

THE ROLE OF MITOCHONDRIA DURING DIFFERENTIATION OF PREADIPOCYTES AND INSULIN INSENSITIVITY OF ADIPOCYTES WITH MITOCHONDRIAL DYSFUNCTION

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Adipocytes play a key role in the regulation of energy metabolism and maintenance of glucose homeostasis in the human body. Recent studies demonstrated that mitochondrial dysfunction may be involved in the pathophysiology of type 2 diabetes, which is characterized by insulin resistance in muscle and adipose tissues. In this study, we attempted to elucidate the role of mitochondria in the differentiation and function of adipocytes. We used the 3T3-L1 preadipocytes to produce adipocytes by appropriate chemical induction. First, we investigated the role of mitochondria during differentiation of 3T3-L1 preadipocytes. The results showed that during adipogenesis the mRNA and protein levels of mitochondrial biogenesis-related genes were up-regulated, and the quantity and function of mitochondria were significantly elevated. Moreover, addition of the mitochondrial respiratory inhibitors at the early phase of differentiation process could block the cell differentiation. These results suggest that elevated mitochondrial biogenesis was required for the differentiation of preadipocytes to support their need of energy to perform normal physiological function. On the other hand, we examined the role of mitochondrial dysfunction in insulin resistance. The results showed a significant decrease in insulin response as indicated by lower glucose uptake and decline in the phosphorylation of AKT in adipocytes with mitochondrial dysfunction. Besides, we observed that the expression of glucose transporter 4 (Glut4) was down-regulated in a time-dependent manner in adipocytes treated with mitochondrial respiratory chain inhibitors. Taken together, our results suggest that mitochondrial dysfunction resulted in higher intracellular H_2O_2 levels that lead to insulin resistance of adipocytes *in vitro* through inactivation of AKT and down-regulation of Glut4 expression. Furthermore, this study has provided a molecular basis for the well-documented observation that some of the patients with distinct mitochondrial diseases, like MELAS and MERRF syndromes, often manifest complications such as diabetes.

Keywords:

Insulin resistance / Mitochondrial dysfunction / Glucose transporter