INTRODUCTION AND OBJECTIVE

Type 1 diabetes mellitus (DM1) is an organ-specific autoimmune disease, mediated by T cells and characterized by the selective destruction of insulin producing pancreatic cells. Glucagon-like peptide-1 (GLP-1) is gastrointestinal hormone that potentiates glucosed-stimulated insulin secretion. Additionally, it stimulate insulin biosynthesis and stimulate proliferation of the beta-cell (Fig.1). After being secreted, GLP-1 have a very short circulating half-life of 3–5 min due to the action of proteases such as dipeptidyl peptidase IV (DPP-4) (Fig. 2).

Recently, a new class of drugs, dipeptidyl peptidase-4 inhibitors (DPP4i), have demonstrated therapeutic efficiency in patients with type 2 diabetes mellitus. Furthermore, the use of DPP-4 inhibitors in experimental models of DM1 have shown protection of pancreatic β cells against apoptosis, stimulation of neogenesis of pancreatic islets as well as improvement in the homeostatic glucose control. They act by blocking degradation of the incretin hormone glucagon-like peptide-1 (GLP-1).

Aim: To evaluate the possible effect of the administration of DPP-4 inhibitor in the treatment of experimental type 1 diabetes.

METHODS

• **Type 1 Diabetes Induction**
  Eight-week-old male C57Bl/6 mice will be lightly anesthetized. Streptozotocin (STZ) will be dissolved in 25mM citrate buffer, at pH 4.5, and will be immediately injected intraperitoneally at a dose of 40 mg/kg, for 5 consecutive days.

• **Blood Glucose Determination and Diabetes Definition**
  Blood samples will be taken from the tail vein of nonfasted alert animals, and glucose levels will be determined with the glucometer system Accu-Chek Active. Mice will be considered diabetic if glycaemia was above 250 mg/dL, on 2 consecutive measurements.

• **Dipeptidyl peptidase-4 Inhibitor administration**
  After mice were considered diabetic, they were placed on either normal chow diet (control group) or diet containing DPP4 (6 g/kg MK0431-Sitagliptin).

• **ELISA**
  Serum active GLP-1 and pancreatic homogenate cytokines (IFN-γ, TNF-α) levels were measured by ELISA 30 days after the DPP4 administration.

• **Flow cytometry analysis**
  The frequency of CD4⁺CD25⁺Foxp3⁺ T cells in spleen was examined by flow cytometry 30 days after the DPP4 administration.

RESULTS

[Graphs and data showing GLP-1 levels, Th1 cytokines, Regulatory T cells, Blood glucose levels]

CONCLUSIONS

DPP-4 inhibitor treatment can be associated with immunomodulation, reducing proinflammatory cytokine in the pancreas and increasing regulatory T cells in experimental type 1 diabetes.