Urine biomarkers reveal mitochondrial dysfunction in diabetic kidney disease

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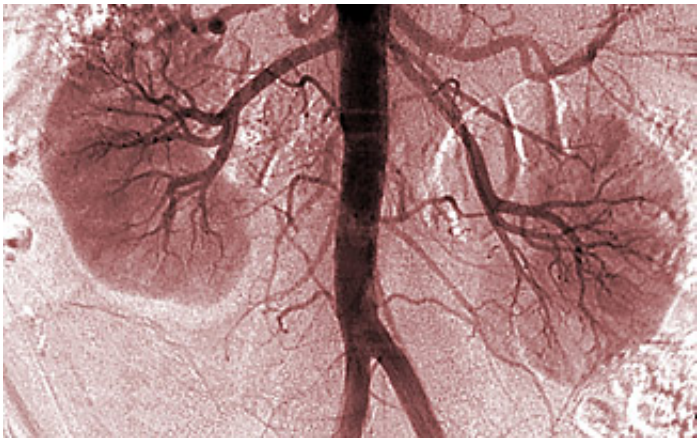

This is an X-ray of human kidneys. Credit: UC San Diego School of Medicine

Researchers at the University of California, San Diego School of Medicine have identified 13 metabolites – small molecules produced by cellular metabolism – that are significantly different in patients with diabetes and chronic kidney disease compared to healthy controls.

Twelve of the 13 metabolites are linked to mitochondrial function, suggesting that suppression of mitochondria – the powerhouses of cells – is a fundamental characteristic of diabetic kidney disease. The findings are published in the November edition of the *Journal of the American Society of Nephrology*.

"This work provides strong evidence that reduced mitochondrial

function is a dominant feature of human diabetic kidney disease," said first author Kumar Sharma, MD, professor of medicine and director of the Center for Renal Translational Medicine at UC San Diego. "We found that a specific cellular pathway, AMPK-PGC1a, likely plays a key role to reduce mitochondrial function and content, which means that new therapeutic approaches that restore and increase mitochondrial function and content could ameliorate or perhaps even arrest chronic kidney disease."

Diabetic kidney disease is the leading cause of end-stage kidney disease, which is the eighth leading cause of death in the United States and a major risk factor for cardiovascular disease, the nation's leading killer. An estimated 26 million American adults have chronic kidney disease (CKD), with millions more at increased risk. These patients often require dialysis or an organ transplant.

The primary causes of CKD are high blood pressure and diabetes. Rates of both CKD and diabetes have risen dramatically in the last decade, particularly among people aged 65 and older. According to the National Kidney and Urologic Diseases Information Clearinghouse, the annual mortality rate for end-stage renal disease rose from 10,478 in 1980 to 90,118 in 2009, though it has declined somewhat in recent years.

After analyzing a total of 193 urine samples from patients with diabetes and CKD, diabetes but no CKD and healthy controls with neither condition, Sharma and colleagues quantified 94 metabolites in the samples. Thirteen metabolites were significantly different between patients with diabetes and CKD versus controls. Twelve remained significant when compared to patients with diabetes but not CKD. Twelve metabolites play a role in mitochondrial metabolism and were present in lower levels in patients with diabetes and CKD, suggesting that this major diabetic complication is at least partly the consequence of suppressed mitochondrial activity.

Sharma said measuring urine metabolites to detect and assess diabetic kidney disease is a major diagnostic step forward. "The urine metabolites can indicate the underlying function of the kidney at a biochemical and intracellular level," he said, "and are well-conserved compared to many cell-based and protein measurements. Urine metabolomics also offers an opportunity to gauge effects of new treatments which will be an advantage to guide precision medicine."

Provided by University of California - San Diego

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