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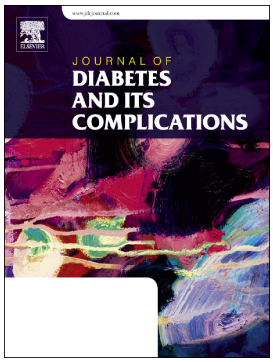

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FGF21 Protects Human Umbilical Vein Endothelial Cells Against High Glucose-Induced Apoptosis via PI3K/Akt/Fox3a Signaling Pathway

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Abstract

Diabetic macroangiopathy is the main cause of morbidity and mortality in patients with diabetes. Endothelial cell injury is a pathological precondition for diabetic macroangiopathy. Fibroblast growth factor 21 (FGF21) is a key metabolic regulator which has recently been suggested to protect cardiac myocytes and vascular cells against oxidative stress-induced injury in vitro and vivo. In this study, we aimed to investigate the protective capacity of FGF21 in human umbilical vein endothelial cells (HUVECs) against high glucose (HG)-induced apoptosis via phosphatidylinositol-3-kinase/protein kinase B (PI3K/Akt)/FoxO3a pathway. Our results show that pretreating HUVECs with FGF21 before exposure to HG increases cell viability, while decreasing apoptosis and the generation of reactive oxygen species. Western blot analysis shows that HG reduces the phosphorylation of Akt and FoxO3a, and induces nuclear localization of FoxO3a. The effects were significantly reversed by FGF21 pre-treatment. Furthermore, the protective effects of FGF21 were prevented by PI3K/Akt inhibitor LY294002. Our data demonstrates that FGF21 protects HUVECs from HG-induced oxidative stress and apoptosis via the activation of PI3K/Akt/FoxO3a signaling pathway.

Keywords: FGF21, eNOS, Oxidative stress, Apoptosis, FoxO3a, Akt