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TAZ is required for the patterning of the juxtamedullay nephron in kidney development

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Objectives: The mammalian Hippo signaling pathway has been implicated in the regulation of cell proliferation, cell death, tissue regeneration, and tumorigenesis. The Hippo pathway is a conserved kinase cassette that regulates cell proliferation, cell death and tissue regeneration by controlling the activity of Yes-associate protein (YAP) and transcriptional coactivator with PDZ-binding motif (TAZ). In kidney development, YAP plays a critical role in branching morphogenesis in the mouse kidney. However the physiological role of TAZ in kidney development remains unclear. Here we investigate the role of TAZ in kidney development using conditional knockout mice.

Methods: We generated the conditional knockout mice in which TAZ was genetically ablated specifically in ureteric bud (UB) lineage ($TAZ^{flox/flox}$;HOXB7-Cre^{+}) or distal tubular epithelial cell (TEC) ($TAZ^{flox/flox}$;Ksp-Cre^{+}).

Results: TAZ deletion in UB ($TAZ^{flox/flox}$;HOXB7-Cre^{+} mice) did not cause any histological defect. However, TAZ deletion in distal tubules ($TAZ^{flox/flox}$;Ksp-Cre^{+}mice) resulted in the formation of renal cyst resembling polycystic kidney disease or glomerulocystic kidney disease. The renal cysts were observed mainly in the juxtamedullay nephron at 11 weeks after birth and the size of the renal cyst was increased with age. No fetal or neonatal lethality were observed. Immunohistochemical analyses revealed that the epithelial cells of renal cysts were positive with claudin-1, Lotus Tetragonolobus Lectin (LTL) or E-cadherin but negative with aquaporin-2.

Conclusions: In summary, our data showed that TAZ alone plays a critical role in the patterning of the juxtamedullay nephron rather than the branching of UB in mouse kidney development.