Wnt5a implicated in CAKUT

New data suggest a role of *Wnt5a* mutations in the formation of duplex collecting systems—one of the most common congenital anomalies of the kidney and urinary tract (CAKUT).

Wnt5a controls cell positioning during the elongation of several tissues. To investigate the role of this gene in mesoderm development, Alan Perantoni and colleagues used a conditional knockout mouse. "This approach allowed us to specifically target the mesoderm and to control the timing of *Wnt5a* recombination and/or inactivation," comments Perantoni.

The researchers report that the kidneys of the mutant embryos had unilateral or bilateral abnormalities; they were duplexed and associated with double ureters. Further investigations indicated a role of *Wnt5a* signalling in early morphogenesis of the intermediate mesoderm before formation of the metanephros. "Formation of the """ duplex collecting system in the *Wnt5a* mutant is likely the result of dysmorphogenesis of the nephric duct, which forms a fused doublet structure on each side of the embryo," explains Perantoni. "This defective structure precedes the double outgrowth of the ureteric bud, which then induces two metanephric domains to form the duplex kidneys."

The researchers plan to further investigate the specific cellular mechanisms that are responsible for proper patterning of the nephric duct. They are also interested in determining whether patients with duplex kidneys have *WNT5A* mutations. "Our model could conceivably prove useful in efforts to rescue this phenotype," says Perantoni.

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