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Two drugs, one result: Preventing the onset of type I diabetes in mice

Type 1 diabetes is an autoimmune disease that affects over one million Americans and results from the selective destruction of pancreatic beta (fl) cells by pathogenic T lymphocytes. Once there is nearly complete elimination of fl cells, individuals lose the ability to maintain blood glucose levels, and severe complications may develop. One way to prevent the onset of diabetes may be to inactivate (tolerize) the pathogenic T lymphocytes, thereby preventing beta cell destruction. In an attempt to induce T cell tolerance, our lab has pioneered two antigen specific drugs containing peptides implicated in diabetes onset, which we have studied in order to determine their potential use as clinically relevant treatments for blocking the onset of disease. One peptide, derived from glutamic acid decarboxylase (GAD2), has been expressed into the hypervariable region (CDR3) of an antibody molecule (Ig). Another peptide, derived from the insulin fl chain (INSfl), was expressed on an Ig in the same manner. The resulting Ig-GAD2 and Ig-INSfl drugs were tested for peptide presentation to T cells via antigen presenting cells. Mice were then treated with each drug, and the disease was delayed in young mice. With chemical aggregation of Igs the anti-inflammatory cytokine IL-10 is upregulated and the inflammatory cytokine is suppressed. Each drug resulted in excellent (63% for Ig-INSfl and 88% for Ig-GAD2) disease suppression. Further studies have shown these two drugs to be invaluable tools for preventing disease onset in older, predisposed mice, which is promising for the suppression of human diabetes in clinical situations.