Oral Treatment with PBI-4050 Reduces Kidney Fibrosis

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INTRODUCTION

PBI-4050, a novel first-in-class orally active compound which is currently in clinical phase Ib/II in DKD/CKD patients, displays antifibrotic activities via a novel mechanism of action. In a double-blind ascending dose (400 to 2400 mg) in healthy volunteers, PBI-4050 was found to be safe and well tolerated up to 2400 mg without any significant adverse effects. Similarly, PBI-4050 was well tolerated in CKD patients with no SAEs observed at 800 mg.

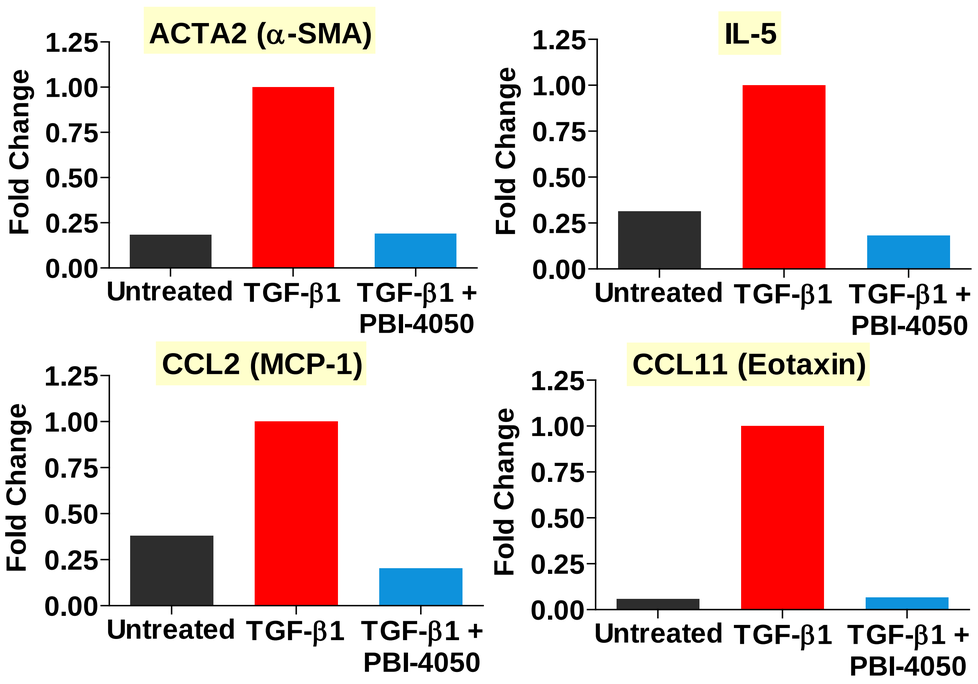
STUDY DESIGN

qPCR: Serum-starved Normal Human Dermal Fibroblasts (NHDF) and human epithelial proximal tubule cells (HK-2) were treated with or without PBI-4050 (500 μM) and TGF-β1 (10 ng/ml) for 24h. qPCR analysis of relative gene expression was performed with RT2 Profiler PCR Array using the ΔΔCt method. mRNA expression levels were normalized against endogenous control levels in each sample and calculated relative to control TGF-β1-treated cells.

