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Nogo-B promotes endoplasmic reticulum stress-mediated autophagy in endothelial cells of diabetic nephropathy

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Objectives : Endothelial cells are the critical targets of injury in diabetic nephropathy (DN) and endothelial cell lesions contribute to the disease progression. Neurite outgrowth inhibitor B (Nogo-B), an endoplasmic reticulum (ER)-resident protein, plays a pivotal role in vascular remodeling after injury and maintains the structure and function of the endoplasmic reticulum. Yet the role of Nogo-B in regulation of ER stress and endothelial cell injury remains largely unknown. Herein, we tested the hypothesis that Nogo-B activates ER stress-mediated autophagy and protects endothelial cells in diabetic nephropathy.
Methods : The level of sNogo-B in serum(34 patients with diabetes) or urinary(17) was measured and 47 healthy controls were used as normal controls. In the vitro, siRNA was used to silence the expression of Nogo-B in Ea.hy926 cells under hyperglycemic condition. In the vivo, adenovirus-induced knockdown of Nogo-B was performed in db/db diabetic mice for 8 weeks. Other testing methods include ELISA, RNA-seq, Immunofluorescence, western blot, transmission electron microscopy(TEM), periodic acid-Schiff(PAS) stain and et al.
Results : The level of Nogo-B was decreased in glomerular endothelial cells in biopsy specimens from DN patients. In vivo and in vitro studies have shown that silencing Nogo-B activated ER stress signaling and suppressed the expression of autophagy-related marker early growth response 1 (EGR1) and microtubule-associated protein light chain 3 (LC3) in endothelial cells in hyperglycemic condition.
Conclusions : These results denote that Nogo-B contributes to ER stress-mediated autophagy and protects endothelial cells in diabetic nephropathy, providing new evidences for understanding the role of ER stress-mediated autophagy in endothelial cells of diabetic nephropathy.