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Rapid CD4 T cell depletion in human-PBL-SCID cells may be mediated by non-cytotoxic macrophage-tropic isolates of HIV. D. E. Mosier, R. J. Galizia, P. D. Masurac, E. B. Torbett, and J. A. Levy. The Scripps Research Institute, La Jolla, CA 92037 and UCSF, San Francisco, CA 94143.

Distinct isolates of human immunodeficiency virus (HIV) differ in their tropism, rate of replication, pathogenicity, and ability to infect distinct target cells. We have compared a panel of molecularly cloned HIV-1 or HIV-2 isolates which differ in their biologic properties for their ability to deplete CD4 T cells in vivo by using them to infect SCID, GM-CSF, and GM-CSF receptor-negative (hu-PBL-SCID) mice. The macrophage-tropic strains HIV-Ig58 and HIV-2cd16, which are non-cytotoxic in vitro, induced the most rapid and extensive CD4 T cell depletion in the hu-PBL-SCID model, whereas HIV-Ig53, which is highly cytotoxic for T cells in vitro, caused the slowest and least extensive CD4 T cell depletion in vivo. The rate of CD4 T cell depletion in hu-PBL-SCID mice was not correlated with viral burden, as HIV-Ig53 showed higher replication capacity than other strains in vivo as well as in vitro. The HIV sequence in the env gene that is associated with macrophage-tropic herpesvirus correlate with enhanced capacity for CD4 T cell depletion in the hu-PBL-SCID model, but not for cytotoxic effects in tissue culture. The rate of CD4 depletion is more dependent on the particular viral strain than the extent of viral replication, implying a role for pathogenic sequences encoded in the env gene.

HIV-specific T cell help in newborns of HIV-infected women. M. Clerici*, A. A. V. Sison#, J. A. Berzofsky*, T. Rakusan*, H. K. Gajdusek, R. A. Gallo, and J. A. Levy. Immunity Section, Laboratory of Clinical Investigation, NIAID, National Institutes of Health, Bethesda, MD 20892. In vivo, T helper cells (TH) function by interleukin 2 (IL-2) production in response to HIV and non-HIV antigens to determine whether HIV-specific TH function of mother and/or infant correlated with absence of mother-to-infant transmission of HIV. Polymorphic chain reaction and viral culture assays were performed to determine HIV infection of the infants. PBMC from 10/25 (40%) mothers tested and from 6/23 (26%) newborns were positive for HIV. All three of the infected newborns were unresponsive to one, and none of the 10 offspring who were responsive to one were born to infants who were infected. No correlation was detected between the mothers' TH-specific TH response and viral transmission of HIV. In vitro T cell reactivity of mother and newborn were not correlated. These results demonstrate that exposure to HIV antigens can occur in utero and that such exposure may be an important factor in the development of the immune system. 

Regulation of interferon-γ production by IL-12, TNF, and IL-10 in SCID splenocytes. E. S. Trippe and E. F. Unanue. Washington Univ. Sch. of Med., St. Louis, Mo 63110.

Listeriosis in SCID mice is an established model of IFN-γ-dependent macrophage activation by NK cells in vivo and in vitro. Through a T-cell independent pathway, infection with Listeria results in the activation of macrophages with high expression of class II MHC molecules. Macrophages that take up Listeria release cytokines that induce NK cells to produce IFN-γ. In this study we demonstrate that IFN-γ production from SCID splenocytes is stimulated by IL-12 and TNF but not by IL-10. IL-12 production is necessary for heat killed Listeria monocytes (hk-M) to stimulate IFN-γ production since neutralization of IL-12 abolishes IFN-γ production. A 10 kD factor, which inhibits IFN-γ production. Thus both IL-12 and TNF are co-stimulators for IFN-γ production. IL-10 inhibits hk-M stimulated IFN-γ production by inhibiting TNF and IL-12 production by SCID splenocytes as well as by inhibiting these cells' ability to respond to IL-12 and TNF. Conditioned media from peritoneal macrophages stimulated with HK-M contains IL-12, TNF and IL-10 which regulate IFN-γ production by NK cells as well as by IL-12 and IL-10 in response to HK-M. IL-12 and IL-10 stimulate IFN-γ production by NK cells whereas IL-10 inhibits it at both the level of the macrophage and the NK cell.

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IL-10 inhibits macrophage (Mφ) co-stimulatory activity by selectively inhibiting the upregulation of B7 expression. L. J. S. de Vries, L. J. E. van den Berg, and E. M. Shevach. U. of Pittsburgh, Pittsburgh, PA 15213 and Immunity Section, Laboratory of Clinical Investigation, NIAID, National Institutes of Health, Bethesda, MD 20892. In vivo, T helper cells (TH) function by interleukin 2 (IL-2) production in response to HIV and non-HIV antigens to determine whether HIV-specific TH function of mother and/or infant correlated with absence of mother-to-infant transmission of HIV. Polymorphic chain reaction and viral culture assays were performed to determine HIV infection of the infants. PBMC from 10/25 (40%) mothers tested and from 6/23 (26%) newborns were positive for HIV. All three of the infected newborns were unresponsive to one, and none of the 10 offspring who were responsive to one were born to infants who were infected. No correlation was detected between the mothers' TH-specific TH response and viral transmission of HIV. In vitro T cell reactivity of mother and newborn were not correlated. These results demonstrate that exposure to HIV antigens can occur in utero and that such exposure may be an important factor in the development of the immune system.

TNF-α upregulates IL-10 expression in human peripheral blood monocytes. R. H. Chang and S. C. Manu. Immunology Section, Laboratory of Clinical Investigation, NIAID, National Institutes of Health, Bethesda, MD 20892. In vivo, T helper cells (TH) function by interleukin 2 (IL-2) production in response to HIV and non-HIV antigens to determine whether HIV-specific TH function of mother and/or infant correlated with absence of mother-to-infant transmission of HIV. Polymorphic chain reaction and viral culture assays were performed to determine HIV infection of the infants. PBMC from 10/25 (40%) mothers tested and from 6/23 (26%) newborns were positive for HIV. All three of the infected newborns were unresponsive to one, and none of the 10 offspring who were responsive to one were born to infants who were infected. No correlation was detected between the mothers' TH-specific TH response and viral transmission of HIV. In vitro T cell reactivity of mother and newborn were not correlated. These results demonstrate that exposure to HIV antigens can occur in utero and that such exposure may be an important factor in the development of the immune system.


Recently, we cloned the human cDNA homologue of P600, a mRNA which is transcribed by activated mouse T2 clones. Both human and mouse P600 proteins were biologically active on human monocytes and B cells. Therefore, we proposed that this novel cytokine be designated interleukin-13 (IL-13). Human IL-13 is a non-glycosylated protein of 132 amino acids with a molecular mass (Mr) of 10 kD. IL-13 induced changes in the morphology of human monocytes. These cells formed long cellular processes and adhered strongly to the substrate when cultured in the presence of IL-13. In addition, IL-13 strongly enhanced the expression of class II MHC antigens on monocytes and induced expression of CD23 (FceRII). Furthermore, IL-13 inhibited the LPS-induced production of monokines including IL-1, IL-6 and IL-8. Taken together, these data indicate that IL-13 has important immunoregulatory activities on human monocytes.