International research team discovers novel genes influencing kidney disease risk

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A team of researchers from the United States and Europe has identified more than a dozen genes that may play a role in the etiology of common forms of kidney disease. The team, known as the CKDGen Consortium, examined common variations in DNA sequences in more than 65,000 individuals of European descent. Common variations in several genes were found to be more frequent among people with poor kidney function or chronic kidney disease than in those with normal kidney function. The researchers further confirmed their findings in more than 20,000 additional individuals. The findings are published in the April 11 edition of *Nature Genetics*.

Chronic kidney disease is a serious public health problem in the U.S. and around the world. Characterized by reduced kidney function or kidney damage, the disease affects approximately 10 percent of adults in the US. Research over the past 10 years has shown that chronic kidney disease increases the risk for cardiovascular diseases such as coronary heart disease and stroke. In addition, the disease can progress to the point where kidney transplant or dialysis is required.

Important risk factors for chronic kidney disease include diabetes and hypertension, although kidney disease clusters in families. The hereditary factors underlying chronic kidney disease have been difficult to determine until recently, when new methods to search for risk genes became available. The CKDGen Consortium applied one of the new methods, called genome-wide association study. In 2008, Johns Hopkins researchers used similar methods to identify common variants for non-

diabetic end stage renal disease, gout and sudden cardiac death.

For the latest study, the CKDGen Consortium team conducted genome-wide association studies among participants of 20 population-based studies. As part of these studies, more than 2,500,000 genetic variants for each study participant were examined in relation to kidney function. The researchers found strong evidence for more than 12 genes influencing chronic kidney disease risk and kidney function.

"We've know for a long time that diabetes, hypertension and family history are strong risk factors for kidney disease, but we have not been able to fully understand why. These findings will ultimately shed light on how and why kidney disease clusters in families and why it occurs in some individuals but not others," said Linda Kao, PhD, MHS, associate professor in the Johns Hopkins Bloomberg School of Public Health's departments of Epidemiology and Biostatistics, and the senior Johns Hopkins author on the study.

"By studying the genes identified in this study, we can learn more about basic mechanisms underlying kidney function and disease. These novel insights can form a foundation to improve prevention and therapy of kidney diseases," said the study's lead author, Anna Köttgen, MD, MPH, an adjunct assistant professor in the Bloomberg School's Department of Epidemiology.

"It is exciting to see research from around the world come together to collaborate and unlock the mysteries of kidney disease genetics. We learned that together we can do a lot more than apart," said Josef Coresh, MD, PhD, MHS, professor in the Bloomberg School's departments of Epidemiology and Biostatistics, and the principle investigator of ARIC, a large study contributing to the discovery.

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