Evidence for Sustained Islet Turnover in Humans with Long-Standing Type 1 Diabetes

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Authors:

JURIS J. MEIER, ANIL BHUSHAN, ALEXANDRA E. BUTLER, ROBERT A. RIZZA, PETER C. BUTLER
Institutions:

Los Angeles, CA; Rochester, MN
Results:

Background. Type-1 diabetes is held to be due to a complete loss of insulin secreting beta cells through autoimmune mediated beta cell destruction. This implies that reversal of the disease requires replacement of beta cells by islet or pancreas transplantation. However some insulin secretion is detectable in many people with long-standing type-1 diabetes, indicating either a small population of surviving beta cells or continued renewal of beta cells subject to ongoing autoimmune destruction. In case of the latter, a novel approach to beta cell replacement in type-1 diabetes would be to inhibit beta cell destruction, potentially leading to reversal of diabetes.

Methods. Pancreatic sections from 42 individuals with type-1 diabetes and 6 non-diabetic individuals were stained for insulin, glucagon, Ki67, cleaved caspase-3, CD3, and CD68. The presence and extent of beta cells as well as the frequency of beta apoptosis and replication were quantified. Islets in both cases of type-1 diabetes and controls were evaluated for the presence and extent of lymphocytes and macrophages. **Results.** Beta cells were identified in 88 % of individuals with type-1 diabetes. The number of beta cells was unrelated to diabetes duration (range 4-67 years), and age at death (range 14-77 years), but was higher ($p<0.05$) in individuals with the lower mean blood glucose. Beta cell apoptosis was three times more frequent in type-1 diabetes than controls ($p < 0.001$) but beta cell replication was absent in both groups. Increased beta cell apoptosis in type-1 diabetes was accompanied by macrophages and T-lymphocytes as well as periductal fibrosis ($p < 0.001$), implying chronic inflammation.

Conclusions. Most people with long standing type-1 diabetes have beta cells that continue to be destroyed in the setting of low-grade inflammation. This implies, by definition, that concomitant new beta cell formation must be occurring, even in the setting of long standing diabetes. We conclude that type-1 diabetes may be reversible by targeted inhibition of beta cell destruction.