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DIFFERENT REGULATION OF THE PINCH-1-ILK-α-PARVIN COMPLEX BY TRANSFORMING GROWTH FACTOR-β1 IN GLOMERULAR CELLS

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Glomerular damage is a major cause of renal failure. Recent studies suggest that a ternary protein complex consisting of PINCH-1, integrin-linked kinase (ILK) and α-parvin, cytoplasmic components of cell-extracellular matrix adhesions, plays pivotal roles in regulation of glomerular cell behavior. This study reports here that transforming growth factor-β1 (TGF-β1), a key factor in the progression of glomerular failure, regulates the PINCH-1-ILK-α-parvin (PIP) complex formation in glomerular podocytes and mesangial cells. Treatment of podocytes with TGF-β1 inhibited the PIP complex formation. Forced disruption of the PIP complex in podocytes activated p38 MAP kinase and promoted apoptosis. Importantly, inhibition of p38 MAP kinase, either with a chemical p38 inhibitor (SB202190) or with a dominant negative form of p38α, alleviated podocyte apoptosis induced by the disruption of the PIP complex. In contrast to an inhibitory role of TGF-β1 in podocytes, TGF-β1 in mesangial cells promoted the PIP complex formation and inhibited caspase-3 activity. Thus, TGF-β1 regulates the PIP complex in a cell type-dependent fashion. Because the PIP complex promotes glomerular matrix deposition and protects podocytes from apoptosis, the TGF-β1-induced up- and down-regulation of the PIP complex likely contribute to the pleiotropic effects of TGF-β1 on different glomerular cell types and hence the progression of glomerular failure.
Key Words: TGF, Podocyte, Mesangial cell, PINCH-1-ILK-parvin, P38