

Control of Immune Tolerance by the Aire protein

Mark S. Anderson, MD, PhD

UCSF Diabetes Center
513 Parnassus Ave. Box 0540
San Francisco, CA 94143-0540

The maintenance of immune tolerance is an essential process to prevent autoimmunity. A critical protein in promoting immune tolerance is the AutoImmune REgulator (Aire). Aire is highly expressed in a mature subset of thymic medullary epithelial cells (mTEC's) where it helps promote immune tolerance by driving the expression of tissue-specific antigens (TSA's). Humans and mice that have genetic mutations in the *Aire* gene develop a multiorgan autoimmune syndrome characterized by immune infiltrates and autoantibodies. Recent work by our group has further defined the autoimmune syndrome present in Aire-deficient mice and studies will be presented analyzing defects in the autoimmune repertoire present in these mice. Additionally, we have generated a novel dominant-negative allele of Aire that has revealed the importance of quantitative changes in thymic TSA expression. Recent work on the imprint of these quantitative changes on the developing immune repertoire will also be presented. Finally, we have uncovered a similar role for Aire outside of the thymus in secondary lymphoid organs. The potential contribution to immune tolerance of these extrathymic Aire-expressing cells (eTAC's) will also be discussed.

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