

Immunology, T cell development
The role of dendritic cells in T cell development and thymic involution
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Co-supervisor/ Collaborator(s) (if any):
Project Description
<p>a) Background:</p> <p>Thymic dendritic cells (DCs) are known to shape T cell-mediated immune responses by deleting auto-reactive T cells and inducing regulatory T cells. It is however unclear, whether thymic DCs are involved in the early T cell development or play a role in thymic involution. Given the cytokine producing capacity of DCs that is frequently dysregulated in aged individual with involuting thymus, we hypothesized that DCs influence early T cell development and thymic involution via production of pro-inflammatory cytokines. Indeed, our preliminary data revealed a critical role of cytokine environment created by thymic DCs in T cell development and thymic involution. Further studies are now required to understand how thymic DC regulates these processes.</p> <p>b) Proposed work:</p> <p>Using a conditional knockout mouse model we have identified perturbed cytokine profiles in aged but not young mice with mutant DCs. Correspondingly, T cell development was largely altered in aging mice with mutant DCs compared to control mice. We will further validate the cytokine effects on T cell development by introducing specific cytokines in vivo, fetal thymic organ culture or thymic slide culture in vitro. The molecular mechanisms by which the introduced mutation in DCs affects cytokine production in an age-dependent manner will be determined.</p>
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