

The effect of imatinib in established fibrosis using human precision-cut kidney slices

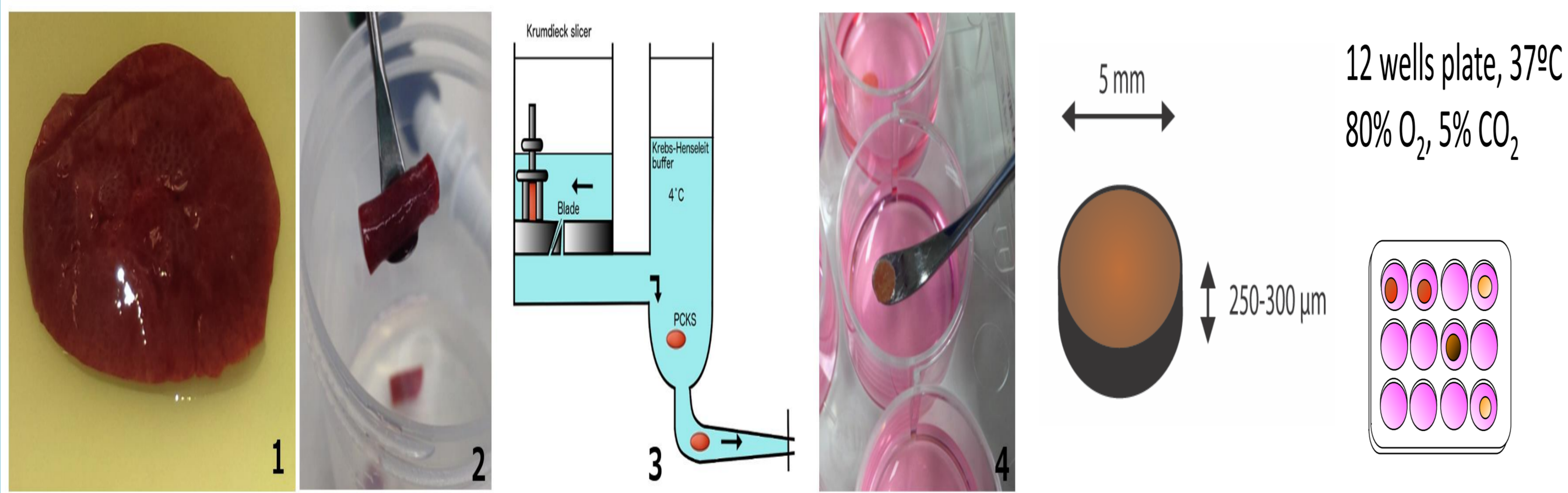
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Introduction

Chronic kidney disease (CKD) poses a major health burden and renal fibrosis is an integral part of the pathophysiological mechanism underlying disease progression. Yet, until now, no effective therapies exist to halt or even reverse kidney fibrosis. Here, we established an *ex vivo* model for antifibrotic drug screening using human fibrotic precision-cut kidney slices (PCKS) and tested the antifibrotic efficacy of imatinib, a tyrosine kinase inhibitor.

