

the main population of TN cells that can develop to DP cells in FTOC.

In conclusion, the thymus appears to be the major site of viral replication and amplification in newborn macaques infected with SHIV-C2/1. As a result of SHIV-C2/1 infection, T-cell progenitors in the thymus were impaired and the CD2⁺TN subpopulation was selectively decreased. Moreover, our findings revealed a substantial reduction of proliferation and impaired maturation of TN cells after peak viremia and the onset of CD4 depletion. However, additional studies are needed to clarify the mechanism by which thymopoiesis is impaired. Our results provide experimental evidence that an X4-utilizing acute pathogenic SHIV infection induced severe thymic atrophy and impairment of thymopoiesis in the early stage of infection. They also provide the basis for a pathogenic model, in which impaired thymopoiesis leads to profound and irreversible peripheral CD4⁺ T cell depletion. In HIV-1-infected children, there are markers of thymic dysfunction that can predict survival outcome. Mathematical models have suggested that thymic dysinvolution in children is more severe than it is in adults, particularly in X4 virus infections (24, 54). Thus, SHIV-C2/1 infection in newborn macaques can be a useful model of HIV-1-infected children that have a rapid course of disease progression.

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