POSTER PRESENTATION

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Suppression of kidney fibrosis by cGMP-dependent protein kinase I

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Background

cGMP is synthesized via nitric oxide- or natriuretic peptide-stimulated guanylyl cyclases and exhibits pleiotropic regulatory functions also in the kidney. Both isoforms of cGKI (α , β) have been detected in arterioles, mesangium and within the cortical interstitium. In contrast to cGKI α , the β -isoform was not detected in the juxtaglomerular apparatus and in medullary fibroblasts.

The aim of this study was to examine the function of cGKI in the renal interstitium, emphasizing a functional differentiation of both isoforms. Interstitium fibroblasts play a prominent role in interstitial fibrosis. Accordingly, cGKI may also be involved in this pathophysiological process.

Results

Kidney fibrosis was induced by unilateral ureter obstruction (UUO). We treated α SM-rescue (expressing cGKI α only in smooth muscle under the control of the SM22 promotor with a cGKI-KO background), cGKI-KO mice (expressing no cGKI) and wt mice with YC-1 (sGC stimulator) which increases cGMP concentration.

Administration of YC-1 showed significantly antifibrotic effects in wt-, but not in α SM-rescue- and cGKI-KO mice, especially regarding the fibrosis marker Col1a1, TGF β and fibronectin. Thereby cGKI α was activated by YC-1 which phosphorylates RhoA and inhibits in turn the profibrotic RhoA/ROCK pathway.

Conclusion

Our results indicate that cGMP/cGKIα acts via RhoA/ ROCK, as an important suppressor of kidney fibrosis.

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