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DEVELOPMENT

Celsr1 and *Vangl2* team up to pattern the kidney

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A new study provides insights into the mechanisms of rostrocaudal patterning during renal development. David Long, Eugenia Papakrivopoulou and colleagues show that two proteins involved in planar cell polarity (PCP) — CELSR1 and VANGL2 — are required for branching of the ureteric tree and glomerular maturation in mice. They also report that patients with spina bifida and *CELSR1* mutations can have renal tract anomalies.

"Previous work from our laboratory and others had implicated PCP in kidney development," explains Long. "We built on these findings by using optical projection tomography and sophisticated computational analysis to identify the precise role of PCP in kidney morphogenesis."

The researchers report that, in wild type mice, the caudal renal compartment expressed lower levels of *Celsr1* than the rostral compartment. Genetic deletion of *Celsr1* resulted in an atrophied ureteric tree, in particular in the caudal compartment of the kidney. "PCP genes have been previously implicated in controlling tubule diameter, but the role of *Celsr1* in kidney patterning had not been described," says Long. In addition, mice with heterozygous compound mutations in *Celsr1* and *Vangl2* had more rudimentary ureteric trees than those with single mutations in either gene, particularly in the caudal compartment. "Although it was known that different PCP genes can genetically interact, the effect of this interaction on rostrocaudal symmetry is a novel finding," comments Long.

As well as defective branching, *Celsr1*-knockout mice had dilated cortical tubules, whereas *Celsr1* and *Vangl2* double mutants had truncated caudal structures, rudimentary tubules, a hypoplastic medulla and impaired glomerular maturation. Both mutants had defective spindle orientation during tubule elongation.

The researchers also found renal defects (including unilateral renal agenesis, hydronephrosis and hydroureter) in five of 13 patients with spina bifida and heterozygous missense or nonsense *CELSR1* mutations. "This is the first report of an association between mutations in PCP genes and a higher incidence of renal malformations," says Long.

In future research, Long and colleagues plan to study the roles of other PCP components during kidney branching morphogenesis.

Lara Crow/NPG

"Our results should encourage further studies to determine whether spina bifida and mutations in other PCP genes coexist with kidney malformations," says Long.

Andrea Aguilar

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