Oral treatment with PBI-4050 reduces kidney fibrosis

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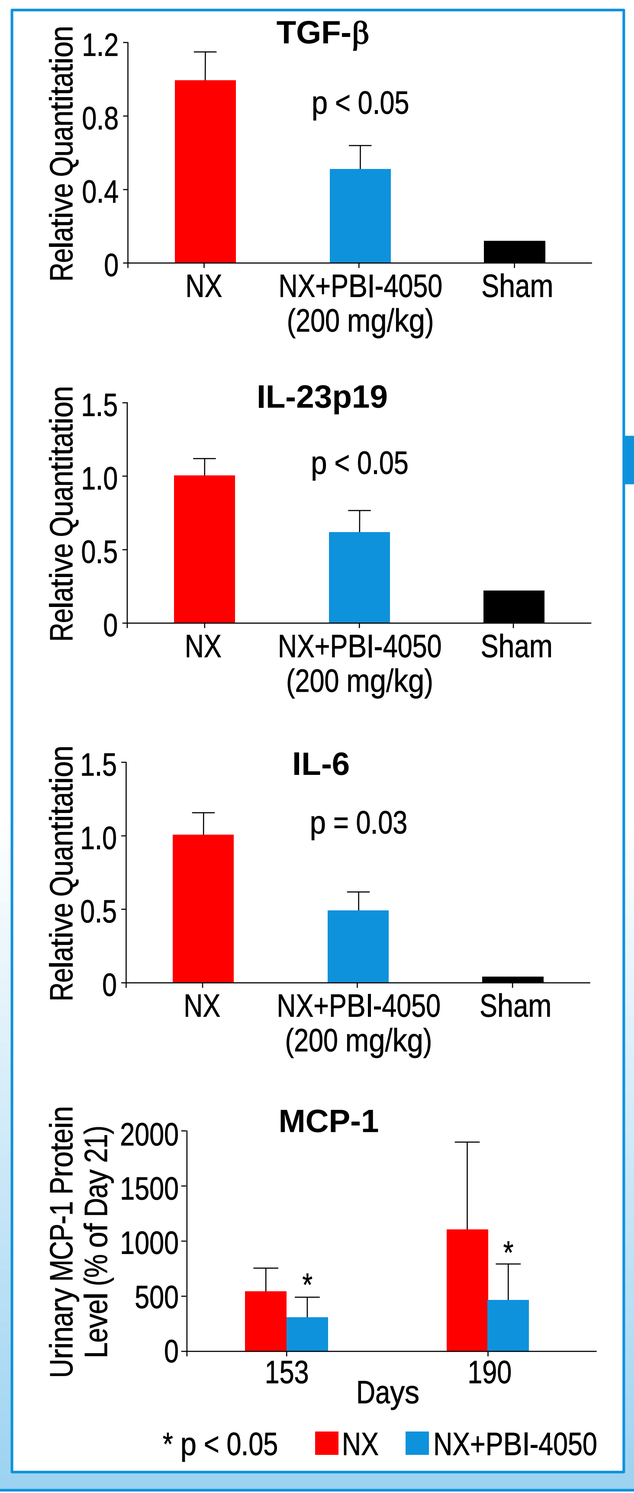
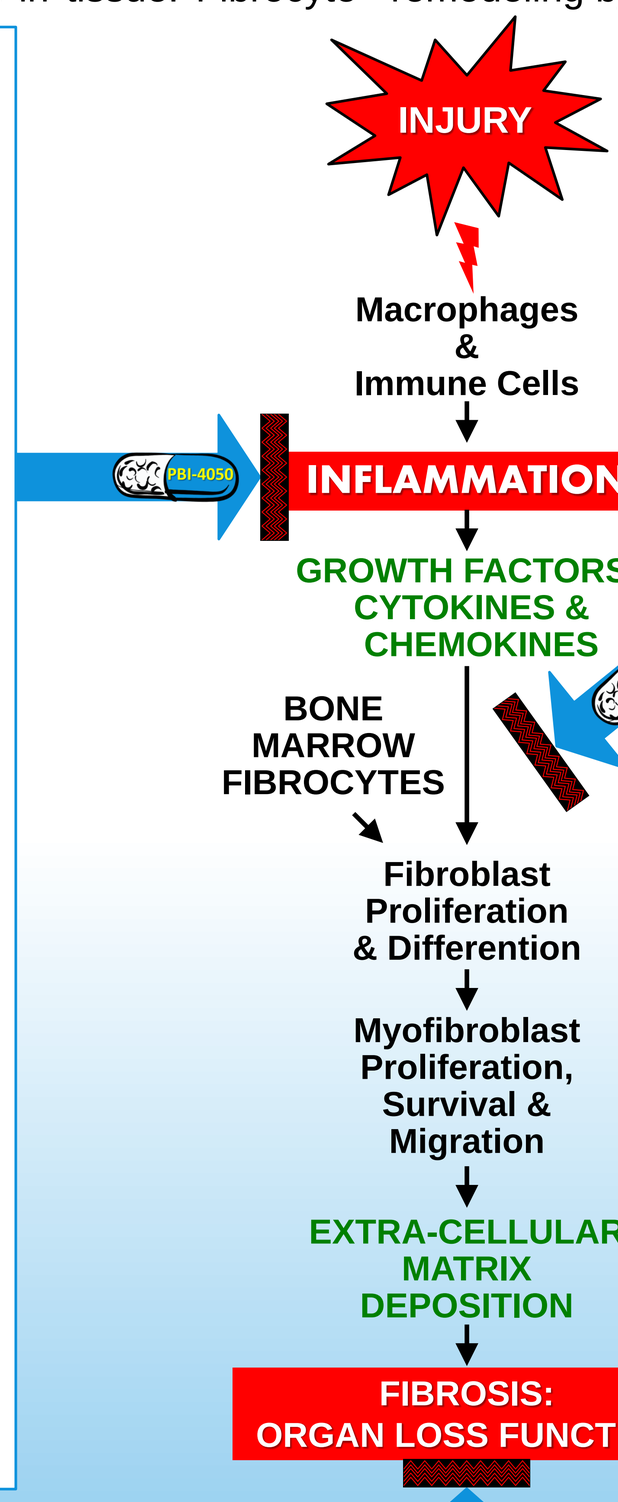
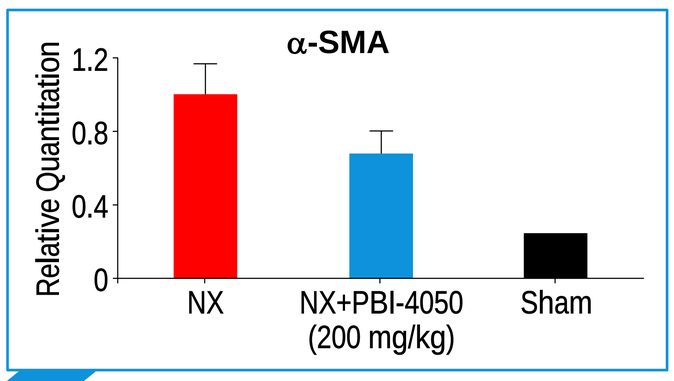
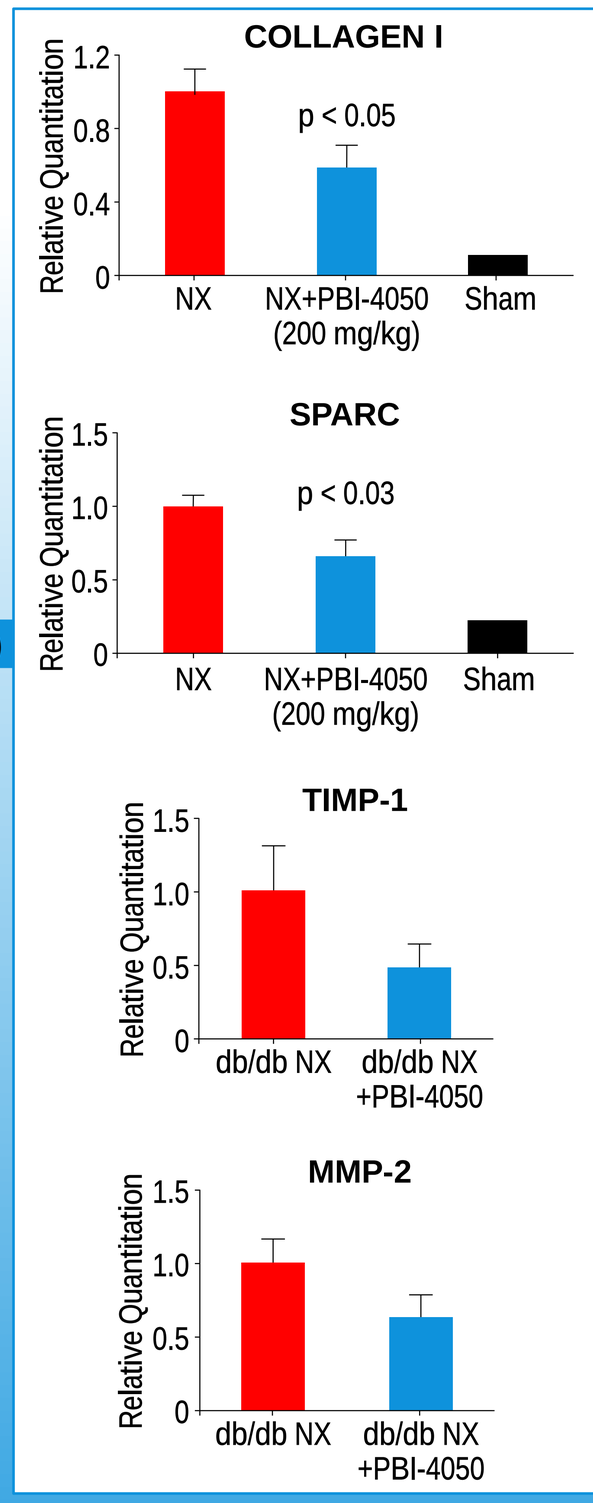
SUMMARY

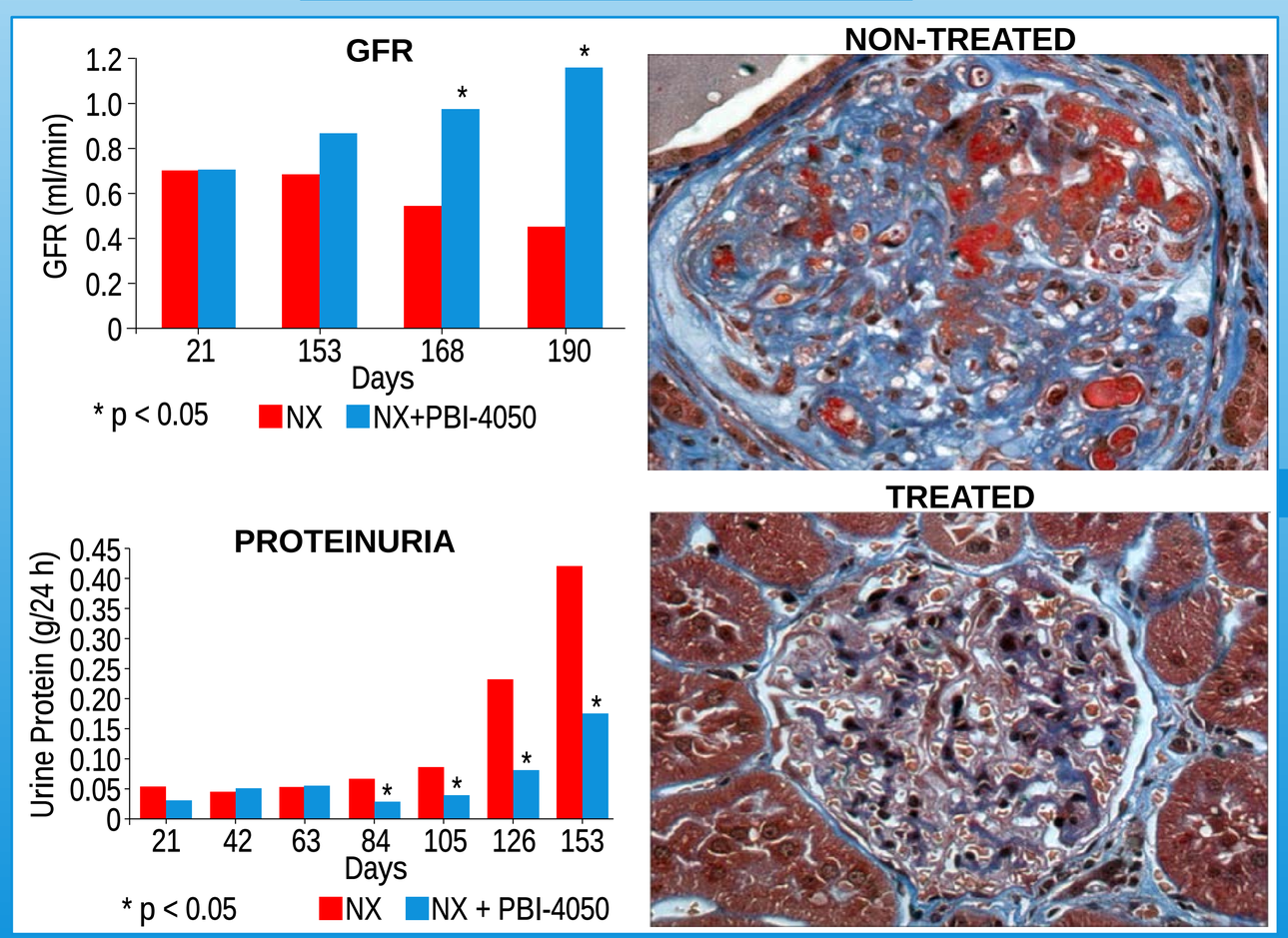
PBI-4050 reduces fibrosis via the regulation of macrophages, T cells, fibrocytes/fibroblasts/myofibroblasts and epithelial cells. In a pro-fibrotic phase, PBI-4050 plays a regulatory role by promoting a Type 1, anti-fibrotic cytokine production phenotype in macrophages and T cells, resulting in a reduction of the over-expression or over-production of TGF-β, MCP-1, CTGF, IL-6 and IL-23. Interestingly, MCP-1 is also an important inducer of fibrocyte precursor migration in tissue. Fibrocyte differentiation, resident fibroblast activation and EMT are the key sources of activated myofibroblasts and successive accumulation of extra-cellular matrix protein deposition and fibrosis. PBI-4050 inhibits fibrocyte differentiation, fibroblast activation and EMT as demonstrated by a reduction in alpha smooth muscle actin (α-SMA), collagen I and SPARC mRNA expression. PBI-4050 also plays a role in tissue remodeling by regulating MMP and TIMP expression.











CONCLUSION

Taken together, these preclinical results suggest that PBI-4050 offers the potential as a novel therapy for the treatment of kidney fibrosis.