IMMUNOLOGY

**FOLLICULAR HELPER
T CELLS IN T1DM**

New research published in the *Journal of Clinical Investigation* demonstrates that patients with type 1 diabetes mellitus (T1DM) have cellular and molecular indicators of the presence of follicular helper T (T_{fh}) cells, which might drive disease pathogenesis upstream of autoantibody generation.

The mechanisms underlying the immunopathogenesis of T1DM have been the focus of intensive research. Previously, findings from studies performed in animal models suggested that the type 1 helper T cell subset of CD4⁺ T helper cells was primarily responsible for autoimmune destruction of the pancreas in T1DM. Our understanding of the nuances of T helper cell differentiation, and the phenotypes and functions of the subsets, has considerably advanced in the past decade. Now, a team of researchers led by senior investigator Lucy Walker at University College London, UK, show that T_{fh} differentiation and skewing towards a T_{fh} phenotype might contribute to development of autoimmunity in T1DM.

The researchers used microarray assays to assess gene expression patterns associated with T helper cell differentiation in a model of T1DM whereby transgenic mice expressed a pancreas-derived self-antigen. They identified a gene expression pattern in the mice that was characteristic of T_{fh} cells; flow cytometry analysis confirmed that T_{fh} cells were enriched in these animals.

Furthermore, analysis of blood from patients with T1DM showed enrichment in a T_{fh}-associated gene expression signature. Analysis of memory T cells of patients with T1DM and healthy controls confirmed that patients had increased numbers of T_{fh} cells. Given that T_{fh} cells are important for interacting with B cells to mediate antibody production, these findings suggest that skewing of T helper cell differentiation toward a T_{fh} phenotype could occur upstream of autoantibody production in patients with T1DM.

These findings could be useful for developing early targeted therapies for patients at risk of T1DM. "If a T_{fh} signature can be detected in people before they develop diabetes mellitus, this information may help to identify which individuals would be the best candidates for preventative therapies," speculates Walker.

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