ALTERED MUCOSAL-ASSOCIATED INVARIANT T CELLS PHENOTYPE IN CHILDREN WITH NEWLY DIAGNOSED TYPE 1 DIABETES BUT NOT IN AUTOANTIBODY-POSITIVE AT-RISK CHILDREN

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ABSTRACT

Introduction: Mucosal-associated invariant T (MAIT) cells are unconventional T cells, enriched in the gut. They express an invariant T-cell receptor and recognize riboflavin metabolites from bacteria presented by MHC-Ib-related protein 1 (MR1) molecules. Alterations in gut microbiota have been reported in patients with type 1 diabetes (T1D), even before the onset of the disease. These changes can potentially alter the frequency or phenotype of circulating MAIT cells. **Methods:** We characterized peripheral blood MAIT cells in a cohort of 51 children with newly diagnosed T1D, 27 at-risk children positive for multiple autoantibodies (AAb+) and 113 age-matched healthy children. Using multi-colour flow cytometry, we analysed the frequency, surface phenotype and cytokine production of MAIT cells. In addition, we characterized the frequency and surface phenotype of blood MAIT cells in 26 patients with long-standing T1D and 25 age-matched healthy controls. **Results:** No significant differences in MAIT cell frequency were observed between the study groups. Further phenotyping revealed that the expression of CD8, CD27, CCR5 and β7 integrin on MAIT cells was lower in children with newly diagnosed T1D compared to AAb+ and healthy children. The frequency of MAIT cells producing IFN-γ was also lower in children with newly diagnosed T1D, but the frequencies of IL-17A- and IL-4-secreting MAIT cells were similar in the study groups. Finally, the capacity of MAIT cells to be activated *in vitro* by *E.coli* bacteria through MR1 was comparable between the study groups. However, none of these changes was observed in adult patients with long-standing T1D. In contrast, a decreased frequency of MAIT cells and increased CD25 expression was observed in adult T1D patients with a short duration after diagnosis. **Conclusion:** There are subtle changes in the circulating MAIT compartment in patients with T1D at the onset of the disease as well as after clinical diagnosis, but not in AAb+ at-risk subjects including progression to clinical disease. Consequently, the alterations in blood MAIT cells are likely associated with the clinical manifestation of the disease rather than being features of earlier T1D autoimmunity.