

## **The Role of TCR-MHC Interactions in Driving the Maturation of Recent Thymic Emigrants**

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### **Abstract:**

A number of studies have suggested that newly differentiated T cells that have left the thymus undergo changes in the periphery. Interpretation of these studies was hampered by the intrinsic technical drawbacks of the methods available to study these recent thymic emigrants (RTEs). A new technique, the development of transgenic mice containing a bacterial artificial chromosome that expresses Green Fluorescent Protein (GFP) under the control of the RAG2 promoter (RAG2p-GFP Tg mice), has greatly facilitated the study of RTE biology by allowing analysis of unmanipulated cells for approximately a two-week window in the periphery.

Based on analysis of RAG2p-GFP Tg mice, our lab has published data demonstrating that RTEs are functionally and phenotypically immature as compared with the rest of the mature naïve T cell pool. RTEs exhibit relatively reduced proliferative capacity and diminished IL-2 secretion (CD4s) and IFN- $\gamma$  secretion (CD8s) in response to TCR stimulation.

These findings raise the possibility that the pool of peripheral T cells is shaped not only by thymic development but also by continued maturation in the periphery. To aid in understanding the significance of this continued peripheral maturation, our lab is investigating the mechanism(s) that drive this maturation. One current hypothesis is that RTE maturation is driven by TCR-mediated signals delivered upon interaction with MHC ligand. According to this hypothesis, this TCR-MHC interaction would mold the RTE TCR repertoire.

To test the prediction that the RTE TCR repertoire differs from that of the rest of the mature naïve T cell compartment, the repertoires were compared in several ways. For the CD4 and CD8 subsets, no dramatic differences were found in TCR V $\alpha$  or V $\beta$  family member representation. However, more discriminating analysis of smaller subpopulations has suggested that the TCR repertoires of CD8<sup>+</sup>GFP<sup>+</sup> and naïve CD8<sup>+</sup>GFP<sup>-</sup> differ, as is the case for the CD4<sup>+</sup>GFP<sup>+</sup> subset in comparison to the naïve CD4<sup>+</sup>GFP<sup>-</sup> subset. This analysis was done using Restriction Fragment Length Polymorphism analysis of CDR3 lengths of selected TCR V $\beta$  to J $\beta$  arrangements. Currently, this result is being substantiated by comparative CDR3 spectratyping of the TCR repertoires expressed by these same subsets.