

Asilomar 2003 Poster Abstract

Presenter: Emily Venanzi

Poster Title: “Aire influences peripheral antigen expression and the development of autoimmunity”

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Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED), also called autoimmune polyendocrine syndrome type I (APS-1), is a monogenic multi-organ autoimmune disease caused by mutations in the *autoimmune regulator (aire)* gene. *Aire* encodes a transcription factor, *aire*, that is expressed primarily in a subset of medullary thymic epithelial cells (mTECs) also responsible for the ectopic expression of various peripheral antigens. To study whether *aire* is involved in transcriptional regulation of these antigens, we created *aire* knockout mice. These mutant mice exhibit autoimmune infiltrates in multiple tissues and produce autoantibodies against many of the same tissues. As expected, an *aire* knockout non-hematopoietic thymic epithelium is required for disease initiation. In comparing the gene expression profiles of wild type and knockout mTECs, we found a specific decrease in expression levels of peripheral antigen genes in *aire*^{-/-} mTECs. This strongly suggests that *aire* plays a role in central tolerance by regulating the thymic transcription of these genes.