

P016 PKB/Akt activity is important for epithelial-mesenchymal transition during renal fibrosis

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Transforming growth factor- β 1 (TGF- β 1) is a primary mediator of cellular damage during diabetic nephropathy, and its upregulation is implicated in epithelial-mesenchymal transition (EMT) associated with renal fibrosis and kidney disease. PKB/Akt and its downstream targets such as GSK3 β have been implicated in the onset and progression of EMT in renal fibrosis. We demonstrate that TGF β 1 can induce PKB/Akt activation in kidney epithelial cells, together with downstream targets such as GSK3 β . LY294002 and wortmannin reduced this TGF β 1-mediated activation. Wild-type, but not mutant PTEN (C124S) also reduced PKB/Akt activation in this regard. Inhibition of PKB/Akt significantly reduced the ability of TGF β 1 to induce EMT in renal epithelial cells, suggesting that PKB/Akt activity is involved in this response. To examine the role of PKB/Akt activation in DN *in vivo*, PKB/Akt activation in kidney sections from both control Wistar and type 2 diabetic Goto-Kakizaki rats (GK) was analysed. Elevated levels of phosphorylated PKB/Akt and its downstream target pGSK3 β were observed in the kidneys of diabetic, but not control Wistar rats, with pronounced staining in the kidney tubules. These data suggest that TGF β 1 mediated PKB/Akt signaling plays an important role in the fibrotic response triggered by the extracellular milieu in diabetic nephropathy.