

Abstract Submission No.: A-0880**Collectin-11 promotes cell proliferation and regulates cell functions in renal fibroblasts via engaging EGFR and TGFRII**

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Objectives : Our previous work in a murine model of renal ischemia/reperfusion injury demonstrated that Collectin-11 (CL-11) promotes the development of renal tubulointerstitial fibrosis and CL-11 stimulates renal fibroblast proliferation. However, the effects of CL-11 on renal fibroblast involved are currently unknown. This study aims to investigate the role of CL-11 in regulating fibroblast behavior and functions, including cell proliferation, ECM, cytokine/chemokine, and growth factor production, as well as the associated signaling pathways and potential receptors for CL-11 binding.

Methods : Murine renal fibroblasts were cultured from renal cortex of C57BL/6 mice. Murine recombinant CL-11 (rCL-11) was used to examine its effects on renal fibroblast proliferation and molecular events. Molecular docking analysis, immunofluorescence confocal microscopy and western blotting of intracellular signaling were used to evaluate the interaction between CL-11 and its related receptors.

Results : Treating renal fibroblasts with rCL-11 led to an increase in the Edu+ cell percentage, PCNA expression, and the S phase cell proportion, providing strong evidence that CL-11 stimulates fibroblasts proliferation. Additionally, we observed that CL-11 upregulates the production of ECM (collagen, fibronectin), proinflammatory cytokines/chemokines (IL-6, TNF- α , IL-11, IL1b, CXCL1), and growth factors (EGF, TGF- β 1, IGF2, PDGF- β). Our study also revealed that EGFR and TGF- β R are constitutively expressed on renal fibroblasts and that CL-11 exhibits high binding affinity with EGFR or TGF- β R. CL-11 colocalizes with EGFR or TGF- β R and activates downstream signaling pathways of EGFR (AKT/mTOR, ERK) and TGF- β R (SMAD2, AKT, ERK), providing compelling evidence that EGFR and TGF- β R serve as receptors for CL-11 binding.

Conclusions : In conclusion, this study demonstrated that CL-11 is an important stimulus for renal fibroblasts, promoting cell proliferation and the production of ECM, proinflammatory cytokines/chemokines, and growth factors. It also revealed that EGFR and TGF- β R are potential receptors for CL-11 binding and action on renal fibroblasts. Furthermore, our findings provide insight into how CL-11 could promote renal tubulointerstitial fibrosis.