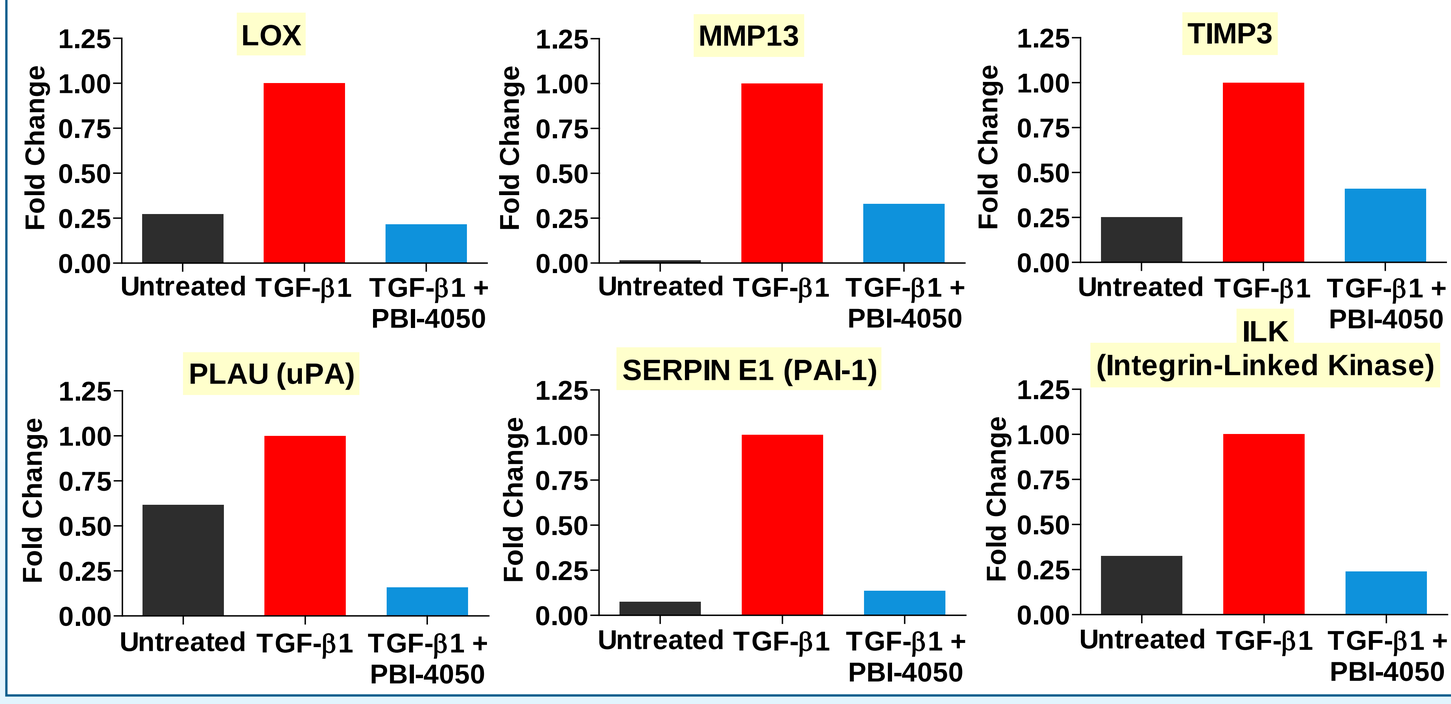
RESULTS

▶PCR array on normal human dermal fibroblasts (NHDF)