Material and Methods

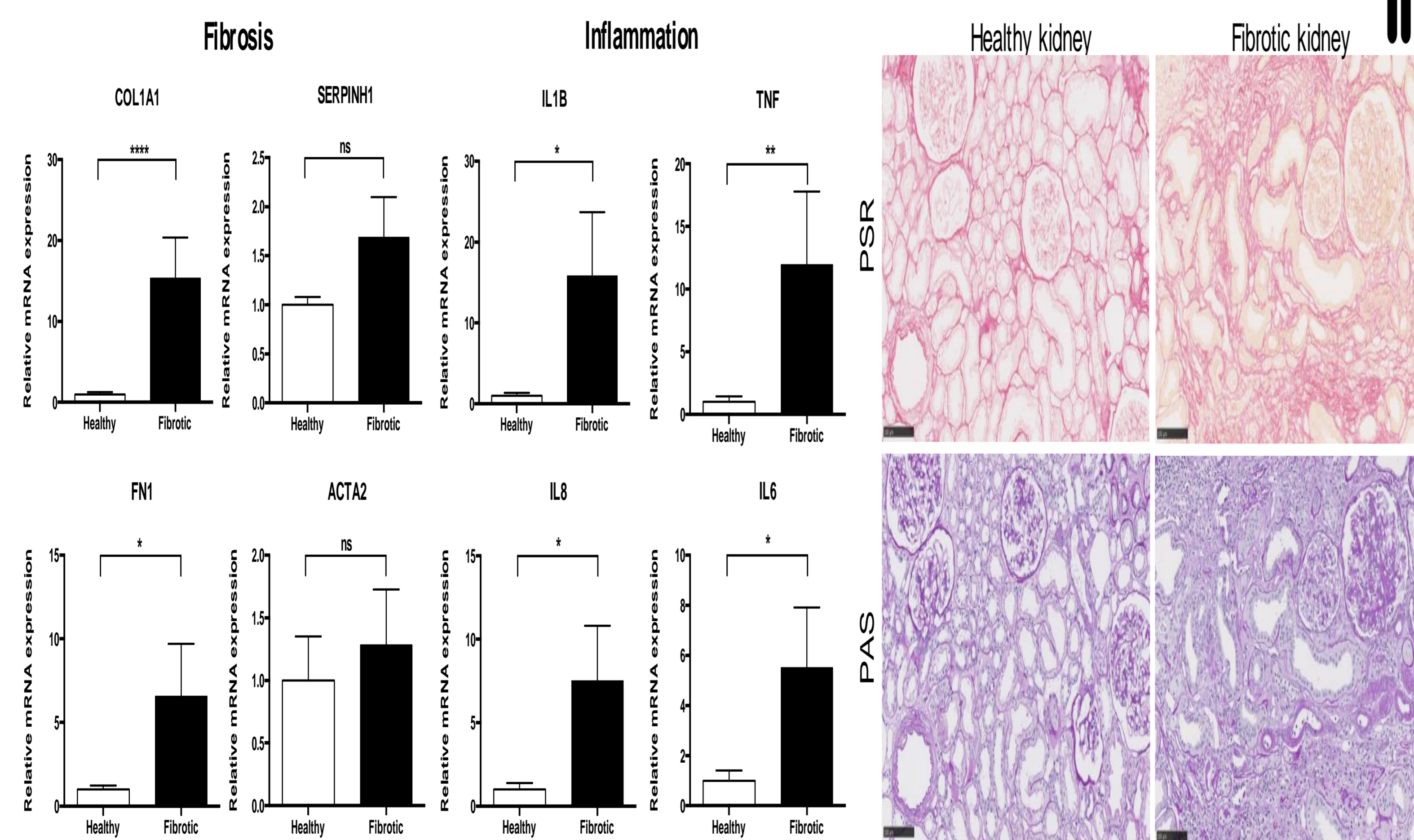


Murine PCKS:
- Healthy kidney from C57BL/6 mice.

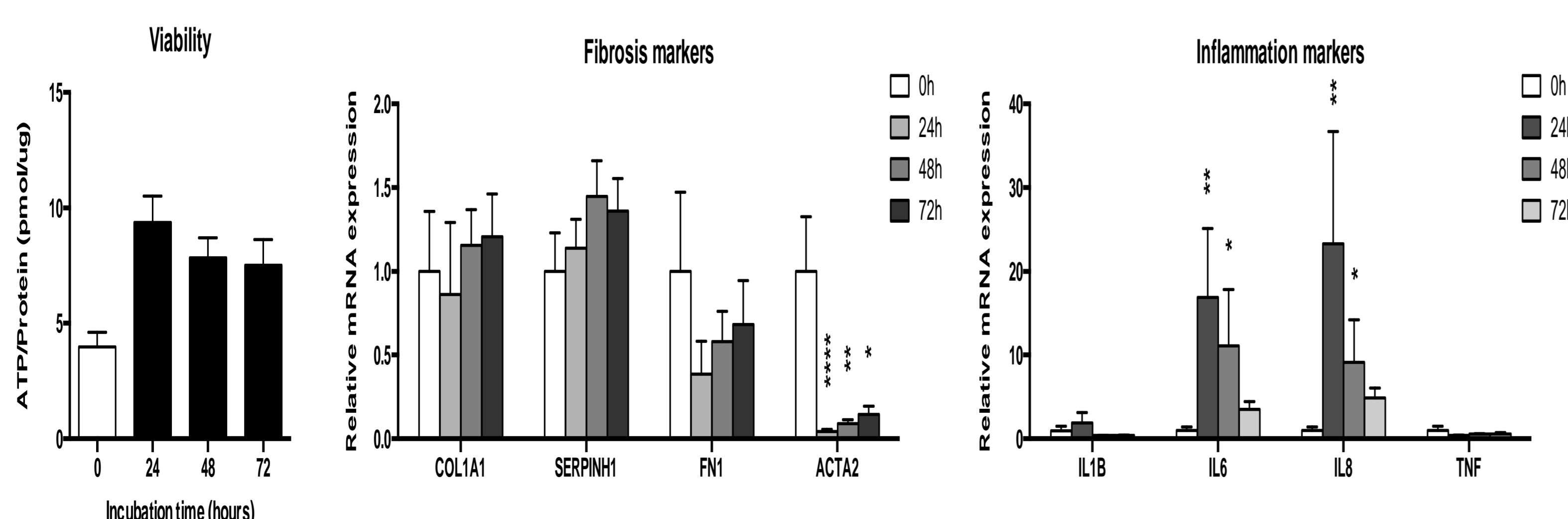
Human PCKS:
- Healthy: healthy part of tumor nephrectomy.
- Fibrotic: ESRD native kidney or non-functioning renal allograft.

