

The increase in thymopoiesis following T cell progenitor therapy is dependent upon the input population and continued interaction between developing T cells and the thymic microenvironment.

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The inclusion of *in vitro* derived T cell progenitor (proT) therapy with hematopoietic stem cell transplant (HSCT) aids in the recovery of the thymus damaged by total body irradiation and improves *de novo* thymopoiesis. To understand the interaction between proTs and the thymic microenvironment, wildtype (WT) mice were lethally irradiated and given T cell deficient donor (Rag1^{-/-}) marrow along with *in vitro* generated proT from WT donors, limiting mature T cell development to infused proT. Donor proTs within the host thymus led to a significant increase in thymic epithelial cell (TEC) numbers by day 21 post-transplant, and increased actively cycling TECs as measured by Ki67 expression and BrdU uptake. However, that gain was temporary and lost by day 28, suggesting that continued signaling from proT cells is required to sustain TEC cycling and mass. We also find a significant improvement in total thymocyte number by day 21 followed by a significant increase in the total mature T cell number in the secondary lymphoid organs by day 28. This protective surge is also temporary, receding by day 60. In this time period, infused DN2 proTs selectively increased thymocyte number while DN3 proTs preferentially led to a greater TEC numbers. Interestingly, an exception in persistence occurs when DN3 proTs are used and the increase in mature T cells in the spleen persists at day 60. As a result of the lack of competition for thymic niches by cells from the Rag1^{-/-} graft, a subpopulation of the infused proT persisted in the thymus in an immature state at day 60. These findings highlight the importance of the interaction between developing T cells and TECs in the proliferation and survival of these critical components of the thymic microenvironment.