

# PBI-4050, an anti-fibrotic compound, regulates the expression of profibrotic cytokines and oxidative stress mediators in a 5/6-nephrectomized rat model



PROMETIC

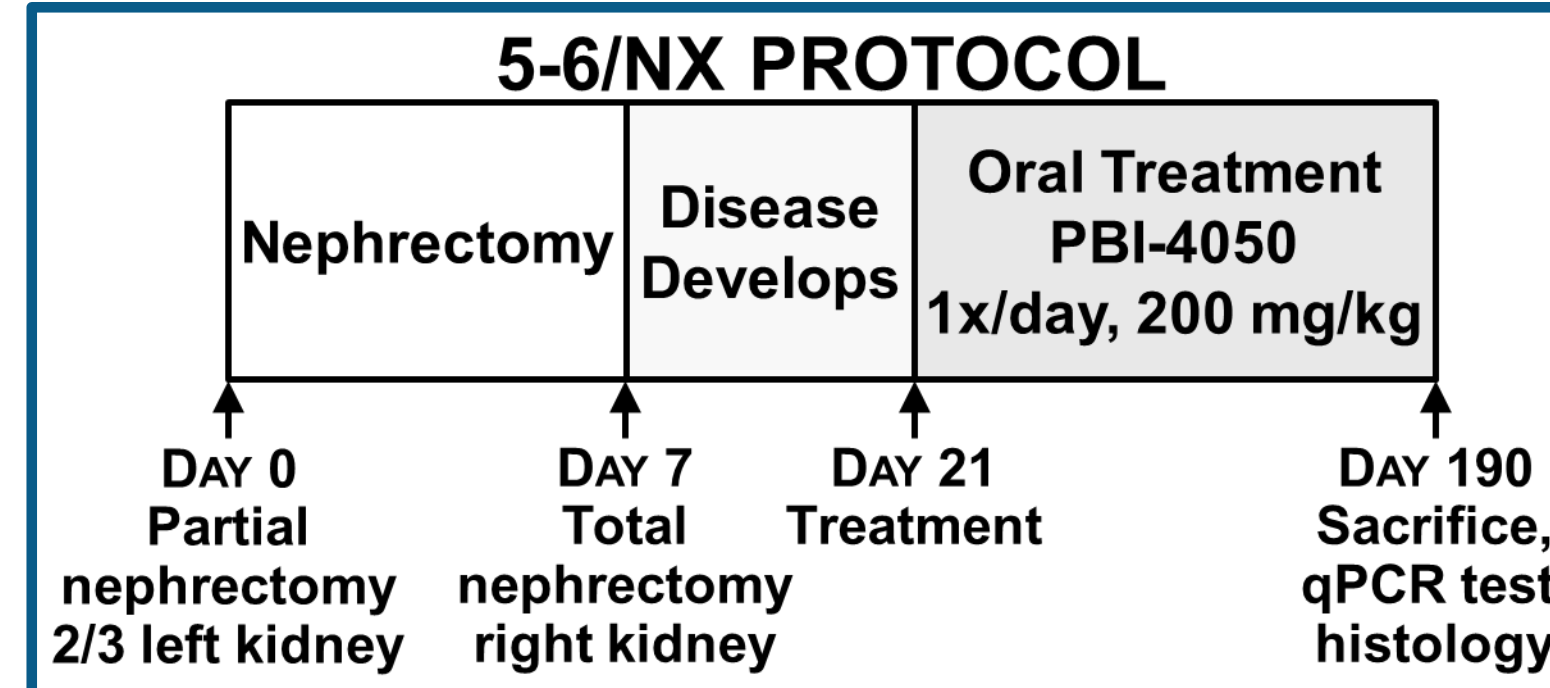
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## BACKGROUND

Progression of fibrosis in the kidney leads to the loss of renal function. Oxidative stress, inflammation, profibrotic cytokines, and matrix remodeling mediators are major players in the evolution of chronic kidney disease (CKD). In the present study, we evaluated the protective effect of PBI-4050 in the 5/6-nephrectomized (NX) rat model of chronic renal failure.

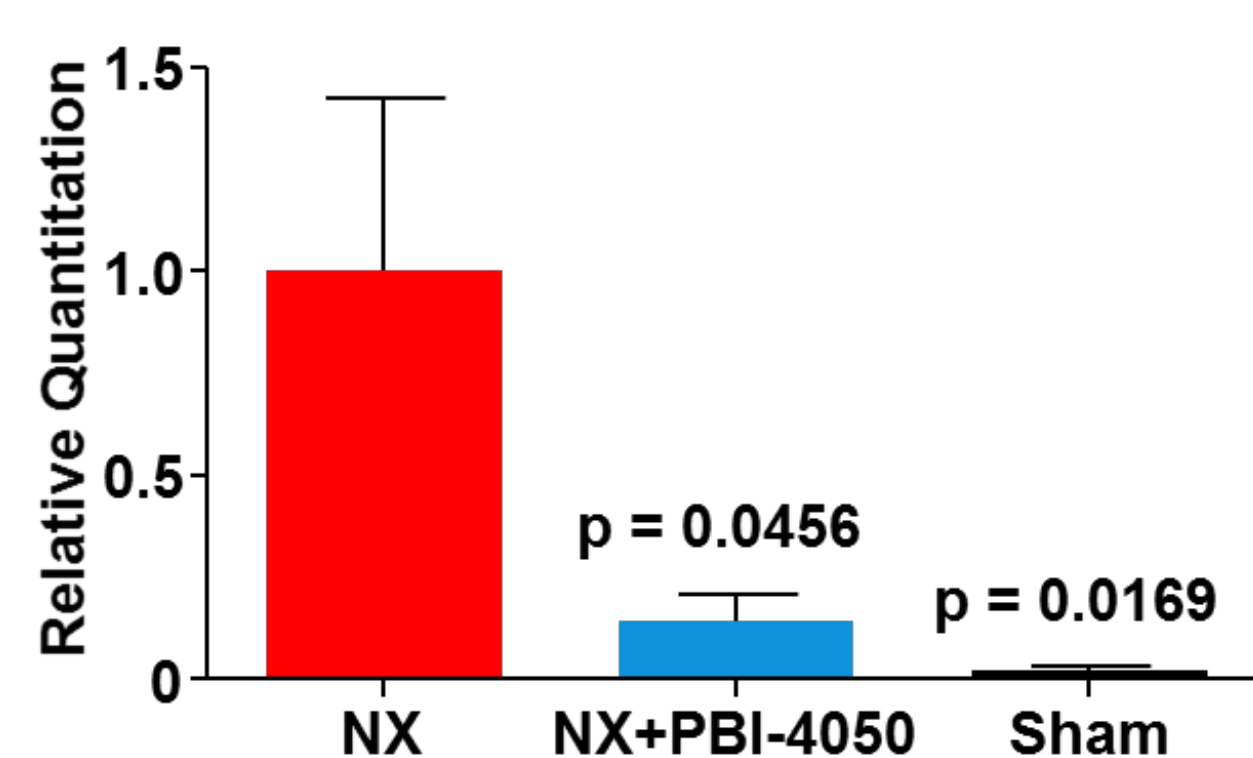
## METHODS



**qPCR:** RNA was isolated from rat remnant kidney using TRIzol® reagent and cDNA was prepared. qPCR analysis of relative gene expression was performed with TaqMan® Gene Expression assays using the Ct method. mRNA expression levels were normalized against GAPDH endogenous control levels in each sample and calculated relative to control NX rats.

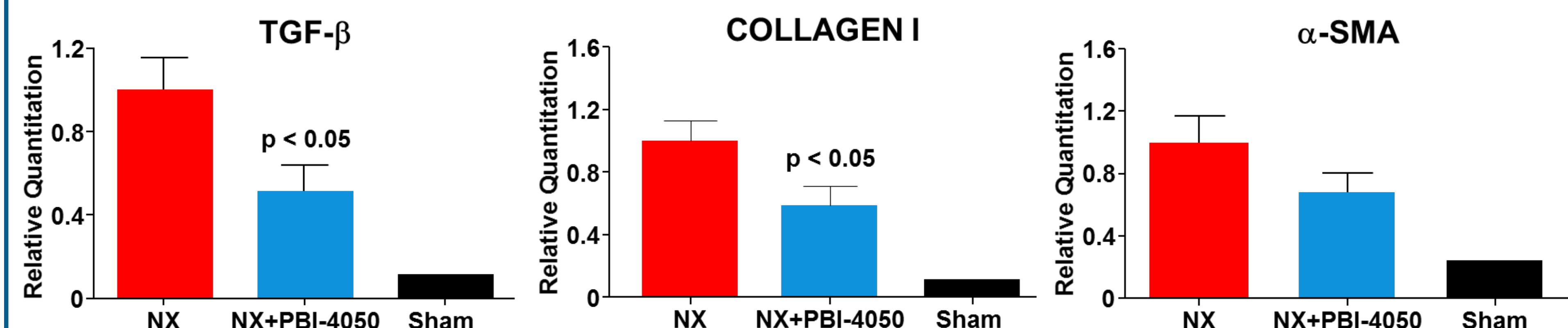
## RESULTS

### 1. Expression of oxidative stress markers



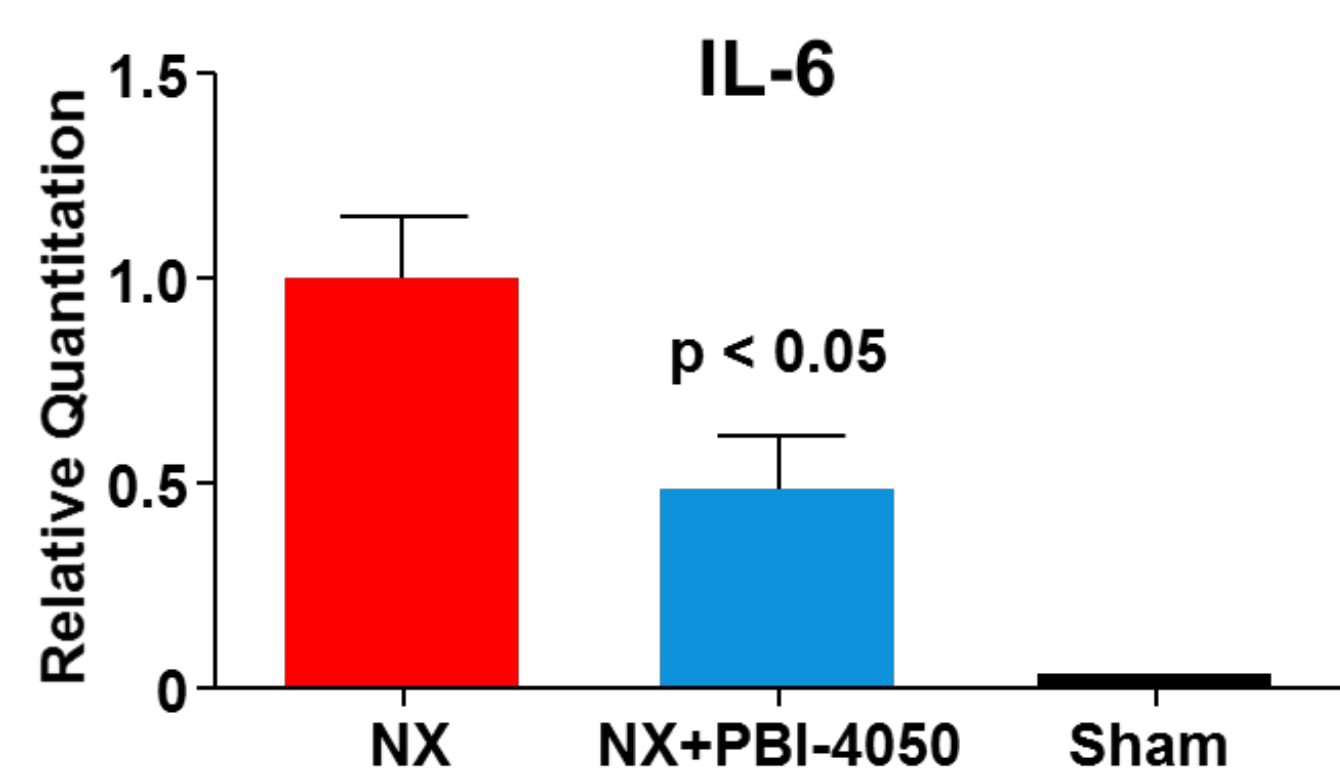
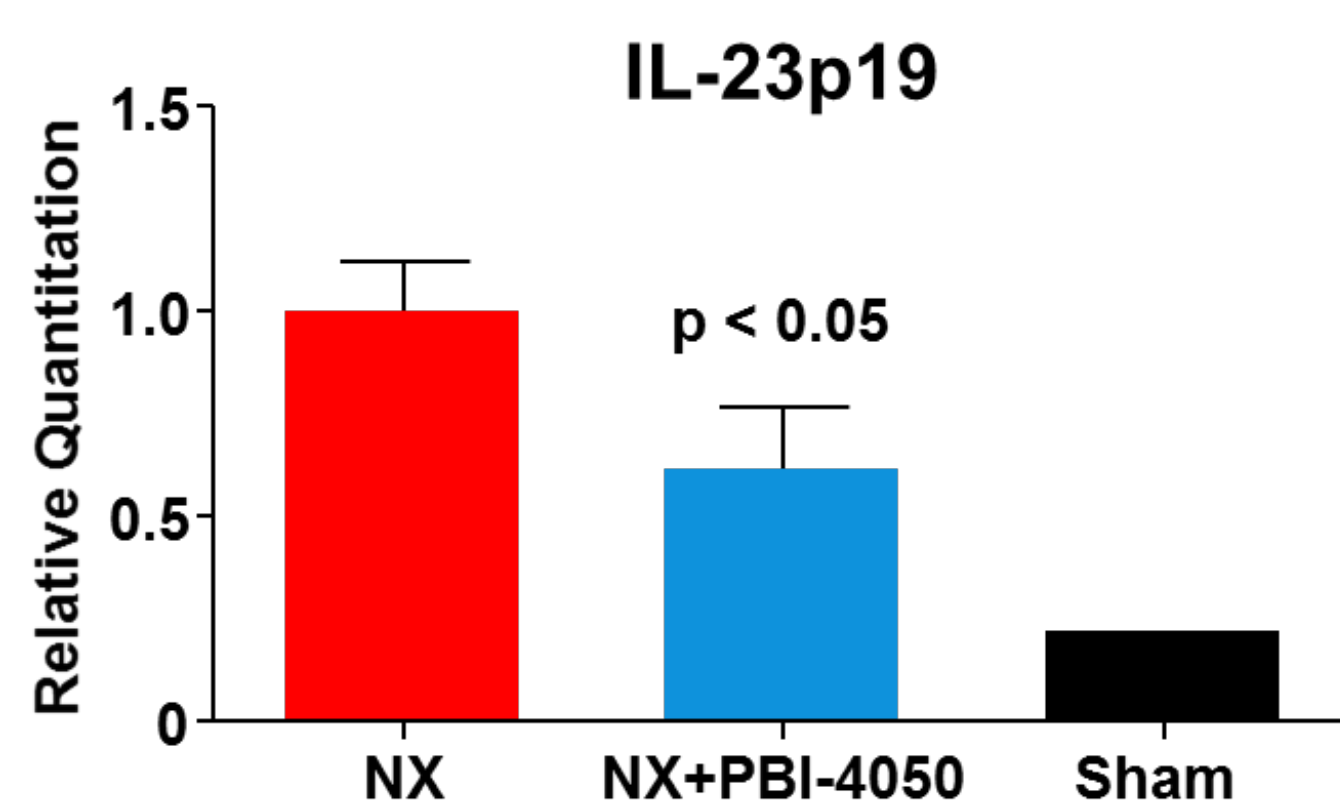
PBI-4050 decreases oxidative stress marker iNOS mRNA expression in the 5/6-NX rat model of CKD.

### 2. Expression of fibrosis markers



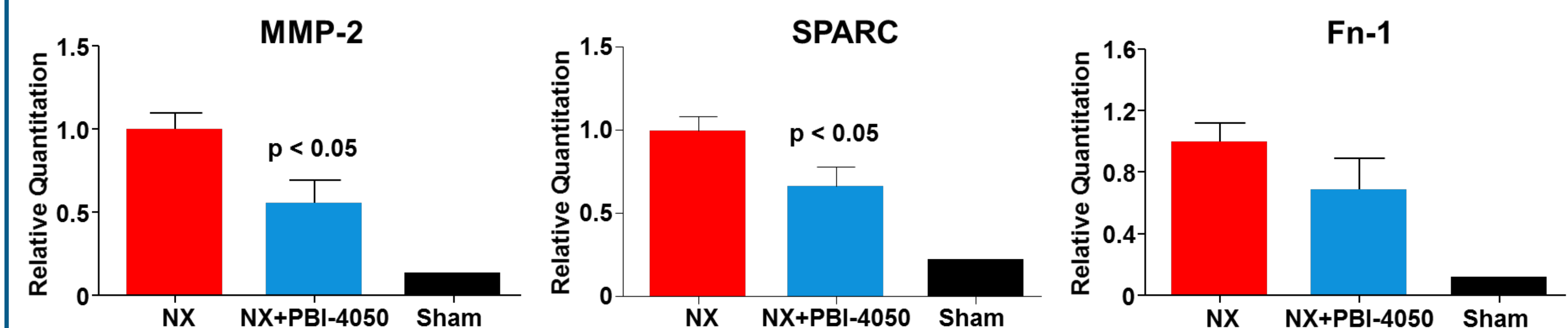
PBI-4050 decreases TGFβ, collagen I and α-SMA mRNA expression in the 5/6-NX rat model of CKD.

### 3. Expression of profibrotic cytokines



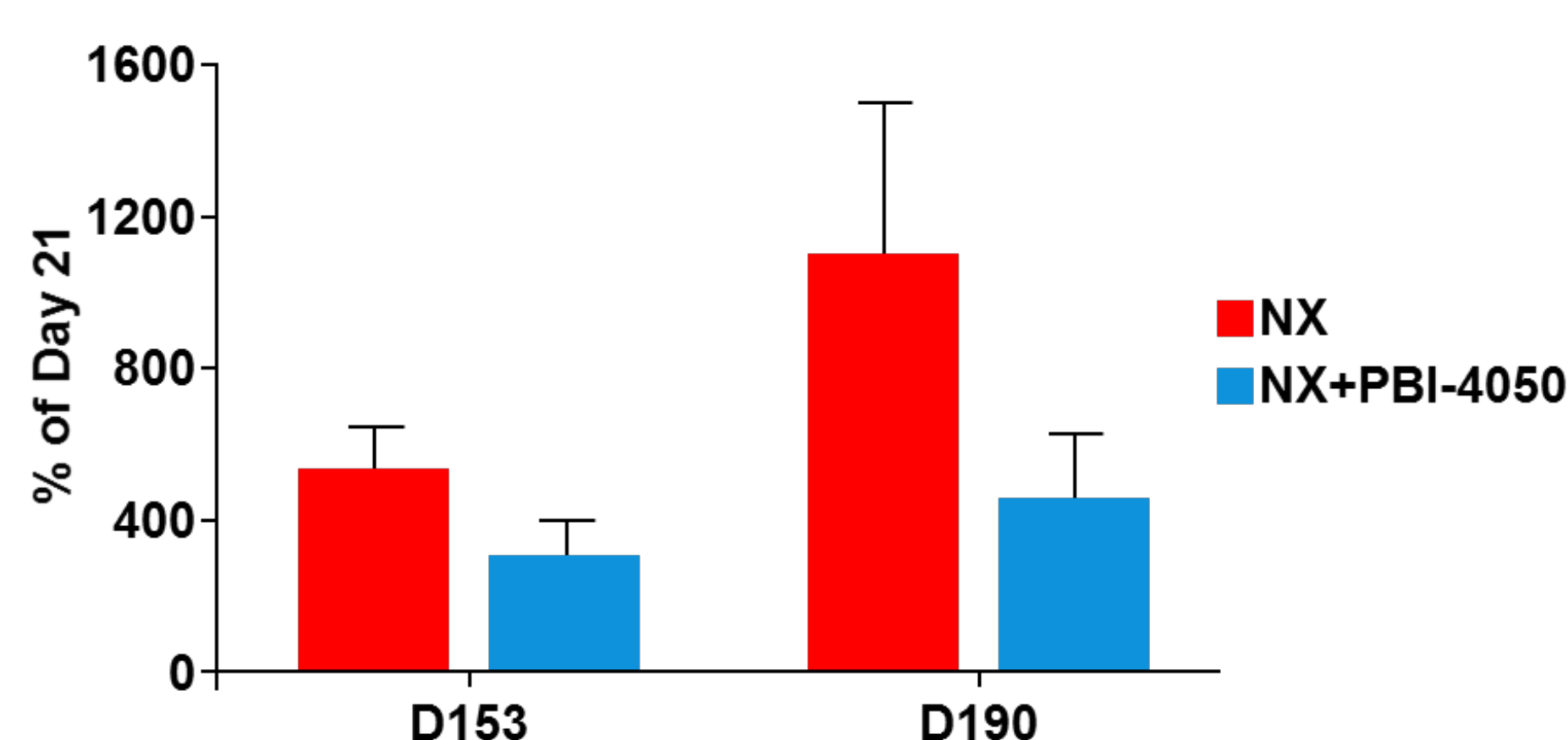
PBI-4050 decreases IL-23p19 and IL-6 mRNA expression in the 5/6-NX rat model of CKD.

### 4. Expression of remodeling markers

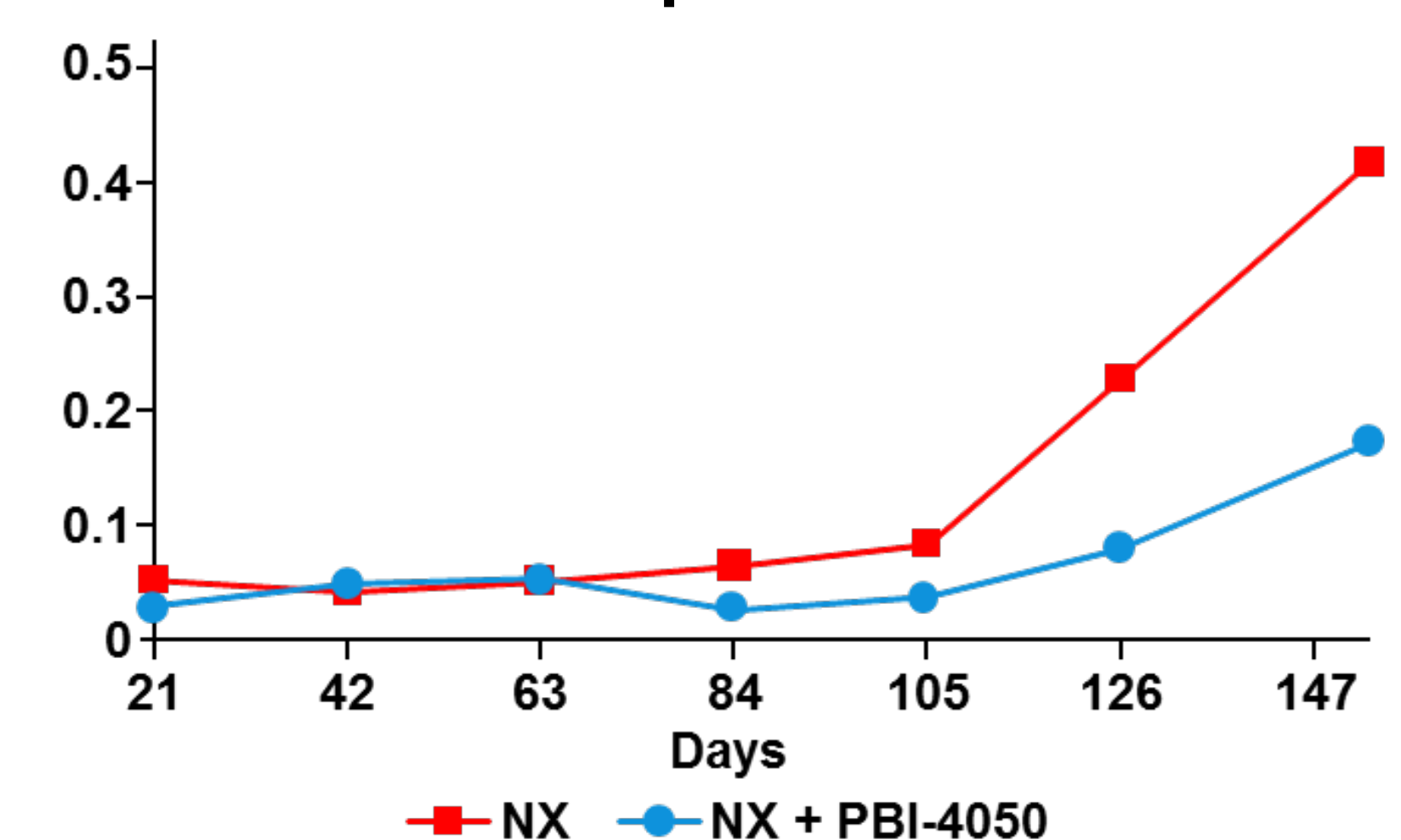


PBI-4050 decreases MMP-2, SPARC and Fn-1 mRNA expression in the 5/6-NX rat model of CKD.

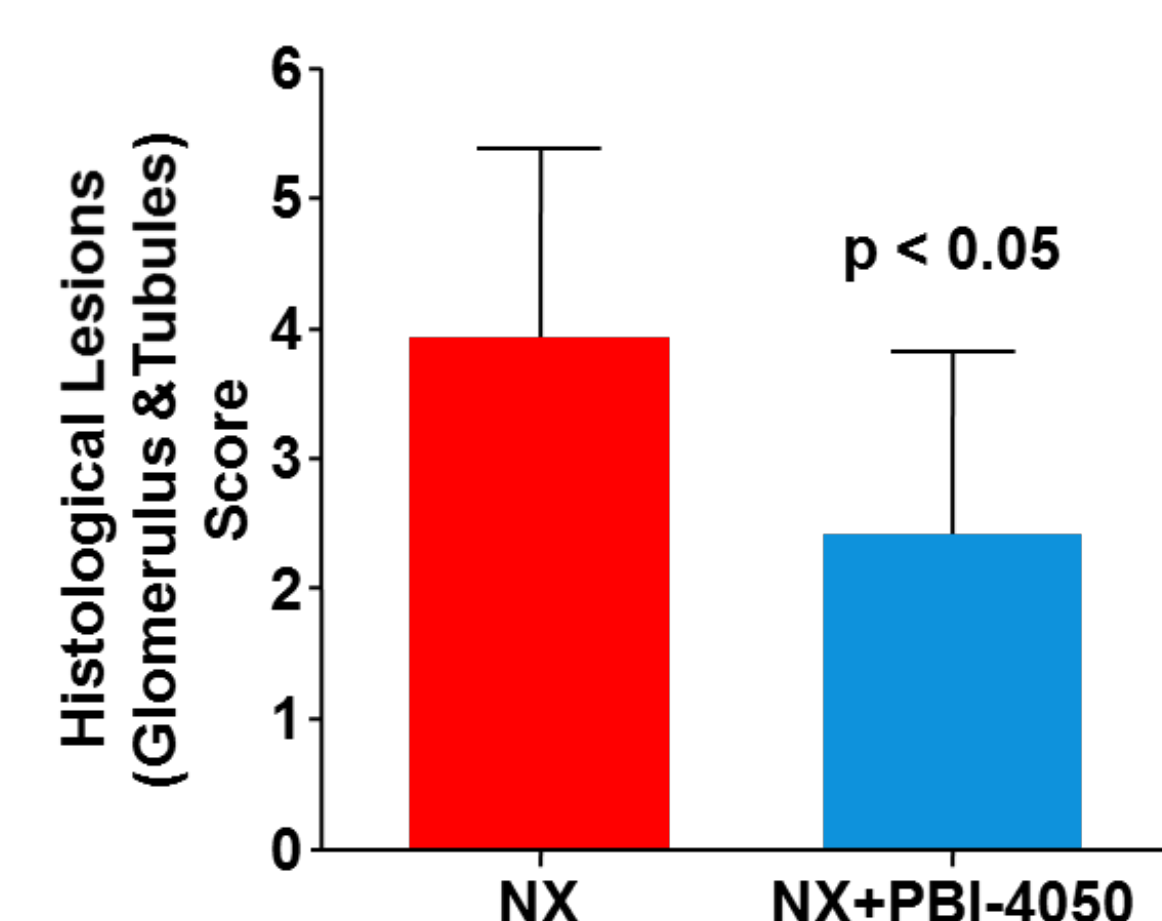
### 5. PBI-4050 reduces urine MCP-1 level



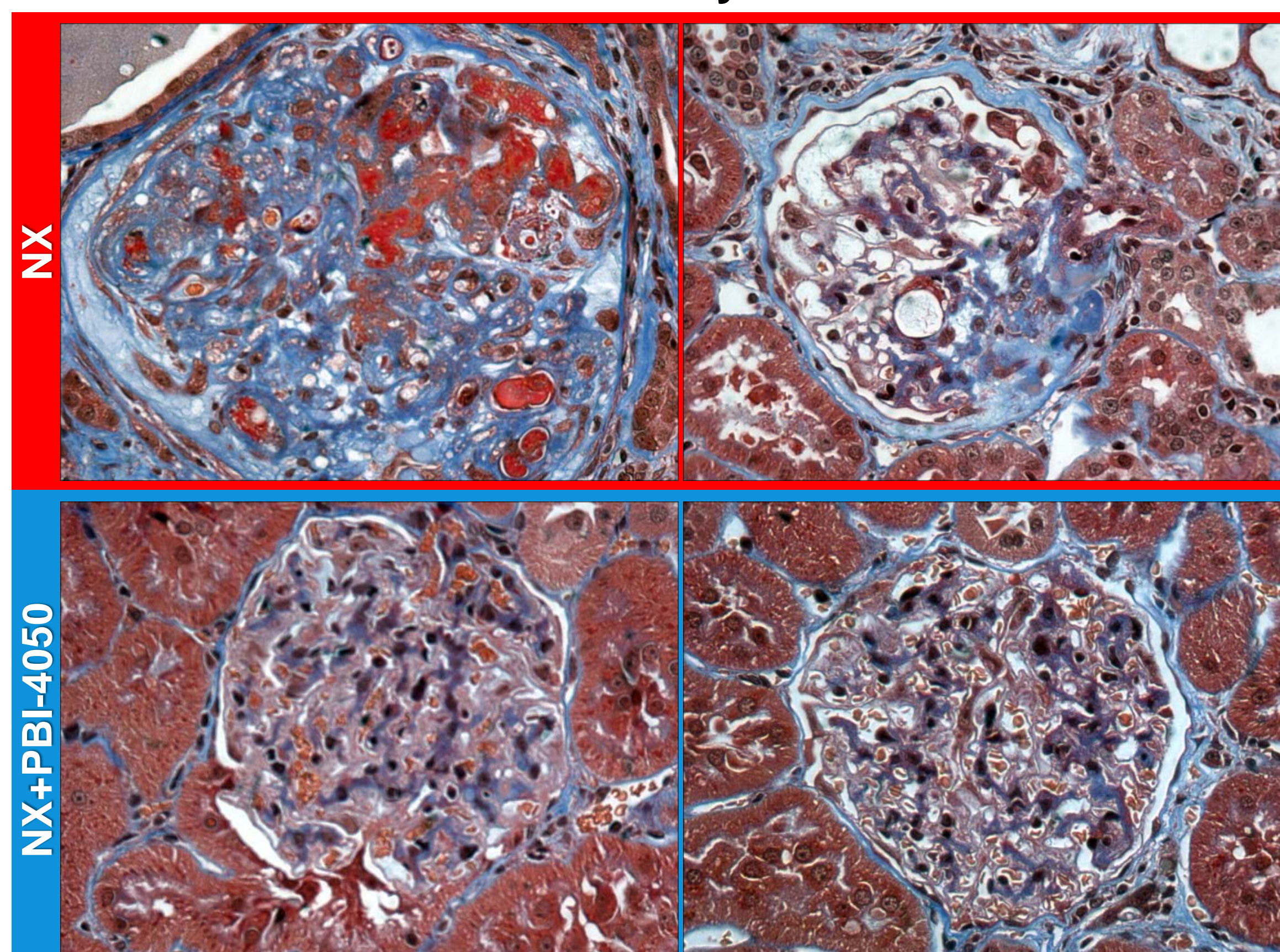
### 6. PBI-4050 reduces proteinuria



### 7. PBI-4050 reduces interstitial and glomerular fibrosis/sclerosis in remnant kidney



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.



## CONCLUSION

Our results demonstrate that PBI-4050 attenuates the development of fibrosis in the 5/6-nephrectomy rat model, and suggest that PBI-4050 may be an efficacious treatment to reduce fibrosis in chronic kidney diseases.