Distinct T-cell signatures observed at different stages of type 1 diabetes development

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A study conducted at the University of Eastern Finland found distinct signatures in CD8$^+$ T cells in blood samples from children with newly diagnosed type 1 diabetes and in autoantibody-positive children who
later developed type 1 diabetes. **The study** was published in the journal *Diabetes*.

Type 1 diabetes is an autoimmune disease which usually develops in childhood. The symptomatic onset of type 1 diabetes results from a T-cell mediated destruction of insulin-producing beta cells in the pancreas.

CD4\(^+\) helper T cells orchestrate the **autoimmune response**, while CD8\(^+\) cytotoxic T cells directly contribute to the destruction of the **beta cells**. Interestingly, a specific blood CD8\(^+\) T-cell **signature** has recently been associated with a beneficial response to immunotherapy treatments aiming to delay the onset of type 1 diabetes.

In the current study, led by Professor Tuure Kinnunen at the University of Eastern Finland, two distinct signatures were detected in a subset of circulating, highly differentiated CD8\(^+\) T cells in children at different stages of type 1 diabetes development.

A proinflammatory signature consisting of an increased frequency of T cells producing proinflammatory cytokines, such as IFN-\(\gamma\) and TNF-\(\alpha\), was detected in children with newly diagnosed type 1 diabetes.

In contrast, in autoantibody-positive at-risk children who later developed type 1 diabetes, an increased frequency of T cells expressing the co-inhibitory receptors KLRG1 and TIGIT was detected.

Importantly, the latter signature resembles the CD8\(^+\) T-cell signature associated with a beneficial response to immunotherapy in earlier studies.

"Our findings suggest that before disease onset, children who later progress to clinical type 1 diabetes have a distinct CD8\(^+\) T-cell profile detectable in their **blood samples**. It could be envisioned that this is a
potential, but eventually failing attempt of the immune system to harness the harmful autoimmune response.

"In the future, these T-cell signatures could potentially be used to develop better biomarkers for evaluating the risk of developing type 1 diabetes, and who would benefit from preventative immunotherapy.

"Additionally, a deeper characterization of these interesting cell types is warranted to better understand the type 1 diabetes disease process," University Teacher Anna-Mari Schroderus, the lead author of the study notes.

This study utilized samples from the unique Finnish DIPP follow-up study where children with a genetic risk for the development of type 1 diabetes are followed from birth. The study also involved researchers from the universities of Turku, Oulu, and Helsinki, and Kuopio University Hospital.

**More information:** Anna-Mari Schroderus et al, Temporal Alterations in CD8\(^+\) T Cells During the Progression from Stage 1 to Stage 3 Type 1 Diabetes, *Diabetes* (2024). [DOI: 10.2337/db24-0159](https://doi.org/10.2337/db24-0159)

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