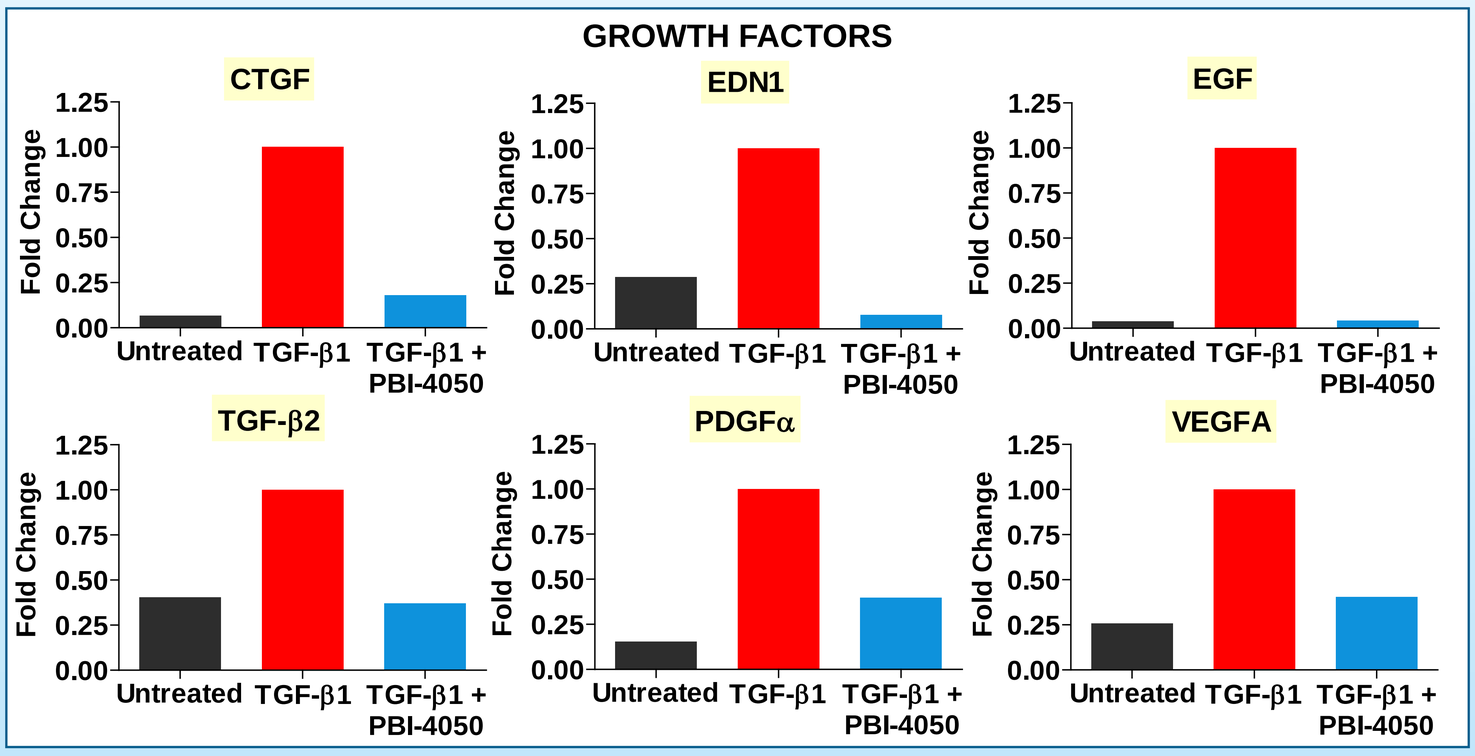
PRO-FIBROTIC/INFLAMMATORY CYTOKINES



REMODELING ENZYMES

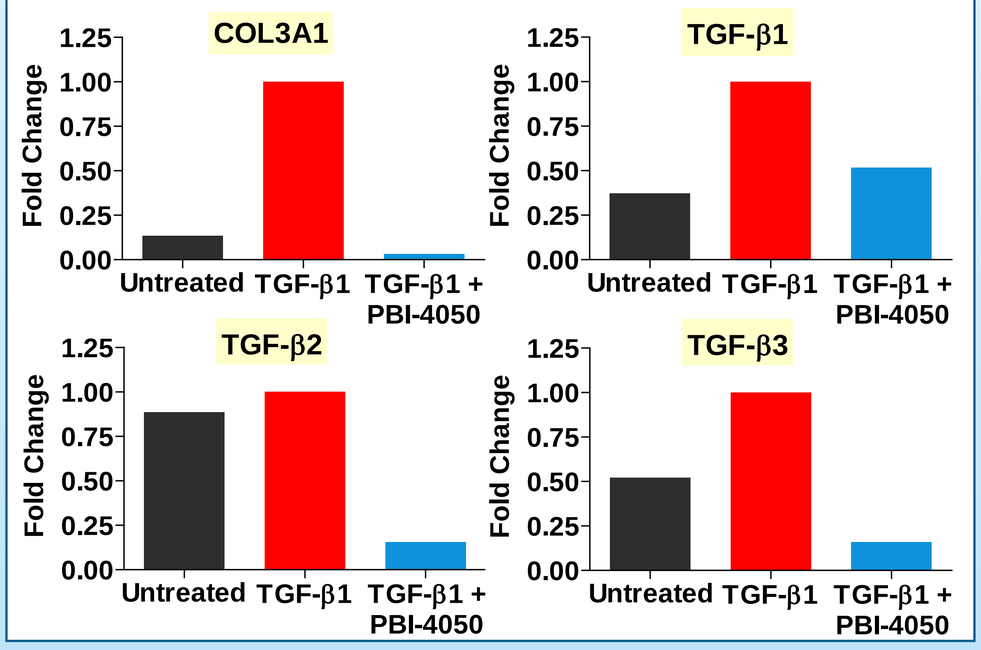


GROWTH FACTORS



▶PCR array on human kidney epithelial cells (HK-2)

