

Abstract

Proc Natl Acad Sci U S A. 2007 Dec 11;104(50):19960-5.

Dramatic increase in naive T cell turnover is linked to loss of naive T cells from old primates.

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OBJECTIVE: The loss of naive T cells is a hallmark of immune aging. Although thymic involution is a primary driver of this naive T cell loss, less is known about the contribution of other mechanisms to the depletion of naive T cells in aging primates.

METHODS: We examined the role of homeostatic cycling and proliferative expansion in different T cell subsets of aging rhesus macaques (RM).

RESULTS: BrdU incorporation and the expression of the G(1)-M marker Ki-67 were elevated in peripheral naive CD4 and even more markedly in the naive CD8 T cells of old, but not young adult, RM. Proliferating naive cells did not accumulate in old animals. Rather, the relative size of the naive CD8 T cell compartment correlated inversely to its proliferation rate. Likewise, T cell receptor diversity decreased in individuals with elevated naive CD8 T cell proliferation. This apparent contradiction was explained by a significant increase in turnover concomitant with the naive pool loss. The turnover increased exponentially when the naive CD8 T cell pool decreased below 4% of total blood CD8 cells.

CONCLUSION: These results link the shrinking naive T cell pool with a dramatic increase in homeostatic turnover, which has the potential to exacerbate the progressive exhaustion of the naive pool and constrict the T cell repertoire. Thus, homeostatic T cell proliferation exhibits temporal antagonistic pleiotropy, being beneficial to T cell maintenance in adulthood but detrimental to the long-term T cell maintenance in aging individuals.

PMID: 18056811

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