Understanding Diabetes - Putative Role of PDGF and LRP-1.

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Glucose homeostasis is a major problem in diabetes. Beta cell death is common both in Type 1 and Type 2 diabetes. Beta cells become damaged or dysfunctional when more insulin is secreted into the blood in order to maintain blood glucose levels either resulting in hyperglycemia or insulin deficiency. Gleevec which is used in the treatment of chronic myeloid leukemia and gastro intestinal stromal tumor's is found to have a significant effect on diabetes also.

LDL receptor related protein also called LRP-1 or CD91 is known to be interacting with more than one ligand. Studies showed that it can interact with cellular receptors such as PDGF.

PDGF signaling is enhanced in diabetes possibly via high glucose levels which could worsen insulin resistance in diabetes. PDGFR signaling is controlled by LRP-1 and is inhibited by Imatinib. Imatinib could modulate PDGF and LRP-1 interaction. To be more precise, PDGF and LRP-1 interaction happens in endothelial cells leading to arteriosclerosis. The same could happen in beta cells leading to their dysfunction and death in Diabetes.

We tried to analyze if PDGF and LRP-1 interaction happens in beta cells. LRP-1 was expressed and is tyrosine phosphorylated when stimulated with Fetal Calf Serum and PDGF stimulator, where the phosphorylation is completely abolished by Tyrosine Kinase inhibitors- Imatinib and Sunitinb.

LRP-1 expression resulted in co-expression of PDGF receptor, but the supplementation of tyrosine kinase inhibitors did not show consistent effects on co-expression. It has been shown that knocking down of LRP-1 decreases PDGF expression, which is a good sign for beta cell survival.

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