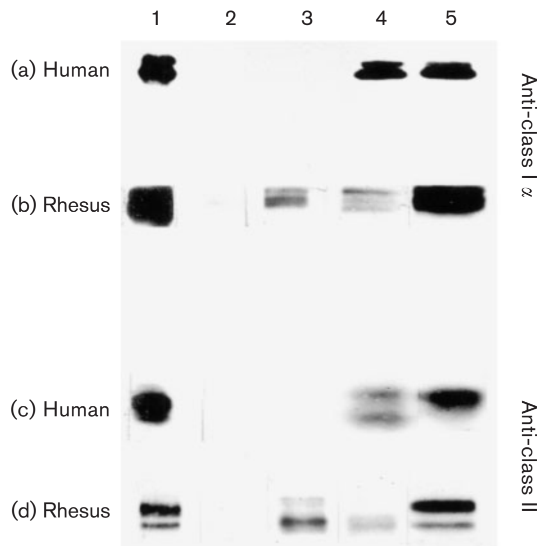

Fig. 2. SIV-infected macaques have antibodies to rhesus MHC molecules but not to human MHC molecules. Unlabelled lysates of human (a, c) or rhesus (b, d) PBMC were electrophoresed directly (1) or first precipitated with macaque pre-inoculation serum (2); serum from SIV-infected macaques (3); serum from SIV-vaccinated macaques (4); monoclonal antibodies against MHC class I and II (5). Separated proteins were Western blotted and probed with monoclonal antibody, HC10, against MHC class I (a, b) or with monoclonal antibody CR3/43 against MHC class II (c, d). A representative result is shown for a SIV-infected and a SIV-vaccinated macaque.

To determine if anti-MHC responses were related to SIV-specific immune responses serial serum samples taken from seven macaques were analysed for the development of anti-rhesus MHC class I α-chain antibody responses and antibody responses to SIV structural components following infection with SIV (Table 1). Pre-inoculation sera did not react with any of the antigens tested. Anti-MHC class I responses usually occurred by 1 month after infection and in three instances were detectable prior to an anti-SIV envelope response. In one animal (K8) the anti-class I response appeared in the absence of responses to SIV Gag p27 and SIV Env gp120. This animal was definitely infected with SIV as evidenced by virus isolation from PBMC and detection of proviral DNA by PCR. Although K8 failed to make a response to gp120 at any time following infection and had a delayed response to SIV gp41, the anti-class I response peaked between 3 and 7 months post-infection. In contrast, animal 3H had no detectable anti-class I response until 3 months after infection but had seroconverted to SIV antigens 1 to 2 months after infection. The lack of correlation between the appearance of the anti-MHC class I response and the appearance of anti-SIV responses suggests that molecular mimicry, at least for MHC class I, is unlikely. The possibility of molecular mimicry cannot be excluded absolutely. It is possible that precipitating anti-MHC antibodies appear before antibodies reactive on Western blots; however, this is not supported by the results from animal 3H where anti-SIV responses precede the anti-MHC class I antibody response. If molecular mimicry does occur then the species-specific recognition of MHC implies a close evolutionary relationship between virus cross-reactive

Table 1. Lack of correlation between serum antibody responses to MHC class I α-chain and to SIV structural proteins

Intensity of response is shown semi-quantitatively on a scale from +/−, for a very weak reaction to + + + for a strong reaction.

