

Thymic Selection: Getting out alive

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Conventional $\alpha\beta$ T cell precursors with a low affinity for self undergo positive selection in the thymic cortex, then migrate to the medulla. During their residency in the medulla, they undergo further maturation to become functionally responsive T cells, after which time they emigrate. In contrast to what was previously thought, we found that thymic emigration occurs rapidly for conventional $\alpha\beta$ T cells (1-2 days) and is dependent on the transcription factor KLF2. On the other hand long-lived antigen-experienced cells (NKT, Treg, memory cells etc.) can be found in the thymus, but this may reflect their re-circulation from the periphery.

T cell precursors with a high affinity for self-antigens commonly die within the thymus—clonal deletion. We used a highly physiologic TCR transgenic model (HY^{cd4}) to show that self-reactive thymocytes die in the cortex. We also show that costimulatory molecules expressed in the medulla were dispensable for deletion, as was migration to the medulla or even an organized medullary epithelium. However, the kinetics of clonal deletion in vivo indicated that apoptosis was asynchronously activated over four days after receiving a high-affinity signal. This inefficient apoptosis mechanism may allow for the generation of self-antigen specific regulatory T cell populations.

References:

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