

Publication

Regulation of PDZ domain containing 1 (PDZK1) Expression by Hepatocyte Nuclear Factor 1 alpha (HNF1 α) in Human Kidney

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In the renal proximal tubule the secretion and reabsorption of glomerularly filtrated compounds is realized by a functional network of uptake and efflux transporters. The activity and localization of several transporters expressed at the apical tubular membrane is regulated by the membrane associated protein PDZ domain containing 1 (PDZK1). We aimed to characterize the transcriptional regulation of this modulator of renal transport. Coexpression analyses of PDZK1 and putative regulators were performed using human kidney samples. Protein and mRNA expression of PDZK1 in renal proximal tubule epithelial cells after adenoviral transfer and siRNA knockdown of transcription factor hepatocyte nuclear factor 1 alpha (HNF1 α) was assessed by quantitative real-time PCR and Western blot analysis. Transactivation of the PDZK1 promoter was quantified in cell-based reporter gene assays. Subsequently, the binding of HNF1 α to the PDZK1 promoter was verified by in silico analyses and chromatin immunoprecipitation assay. HNF1 α positively regulated the promoter activity of PDZK1. Adenoviral overexpression of HNF1 α in renal proximal tubule epithelial cells (RPTEC) increased PDZK1 mRNA and protein expression, whereas siRNA knockdown of HNF1 α resulted in decreased expression of PDZK1. Our results show that HNF1 α , which has previously been described as a modulator of several transporters of the renal transportosome, is also a key determinant of PDZK1 transcription.

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