		Antibody response to:						
			SIV Env		SIV Gag			
Animal no.	Months post-infection	Simian MHC class I α	gp120	gp32/41	p55	p27	p17	SIV RT p68/59
32H	0	−	−	−	−	−	−	−
	1	+ + +	+/−	−	+ +	+ + +	+/−	+ +
	2	+	+ +	+ + +	+ +	+ + +	+/−	+ + +
	5	+ + +	+ + +	+ + +	+ + +	+ + +	+ +	+ + +
	12	+ +	+ + +	+ + +	+ + +	+ + +	+	+ + +
K8	0	−	−	−	−	−	−	−
	1	+	−	−	−	−	−	+/−
	2	+	−	−	−	−	+/−	+ +
	3	+ + +	−	−	−	−	−	+ +
	4	+ + +	−	+/−	−	−	−	+ +
	7	+ + +	−	+ + +	+/−	+	+/−	+ +
	9	+ +	−	+ + +	−	−	+	+
	12	+ +	−	+ + +	−	+/−	+	+
I4	0	−	−	−	−	−	−	−
	1	+ +	−	−	+ +	+ + +	+	+ + +
	2	+ +	+	+ +	+ + +	+ + +	+ +	+ + +
	3	+ +	+ +	+ + +	+ + +	+ + +	+ +	+ + +
	4	+ +	+ + +	+ + +	+ + +	+ + +	+ +	+ + +
	12	+ +	+ + +	+ + +	+ + +	+ + +	+ +	+ + +
44H	0	−	−	−	−	−	−	−
	1	+ +	−	+/−	+ + +	+ + +	+ + +	+ + +
	2	+ +	−	+ + +	+ + +	+ + +	+ + +	+ + +
	3·5	+ +	+	+ + +	+ + +	+ + +	+ + +	+ + +
I67	0	−	−	−	−	−	−	−
	1	−	−	+	+	+ + +	+ + +	+ +
	2	+ + +	−	+ + +	+ + +	+ + +	+ + +	+ + +
	3	+ + +	+	+ + +	+ + +	+ + +	+ + +	+ + +
	4	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +
	11	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +
27H	0	−	−	−	−	−	−	−
	1	+/−	−	−	+ + +	+ + +	+ +	+ + +
	2	+	+ + +	+ +	+ + +	+ + +	+ + +	+ + +
	3	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +
3H	0	−	−	−	−	−	−	−
	1	−	+/−	−	+ + +	+ + +	+ + +	+ + +
	2	−	+ + +	+ +	+ + +	+ + +	+ + +	+ + +
	3	+	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +
	4	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +

region(s) and host species perhaps conferring some selective advantage on the virus.

Other hypotheses to explain our findings include: early immune dysregulation induced by infection with SIV leading to a breakdown of tolerance; massive destruction of lymphocytes leading to enhanced presentation of cellular components and presentation of altered or immature MHC molecules due to acquisition by newly synthesized virions. Whilst the acquisition of host cell molecules by HIV and SIV is well documented, little is known about the physical state of these molecules. There may be structural constraints imposed by the virion-encoded proteins leading to selectivity of host cell molecule incorporation. For example, incorporation of MHC class II may require association with gp41 and the incorporation of MHC class I is haplotype dependent (Poon *et al.*, 2000). This may, at least in part, explain the species specificity reported in the present study. Antibodies to other, as yet unidentified host cell proteins, seen in this study, may arise in a similar manner. It is known that in addition to MHC molecules immunodeficiency viruses can incorporate molecules such as complement

control proteins (Saifuddin *et al.*, 1995) and adhesion molecules that have significant species variability.

Do anti-MHC antibody responses have functional significance? Recently, it has been shown that human antibodies to MHC alloantigens mediate lysis and neutralization of HIV-1 primary isolates in the presence of complement (Spear *et al.*, 2001). Anti-MHC class I antibodies may also have a role in virus clearance through opsinization (Benkirane *et al.*, 1994). Although antibodies induced by alloimmunization with a B-lymphoblastoid cell line (B-LCL) failed to protect macaques against SIV infection (Polyanskaya *et al.*, 1997), the anti-MHC response induced was incomplete. In another study, immunization of macaques with allogeneic lymphocytes protected 50 % of animals challenged (E. J. Stott and others, personal communication). The finding that infection-related antibodies recognize virion-acquired host cell proteins needs further investigation as this may suggest novel targets for anti-envelope vaccine design.

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REFERENCES

Arthur, L. O., Bess, J. W., Jr, Sowder, R. C., II, Benveniste, R. E., Mann, D. L., Chermann, J. C. & Henderson, L. E. (1992). Cellular proteins bound to immunodeficiency viruses: implications for pathogenesis and vaccines. *Science* **258**, 1935–1938.

Arthur, L. O., Bess, J. W., Jr, Urban, R. G., Strominger, J. L., Morton, W. L., Mann, D. L., Henderson, L. E. & Benveniste, R. E. (1995). Macaques immunized with HLA-DR are protected from challenge with simian immunodeficiency virus. *J Virol* **69**, 3117–3124.

Benkirane, M., Blanc-Zouaoui, D., Hirn, M. & Devaux, C. (1994). Involvement of human leukocyte antigen class I molecules in human immunodeficiency virus infection of CD4-positive cells. *J Virol* **68**, 6332–6339.

Bergmeier, L. A., Walker, J., Tao, L., Cranage, M. & Lehner, T. (1994). Antibodies to human and non-human primate cellular and culture medium components in macaques vaccinated with the simian immunodeficiency virus. *Immunology* **83**, 213–220.

Cantin, R., Fortin, J.-F., Lamontagne, G. & Tremblay, M. (1997). The presence of host-derived HLA-DR1 on human immunodeficiency virus type 1 increases viral infectivity. *J Virol* **71**, 1922–1930.

Cantin, R., Martin, G. & Tremblay, M. J. (2001). A novel virus capture assay reveals a differential acquisition of host HLA-DR by clinical isolates of human immunodeficiency virus type 1 expanded in primary human cells depending on the nature of producing cells and the donor source. *J Gen Virol* **82**, 2979–2987.

Chan, W. L., Rodgers, A., Hancock, R. D., Taffs, F., Kitchin, P., Farrar, G. & Liew, F. Y. (1992). Protection of simian immunodeficiency virus-vaccinated monkeys correlates with anti-HLA class I antibody response. *J Exp Med* **176**, 1203–1207.

Chan, W. L., Rodgers, A., Grief, C. & 8 other authors (1995). Immunization with class I human histocompatibility leukocyte antigen can protect macaques against challenge infection with $SIV_{mac-32H}$. *AIDS* **9**, 223–228.

Cranage, M. P., Baskerville, A., Ashworth, L. A. E. & 7 other authors (1992a). Intrarectal challenge of macaques vaccinated with formalin-inactivated simian immunodeficiency virus. *Lancet* **339**, 273–274.

Cranage, M. P., Ashworth, L. A. E., Greenaway, P. J., Murphey-Corb, M. & Desrosiers, R. C. (1992b). AIDS vaccine developments. *Nature* **355**, 685–686.

Cranage, M. P., Polyanskaya, N., McBride, B. & 12 other authors (1993). Studies on the specificity of the vaccine effect elicited by inactivated simian immunodeficiency virus. *AIDS Res Hum Retrovir* **9**, 13–22.

Daniel, V., Schimpf, K. & Opelz, G. (1989). Lymphocyte autoantibodies and alloantibodies in HIV-positive haemophilia patients. *Clin Exp Immunol* **75**, 178–183.

De La Barrera, S., Fainboim, L., Lugo, S., Picchio, G. R., Muchnik, G. R. & De Bracco, M. M. E. (1987). Anti-class II antibodies in AIDS patients and AIDS-risk groups. *Immunology* **62**, 599–604.

De Santis, C., Robbioni, P., Longhi, R., Lopalco, L., Siccardi, A. G., Beretta, A. & Roberts, N. J., Jr (1993). Cross-reactive response to human immunodeficiency virus type 1 (HIV-1) gp120 and HLA class I heavy chains induced by receipt of HIV-1-derived envelope vaccines. *J Infect Dis* **168**, 1396–1403.

De Santis, C., Lapalco, L., Robbioni, P., Longhi, R., Rappocciolo, G., Siccardi, A. G. & Beretta, A. (1994). Human antibodies to immunodominant C5 region of HIV-1 gp120 cross-react with HLA class I on activated cells. *AIDS Res Hum Retrovir* **10**, 157–162.

Dorsett, B., Cronin, W., Chuma, V. & Iochim, H. L. (1985). Anti-lymphocyte antibodies in patients with the acquired immune deficiency syndrome. *Am J Med* **78**, 621–626.

Fortin, J.-F., Cantin, R., Lamontagne, G. & Tremblay, M. (1997). Host-derived ICAM-1 glycoproteins incorporated on human immunodeficiency virus type 1 are biologically active and enhance viral infectivity. *J Virol* **71**, 3588–3596.

Golding, H., Shearer, G. M., Hillman, K. & 7 other authors (1989). Common epitope in human immunodeficiency virus (HIV) 1-gp41 and HLA class II elicits immunosuppressive autoantibodies capable of contributing to immune dysfunction in HIV 1-infected individuals. *J Clin Invest* **83**, 1430–1435.

Grassi, F., Menervi, R., Gullberg, M. & 9 other authors (1991). Human immunodeficiency virus type 1 gp120 mimics a hidden monomorphic epitope borne by class I major histocompatibility complex heavy chains. *J Exp Med* **174**, 53–62.

Habeshaw, J. A. (1994). HLA mimicry by HIV-1 gp120 in the pathogenesis of AIDS. *Immunol Today* **15**, 39–40.

Henderson, L. E., Sowder, R., Copeland, T. D., Oroszlan, S., Arthur, L. O., Robey, W. G. & Fischinger, P. J. (1987). Direct identification of class II histo-compatibility Dr proteins in preparations of human T-cell lymphotropic virus type III. *J Virol* **61**, 629–632.

