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Eph-receptor tyrosine kinase signaling in urogenital development

Christiane Peuckert Uppsala University, Sweden

Obstructive nephropathy belongs to congenital anomalies of the kidney and the urogenital tract (CAKUT), which are the most frequent causes of early renal failure. Several developmental abnormalities can underlie obstructive nephropathy such as ectopically or blind ending ureters, a duplex collecting system or duplex kidney and posterior urethral valves. Although, recent research using mouse models suggests roles for several genes in facilitating proper ureter insertion and development, underlying molecular mechanisms for congenital obstructive nephropathy in humans remain poorly understood. Eph receptors constitute the largest known family of receptor tyrosine kinases and are involved in the modulation of the cytoskeleton. Consequently, Eph signaling regulates cell adhesion and migration, which are important for mechanisms as cell segregation, border formation, adhesion during embryonic fusion events and axon guidance in the developing embryo. We have performed a detailed analysis of a battery of different Eph and ephrin mutant and signaling deficient mice. Impaired Eph signaling leads to severe hydronephrosis and hydroureter. We found that, Eph-mediated signaling is crucial for a number of developmental steps, as ureteric bud induction, ureter muscularization, innervation and insertion, all processes which, if disturbed individually, can potentially lead to impaired urine drainage. Our data suggest that the ligands ephrin-B2 and ephrin-A5 interact redundantly with several Eph receptors in forward and reverse mode. Based on our and on the studies of others, genes coding for ephrins and Eph receptors should be considered in the etiology of CAKUT.

Biography

Christiane Peuckert has completed her PhD from the University of Jena, Germany, where she studied Eph-ephrin signaling during embryonic brain development. In 2007, she joined the Department of Neuroscience at Uppsala University in Sweden for her Post-doctoral studies to investigate neurotransmission in brain and spinal cord and the role of Eph-mediated signaling in early kidney development. Since 2012, she is a Senior Researcher at Uppsala University and is focusing on cell-cell communication during Organogenesis.

c.peuckert@neuro.uu.se

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