

IL-21 Production by CD4+ Effector T Cells and Frequency of Circulating Follicular Helper T Cells Are Increased in Type 1 Diabetes Patients

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Abstract : Type 1 diabetes is caused by autoimmune destruction of insulin-secreting beta cells in the pancreas. T cells are known to play an important role in this immune-mediated destruction; however, there is no general consensus regarding alterations in cytokine production or T cell subsets in peripheral blood of patients with type 1 diabetes. Using polychromatic flow cytometry of peripheral blood mononuclear cells (PBMCs), we assessed production of the proinflammatory cytokines IL-21, IFN- γ and IL-17 by memory CD4 T effector (Teff) cells in 69 patients with type 1 diabetes and 61 healthy donors. We found a 21.9% (95% CI 5.8, 40.2; $p = 3.9 \times 10^{-3}$) higher frequency of IL-21(+) CD45RA(-) memory CD4(+) Teffs in patients with type 1 diabetes (geometric mean 5.92% [95% CI 5.44, 6.44]) compared with healthy donors (geometric mean 4.88% [95% CI 4.33, 5.50]). In a separate cohort of 30 patients with type 1 diabetes and 32 healthy donors, we assessed the frequency of circulating T follicular helper (Tfh) cells in whole blood. Consistent with the increased production of IL-21, we also found a 14.9% increase in circulating Tfh cells in the patients with type 1 diabetes (95% CI 2.9, 26.9; $p = 0.016$). Analysis of IL-21 production by PBMCs from a subset of 46 of the 62 donors immunophenotyped for Tfh showed that frequency of Tfh cells was associated with the frequency of IL-21+ cells ($r^2 = 0.174$, $p = 0.004$). These results indicate that increased IL-21 production is likely to be an aetiological factor in the pathogenesis of type 1 diabetes that could be considered as a potential therapeutic target.

Keywords : T follicular helper cell, IL-21, IL-17, type 1 diabetes

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