Role of TNFα in diabetes mellitus

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Diabetes Mellitus is a kind of world spread metabolic disorder, known with prolonged high levels of glucose. Diabetes type 2 (T2DM), constitutes about 90% of cases, showing polydipsia, polyphagia, polyuria as its symptoms. Insulin resistance (IR) is a feature of diabetes in which due to various factors, Insulin signaling pathway is disturbed and phosphorylated Insulin receptor substrate 1 (IRS-1) is inhibited. Liver Insulin resistance is the main cause of high fasting blood glucose (Hyperglysemia), since up to 50-60% of hepatic glucose is produced through gluconeogenesis procedure. IR is caused by the presence of free fatty acids (FFAs) in plasma, leading stimulation of gluconeogenesis and increased glucose production. Cytokines like TNFα, IL1β, IL6 can also interfere Insulin signaling and cause IR. TNFαs play various roles in body. It causes IR in different tissues by Jun NH2-terminal kinase (JNK) dependent phosphorylation of serine, inhibiting the activity of phosphatidylinositol 3-kinase (PI3K) enzyme in Insulin signaling pathway and reducing GLUT-4 or IRS-1 expression. To investigate the expression of TNFα, Hepatocellular carcinoma cells (HepG2) cells were cultured in DMEM medium, containing palmitate (PA) and high in glucose. TNFα gene expression was prevented using short hairpin RNA (sh-RNA) lentiviral particles to investigate the effects in hepatocyte cells and results were evaluated using western blot. Increased expression of TNFα was observed in HepG2 cells that were IR induced by PA. The results of the western blot showed reduced expression in the absence of TNFα gene in these cells compared to the control samples. Also the amount of phosphorylation of IRS-1 increased in the cells that TNFα decreased.

In nutshell, based on the evidence, PA can increase the expression of cytokine in the inflammatory pathway, including TNFα in hepatocyte cells, by making disturbance in Insulin signaling and resistance.

References:
