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EC PHARMACOLOGY AND TOXICOLOGY
Opinion

UCP-2 and Adiponectin in Diabetes

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Received: April 06, 2021; **Published:** April 30, 2021

The diagnostic sign of Diabetes mellitus (DM) is high blood sugar or hyperglycemia which occurs either due to no/inadequate insulin secretion (DM1), and no/inadequate insulin action (DM2). Insulin is a hormone secreted into the bloodstream by the β-cells in the pancreas in response to high blood sugar to regulate the glucose levels in blood. When carbohydrate rich meal is eaten, glucose with help of glucose transporters enter the β-cells where after going through various metabolic pathways ATP is released and the ATP to ADP ratio causes secretion of insulin. In DM2 because body's cells do not respond to insulin a condition called insulin resistance develops. Though the cause of DM1 and DM2 are different, the chronic complications such as cardiomyopathy, retinopathy, nephropathy etc. of both the disease are similar and are related to oxidative stress or the generation of free radicals. Today diabetes is one of the most researched disease, with multiple documented molecular pathways. Multiple pathways are responsible for the development of insulin resistance at a molecular level still a lot remains to be understood. One of it being the interaction of two molecules: Adiponectin and Uncoupling protein 2 (UCP2).

Adiponectin is secreted by the adipose tissue and plays an important role in glucose homeostasis. A significant amount of experimental documentation indicates that adiponectin is an insulin-sensitizing hormone. Recent studies indicate that low blood adiponectin concentration are correlated with insulin resistance and T2DM. Regulation of glucose metabolism and insulin sensitization is done by adiponectin via phosphorylation and activation of AMPK which modulates fatty acid uptake, oxidative metabolism, glucose transport, glycolysis and mitochondrial biogenesis. Adiponectin also has anti-inflammatory and antioxidant properties and decreased adiponectin in diabetes promotes inflammation and oxidative stress leading to diabetic complications [1]. Therefore, adiponectin represents a potential candidate in understanding diabetes.

Uncoupling proteins (UCPs) are mitochondrial transporter proteins which lowers mitochondrial membrane potential and regulates glucose disposal rate, insulin secretion, and prevents oxidative stress. Uncoupling protein 2 (UCP2) is expressed in the pancreatic β-cells in diabetes and it negatively regulates insulin meaning with increased expression of UCP 2 the ability of β-cells to secrete insulin decreases. Whenever there is an increase in blood glucose levels the mitochondrial membrane potential increases resulting in generation of free radicals causing enhancement of UCP2 expression. UCP2 causes decrease in mitochondrial membrane potential, acts as an antioxidant reducing oxidative stress and decreases ATP production which is the key to insulin secretion thus reducing insulin secretion. It is now well documented in animal models of T2DM that UCP2 expression is significantly increased [2]. Therefore, UCP2 represents a potential candidate in understanding diabetes.

The above discussion indicates that in diabetes the expression of UCP2 increases and of adiponectin decreases. In 2007 Chevillotte., et al. observed that UCP 2 null mice the expression of adiponectin in adipose tissue is reduced. They documented that action of UCP2, on ROS production plays a vital role in negative regulation of adiponectin gene expression meaning when UCP2 is not there oxidative stress occurs which reduces adiponectin expression. In other words their findings suggest that when UCP2 levels in adipose tissue increases they reduce oxidative stress and positively induce adiponectin gene expression and therefore may favor insulin sensitivity [3]. In a study

by Mahadik., et al. UCP2 gene expression was evaluated in human adipose tissue of diabetic patients and its association with adiponectin was studied to get a perception about their correlation. They found that UCP2 gene and adiponectin gene expression were both significantly reduced in diabetic patients compared with controls [4]. Adiponectin treatment in liver causes UCP2 up-regulation [5]. Decrease in UCP2 expression causes an increase in another adipocytokine TNFα which directly downregulates adiponectin contrarily increased concentration of adiponectin increases UCP2 expression in the aorta thus attenuating the vascular damage [6]. In T2DM their is upregulation of UCP2 in pancreatic cell which is accompanied by oxidative stress and downregulation of adiponectin which is contrary to the above correlation of UCP2 oxidative stress and adiponectin. It would be interesting to study the association to find new therapeutic targets.

Conflict of Interest

There is no conflict of interest.

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Volume 9 Issue 5 May 2021