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Role of regulatory T cells in mother to child transmission of HIV

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Abstract

Mother-to-child transmission of HIV-1 occurs in a minority of HIV-infected mother-infant pairs, even without any interventions. The mechanisms that protect the majority of HIV-exposed infants from infection are unclear. T regulatory cells (Treg) have important immunomodulatory functions, but their role in the fetus as well as in mother-to-child transmission of HIV is understudied. Methods: We studied available cryopreserved peripheral blood mononuclear cells from HIV-exposed infants from the breastfeeding, antiretrovirals and nutrition (BAN) study cohort in Malawi: 64 infants were HIV-uninfected and 28 infants were HIV-infected at birth. We quantified the frequency of Treg cells (CD4+CD25+FoxP3+), and activated CD4+ and CD8+ T cells (CD38+HLADR+) by flow cytometry at birth, 6 weeks and 6, 9 and 12 months of age. Descriptive statistics were performed to describe the distributions of these lymphocyte markers according to HIV infection status; and Student's t-tests and Wilcoxon-Rank Sum tests to perform comparisons between HIV- infected and uninfected infants. Results: T cell activation increased rapidly in the first 6 weeks of life more pronounced on CD8+T cells; a further increase in activation was observed at the time of weaning from breastfeeding at 6 months of age.

In contrast, the frequency of Treg was stable over the first 6 weeks of life (median, 0.5%), slightly decreased between 6 weeks and 6 months (median at 6 months, 0.3%) and then slightly increased between 6 months (time of weaning) and 12 months of age (median, 0.45%). HIV-infected infants had significantly higher frequencies of activated T cells than uninfected infants (P<0.01), as expected. At the time of birth, HIV-exposed uninfected infants had higher levels of Treg, compared to infants infected in utero (Figure, P=0.03). Among infants with negative HIV tests at birth, Treg % tended to be higher in those who were HIV-infected by 6 months of life, compared with those who remained uninfected (median, 1.25% vs. 0.55%). Conclusions: This study provides evidence that Treg may play a role in preventing mother-to-child transmission of HIV, and perhaps even delaying detection of HIV infection in the infant, likely by suppressing immune activation in the fetus and infant. Better characterization of the role of Treg in fetal and neonatal immunity may provide a valuable complementary approach to achieve eradication of mother-to-child transmission of HIV.

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