Transgenic overexpression of human Bcl-2 in islet beta cells inhibits apoptosis but does not prevent autoimmune destruction.

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Insulin-dependent diabetes mellitus results when > 90% of the insulin-producing beta cells in the pancreatic islets are killed as a result of autoimmune attack by T cells. During the progression to diabetes, islet beta cells die as a result of different insults from the immune system. Agents such as perforin and granzymes, CD95 ligand and tumor necrosis factor-alpha, or cytokines and free-radicals have all been shown to cause beta cell apoptosis. The anti-apoptotic protein, Bcl-2, might protect against some of these stimuli. We have therefore generated transgenic mice expressing human Bcl-2 in their islet beta cells. Although Bcl-2 was able to prevent apoptosis induced by cytotoxic agents against beta cells in vitro, Bcl-2 alone could not prevent or ameliorate cytotoxic or autoimmune beta cell damage in vivo.

JOURNAL ARTICLE Age of Onset Animal Antigens, CD80/BIOSYNTHESIS/GENETICS *Apoptosis CD8-Positive T-Lymphocytes/IMMUNOLOGY Diabetes Mellitus, Insulin-Dependent/CHEMICALLY INDUCED/ *IMMUNOLOGY Disease Models, Animal Drug Resistance Human Interleukin-2/BIOSYNTHESIS/GENETICS Islets of Langerhans/*IMMUNOLOGY Mice Mice, Transgenic Proto-Oncogene Proteins c-bcl-2/*BIOSYNTHESIS/GENETICS Staurosporine/PHARMACOLOGY Streptozocin/PHARMACOLOGY Support, Non-U.S. Gov't