

“A role of the autoimmune regulator (AIRE) gene in the peripheral antigen presenting cells”

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Patients with autoimmune polyendocrine syndrome type I suffer from endocrine and non-endocrine manifestations due to mutations in the transactivating autoimmune regulator gene (AIRE). AIRE is mainly expressed in the thymus and in the spleen, implicating a role in central and peripheral tolerance. Here we show an exaggerated ability of Aire^{-/-} antigen-presenting cells (APCs) to activate T cell hybridomas. In addition, Aire^{-/-} APCs stimulated naïve polyclonal CD4⁺ T cells more efficiently than the littermate wild type APCs. Microarray analysis of APCs from Aire^{-/-} mice displayed a differential regulation of 68 genes, including the increased expression of VCAM-1 verified at the protein level in APS I patients. The increased ability to stimulate T cell hybridomas could be blocked with VCAM-1 antibody. The exaggerated T cell response along with elevated Vcam-1 expression was not a consequence of existing autoimmunity or autoreactive T cells, since APCs from OT-II transgenic TCR on an Aire-deficient background displayed similar results. Furthermore, elevated expression of Vcam-1 was not due to increased inflammation as judged by normal levels of cytokine expression. Our findings show that there is an exaggerated antigen-dependent activation of T cells in Aire^{-/-} mice that is partly mediated by over-expression of Vcam-1 on antigen-presenting cells. These results implicate a role for AIRE/Aire in the peripheral tolerance.