Hoxie, J. A., Fitzharris, T. P., Youngbar, P. R., Mathews, S. D. M., Rackowski, J. L. & Radka, S. F. (1987). Non-random association of cellular antigens with HTLV-III virions. *Hum Immunol* **18**, 39–52.

Kion, T. A. & Hoffmann, G. W. (1991). Anti-HIV and anti-MHC antibodies in alloimmune and autoimmune mice. *Science* **253**, 1138–1140.

Langlois, A. J., Weinhold, K. J., Mathews, T. J., Greenberg, M. L. & Bolognesi, D. P. (1992). Detection of anti-human cell antibodies in sera from macaques immunized with whole inactivated virus. *AIDS Res Hum Retrovir* **8**, 1641–1652.

Meier, T., Arni, S., Malarkannan, S., Poincelet, M. & Hoessli, D. (1992). Immunodetection of biotinylated lymphocyte-surface proteins by enhanced chemiluminescence: a nonradioactive method for cell-surface protein analysis. *Anal Biochem* **204**, 220–226.

Müller, C., Kukel, S., Schneweis, K. E. & Bauer, R. (1994). Anti-lymphocyte antibodies in plasma of HIV-1-infected patients

preferentially react with MHC class II-negative T cells and are linked to antibodies against gp41. *Clin Exp Immunol* **97**, 367–372.

Nguyen, D. H. & Hildreth, J. E. (2000). Evidence for budding of human immunodeficiency virus type 1 selectively from glycolipid-enriched membrane lipid rafts. *J Virol* **74**, 3264–3272.

Ozturk, G. E., Kohler, P. F., Horsburgh, C. R., Jr & Kirkpatrick, C. H. (1987). The significance of anti-lymphocyte antibodies in patients with acquired immune deficiency syndrome (AIDS) and their sexual partners. *J Clin Immunol* **7**, 130–139.

Polyanskaya, N., Sharpe, S., Cook, N., Leech, S., Banks, J., Dennis, M., Hall, G., Stott, J. & Cranage, M. (1997). Anti-major histocompatibility complex antibody responses to simian B cells do not protect macaques against SIV_{mac} infection. *AIDS Res Hum Retrovir* **13**, 923–931.

Poon, D. T., Coren, L. V. & Ott, D. E. (2000). Efficient incorporation of HLA class II onto human immunodeficiency virus type 1 requires envelope glycoprotein packaging. *J Virol* **74**, 3918–3923.

Riera, N. E., Galassi, N., de la Berrera, S., Rickard, E., Muchinik, G., Perez-Bianco, R. & de Bracco, M. M. E. (1992). Anti-leukocyte antibodies as a consequence of HIV infection in HIV^{+} individuals. *Immunol Lett* **33**, 99–104.

Rossio, J. L., Bess, J., Jr, Henderson, L. E., Cresswell, P. & Arthur, L. O. (1995). HLA class II on HIV particles is functional in superantigen presentation to human T cells: implications for HIV pathogenesis. *AIDS Res Hum Retrovir* **11**, 1433–1439.

Saifuddin, M., Ghassemi, M., Patki, C., Parker, C. J. & Spear, G. T. (1994). Host cell components affect the sensitivity of HIV type 1 to complement-mediated virolysis. *AIDS Res Hum Retrovir* **10**, 829–837.

Saifuddin, M., Parker, C. J., Peebles, M. E., Gorny, M. K., Zolla-Pazner, S., Ghassemi, M., Rooney, I. A., Atkinson, J. P. & Spear, G. T. (1995). Role of virion-associated glycosylphosphatidylinositol-linked proteins CD55 and CD59 in complement resistance of cell line-derived and primary isolates of HIV-1. *J Exp Med* **182**, 501–509.

Spear, G. T., Olinger, G. G., Saifuddin, M. & Gebel, H. M. (2001). Human antibodies to major histocompatibility complex alloantigens mediate lysis and neutralization of HIV-1 primary isolate virions in the presence of complement. *J Acquir Immune Defic Syndr* **26**, 103–110.

Stott, E. J. (1991). Anti-cell antibody in macaques. *Nature* **353**, 393.

Stott, E. J., Almond, N., West, W., Kent, K., Cranage, M. P. & Rud, E. (1994). Protection against simian immunodeficiency virus infection of macaques by cellular or viral antigens. *Neuviéme Colloque des Cent Gardes* 219–224.

Tremblay, M. J., Fortin, J.-F. & Cantin, R. (1998). The acquisition of host-encoded proteins by nascent HIV-1. *Immunol Today* **19**, 346–351.