$5.9 Million Grant to UC San Diego for Paradigm-Shifting Diabetes Research

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Kumar Sharma, MD, FAHA, professor of medicine at the University of California, San Diego School of Medicine and director of the Center for Renal Translational Medicine, has received a $5.9 million grant from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), part of the National Institutes of Health, to study kidney complications related to type 1 and type 2 diabetes.

Renal complications of diabetes represent one of the major public health problems facing industrialized nations. In patients with type 1 diabetes, diabetic kidney disease is the leading cause of excess mortality.

"Each year in the United States, more than 100,000 people are diagnosed with kidney failure, a serious condition in which the kidneys fail to rid the body of toxins," said Sharma. "Diabetes is the most common cause of kidney failure, accounting for nearly 44 percent of new cases, so it is critical that we gain a better understanding of kidney complications associated with the disease. Even with early kidney disease there is a major impact on the cardiovascular system and there is a great need to understand the kidney-cardiovascular connections."

The NIDDK grant awards "groundbreaking original research addressing fundamental questions or major obstacles in type 1 diabetes research, including studies that challenge current dogma."

Scientists have long believed that that excess calories are processed via hyper-functioning mitochondria, the so-called "energy factories" of the cell, resulting in accumulation of reactive oxygen species. Sharma's studies, in collaboration with UCSD researchers Laura Dugan, MD, and Robert Naviaux, MD, PhD, will directly examine this hypothesis using live animal imaging and mitochondrial measurements.

To determine if mitochondrial function is actually reduced in humans, Sharma and his colleagues will evaluate the urine metabolome - measuring and analyzing metabolites, such as end-products of sugar, protein and fat metabolism, in the urine of patients with diabetes at specific times and under specific conditions. The grant will further define this analysis, allowing the researchers to use data from two large, well-characterized cohorts of patients from the Chronic Renal Insufficiency Cohort (CRIC) and the Finnish Diabetic Nephropathy Study (Finn-Diane), along with collaborators from the University of Pennsylvania and Helsinki, Finland. They will also determine if epigenetic modification of specific genes underlies the alteration in mitochondrial function in patients and in animal models.

"Using systems-biology and imaging approaches, we hope to link measurement of mitochondrial function to metabolic alterations in the kidney - an approach that challenges prevailing theories about hyperglycemia-induced kidney disease," said Sharma. "By characterizing the urine metabolome and epigenome in patients with diabetes and kidney disease, we hope to gain a better understanding of the basis of kidney complications associated with type 1 and type 2 diabetes."

Additional project collaborators at UC San Diego School of Medicine include Daniel O'Connor, MD, Trey Ideker, PhD, Joachim Ix, MD, MAS, Anne Murphy, PhD, Bruce Barshop, MD, PhD, and Bing Ren, PhD.

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