

New target for treating prediabetes in patients with kidney disease

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Insulin resistance, or [prediabetes](#), in individuals with kidney disease may be caused by the progressive retention of certain compounds that are normally excreted by the kidneys in healthy individuals, according to a study appearing in an upcoming issue of the *Journal of the American Society of Nephrology (JASN)*. The findings might be used to prevent insulin resistance in kidney disease patients, which could lower their risk of developing [heart problems](#).

Cardiovascular disease is the number one killer of patients with [chronic kidney disease](#) (CKD), and insulin resistance—a lowered level of response to insulin circulating in the blood—is an important cardiovascular risk factor in these patients. It's not clear why patients with CKD often develop insulin resistance, but the retention of compounds that are normally removed from the blood and excreted in the urine may play a role. One such compound is p-cresyl sulfate (PCS), a toxin that is produced by [gut bacteria](#). PCS is retained in CKD patients, and it is poorly removed by most dialysis techniques.

Christophe Soulage, PhD, Denis Fouque, MD, PhD, and Laetitia Koppe, MD ([INSERM](#) & Université de Lyon, in Villeurbanne, France) led a team that sought to determine whether PCS contributes to CKD-associated insulin resistance. They found that administering PCS to mice with normal kidney function for four weeks triggered insulin resistance, loss of fat mass, and a redistribution of lipids in the muscles and liver, mimicking features associated with CKD.

The researchers also found that mice treated with PCS exhibited altered insulin signaling in skeletal muscles. In addition, when mice with CKD were treated with a [prebiotic](#) that reduces blood levels of PCS, insulin resistance and lipid abnormalities were prevented.

Taken together, these findings suggest that PCS contributes to insulin resistance and that targeting

PCS may help improve the health of patients with CKD.

"Because [insulin resistance](#) is an important [cardiovascular risk factor](#), novel therapeutic approaches like prebiotics that could decrease PCS more substantially than currently available strategies must be developed, especially since this toxin is not very efficiently removed by dialysis," said Dr. Soulage.

More information: The article, entitled "p-Cresyl sulfate promotes insulin resistance associated with CKD," will appear online at jasn.asnjournals.org/ on December 20, 2012.

Provided by American Society of Nephrology

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