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Therapeutic ultrasound as novel approach to ameliorate insulin secretory deficiency in Type-2 Diabetes Mellitus

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Statement of the Problem: In Type 2 Diabetes Mellitus (T2DM), the typical biphasic pattern of insulin secretion is disrupted. Treatment with ultrasound can stimulate insulin secretion from both human pancreatic islets and rat insulinoma INS 832-13 cells. Insulin secretion can be also stimulated by activation of mechanosensitive channels, namely transient receptor potential vanilloid (TRPV) and Piezo channels. Isoforms of these channels have been recently implicated in glucose stimulated insulin secretion. However, very little is known about the possible regulatory effect of ultrasound on expression and function of mechanosensitive channels in the pancreas. Methodology & Theoretical Orientation: In this study, using INS 832-13 cells as a model secretory system, we examined the expression of TRPV isoforms 1-6 and Piezo 1 & 2, and the possible sonogenetic effect of ultrasound on expression of these mechanosensitive genes. Findings: Using RT-qPCR, we found that INS 832-13 cells predominately express TRPV1, TRPV2, and Piezo1 channel isoforms. We then treated the INS cells with continuous ultrasound application for 5 min at a frequency of 800 kHz and intensity of 0.5 W/cm2 to stimulate insulin release from these cells. However, this short-term (≤ 1h) ultrasound stimulation had no significant effect on gene expression (mRNA) levels of any of the three channel proteins. In contrast to gene expression studies, protein expression analysis revealed a moderate (20-50%) increase in intracellular insulin levels following INS cell stimulation with high (20 mM) glucose or ultrasound treatment. Conclusion & Significance: Our current data suggest that, at least in short term, ultrasound and glucose stimulated-insulin release do not depend on the change in expression levels of these genes, implying involvement of post-transcriptional and/or secretory mechanisms in acute ultrasound-stimulated insulin release. Thus, understanding the mechanism of ultrasound induced insulin secretion could lead to targeted, noninvasive therapies for T2DM patients.

Biography

Aleksandra Jeremic has his expertise in molecular endocrinology, high resolution imaging and passion in improving the health and wellbeing of people suffering from T2DM. in collaboration with Prof. Vesna Zderic lab from GW Biomedical engineering department, his lab is investigating molecular mechanisms by which therapeutic ultrasound stimulates gene-expression and insulin release from pancreatic beta-cells. These sono-genetics studies opened a new perspective for exploring ultrasound as a novel therapeutic approach to ameliorate secretory and genetic defects in diseases such as type-2 diabetes mellitus and cardiopathy.