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Cdc42-Interacting Protein-4 Promotes TGF-?1-Induced Epithelial-Mesenchymal Transition and Extracellular Matrix Deposition in Renal Proximal Tubular Epithelial Cells

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Abstarc :

Cdc42-interacting protein-4 (CIP4) is an F-BAR (Fer/CIP4 and Bin, amphiphysin, Rvs) family member that regulates membrane deformation and endocytosis, playing a key role in extracellular matrix (ECM) deposition and invasion of cancer cells. These processes are analogous to those observed during the initial epithelial-mesenchymal transition (EMT) of renal tubular epithelial cells. The role of CIP4 in renal tubular EMT and renal tubulointerstitial fibrosis was investigated over the course of the current study, demonstrating that the expression of CIP4 increased in the tubular epithelia of 5/6-nephrectomized rats and TGF-?1 treated HK-2 cells. Endogenous CIP4 evidenced punctate localization throughout the cytosol, with elevated levels observed in the perinuclear region of HK-2 cells. Subsequent to TGF-?1 treatment, CIP4 expression increased, forming clusters at the cell periphery that gradually redistributed into the cytoplasm. Simultaneously, EMT induction in cells was confirmed by the prevalence of morphological changes, loss of E-cadherin, increase in ?-SMA expression, and secretion of fibronectin. Overexpression of CIP4 promoted characteristics similar to those commonly observed in EMT, and small interfering RNA (siRNA) molecules capable of CIP4 knockdown were used to demonstrate reversed EMT. Cumulatively, results of the current study suggest that CIP4 promotes TGF-?1-induced EMT in tubular epithelial cells. Through this mechanism, CIP4 is capable of inducing ECM deposition and exacerbating progressive fibrosis in chronic renal failure.

Key Word :
Cdc42-interacting protein-4, epithelial-mesenchymal transition, renal proximal tubular epithelial cells, ?-catenin, TGF-?1-induced

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