MicroRNA-146a controls IFN-γ production and functional plasticity in γδ T cells by targeting Nod1

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BACKGROUND AND OBJECTIVES

γδ T cells have emerged as key providers of the proinflammatory cytokines interleukin 17 (IL-17) and interleukin-22 (IFN-γ) in various models of infection, inflammation and autoimmunity. Our previous epigenetic and transcriptional analyses have shown that whereas CD27+/γδ T cells are committed to IFN-γ expression, the IL-17 producing CD27− subset has limited plasticity to co-express both cytokines under inflammatory conditions (Schmolka et al. Nat Immunol 2013). To further understand the molecular control of this plasticity we now investigated the potential role of microRNA (miRNA)-mediated post-transcriptional regulation.

RESULTS

1. Expression analysis: mir-146a is differentially expressed in γδ T cell subsets

2. Gain-of-function: mir-146a reduces IFN-γ production by γδ T cells

3. Loss-of-function: Loss of mir-146a increases IFN-γ and IFN-γ/IL-17 γδ T-cell subsets

4. Listeria infection: increased IFN-γ and IL-17 γδ T cells in mir-146a−/− mice

5. Ago2IP: mRNA targets of mir146a

6. Nof1 is required for IFN-γ production and functional plasticity in γδ T cells

TAKE-HOME MESSAGE

(Schmolka et al. Sci Immunol: in press)