The role of the transcription factor GATA3 in kidney function and disease

From 2013-05-01 to 2015-04-30, closed project

Objective

Mutations in GATA3, a dual zinc-finger transcription factor, cause the autosomal dominant hypoparathyroidism, deafness, renal dysplasia (HDR) syndrome, and down-regulation of GATA3 results in clear cell renal cell carcinoma. The renal abnormalities in HDR patients consist of cysts, renal aplasia/hypoplasia, mesangioproliferative glomerulonephritis, and vesicoureteral reflux. In the developing kidney, GATA3 is expressed in the ureteric bud along the branching process that gives rise to the collecting system of the definitive kidney, as well as in the glomerular mesangium and adjacent endocapillary cells. Nephric duct-specific inactivation of Gata3 leads to ectopic ureter budding as a result of premature nephric duct cell differentiation and loss of Ret receptor expression, leading to urogenital malformations such as kidney dysplasia, duplex systems, as well as vas deferens hyperplasia and uterine agenesis. While GATA3 has been identified to have a role in the developing kidney, little is known about its role in the adult kidney and the cellular pathways it regulates. Moreover, GATA3 has been shown to have a protective role in glomerulonephritis, however the molecular mechanisms of this process are unknown. Thus, the overall aim of this project is to define the role of GATA3 in normal adult kidney and in kidney models of glomerular disease. The specific aims are to: 1) assess the expression pattern of GATA3 in normal adult kidneys and in kidneys with glomerulonephritis; 2) determine whether heterozygous Gata3 +/- mice are more susceptible to an earlier/more severe form of glomerulonephritis compared with wild-type mice; 3) investigate the role of GATA3 in the Wnt/beta-catenin pathway; and 4) identify the target genes of GATA3 in normal adult kidneys using ChIP-Seq. An integration of these data will advance our understanding of the cellular pathways regulated by GATA3 in the kidney and the molecular mechanisms giving rise to glomerular disease.
Coordinator

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Subjects

Scientific Research

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