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Poster presentation

P03-09. Preserved adaptive immune responses and limited immune activation in CD4-low SIV-positive sooty mangabeys

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Background

We previously reported a dramatic and sustained CD4+ T cell decline (<80/μl blood) in two SIV+ sooty mangabeys that was associated with a multi-tropic SIV infection (R5/X4/R2) (Milush et al., J Immunol, 2007). These "AIDS defining" CD4+ T cell levels have been maintained for more than eight years in association with low levels of immune activation and no clinical signs of simian AIDS.

Methods

Three additional mangabeys were inoculated with plasma from a CD4-low mangabey and phenotypic/functional changes in multiple immune cell subsets were monitored via flow cytometry. Monocyte TNF-alpha production was assessed following 6-hour *ex vivo* whole blood stimulations with 10 μg/ml LPS. An influenza vaccine was administered during chronic infection and the resulting antibody response was measured via hemagglutination inhibition and microneutralization assays.

Results

By 20 days post passage, all three SIV-positive mangabeys experienced a severe decline of CD4+ T cells in the blood (40–80 cells/μl), lymph nodes, and GALT. Despite global CD4+ T cell depletion, chronic infection was characterized by low levels of immune activation. SIV specific antibodies and CTL were detectable in all CD4-low mangabeys and, notably, all animals mounted a clear neo-response to influenza vaccination. *Ex vivo* LPS stimulation revealed a reduced monocyte TNF-alpha response in SIV-infected mangabeys (approximately 5% of monocytes responding). In contrast, chronically SIV-infected rhesus macaques exhibited a high monocyte TNF-alpha response that was comparable to uninfected controls (approximately 25% of monocytes responding). The reduction of mangabey monocyte TNF-alpha responses occurred early (by 7 days) following SIV infection.

Conclusion

Multi-tropic SIV was passaged to uninfected mangabeys and induced dramatic systemic CD4+ T cell loss without clinical signs of simian AIDS. The suppression of monocyte inflammatory cytokine production (TNF-alpha) may contribute to the maintenance of low immune activation and preserved adaptive immune responses even in the face of dramatic CD4+ T cell depletion.