Review of New Immunology Technologies at CROI

Poster 676

	HIV exposed uninfected neonates		HIV exposed uninfected at 12 month	
	Exposed	Control	Exposed	Control
CD3+ T cells	2251.4 (±192.4)	1820 (±151)	4148 (±362.5)	3352 (±181.4)
CD4+ T cells	1467 (±109.8)	1267 (±103.8)	2552 (±227.8)	1995.8 (±135)
CD8+ T cells	652.6 (±59)	539 (±47.7)	1207 (±145.1)	980 (±60.4)
B cells	698.7 (±68.1)	699.4 (±66)	1887 (±295.9)	1407 (±105.6)
NK cells	2203.4 (±239.3)	2485.6 (±269)	1539 (±204.7)	750 (±66.5)
CD45+ CD34+	116 (±12.8)	113 (±8.9)	37.5 (±5.6)	53.8 (±9.6)±

- HIV exposed uninfected neonates are born with markers of immune activation and a decrease in percentage of naïve T cells
- Cell activation persists until 12 months of age

Innate Immune Cells

- Has anti-tumor & anti-microbial activities
- May play a pivotal role in autoimmunty and asthma
- Rapidly release high levels of IL-4 and IFNγ upon activation (TCR)
- Various subsets of inKT cells have been described that may drive Th1 & Th2 responses

- Spontaneously kill tumor cells
- Control viral infections (early phase of infection)
- Important source of cytokines: IFNγ, TNFα, GM-CSF, IL-13, chemokines (RANTES, MIP 1a)
- NK cell function regulated by a complex balance of inhibitory and stimulatory receptors

- Migrate from blood to secondary lymphoid tissues
- Potent producers of INFα; control viral infections
- Indirectly activates T cells, macrophages, NK cells, & NKT cells

- Intercept invading pathogens in periphery
- Migrate to secondary lymphoid tissues
- Present antigens to specific naïve T cells

Reduced ability of newborns to produce CCL3 is associated with increased susceptibility to perinatal HIV-1 transmission

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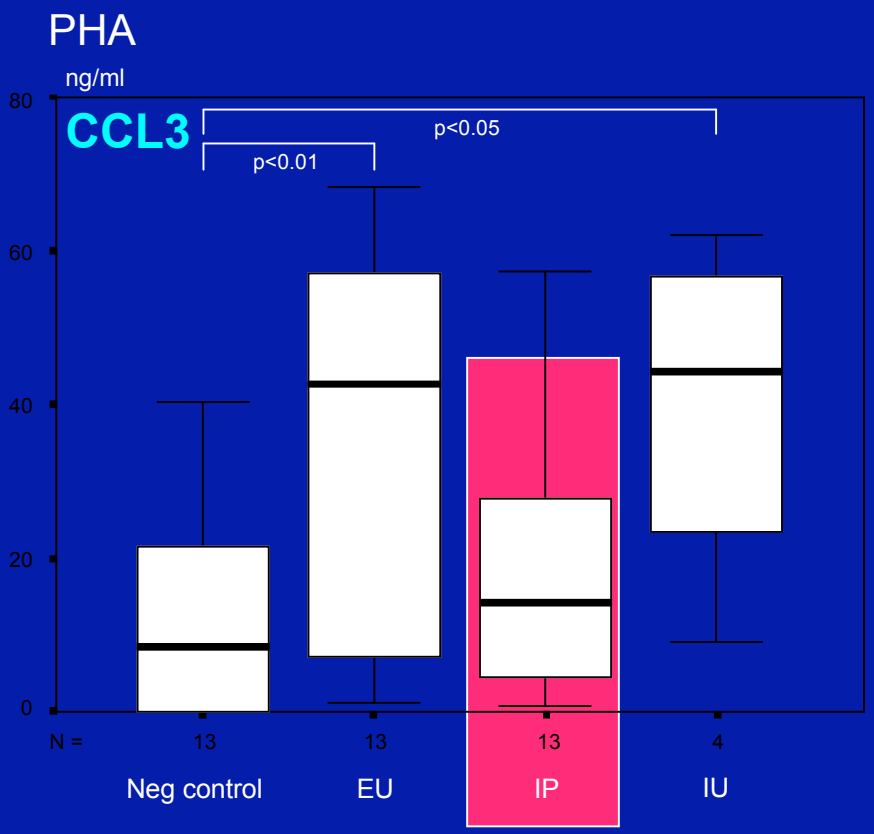
Background

- Early in life – immune system of the infant is more reliant on innate immunity than specific immunity (immunologically inexperienced). The innate immune system may be critical in the prevention of perinatal HIV infection

CC chemokines CCL3, CCL4 and CCL5

- The natural ligands for CCR5 (HIV coreceptor)
- Mediate inhibition of infection with macrophage-tropic HIV isolates
- Significant body of evidence showing the positive influence of CC chemokines in context of HIV-1 infection in adults
- Prototype vaccine studies in rhesus macaques – production of CC chemokines by CD8 T cells associated with protective immunity
- One study: Env T-helper cell responses associated with enhanced expression of chemokines. Postulated that CC chemokines may mediate non-cytolytic inhibition of HIV vertical transmission Wasik et al., 1999. J. Immunol. 162:4355-4364
- Plasma levels of the CC chemokines are elevated in newborns compared to their mothers

CCL3 production of HIV transmitting and non transmitting mothers



Mothers that transmit HIV-1 to their infants during labour and delivery (IP) display a phenotype of deficient production of CCL3, suggesting genetic mechanism

Candidates for reduced CCL3 production?

- CCL3-L1 Copy number
- SNPs in CCL3 or CCL3-L1