# UROTENSIN II AND RELAXIN-2: OPPOSITE ACTIONS AND POTENTIAL THERAPEUTIC IMPLICATIONS IN RENAL FIBROSIS

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## OBJECTIVES

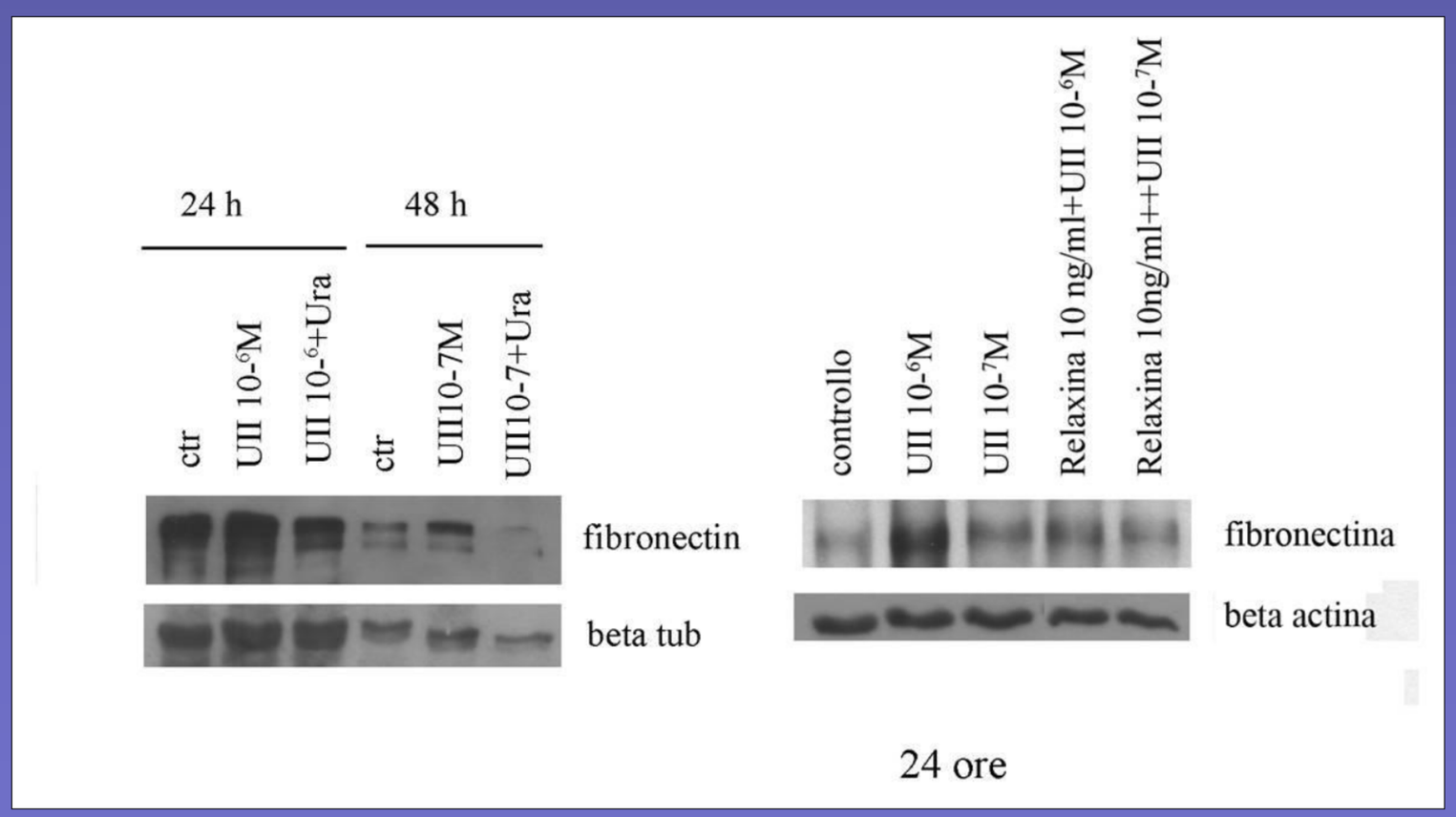
**Tubulointerstitial fibrosis is the final common pathway of diseases that evolve towards chronic kidney disease (CKD) [1]. A key regulator of tissue fibrosis is TGF-β1 (transforming growth factor β1), whose expression is induced by numerous profibrotic stimuli.**
**Our aim has been to evaluate the role of urotensin II (UII), urantide (Ura) and relaxin-2 (RLX) in an in vitro model of renal fibrosis.**

## METHODS

**We used an experimental model of renal tubular epithelial cells belonging to the cell line LLC-PK1, derived from the kidney of healthy male pig. We evaluated the effects on the fibrotic process of the addition of UII, Ura (powerful antagonist of UII's receptor) and RLX, by using antibodies against fibronectin, a marker of fibrosis, in western blot analysis.**

## RESULTS

**After addition of UII, the most potent vasoconstrictor present in mammals [2], we observed the formation of fibrotic tissue; this was documented by the increased expression of fibronectin, which was greater using a concentration of UII equal to 10-6 M. The profibrotic action of UII at this concentration is even higher than that of TGF-β1. We have also observed, for the first time, that Ura is able to reduce fibronectin expression in the context of renal fibrosis; these data confirm the antifibrotic action that Ura seems to exert in myocardial fibrosis, where it abolishes the UII-induced TGF-β1 formation. Finally, we studied the effect of the addition of RLX, pleiotropic hormone able to interfere with the synthesis of collagen and other extracellular matrix components [3]; we noted that this factor mimics the antifibrotic action of Ura in our model of UII-induced fibrosis.**




## CONCLUSIONS

**Our data demonstrate that molecules such as Ura or RLX are able to reverse the tubulo-interstitial fibrosis induced by UII. These results are particularly important because UII and RLX are endogenous substances whose dysregulation (high UII, low RLX) has been linked to numerous pathophysiological states including atherosclerosis, heart failure, hypertension, renal impairment [4,5]. Moreover, no data exist on the interactions between RLX and UII in the molecular pathways of renal fibrosis. Hence, it is possible to imagine a future pharmacological use of Ura and RLX in the treatment of pathological conditions, such as CKD, which are currently considered incurable precisely because secondary to the replacement of normal parenchyma with fibrotic and then not working tissue.**

## REFERENCES:

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