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Role of chemotactic chemokine CXCL16, ADAM10 and ADAM17 in T-cells recruitment to the pancreatic B-cells and initiation of Type 1 diabetes mellitus in Mice: Modulatory action of Simvastatin

Background:

T cell trafficking into pancreatic islets drives the immunological response in type 1 diabetes mellitus (T1DM). It is unknown how A Disintigrin And Metalloproteinase 10 (ADAM10) and 17 (ADAM17) affect the migration of pancreatic T cells into the pancreatic islets during T1DM.

Objective:

The purpose of this study was to examine how ADAM10 and ADAM17 contribute to the development of T1DM and the potential protective effects of simvastatin (SIM) in T1DM caused by STZ.

Methods: Balb/c mice were divided into four groups of ten each. Control group received buffer while SIM group received 50 mg/kg, i.p daily for 12 days. STZ (55 mg/kg, i.p.) was administered to the diabetic group for 5 consecutive days. The SIM + STZ group was given STZ (55 mg/kg, i.p.) for 5 days straight and SIM (30 mg/kg, i.p.) every day for 12 days. Evaluation for pancreatic CXCL16, pancreatic ADAM10, nuclear factor-kB, and pancreatic T-cell expression was performed as well as biochemical, inflammatory, and apoptotic markers.

Results:

The STZ group showed a significant rise in biochemical, inflammatory, and apoptotic parameters as well as membrane-bound ADAM10, ADAM17, CXCL16, nuclear factor-kB (NF- kB), and infiltrating T-cell expression in the pancreatic islets. The biochemical and inflammatory parameters of SIM therapy in the presence of STZ were significantly improved. In addition, the expression of CXCL16, ADAM10, ADAM17, NF-B, T-cell migration, and apoptosis in the pancreatic islets were reduced as well.

Conclusion:

The work results shed the light on ADAM10 and ADAM17 role in promoting pancreatic b-cell death in T1DM. SIM improved STZ-induced changes in T1DM in mice. Therefore, CXCL16 and ADAM10/ADAM17 may serve as novel therapeutic targets for T1DM.

Keywords: Diabetes mellitus type 1, CXCL16, ADAM10, ADAM17, Simvastatin.

Biography:

Mostafa Darwish, has his expertise in molecular pharmacology regarding mechanisms of cisplatin nephrotoxicity and the influence of drugs or substrates on transporting system like OCT2 in tubules on cisplatin excretion from his master work. In addition, he studied the role of chemokines in initiation as well as development of diabetes mellitus in his Ph.D. He studied the role of the chemotactic chemokine CXCL16 and its processing enzymes ADAM 10 and ADAM17 in pancreas of diabetic mice. He has a very good experience in animal modeling and molecular imaging techniques like immunofluorescence and western blotting.

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