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Peripheral blood leukocytes (PBL) from HIV-seropositive pregnant women and cord blood leukocytes (CBL) from their offspring were studied for in vitro T helper cell (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 is correlated with absence of mother-to-infant transmission of HIV. Polymerase chain reaction and viral culture assays were performed to determine HIV infection of the infants. PBL from 10/23 (43%) mothers tested and from 10/23 (43%) newborns CBL samples responded to two or more of five synthetic gpl60 envelope (envelope) peptides. Three of the 23 offspring were shown to be HIV-infected. All three of the infected newborns were unresponsive to one, and some of the 10 offspring who were responsive to one or more at birth were found to be infected. No correlation was detected between the mothers’ TH-specific TH response and viral transmission of HIV. CD4 TH reactivity of mother and newborn were not correlated. These results demonstrate that exposure to HIV antigens can occur in utero, and that such exposure can result in priming of the fetal T helper cell compartment. These results also raise the possibility that HIV-specific TH immunity may be protective in utero or in neonates.

**CYTOKINES AS REGULATORS OF MYELOID CELL BIOLOGY (1024-1027)**

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**REGULATION OF INTERFERON-{gamma} PRODUCTION BY IL-12, TNF AND IL-10 IN SCDI SPLEOCYTES.** C. S. Triepe and F. S. Haaske.

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Listeriosis in SCD mice is an established model of IFN-γ-dependent macrophage activation by NK cells in vitro and in vivo. 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 SCDI splenocytes is stimulated by IL-12 and TNF at high levels, whereas IL-10, IL-12 production is necessary for heat killed Listeria monocytogenes (hk-LM) to stimulate IFN-γ production once neutralization of IL-12 abolishes IFN-γ production.

Both IL-12 and TNF are co-stimulators for IFN-γ production. IL-10 inhibits IFN-γ production by inhibiting TNF and IL-12 production by SCDI splenocytes as well as by inhibiting these cells' ability to respond to IL-12 and TNF. Conditioned media from peritoneal macrophages stimulated with IL-12 and IL-10 which regulate IFN-γ production by NK cells express 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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**TNF-α UPREGULATES IL-10 EXPRESSION IN HUMAN PERIPHERAL BLOOD MONOCYTES.** Chingchial Wangenstrom and Werner Strober.

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In previous studies it has been shown that LPS induces an initial burst of inflammatory monokine production in human monocytes, which is followed by substantial IL-10 production; the IL-10 down-regulates the monokine production as well as IL-10 production itself. In the present studies we found that the hypothesis that one of the inflammatory monokines is responsible for IL-10 production, we tested the hypothesis that one of the inflammatory monokines is responsible for IL-10 production. We found that TNF-α upregulates IL-10 production by human monocytes. In vitro, LPS and IFN-γ co-stimulated IL-10 production by monocytes and IL-10 production by monocytes decreased when the cells were cultured in the presence of anti-TNF-α antibody. The induced IL-10 mRNA by TNF-α in monocytes is dose-dependent and begins between 8-24 hr following the addition of TNF-α to the cells. These results demonstrate that exposure to HIV antigens can occur in utero, and that such exposure can result in priming of the fetal T helper cell compartment. These results also raise the possibility that HIV-specific TH immunity may be protective in utero or in neonates.

**IL-10 INHIBITS MACROPHAGE (Mφ) CO-STIMULATORY ACTIVITY BY SELECTIVELY INHIBITING THE UPREGULATION OF B7 CO-STIMULATORY GENE EXPRESSION.** L. H. de Vries, P. J. van de Wetering, and E. M. Shevach.

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Recently, we have investigated whether the inhibitory effects of IL-10 on Con A induced T cell proliferation or IL-2 production by resting murine T cells were only observed when Mφ, but not when activated B cells, dendritic cells or L cells, were used as accessory cells (ACs). To further elucidate the mechanism of action of IL-10 on the inhibition of Mφ co-stimulatory activity, we have used a system in which Mφ develop into effective co-stimulator cells and the effect of IL-10 on this process can be examined at the absence of T cells. After culture, resting Mφ have no co-stimulatory activity for soluble anti-CD3 induced T cell proliferation nor do they express B7. In contrast, Mφ activated by culture, LPS, or IFN-γ for 24 hr then fixed were effective AC, expressed B7 and the co-stimulatory activity was related to their level of cell surface B7 expression. Addition of IL-10 during the process of Mφ activation resulted in both a marked reduction in co-stimulatory activity and in the upregulation of IL-10 expression. The inhibitory effect of IL-10 on the upregulation of B7 was selective since the upregulation of both ICAM-1 and MHc class II antigens was not affected. Furthermore, the defective co-stimulatory activity of both resting and IL-10 treated Mφ could not be recovered by the addition of IL-10 or IFN-γ production, the regulation of B7 expression and Mφ co-stimulatory activity by IL-10 may play an important role in the generation of Th2 cells or in the induction of T cell energy.

**IL-13 AFFECTS HUMAN MONOCYTE MORPHOLOGY, PHENOTYPE AND FUNCTION.** R. de Waal Malefyt, C. Engler and J. E. de Vries.

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Recently, we cloned the human cDNA homologue of P600, a mRNA which is transcribed by activated mouse Th2 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 aa 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 (FeCIII). 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.