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Targeting memory T cells in type 1 diabetes.

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Abstract

Type 1 diabetes (T1D) is a chronic autoimmune disease that leads to progressive destruction of pancreatic beta cells. Compared to healthy controls, a characteristic feature of patients with T1D is the presence of self-reactive T cells with a memory phenotype. These autoreactive memory T cells in both the CD4(+) and CD8(+) compartments are likely to be long-lived, strongly responsive to antigenic stimulation with less dependence on costimulation for activation and clonal expansion, and comparatively resistant to suppression by regulatory T cells (Tregs) or downregulation by immune-modulating agents. Persistence of autoreactive memory T cells likely contributes to the difficulty in preventing disease progression in new-onset T1D and maintaining allogeneic islet transplants by regular immunosuppressive regimens. The majority of immune interventions that have demonstrated some success in preserving beta cell function in the new-onset period have been shown to deplete or modulate memory T cells. Based on these and other considerations, preservation of residual beta cells early after diagnosis or restoration of beta cell mass by use of stem cell or transplantation technology will require a successful strategy to control the autoreactive memory T cell compartment, which could include depletion, inhibition of homeostatic cytokines, induction of hyporesponsiveness, or a combination of these approaches.