Subset of self-destructive immune cells may selectively drive diabetes

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New research identifies a distinctive population of immune cells that may play a key role in the pathogenesis of diabetes. The research, published by Cell Press and available online in the April 21st issue of *Immunity*, sheds new light on the pathogenesis of diabetes and may lead to the development of new more selective therapeutic strategies for diabetes and other autoimmune diseases of the accessory organs of the digestive system.

Type 1 diabetes (T1D) is a chronic autoimmune disease that develops when the immune system destroys insulin-producing cells in the pancreas. Previous work using a mouse model of diabetes (nonobese diabetic or "NOD" mice) demonstrated that multiple types of immune cells are necessary for the development of T1D, including two different types of T cells, CD4+ and CD8+ T cells, as well as B cells. The individual roles and interactions of these cells in the pathogenesis of T1D are not well understood.

"We do know that the cytokine interleukin (IL)-21 is produced by CD4+ T cells and plays a critical role in autoimmune diseases, and that IL-21 contributes to the proliferation, differentiation and survival of motile types of immune cells," explains senior study author, Dr. Cecile King from the Garvan Institute of Medical Research. "However, how IL-21 mediates its effect on autoimmune disease pathogenesis remains an important unanswered question."

Dr. King and colleagues discovered a subset of CD4+ T cells that produce IL-21 and that express a protein called chemokine receptor 9 (CCR9). In healthy humans, CCR9 is found primarily in T cells that selectively migrate to the gut and is thought to play a role in several inflammatory disorders of the gastrointestinal tract. The researchers showed that this newly identified subset of CD4+ cells also infiltrate the pancreas and other accessory organs of the digestive system and "help" CD8+ cells to elicit T1D.

"We identified a subset of CD4+ T cells that may contribute to the regional specification of organ-specific autoimmune disease," concludes Dr. King. "Recent studies have demonstrated that IL-21 is critical for the maintenance of CD8+ T cells during chronic infection. In our study we showed that IL-21 is also important for the survival of diabetogenic CD8+ T cells. Further studies are needed to confirm that this population of cells is necessary for autoimmune diseases that afflict accessory organs of the digestive system and to explore the possibility that targeting this cell population as a potential therapeutic strategy for diabetes."

More information: McGuire et al.: "A Subset of Interleukin-21+ Chemokine Receptor CCR9+ T Helper Cells Target Accessory Organs of the Digestive System in Autoimmunity." *Immunity* , April 22, 2011

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