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# E3 Ubiquitin Ligase Regulate Renal Fibrosis through TGF-β Induced Epithelial-mesenchymal Transition

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**Aim:** Notch signaling pathway is involved in cell fate specification and plays critical role in kidney development and development of renal fibrosis. Mind bomb-1 (Mib1) encodes an E3 ubiquitin ligase required for the initiation of Notch signaling. Recent study showed that the renal collecting duct plays a pivotal role in renal fibrosis. In this study, we investigated the role of E3 ubiquitin ligase in renal fibrosis by using conditional knockout mice in which Mib1 is genetically ablated specifically in renal collecting duct epithelial cell.

**Methods:** Mib1-floxed mice were crossed with aquaporin (AQP) 2-Cre mice to generate principal cell-specific Mib1 knockout mice (Mibflox/flox; AQP2-Cre+). Unilateral ureteral obstruction (UUO) was performed and mice were sacrificed 3, 7 and 14 days after UUO.

**Results:** After UUO, we observed the decreased expression of AQP2 in wild-type (WT) mice, which was substantially decreased in the Mibflox/flox; AQP2-Cre+ mice compared to those of UUO-kidneys of WT mice. Renal fibrosis were markedly more induced in Mibflox/flox; AQP2-Cre+ than in WT control mice. The expression of TGF-β was more increased in Mibflox/flox; AQP2-Cre+ than in WT control mice. The expression of epithelial-mesenchymal transition (EMT) markers including α-smooth muscle antibody and vimentin were more increased in Mibflox/flox; AQP2-Cre+ than in WT control mice.

**Conclusions:** Our data suggest that renal collecting duct principal cell specific deletion of E3 ubiquitin ligase increased expression of TGF-β and enhanced renal fibrosis via EMT after UUO.

**Key Words:** Notch, Fibrosis, Epithelial-mesenchymal transition