Genetics of Kidney Development: Pathogenesis of Congenital Anomalies of Kidney and Urinary Tract

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Widespread use of fetal ultrasound screening has increasingly revealed diverse malformations of kidney and urinary tract. The true incidence of congenital anomalies of kidney and urinary tract (CAKUT) is unknown, but estimated to be higher than reported. Because they constitute major causes of chronic renal insufficiency in childhood, even after the surgical correction, CAKUT draw serious concerns nowadays. Recent works suggest significant evidence that these disorders have a genetic basis, and familial aggregation and concurrent presence of various anomalies indicate common genetic background in them.

Normal development of kidney and urinary system is a complex process, which results from interaction between the ureteric bud and renal mesenchyme. After the report that metanephric mesenchyme and ureteric bud failed to differentiate when cultured separately but they formed nephrons and collecting ducts when recombined, diverse molecules expressed during kidney differentiation were investigated as a candidate for CAKUT. Genetically engeneered mice model revealed various molecules considered important in urinary tract development, which were involved in cell survival, proliferation, and differentiation. Mutant mice of such genes showed agenesis, dysplasia and hypoplasia of kidney which represent defects on regulation of metanephric formation, epithelial morphogenesis, and nephron numbers.

Results of human and animal studies on various genes have been reported. Same phenotype of CAKUT can be result from mutation of different genes (e.g., null mutations of either WT1 or PAX2 transcription factor genes causes renal agenesis), and mutation of single gene may result in a variety of malformations (e.g., null mutation of angiotensin ? receptor type 2, Agtr 2), and so far, candidate genes suggested are also expressed in many other organs, indicating the presence of nephrogenesis specific genes questionable.

Studies on renal development have rapidly increased recently, but above observations demonstrate that our knowledge in this field is still crude and superficial and more investigations are needed to elaborate the process and disruption of nephrogenesis.