Retinaldehyde dehydrogenase activity is triggered during allograft rejection and it drives Th1/Th17 cytokine production

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Retinoic acid (RA), a vitamin A metabolite, has been attributed to relevant functions in adaptive immunity. On T cells, the disruption on RA signaling alters both CD4+ and CD8+ T cells effector function. In this study, we evaluated the contribution of RA synthesis during the immune response using an in vivo skin transplantation model. Our data indicates that the frequency and number of cells containing an active retinaldehyde dehydrogenase (RALDH), a key enzyme for RA synthesis, is increased during skin transplant rejection. In addition, we found that the expression of the mRNA coding for the isoform RALDH2 is up-regulated on graft rejecting draining lymph nodes (dLNs) cells. Lastly, we observed that IFN-? and IL-17 production by ex vivo re-stimulated dLNs cells is greatly increased during rejection, which it turns depends on RA synthesis, as shown in experiments using a specific RALDH inhibitor. Altogether, our data demonstrate that RA synthesis is incremented dur