



TCR+CD8+ T cell in health and disease: a novel and functionally active subpopulation of T-cells enriched within the gut

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These 'conventional' T cells express either CD4 or CD8 $\alpha\beta$ co-receptors and can be reliant on these molecules for the recognition of MHC-II and MHC-I respectively. In the last two decades, T cells bearing receptors reactive to lipid and small molecule antigens have been discovered. These include Mucosal-Associated Invariant T (MAIT) cells, which are restricted by the monomorphic MHC molecule MR1.

Using MR1-tetramers we showed that MAIT cell co-receptor expression is discordant with conventional T cells. MAIT cells predominantly express CD8 $\alpha\alpha$ or to a lesser extent can be deficient of co-receptor molecules. The high frequency of CD8 $^+$ MAIT cells suggests that the CD8 co-receptor may influence immune outcomes in this population of cells. Using a CD8 α transduced cell line, we have determined that CD8 $\alpha\alpha$ is capable of binding to MR1-tetramers in the absence of a T cell receptor (TCR) and fails to bind to MR1-tetramers mutated at residues shown to abrogate the CD8 interaction with MHC-I. Our observations suggest that MAIT cells use the CD8 co-receptor in a similar manner as conventional T cells to bind MHC-I, whereby CD8 can bind MR1 to enhance the overall avidity of the MAIT TCR interaction with MR1. We aim to characterize the CD8 interaction with MR1 quantitatively and determine its importance in MAIT cell biology.

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TCR $\gamma\delta^+$ CD8 $\alpha\beta^+$ T cell in health and disease: a novel and functionally active subpopulation of T cells enriched within the gut

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$\gamma\delta$ T-cells have been implicated in the pathogenesis of immune-mediated diseases such as inflammatory bowel disease (IBD). However, a potential role of different immune cell subsets in IBD and also in the process of mucosal healing upon treatment is unknown. $\gamma\delta$ T-cells have been divided into CD8 $\alpha\alpha^+$ and CD8 $^+$ T-cells. By using flow cytometry and RT-PCR, we described for the first time a novel subset of human $\gamma\delta$ T-cells expressing CD8 $\alpha\beta$ heterodimers on their surface. We found that these TCR $\gamma\delta^+$ CD8 $\alpha\beta^+$ T-cell subset exist in both human peripheral blood as well as in the gut, however they were differentially enriched within the gut. TCR $\gamma\delta^+$ CD8 $\alpha\beta^+$ T-cells displayed high cytotoxic activity by expressing Fas Ligand on their surface and also producing Granzyme B and Perforin. We showed that these cells can produce INF γ and TNF α but they did not show the ability to produce IL-17 in healthy individuals. In patients with IBD, we found a decrease in the percentage of intestinal CD8 $\alpha\beta^+$ $\gamma\delta$ T-cells compared to healthy controls. Moreover, the percentage of TCR $\gamma\delta^+$ CD8 $\alpha\beta^+$ T-cells out of $\gamma\delta$ T-cells showed a negative correlation with Crohn's disease activity. Three months of anti-TNF α (adalimumab) therapy increased the percentage of TCR $\gamma\delta^+$ CD8 $\alpha\beta^+$ T-cells close to the level of healthy controls. These results suggest that TCR $\gamma\delta^+$ CD8 $\alpha\beta^+$ T-cells might possibly play a role in gut inflammation and also intestinal wound healing after anti-TNF α treatment. These results are likely to have implications for the development of novel therapies to treat mucosal inflammatory diseases.

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A broad family of MR1-restricted T cells

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