Gene variant influences chronic kidney disease risk

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A team of researchers from the United States and Europe has identified a single genetic mutation in the CUBN gene that is associated with albuminuria both with and without diabetes. Albuminuria is a condition caused by the leaking of the protein albumin into the urine, which is an indication of kidney disease.

The research team, known as the CKDGen Consortium, examined data from several genome-wide association studies to identify missense variant (I2984V) in the CUBN gene. The association between the CUBN variant and albuminuria was observed in 63,153 individuals with European ancestry and in 6,981 individuals of African American ancestry, and in both the general population and in individuals with diabetes. The findings are published in the March 2011 edition of *JASN*.

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 U.S. Elevated levels of urinary albumin (albuminuria) are a cardinal manifestation of chronic kidney disease. Higher levels of albuminuria, even within the low normal range, are associated with not only increased risks of end-stage renal disease, requiring kidney transplant or dialysis, but also cardiovascular disease and mortality.

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.

"The significance of this finding is that even though the field has known about cubilin (the protein encoded by CUBN) function from experimental animal studies, our study was the first to establish the link between a genetic variation in this gene and albuminuria," 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. "The identification of CUBN and its association with albuminuria will lead to a multitude of follow-up work that will help us begin to understand the mechanism behind albuminuria and, hopefully, will ultimately lead to novel treatment targets."

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