Received date: 17-03-2023 | Accepted date: 20-03-2023 | Published date: 08-05-2023

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

Mostafa A Darwish[1], Mohamed S Abdel-Bakky[2,3], Abdulmajeed Alqasoumi[2], Waleed M Altowayan[2] and **Elham Amin[1,2]**
[1]Beni- Suef University, Egypt
[2]Qassim University, KSA
[3]Al-Azhar University, Egypt

T cell mediates immune response in type 1 diabetes mellitus (T1DM) through its trafficking into pancreatic islets. The role of A Disintigrin And Metalloproteinase 10 (ADAM10) and 17 (ADAM17) in pancreatic T-cells recruitment into the pancreatic islets during T1DM is not known. This study aimed to investigate the role of ADAM10 and ADAM17 in T1DM development and possible protective role of simvastatin (SIM) in STZ-induced T1DM. Balb/c mice were classified into 4 groups, 10 each. Diabetic group; received STZ (55 mg/kg, i.p.) for 5 consecutive days. Control group received buffer while SIM group received 50 mg/kg, i.p daily for 12 days. SIM + STZ group; received SIM (30 mg/kg, i.p.) daily for 12 days and STZ (55 mg/kg, i.p.) for 5 consecutive days. Biochemical, inflammatory and apoptotic markers as well as pancreatic CXCL16, pancreatic ADAM10, nuclear factor-kB, and pancreatic T-cells expression were analyzed. Significant increase in biochemical, inflammatory and apoptotic parameters as well as the expression of membranous ADAM10, ADAM17, CXCL16, nuclear factor-kB (NF- κB), and infiltrated T-cells in the pancreatic islets were found in STZ group. SIM treatment in the presence of STZ was markedly improved biochemical and inflammatory parameters as well as it reduced the expression of CXCL16, ADAM10, ADAM17, NF-κB, T-cells migration and apoptosis in the pancreatic islets. 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.

Recent Publications:

1. Moustafa Fathy, Mostafa A Darwish, Al-Shaimaa M Abdelhamid, Gehad M Alrashedy, Othman Ali Othman, Muhammad Naseem, Thomas Dandekar, Eman M Othman. (2022). Kinetin Ameliorates Cisplatin-Induced Hepatotoxicity and Lymphotoxicity via Attenuating Oxidative Damage, Cell Apoptosis and Inflammation in Rats. Biomedicine, 10 (7), 1620.

2. Abdel-Bakky, M. S., Alqasoumi, A., Altowayan, W. M., Amin, E., & Darwish, M. A. (2022). Resveratrol inhibited ADAM10 mediated CXCL16- cleavage and T-cell recruitment to Pancreatic B-cells in type 1 diabetes mellitus in mice. pharmaceutics, 14(3), 594.

3. E. Amin, M.S. Abdel-Bakky, M.A. Darwish, H.A. Mohammed, S. Chigurupati, K. A. Qureshi, M. H. Hassan. (2022). The Glycemic Control Potential of Some Amaranthaceae Plants, with Particular Reference to In Vivo Antidiabetic Potential of Agathophora alopecuroides. Molecules, 27 (3), 973.

4. Abdel-Bakky, M. S., Alqasoumi, A., Altowayan, W. M., Amin, E., & Darwish, M. A. (2021). Simvastatin mitigates streptozotocin-induced type 1 diabetes in mice through downregulation of ADAM10 and ADAM17. Life Sciences, 120224.

5. Darwish, Mostafa A., Amira M. Abo-Youssef, Bassim A. shehata, Ali A. Abo-Saif, Mohammed S. Abdelbakky. Resveratrol inhibits macrophage infiltration of pancreatic islets in streptozotocin-induced Type-I diabetic mice via attenuation of CXCL16/ NF-κB p65 signaling pathway. Life sciences 272 (2021): 119250.

Biography

Mostafa Darwish was graduated from faculty of pharmacy and ranked the first throughout the five years of study. He 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.

mostafa.darwish@nub.edu.eg