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An increase in insulin sensitivity of 3T3-L1 adipocytes induced by transmembrane tumor Necrosis Factor –α

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Abstract

Tumor necrosis factor (TNF)-α is a proinflammatory cytokine that links obesity and insulin resistance. However, the effect of transmembrane TNF-α (tmTNF-α) on insulin resistance remains unknown. Here, we demonstrated that high concentration of glucose(25mM) significantly reduced insulin-induced glucose uptake by 3T3-L1 adipocytes that was concomitant with a decrease in tmTNF-α expression but an increase in soluble TNF-α(sTNF-α) secretion. This insulin resistance, however, could be reversed in part by neutralization of TACE using a specific antibody to prevent the cleavage of tmTNF-α into sTNF-α, as manifested by enhancement of insulin-induced glucose uptake, pointing out a possible different role of tmTNF-α in insulin resistance. Then, we stimulated 3T3-L1 adipocytes with exogenous tmTNF-α and sTNF-α respectively, and found that sTNF-α inhibited insulin-induced tyrosine phosphorylation of IRS-1 and AKT phosphorylation, leading to suppression of the glucose uptake induced by insulin. In contrast, tmTNF-α has been shown to elevate insulin-induced glucose uptake by twofold as a result of promoting the insulin signaling. Furthermore, we found that tmTNF-α downregulated the expression of IL-6 and MCP-1 through inactivation of NF-κB and upregulated the expression of adiponectin through PPAR-γ in 3T3-L1 adipocytes. Inhibition of PPAR-γ expression by GW9662, an inhibitor of PPAR-γ, could decrease tmTNF-α-induced adiponectin transcription, blocking tmTNF-α-enhanced AKT phosphorylation and glucose uptake. These data suggest that tmTNF-α may contribute to the improvement of insulin resistance, which is opposite to sTNF-α, thereby specific blockage of tmTNF-α conversion into sTNF-α may be useful to increase insulin sensitivity for the clinical treatment of type 2 diabetes.

Biography

Wenjing Zhou earned her bachelor of medicine at the age of 23 years from Tongji Medical College. She is studying for her Ph.D in the department of Immunology, Tongji Medical College. “Mechanism of tmTNF-α improving insulin resistance” is her first subject, and she is writing the first paper about her research.