Type 1 diabetes vaccine candidates promote human Foxp3+Treg induction in humanized mice

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Immune tolerance is executed partly by Foxp3$^+$regulatory T (Treg) cells, which suppress autoreactive T cells. In autoimmune type 1 diabetes (T1D) impaired tolerance promotes destruction of insulin-producing β-cells. The development of autoantigen-specific vaccination strategies for Foxp3$^+$Treg-induction and prevention of islet autoimmunity in patients is still in its infancy. Here, using human haematopoietic stem cell-engrafted NSG-HLA-DQ8 transgenic mice, we provide direct evidence for human autoantigen-specific Foxp3$^+$Treg-induction in vivo. We identify HLA-DQ8-restricted insulin-specific CD4$^+$T cells and demonstrate efficient human insulin-specific Foxp3$^+$Treg-induction upon subimmunogenic vaccination with strong agonistic insulin mimetopes in vivo. Induced human Tregs are stable, show increased expression of Treg signature genes such asFoxp3, CTLA4, IL-2Rα and TIGIT and can efficiently suppress effector T cells. Such Foxp3$^+$Treg-induction does not trigger any effector T cells. These T1D vaccine candidates could therefore represent an expedient improvement in the challenge to induce human Foxp3$^+$Tregs and to develop novel precision medicines for prevention of islet autoimmunity in children at risk of T1D.

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