

Glucagon-Like Peptide-1(GLP-1) Receptor Agonists Effects in Cell Culture Models of Type 1 Diabetes

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The use of GLP-1 agonists, including Ozempic and Exenatide, has increased by almost 40-fold between 2017 and 2021. These drugs are widely used to regulate glucose metabolism in type 2 diabetes and weight loss for obesity treatment; they can also reduce insulin doses in patients with type 1 diabetes (T1D). However, with the widespread use of this treatment, systemic effects on other organs and cells are unknown. This research aims to evaluate the effects of Exenatide on Fibroblastic Reticular Cells (FRCs), a subpopulation of stromal cells found in lymph nodes and involved in maintaining self-tolerance to prevent autoimmune diseases such as T1D. This work will determine whether Exenatide affects FRC phenotypic identity, possibly impacting tolerance mechanisms and worsening autoimmune diseases. This research was conducted by measuring changes in metabolic activity, phenotype, and viability of FRCs post-Exenatide treatment compared to non-treated controls and Nit-1s, insulin-producing cells, as an additional control. Using immunostaining, I found that, although FRCs are not insulin-producing cells, they express the GLP-1 receptor. Next, the effects of FRC treatment, with concentrations of Exenatide ranging from 300nM to 3µM for 24, 48 & 72 hour time periods, was evaluated. The 900nM concentration increased the metabolic activity of FRCs in vitro, compared to control. In addition, downregulation of immune tolerance-related genes, such as TGFB2, was found at all time points and concentrations following treatment. These preliminary studies identify a novel GLP-1 effect on FRC mechanisms establishing a need to investigate additional off-target effects of GLP-1s in metabolic pathways and on autoimmunity.

Awards Won:

