Oral Treatment with PBI-4547, a Novel First-in-class Anti-diabetic and Anti-fibrotic Compound, Improves Glomerular Function and Prevents Podocyte Injury in the Diabetic db/db Mouse Model

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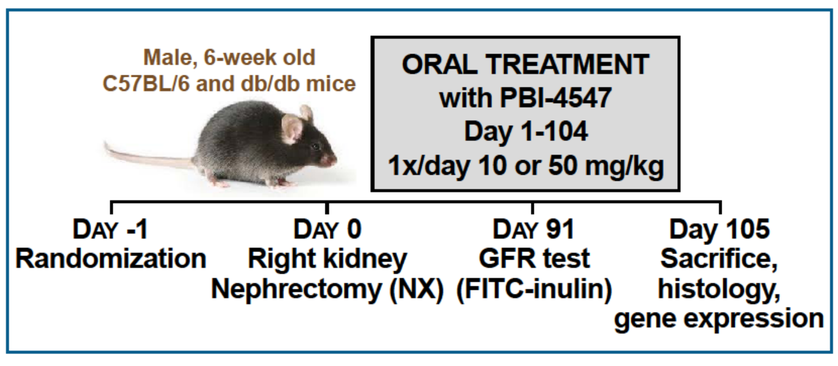
INTRODUCTION

Diabetic nephropathy is one of the most common complications of diabetes and a leading cause of end-stage renal disease worldwide. Glomerular injury plays a pivotal role in the development of diabetic nephropathy.

The aim of this study was to investigate the protective effect of PBI-4547 on kidney function and structure in the uninephrectomized (NX) diabetic (db/db) mouse model.

STUDY DESIGN

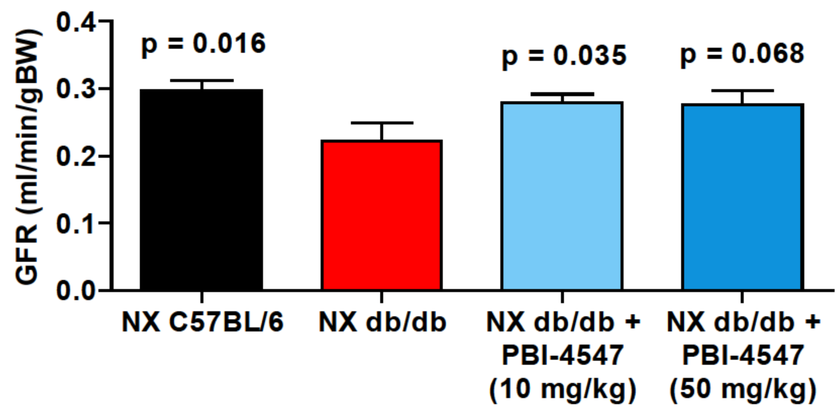
Total nephrectomy of the right kidney was performed on day 0 and animals were treated with vehicle or PBI-4547 (10 or 50 mg/kg, oral once a day) from day 1 through 104. Kidney function (GFR) and kidney mesangium lesions were examined (PAS staining). Relative gene expression (ΔΔCt) was performed on kidney tissue using mouse TaqMan® Gene Expression Assay normalized to NX db/db mice.



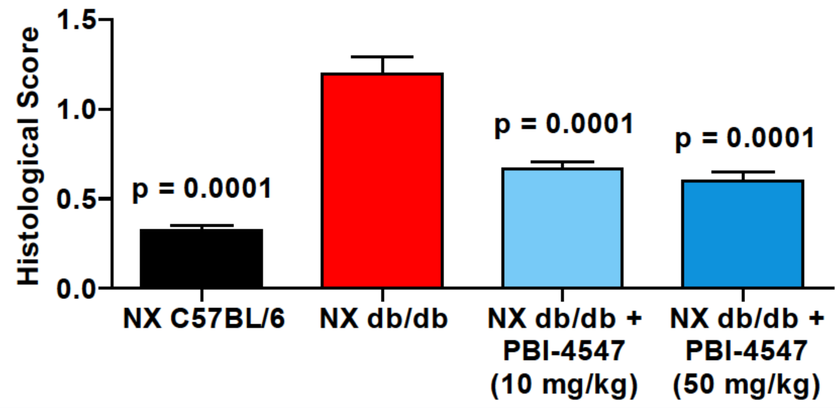
RESULTS

▶ Effect of PBI-4547 on kidney function and structure

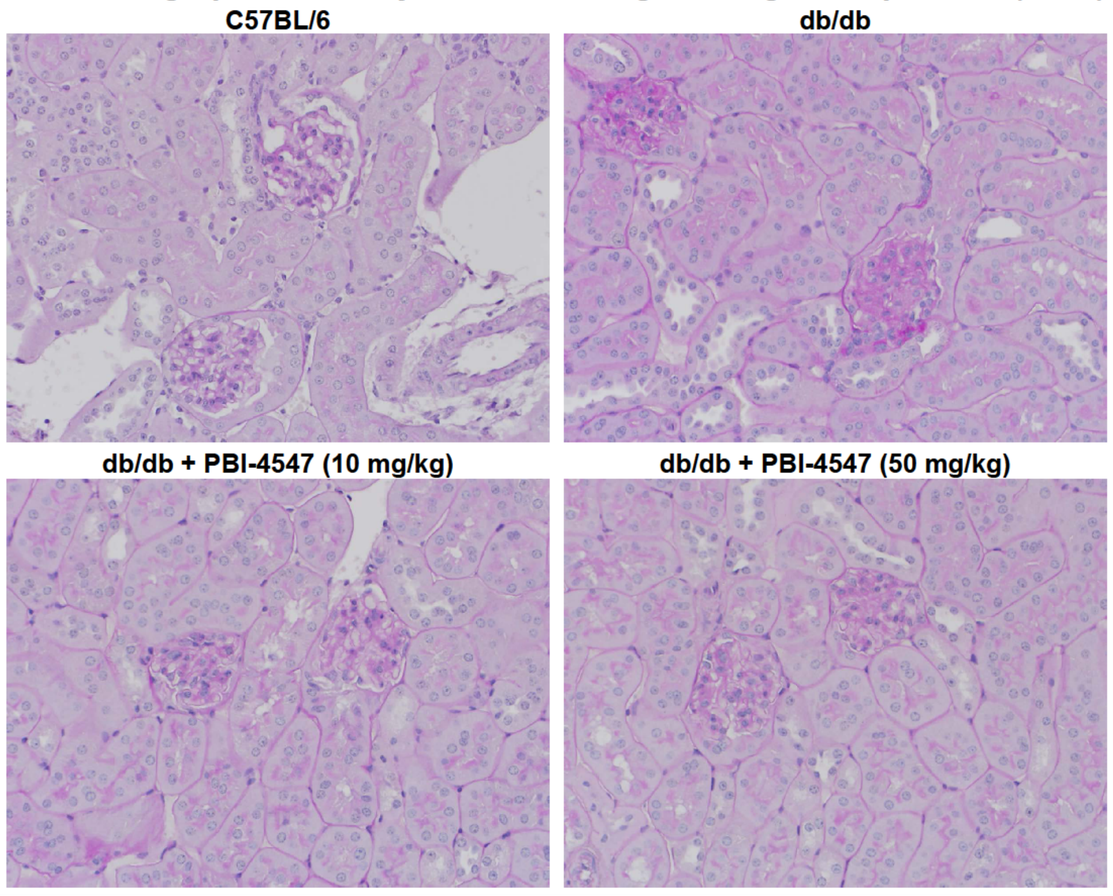
PBI-4547 increases kidney function (GFR).



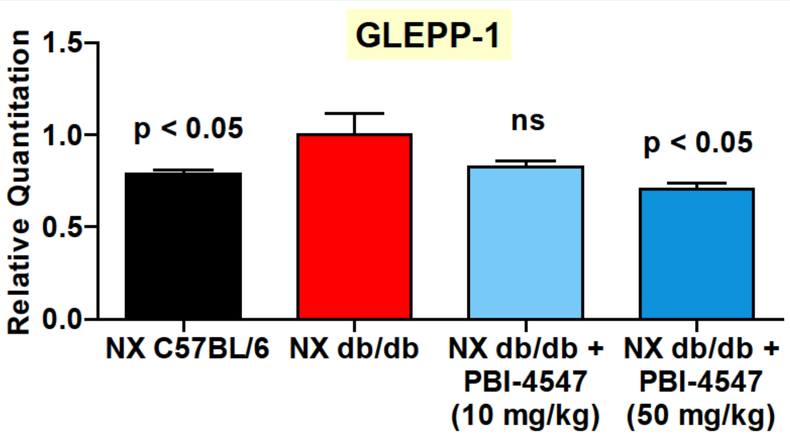
PBI-4547 reduces mesangium lesions.



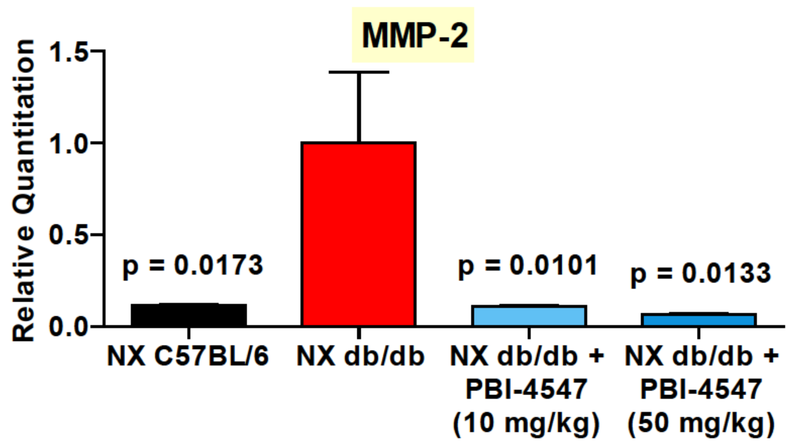
Photomicrographs of kidney tissue showing mesangium expansion (X100).

