P41 Activation of NFKB-JMJD3 signaling promotes bladder fibrosis via boosting bladder smooth muscle cell proliferation and collagen accumulation

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Jianzhong A., Wang K., Wei Q., Li H.

Sichuan University, Department of Urology, Chengdu, China

Introduction & Objectives: Chronic cystitis causes the hyperplasia and/or fibrosis of bladder wall, and further decreases the compliance of bladder. To study the underlying mechanism involved in cystitis induced bladder fibrosis, we investigated the role of NFKB-JMJD3 signaling in human bladder smooth muscle cell (hBSMC) proliferation and deposition of extracellular matrix (ECM).

Materials & Methods: Lipopolysaccharides (LPS) was used to induce hBSMC inflammation, and the cell proliferation was investigated using EdU, CCK8 and flow cytometry assays. Moreover, the ECM components of hBSMCs were analyzed using immunofluorescence and western blotting. Finally, the role of NFKB-JMJD3 signaling in regulating cell proliferation and ECM accumulation was unraveled using their selective antagonists.

Results: By using a selective inhibitor of JMJD3, we demonstrated that LPS increased hBSMC proliferation by upregulating JMJD3 and its downstream CCND1 expression. Interestingly, JMJD3 expression was also markedly affected by NFKB activity. Inhibition of NFKB decreased hBSMC proliferation by downregulating CCND1 expression. Furthermore, LPS promoted collagen I and III expression by regulating NFKB-JMJD3 signaling.

Conclusions: NFKB-JMJD3 signaling play an important role in bladder fibrosis by regulating hBSMC proliferation and its ECM accumulation, and our findings, at least partially, uncovered the underlying mechanism of cystitis caused bladder dysfunction, and paved a new avenue for the effective treatment of patients with bladder cystitis.