RESULTS

A. PBI-4050 decreases CTGF, collagen I and α-SMA mRNA expression in normal rat kidney fibroblasts

Analysis of the expression of fibrosis markers by qPCR in NRK-49F cells showed a significant reduction of the TGF-β1 (5 ng/ml)-induced expression of CTGF, collagen I and α-SMA in PBI-4050-treated cells.

B. PBI-4050 decreases CTGF and collagen I mRNA expression in human kidney proximal tubule epithelial cells

Analysis of the expression of fibrosis markers by Real-Time qPCR in HK-2 cells showed a significant reduction of the TGF-β1 (10 ng/ml)-induced expression of CTGF and collagen I in PBI-4050-treated cells.

C. PBI-4050 decreases collagen I, α-SMA and TGF-β1 mRNA expression in the 5/6-NX rat model of CKD

Analysis of the expression of fibrosis markers by Real-Time qPCR in the remnant kidney of 5/6-NX rats showed a reduction of the expression of collagen I, α-SMA and TGF-β1 in PBI-4050-treated animals.

D. PBI-4050 reduces interstitial and glomerular fibrosis/sclerosis in remnant kidney in the 5/6-NX rat model of CKD

Histological examination of the remaining renal tissue of 5/6-NX rats revealed reduced lesions and fibrosis (blue-colored collagen deposition) in PBI-4050-treated rats, resulting in a significant reduction of the score of histological glomerular and tubular lesions.

CONCLUSIONS

- PBI-4050 significantly inhibits TGF-β1-induced overexpression of the pro-fibrotic markers collagen I and CTGF in rat kidney fibroblasts and human kidney proximal tubule epithelial cells; inhibition of collagen I and TGF-β1 is also observed in vivo in the 5/6-NX rat model.

- PBI-4050 inhibits fibroblast differentiation into myofibroblasts, as indicated by the significant reduction in the expression of the myofibroblast marker α-SMA in rat kidney fibroblasts as well as in the 5/6-NX rat model.

- These results suggest that PBI-4050 is a potential novel therapy for chronic kidney disease by reduction of fibrosis and myofibroblast differentiation.