EPITHELIAL-TO-MESENCHYMAL TRANSITION



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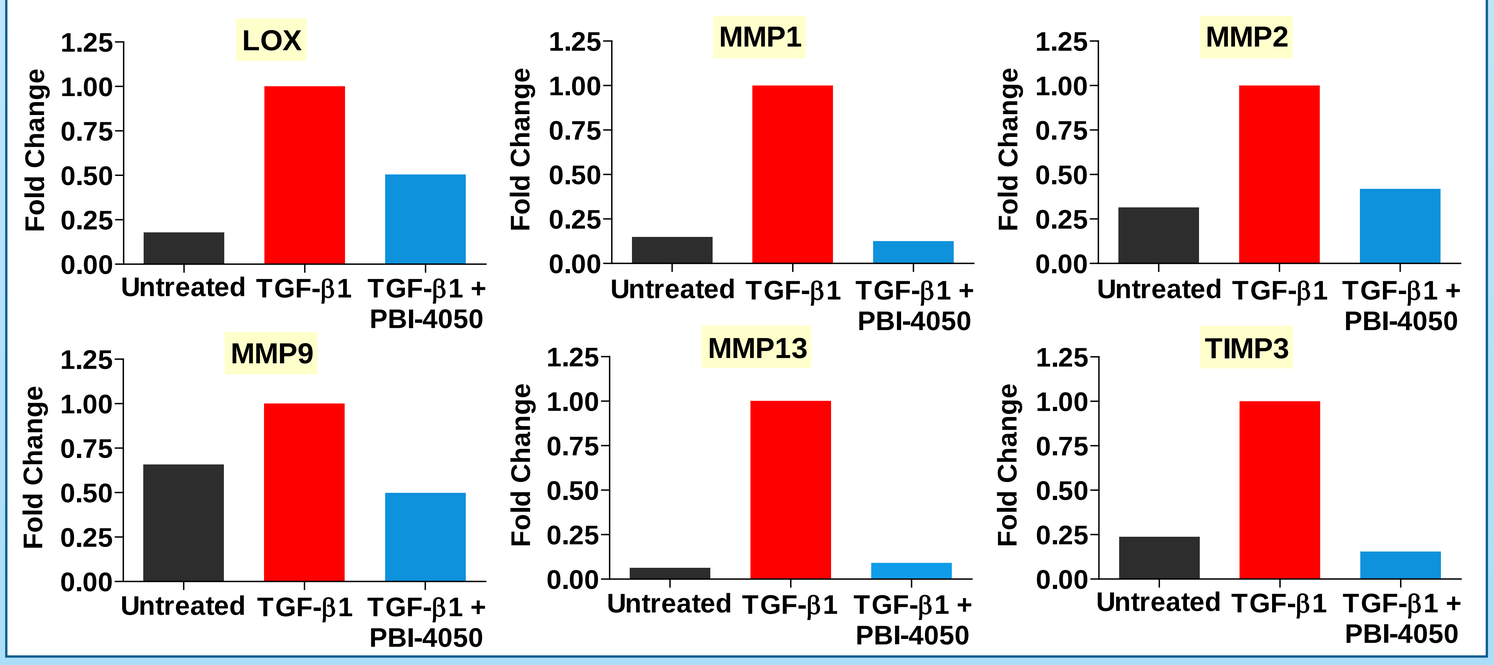
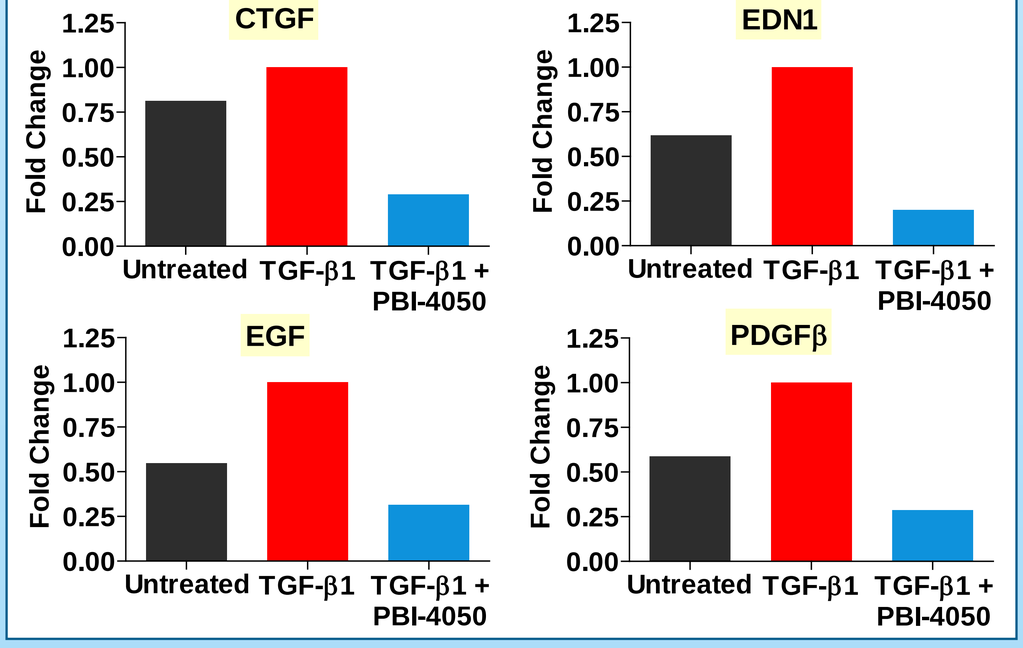


GROWTH FACTORS



CONCLUSION

PBI-4050, which is currently in clinical phase Ib/II in DKD/CKD patients, displays significant antifibrotic activity by regulating pro-fibrotic growth factors and remodeling enzymes, resulting in improved kidney function.