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Molecular and cellular basis of T cell lineage commitment: An overview

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All multicellular organisms initially develop from a single fertilized cell that differentiates into all different cell types, each with distinct and highly specialized functions. Cellular development is the highly complex process by which heterogeneous populations of cells arise with increasingly complex molecular functions and with the capability of performing increasingly specialized tasks. Every step of cellular differentiation generates increased molecular complexity, increased specialization, and the acquisition of greater and greater functional abilities. However, concomitant with increased complexity, specialization, and functional ability, the developmental potential of differentiating cells becomes increasingly limited with the end result that the cells adopt a specific cell fate and terminally differentiate into a specific cell type. So from the perspective of an individual cell, development results in steadily increasing specialization and steadily diminishing potential for alternative developmental outcomes.

Cells of the immune system derive from multipotent hematopoietic stem cells that ultimately differentiate into highly specialized immune cells, and they do so in response to signals initiated by various environmental stimuli. The last few years have seen an explosion in our knowledge of hematopoietic stem that can be signaled to differentiate into mature T lymphocytes in the thymus, the transcription factors that are major players in determination of T cell lineage fate, and the environmental signals that stimulate T cell differentiation. This issue of Seminars in Immunology is focused on key steps in the development of T cells from early hematopoietic precursor cells, to their differentiation and positive selection in the thymus, to their differentiation into functional effector T cells in the periphery.

In this issue, the mechanism by which Notch signaling elicits T cell fate and promotes early T cell development in the thymus is thoughtfully considered by Bhandoola and coworkers [1] and by Pear and coworkers [2]. Taylor and coworkers describe a novel interplay between Notch and IL-7 signaling in the thymus and discuss important differences between murine and human thymocyte development [3]. The evolution of *in vitro* models of thymocyte positive selection, and what has been learned from them, is reviewed by Zuniga-Pflucker and colleagues [4]. Takahama et al. [5] discuss and describe the surprising discovery of a unique proteosome component in cortical thymic epithelial cells that is important for the generation of MHC class I selecting peptides for $CD8^+$ T cells. Bosselut et al. [6] describe how ‘sensor’ transcription factors in immature thymocytes are activated during positive selection to

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induce the differentiation of thymocytes into mature T cells with specific effector functions. And Nakayama and coworkers describe the interplay between TCR and cytokine signals involved in the peripheral differentiation of T helper cell subsets with different effector functions [7].

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