

Abstract Submission No.: A-1029

IGF-2 triggers epithelial-mesenchymal transition in mesothelial cells and contributes to the pathogenesis of dialysis-related peritoneal fibrosis.

Siqi Zheng, Wenxue Hu, Guanglan Li, Ganyuan He, Xinling Liang

Department of Internal Medicine-Nephrology, Guangdong Provincial Peoples Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangzhou, China, China

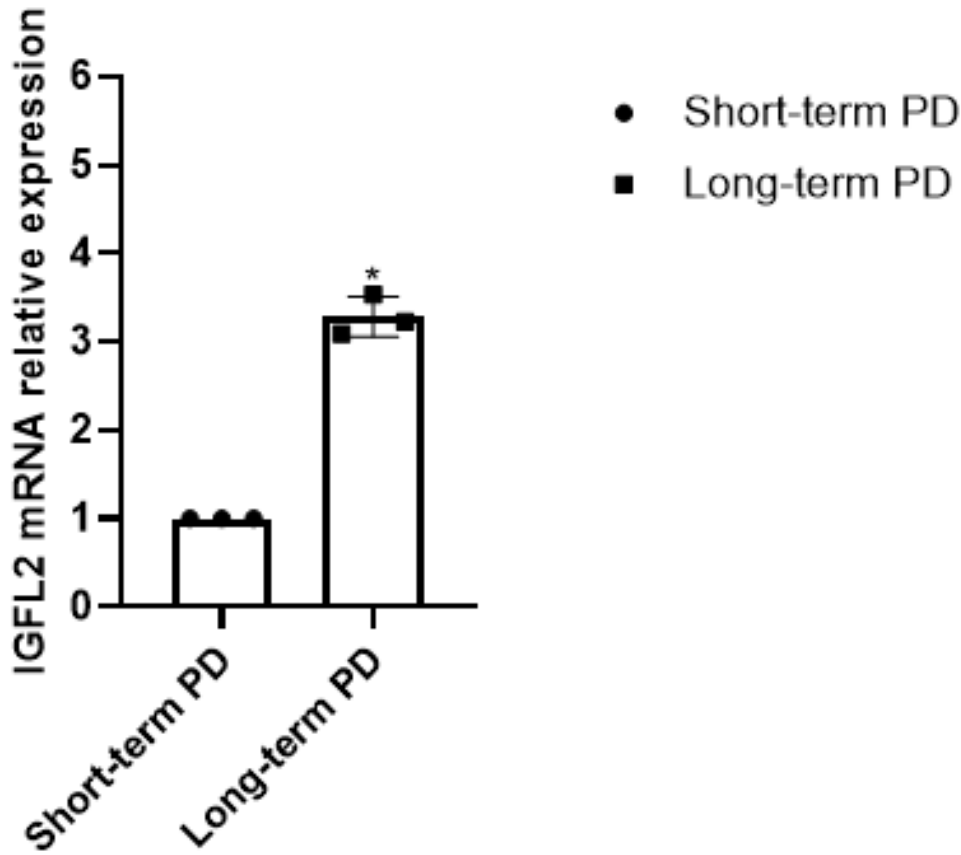
Objectives : To investigate the effect of IGF-2 in TGF- β induced epithelial-mesenchymal transition (EMT) in mesothelial cells (MCs), and evaluate the morphological and molecular changes in a mice model of peritoneal dialysis-related fibrosis.

Methods : In vivo, we established peritoneal fibrosis model in IGF-2 wild-type and IGF-2 global deficient mice by daily intraperitoneal injection of peritoneal dialysis fluids (PDF) containing 4.25% glucose at a dose of 100 ml/kg daily for 4 weeks to assess the effect of IGF-2 on peritoneal morphology and markers related to fibrosis and epithelial-mesenchymal transition (EMT). Meanwhile, we collected overnight effluent samples from patients with continuous ambulatory peritoneal dialysis (CAPD) (2,000 ml) applied scRNA-seq to analyze cell composition and properties. In vitro, we treated MeT-5A cells with TGF- β (5ng/ml) to stimulate EMT and then transfected with IGF-2 siRNA to explore the potential mechanism of IGF-2 in peritoneal fibrosis.

Results : IGF-2 expressed highly in mesothelial cells isolated from the PD effluents of continuous ambulatory peritoneal dialysis (CAPD) patients. In vivo and in vitro study showed that IGF-2 promoted TGF- β or high glucose induced fibrosis, significantly elevated the levels of markers of EMT including α -smooth muscle actin (α -SMA), fibronectin and reduced the levels of E-cadherin. While, inhibition of IGF-2 could relieve the fibrosis. Furthermore, which had been cleared was that IGF-2 alleviated fibrosis by facilitating the activation of the mTOR signaling pathway.

Conclusions : Our study demonstrate that IFG-2 plays a important role in the pathogenesis of dialysis-related peritoneal fibrosis by triggering epithelial-mesenchymal transition in mesothelial cells and suggest implication of the mTOR pathway in mediating the effects of IGF-2 in EMT of MCs.

IGF-2 mRNA relative expression.png



IGF-2 mRNA relative expression.png