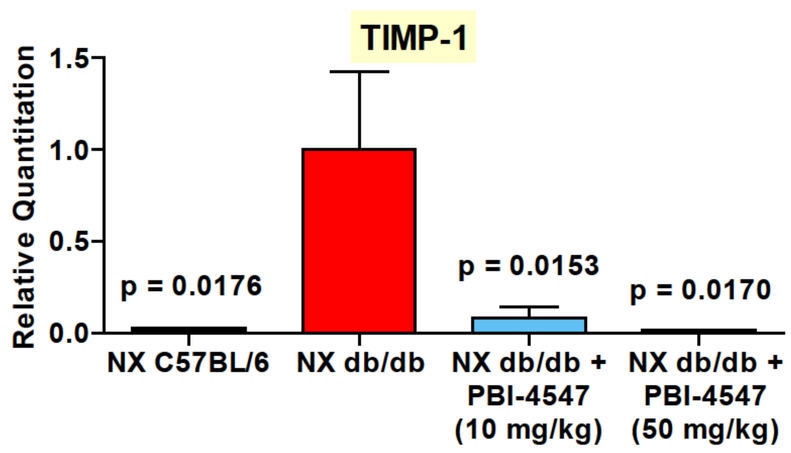


▶ Effect of PBI-4547 on glomerular podocyte integrity

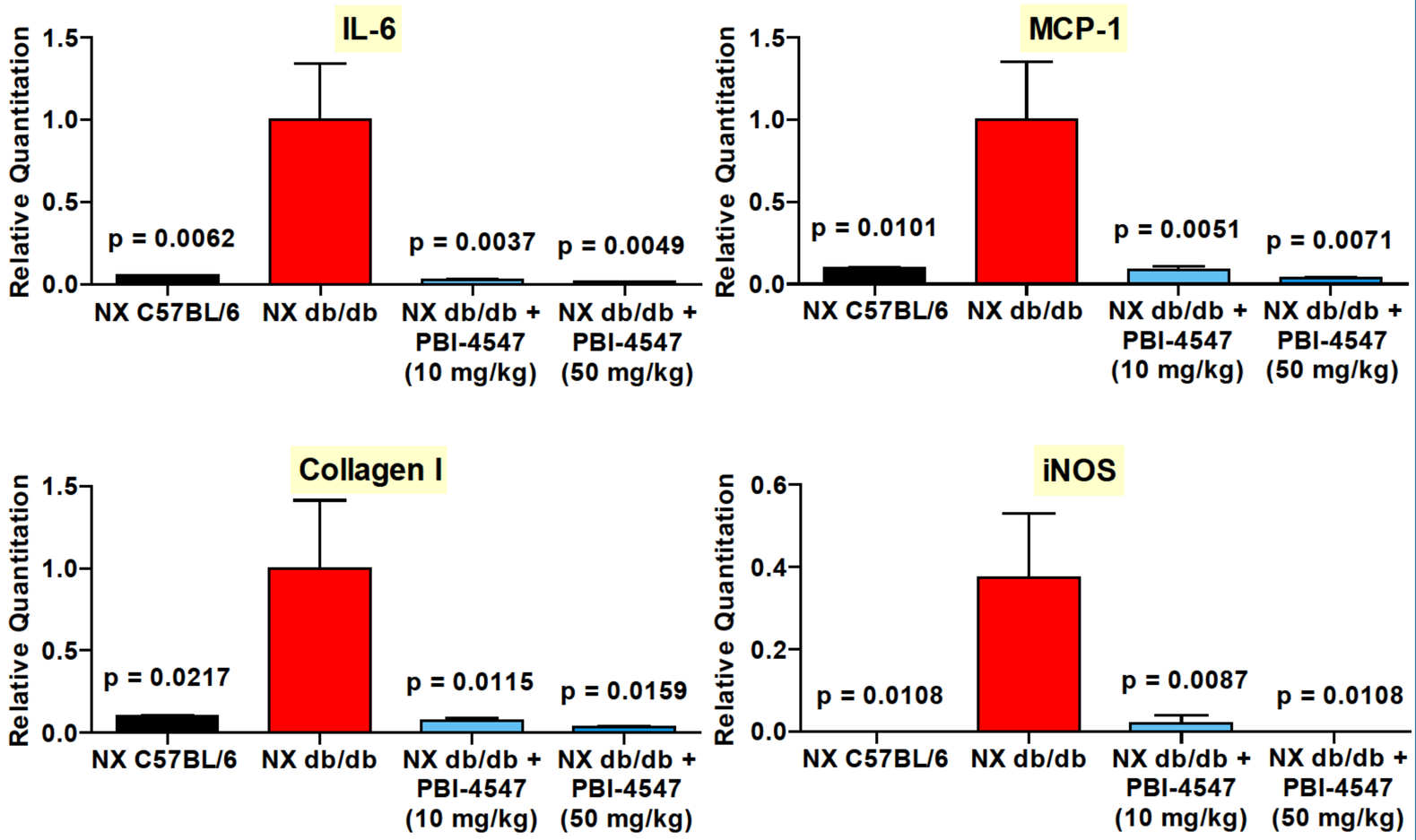


▶ Effect of PBI-4547 on remodeling markers





▶ Effect of PBI-4547 on inflammatory/profibrotic and oxidative stress gene expression



CONCLUSION

PBI-4547:

- Improves kidney function (GFR)
- Preserves kidney structure
  - Reduces mesangium lesions
  - Maintains glomerular integrity (GLEPP-1)
- Regulates expression of inflammatory/fibrotic markers in kidney

Taken together, these results suggest that PBI-4547 offers the potential as a novel therapy for diabetic nephropathy by improving kidney function and structure.

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