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Researchers identify new genetic cause for chronic kidney disease

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A new single-gene cause of chronic kidney disease has been discovered that implicates a disease mechanism not previously believed to be related to the disease, according to new research from the University of Michigan.

The research was published July 8 in the journal *Nature Genetics*.

"In developed countries, the frequency of chronic kidney disease is continually increasing for unknown reasons. The disease is a major health burden," says Friedhelm Hildebrandt, M.D., the paper's senior author and professor of pediatrics and of human genetics at C.S. Mott Children's Hospital.

Using whole exome sequencing, Hildebrandt and his colleagues studied a model disorder for renal fibrosis, nephronophthisis, and detected a new single-gene cause of CKD that implicates a disease mechanism formerly not related to CKD — DNA damage response signaling (DDR).

"Since DNA damage is cause by a whole variety of chemical compounds it may now be important to see whether certain 'genotoxins' may play a role in the increase of CKD," says Hildebrandt who is also an investigator for the Howard Hughes Medical Institute.

The researchers identified mutations of Fanconi anemia-associated nuclease 1 (FAN1) as causing karyomegalic interstitial nephritis (KIN) in patients with CKD. Depletion of fan1 in a zebrafish model of disease

revealed increased DDR, apoptosis, and kidney cysts akin to nephronophthisis.

"Our findings implicate susceptibility to environmental genotoxins and inadequate DNA repair as novel mechanisms of renal fibrosis and CKD," Hildebrandt said.

Provided by University of Michigan Health System