Results – Fibrotic human PCKS

A - Characterization of human renal fibrotic tissue

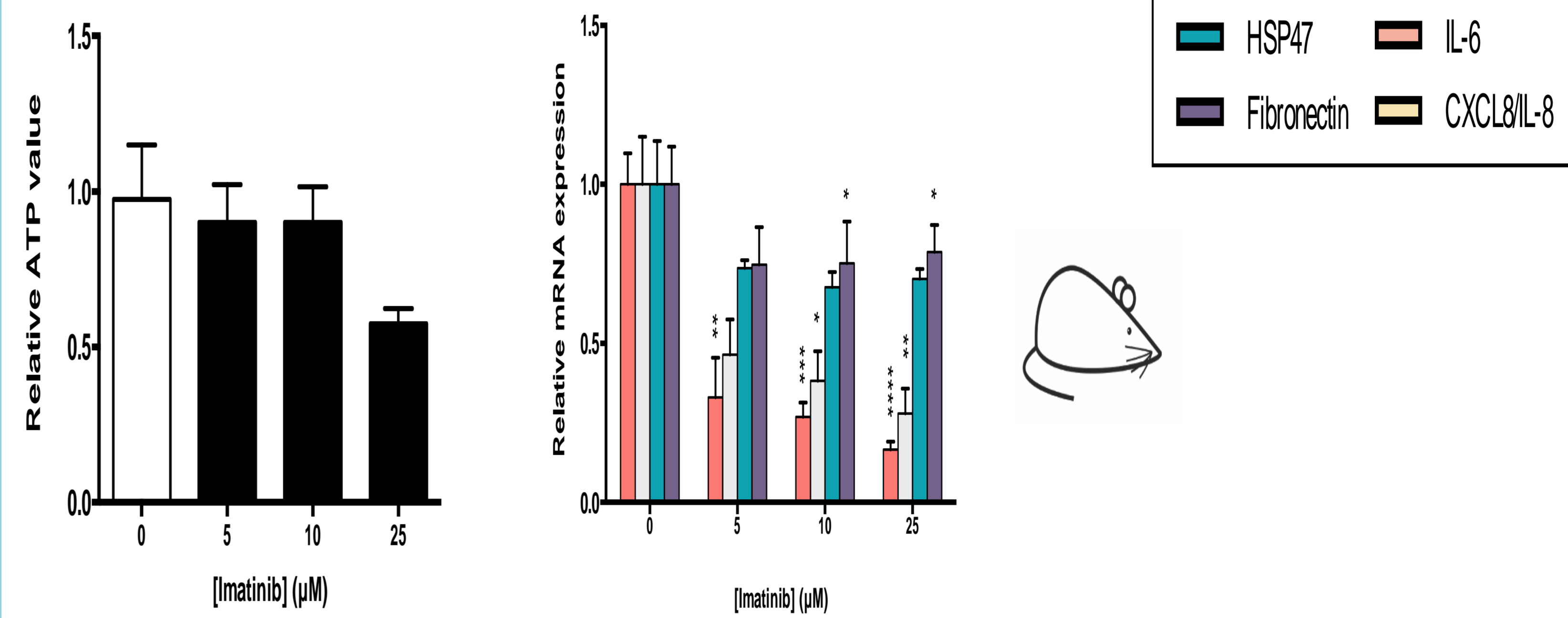


B - Inflammatory and fibrotic response during culture of fibrotic human PCKS

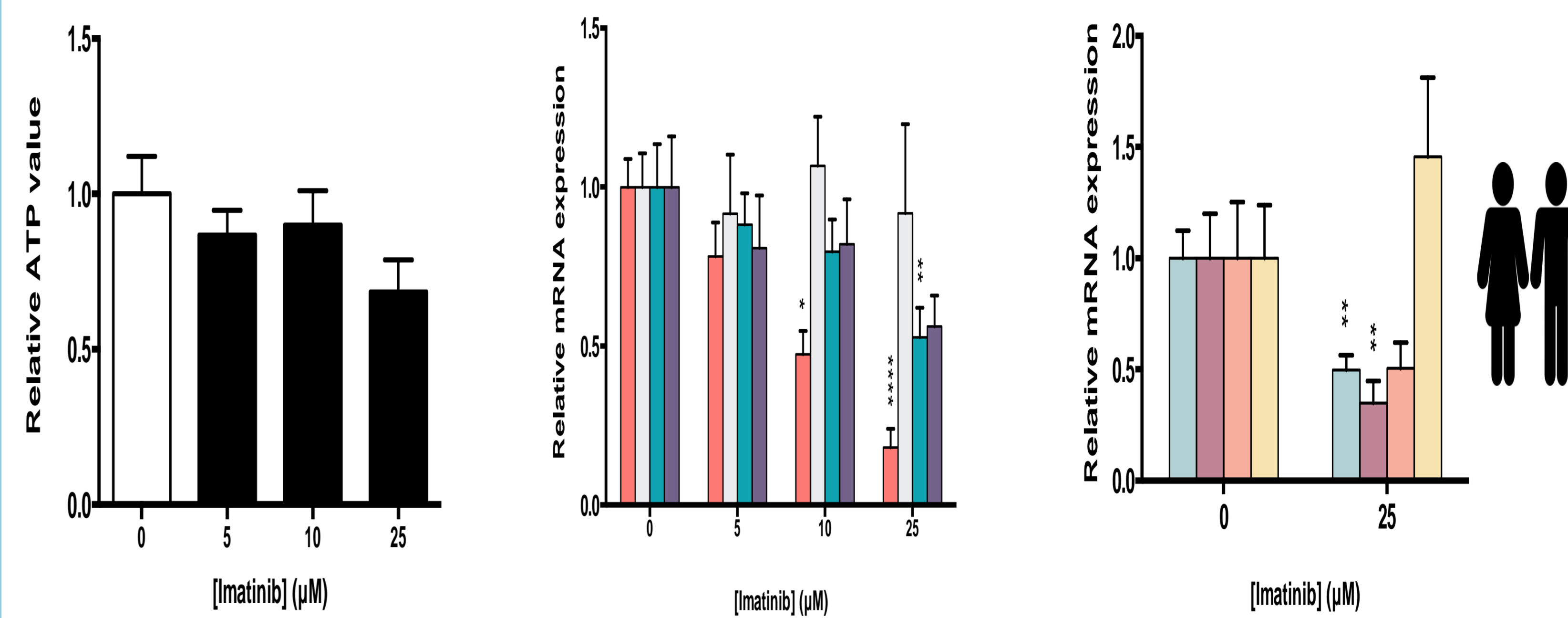


Results – Effect of imatinib in PCKS

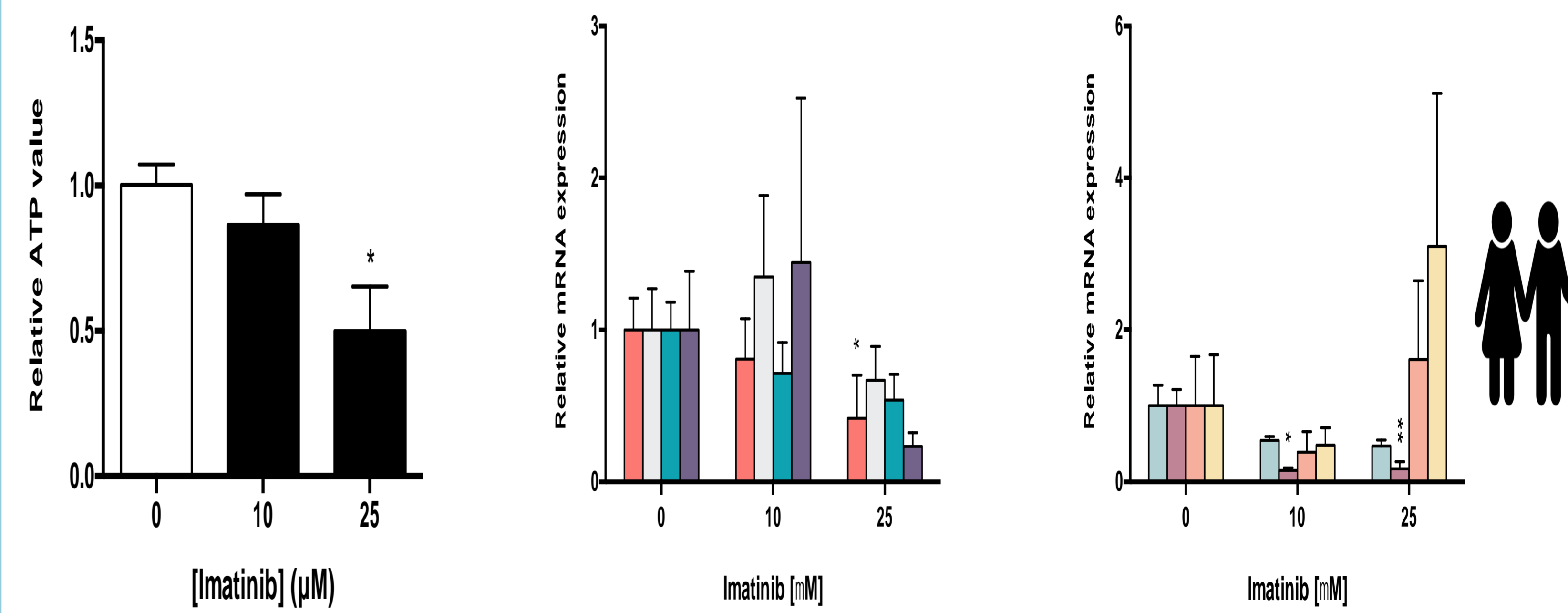
C. Healthy murine PCKS



D. Healthy human PCKS



E. Fibrotic human PCKS



Conclusion

- Diseased renal tissue shows fibrotic profile on mRNA and protein level.
- Time-dependent pathological changes during incubation.
- Imatinib mitigates early onset of fibrosis and inflammation.
- Imatinib elicits toxicity in established fibrosis model.

PCKS prepared from murine and human renal tissue can successfully be used for antifibrotic drug screening.

