Metabolic Control of FoxP3 Expression in Type 1 Diabetes

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Type 1 Diabetes (T1D), is an autoimmune disease characterized by T cell-mediated destruction of insulin-secreting pancreatic beta-cells in genetically susceptible individuals. The T1D involves a complex interaction between pancreatic beta-cells and both innate and adaptive immune system, which undoubtedly changes during the progression of the disease. Altered of both suppressive function and number of regulatory T cells (Tregs) were reported to contribute to the loss of immune tolerance in autoimmune diabetes. The use of Tregs to restore immune tolerance is considered an attractive novel approach to control autoimmune diseases. The transcriptional factor FoxP3, a master gene of Treg cells, has a key role in the control of regulatory activity of this specific T cell subset. Recent experimental evidence has shown that specific metabolic programs control lymphocyte differentiation and function. Here we analyzed the link between metabolism and Treg cell function in subjects with T1D. Specifically, we assessed the capacity of different metabolic programs (either glycolysis or beta oxidation) to control in vitro differentiation of inducible Treg cells (iTreg). We observed that in T1D subjects the altered expression in the Foxp3 gene depends on an altered capacity of iTreg cells to induce proper metabolic switches between glucose oxidation and mitochondrial respiration. Taken together these data suggest that metabolism influences FoxP3 expression and that manipulation of specific metabolic programs may pave the way to the control of immune tolerance during autoimmune disease.