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Inhibition Mechanisms of Type 2 Diabetes
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Abstract
Type 2 Diabetes (T2D) is the most common form of diabetes mellitus which affects approximately 8.3% of the population (diabetes.org 2013). T2D is most often brought on by reduced sensitivity to insulin receptors. This is thought to be caused by a mutation in the gene Insulin Receptor Substrate-1 (IRS-1). It is the suppression of IRS-1 that leads to inactivation of signaling molecules insulin signaling pathways causing insulin resistance (Victor D. H. et al). This literature review will focus on the major mechanisms of inhibition of the insulin signaling pathways. Mice that were bred lacking the Atk2 signaling pathway (associated with IRS-1 gene) revealed age-inhibition of the insulin signaling pathways. Mice were bred lacking Atk2 signaling pathways (Atk2/IRS-1 > FOXO1>PEPCK). This suggests that the Akt2 pathway is crucial for glucose metabolism (Garofalo 2003; Guo 2013). Future research will focus on activating IRS-1 and Atk2 as a therapeutic modality for the treatment and prevention of type 2 diabetes and other metabolic diseases.

Pathophysiology of Diabetes
- Insulin and glycogen are hormones produced in the pancreas and are the two main hormones involved in regulating the level of glucose in the blood.
- The pancreas contains about 1 million groups of cells called islets. There are two kinds of pancreatic islets: α (alpha) and β (beta) cells. Alpha cells secrete glycogen and β cells secrete glucagon.
- On a molecular level glucose homeostasis is triggered by a signaling cascade
  - Atk2/IRS-1>FOXO1>PEPCK
  - T2D results from a combination of increased insulin resistance due to reduced sensitivity to insulin receptors (i.e. IRS-1) and prolonged deterioration of β cell function.

IRS-1 and Atk2 Signaling Pathways
- Mice were bred lacking Atk2 signaling pathways which are associated with the IRS-1 gene.
- At 22 weeks of age loss of adipose (fat) tissue, increase in hyperglycemia (high blood sugar), and increased insulin resistance were observed.
- This suggests that the degradation of the Atk2 signaling pathways causes the sensitivity of insulin receptors (e.g. IRS-1) to be reduced.
- This may be an important step in the development of insulin resistance/diabetes.

Next Steps/Future Research
- Activating IRS and Atk2 for future treatment and prevention of diabetes (Garofalo 2003; Guo 2013)
- Demonstrate how signaling pathways can be modulated unfolding β cell failure (Shouhong et al 2010).

References: