Journal of Clinical Endocrionology Research

Extended Abstract
Vol. 3, Iss. 1
2020

Pharma Europe 2016 : Effect of some gut hormones in the generation of insulin producing cells from mesenchymal stem cells - Hala El Mesallamy - Ain Shams University

Hala O El Mesallamy

Biochemistry Department, Egypt

Diabetes mellitus is a complex metabolic disease with a huge worldwide prevalence. In vitro generation of □-cells from stem cells may provide bases for diabetes cell therapy. We examine the effect of gut hormones including glucagon like peptide1(GLP-1) and obestatin in generation of IPCs in-vitro from WJ-MSCs in comparison to exendin-4. WJ-MSCs were isolated from umbilical cords and characterized by immunophenotyping and in vitro differentiation into adipocytes as an example of mesenchymal lineages. WJ-MSCs under proliferation conditions were incubated with either10nM exendin-4, 10nM GLP-1 and 100nM obestatin. Moreover, WJ-MSCs were induced to differentiate into IPCs using either of those factors using short differentiation protocol (10 days) and long differentiation protocol (30 days). The stem cell markers, nestin and Oct-4; and □-cells differentiation markers, Pdx-1, Maf-A and Isl-1, were assessed by qRT-PCR, while, the functionality of the generated IPCs was assessed by glucose stimulated insulin secretion (GSIS).WJ-MSCs exhibit all characteristics of MSCs including plastic adherence, expression of mesenchymal CDs and lacking hematopoietic ones beside their ability to differentiate into adipocytes. Incubation of these cells with either exendin-4, GLP-1 and obestatin under proliferation conditions decreased the expression of stem cell markers, nestin and Oct-4, indicating the exit of these cells from stemness state. Interestingly, using obestatin in short protocol managed to induce expression of Pdx-1 and Maf-A, as was the case with exendin-4. However, GLP-1 failed to show this. In addition, in long protocol, exendin-4, GLP-1 and obestatin generated IPCs showing increased expression of Pdx-1, Maf-A and Isl-1. As for GSIS, both GLP-1 and obestatin showed higher secretion of insulin but failed to show response to increased glucose concentrations. These results may indicate that obestatin can be potentially used in the differentiation protocols for the generation of IPCs from MSCs.

The classic symptoms of untreated diabetes are unintended weight loss, polyuria (increased urination), polydipsia (increased thirst), and polyphagia (increased hunger). Symptoms may develop rapidly (weeks or months) in type 1 diabetes, while they usually develop much more slowly and may be subtle or absent in type 2 diabetes. Several other signs and symptoms can mark the onset of diabetes although they are not specific to the disease. In addition to the known ones above, they include blurred vision, headache, fatigue, slow healing of cuts, and itchy skin. Prolonged high blood glucose can cause glucose absorption in the lens of the eye, which leads to changes in its shape, resulting in vision changes. Long-term vision loss can also be caused by diabetic retinopathy. A number of skin rashes that can occur in diabetes are collectively known as diabetic dermadromes. In beta cells, insulin release is stimulated primarily by glucose present in the blood. As circulating glucose levels rise such as after ingesting a meal, insulin is secreted in a dose-dependent fashion. This system of release is commonly referred to as glucose-stimulated insulin secretion (GSIS). There are four key pieces to the "Consensus Model" of GSIS: GLUT2 dependent glucose uptake, glucose metabolism, KATP channel closure, and the opening of voltage gated calcium channels causing insulin granule fusion and exocytosis. Voltage-gated calcium channels and ATP-sensitive potassium ion channels are embedded in the plasma membrane of beta cells. These ATP-sensitive potassium ion channels are normally open and the calcium ion channels are normally closed. Potassium ions diffuse out of the cell, down their concentration gradient, making the inside of the cell more negative with respect to the outside (as potassium ions carry a positive charge). At rest, this creates a potential difference across the cell surface membrane of -70mV. When the glucose concentration outside the cell is high, glucose molecules move into the cell by facilitated diffusion, down its concentration gradient through the GLUT2 transporter. Since beta cells use glucokinase to catalyze the first step of glycolysis, metabolism only occurs around physiological blood glucose levels and above. Metabolism of the glucose produces ATP, which increases the ATP to ADP ratio. The ATP-sensitive potassium ion channels close when this ratio rises. This means that potassium ions can no longer diffuse out of the cell. As a result, the potential difference across the membrane becomes more positive (as potassium ions accumulate inside the cell). This change in potential difference opens the voltage-gated calcium channels, which allows calcium ions from outside the cell to diffuse in down their concentration gradient.[9] When the calcium ions enter the cell, they cause vesicles containing insulin to move to, and fuse with, the cell surface membrane, releasing insulin by exocytosis into the hepatic portal vein People (usually with type 1 diabetes) may also experience episodes of diabetic ketoacidosis (DKA), a metabolic disturbance characterized by nausea, vomiting and abdominal pain, the smell of acetone on the breath, deep breathing known as Kussmaul breathing, and in severe cases a decreased level of consciousness. A rare but equally severe possibility is hyperosmolar hyperglycemic state (HHS), which is more common in type 2 diabetes and is mainly the result of dehydration. Treatment-related low blood sugar (hypoglycemia) is common in people with type 1 and also type 2 diabetes depending on the medication being used. Most cases are mild and are not considered medical emergencies. Effects can range from feelings of unease, sweating, trembling, and increased appetite in mild cases to more serious effects such as confusion, changes in behavior such as aggressiveness, seizures, unconsciousness, and (rarely) permanent brain damage or death in severe cases.

This work is partly presented at 5th Annual European Pharma Congress July 18-20, 2016 held at Berlin, Germany

Biography

Prof. Hala El Mesallamy works as Head of Biochemistry Department (since 2001) Professor of Biochemistry since 2006 and served as Vice Dean for Postgraduates Affairs and Scientific research (2013-2015),), ExVice Dean for Community and Environmental Affairs (2007-2009), Member in the permanent committee (since 2013), Faculty of Pharmacy, Ain Shams University. Member in Council Patent of Academy of Scientific Research and Technology in Ministry of Scientific Research (2009-2011), Lecturer and Consultant in Unesco (since 2008), Reviewer in Some International Journals,) Member in the Counseling committee for special prices (since 2012).

hala_elmosalamy@hotmail.com

This work is partly presented at 5th Annual European Pharma Congress July 18-20, 2016 held at Berlin, Germany