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Thioredoxin-interacting protein deficiency ameliorates diabetic retinal angiogenesis

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Abstract

Diabetic retinopathy is the leading cause of blindness among working-aged adults around the world. Hyperglycemia and intraocular vascular endothelial growth factor (VEGF) over-accumulation are essential for the progression of diabetic retinopathy, which eventually results in proliferative diabetic retinopathy, characterized by pathologic angiogenesis and impaired vision. Thioredoxin-interacting protein (TXNIP) was highly induced in retinal endothelial cells under diabetic conditions. However, the role of TXNIP in diabetes-associated retinal angiogenesis remains elusive. Here, we investigated whether the absence of TXNIP alters diabetes-associated retinal angiogenesis. Exposure of human retinal microvascular endothelial cells (HRMECs) to moderately high glucose (MHG) promoted cell migration and tube formation, but not proliferation. Knockdown of TXNIP suppressed moderately high glucose (MHG)-induced reactive oxygen species (ROS) generation, migration, tube formation and activation of Akt/mTOR pathway in HRMECs. Moreover, gene silencing of TXNIP inhibited VEGF-induced angiogenic response by blocking VEGFR2 and downstream signal pathway Akt/mTOR activation in HRMECs. Furthermore, TXNIP knockout inhibited VEGF or VEGF and MHG-induced retinal angiogenesis *ex vivo* compared with wild-type mice. In conclusion, our study demonstrated that TXNIP deficiency inhibited VEGF or/and MHG-induced angiogenic response in HRMECs and mice retinas and suggested TXNIP may be a potential therapy target for treating proliferative diabetic retinopathy.

Keywords

Proliferative diabetic retinopathy, TXNIP, Angiogenesis, VEGFR2, Akt/mTOR.

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