PPARγ and Adiponectin: Interplay of Two Key Regulators of Metabolism

Nowadays, obesity has become widely spread across the United States and many parts over the world, increasing the risk of developing various metabolic diseases, such as cardiovascular disease, type 2 diabetes and certain types of cancer (1). As the major component of adipose tissue, adipocytes are generated through adipogenesis, which is regulated by various transcription factors and endocrine modulators (2). PPARγ is the most critical transcription factor that functions as a master switch in controlling adipocyte differentiation and development, also important in controlling glucose homeostasis and insulin sensitivity (3). In adipocytes, the lipid droplet encompasses greater than 95% of the entire cell body and serves as storage for triglycerides. Hence the adipocyte is traditionally viewed as a cell that is primarily involved in energy storage. However, as more and more adipokines are discovered in the past two decades, adipose tissue has been identified as a metabolically active endocrine organ (4). Adiponectin, first described in 1995 by Harvey F. Lodish (5), is one of the most abundant adipokines in adipocytes. It is involved in regulating glucose level and fatty acid oxidation, exhibiting antidiabetic and antiatherogenic effects (4). Recent studies find that activation of PPARγ improves the secretory profile of adipose tissue and PPARγ activity correlates with the level of adiponectin (6). Further studies show that PPARγ regulates adiponectin level by direct activation of adiponectin gene transcription by binding to the PPAR response element (PPRE) on the upstream of the transcription start site of adiponectin (7). In addition, there is evidence indicating that PPARγ increases adiponectin secretion by stimulating the expression components of the adiponectin secretory pathway such as ER resident protein 44 kDa (ERp44) which plays a major role in the posttranslational processing of adiponectin and determines the oligomer composition of the secreted product (8). These results indicate that adiponectin and its signaling pathway are downstream targets of PPARγ.

References