



Regulation of insulin biosynthesis, secretion, and degradation by IRE1 α in pancreatic β -cells

Keywords: Diabetes, ER Stress, IRE1, pancreas, insulin, WFS1

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Applications

Novel therapeutic targets for regulation of insulin in the treatment of diabetes.

Background

The treatment of diabetes involves maintaining homeostatic levels of insulin so that glucose levels remain within a normal range. Misregulation of glucose levels can result from defective insulin biosynthesis, secretion, and/or degradation. The production and secretion of insulin originates from pancreatic β -cells. The Endoplasmic Reticulum plays a critical role in the biosynthesis of insulin, where its precursors are processed prior to secretion. ER stress can result in misregulation of insulin production, resulting in defects in glucose metabolism

Technology

UMass Medical School investigator Dr. Fumihiko Urano and colleagues have elucidated the pathways regulating insulin biosynthesis and secretion in the pancreas. The primary mediator of insulin regulation in pancreatic β -cells has been shown by Dr. Urano et al. to be IRE1 α , an ER stress protein involved in the proper folding of proteins in the cell prior to secretion. The proper activation of IRE1 α plays an important role in the activation of proinsulin production. They have demonstrated that high levels of glucose result in hyperactivation of IRE1 α in the degradation of insulin mRNA. Furthermore, inhibition of IRE1 α expression or its activation by phosphorylation inhibits insulin biosynthesis. This mechanism correlates with alterations in expression of ER stress-related proteins such as WFS1. These findings suggest that IRE1 α and WFS1 may be therapeutic targets for insulin and glucose regulation in the treatment of diabetes.

Salient Features and Competitive Advantages

- ✚ **Novel Targets for Drug Discovery:** IRE1 α and WFS1 can be used in the screening for novel therapeutics for the treatment of diabetes.
- ✚ **Novel Targets for Drug Development:** Modulation and measurement of IRE1 α and WFS1 expression and activation can be used to validate therapeutics in the research and development stages for ER Stress-related diseases.
- ✚ **Market potential:** The Global Diabetes drugs treatment market was valued of \$15 billion in 2005. The Global Diabetes Market Will Exceed \$21 Billion by 2011.

Publications

J. Biol. Chem. 280:39609-39615 (2005)
Cell Metabolism 4: 245-254 (2006)
PLoS ONE 3:e1648 (2008)

Business Opportunity

UMass OTM is seeking statements of interest from parties interested in licensing and/or sponsoring collaborative research to further develop, evaluate, or commercialize this technology.

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