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New Bioinformatic Analysis Reveals Role of Proteins in Diabetic Kidney Disease

MDM2 emerges as key; Software could expose metabolomic information of other diseases

A new bioinformatic framework developed by researchers at University of California San Diego School of Medicine has identified key proteins significantly altered at the gene-expression level in biopsied tissue from patients with diabetic kidney disease, a result that may reveal new therapeutic targets.

Kumar Sharma, MD, director of the Institute for Metabolomic Medicine and the Center for Renal Translational Medicine at UC San Diego School of Medicine.

In a recently published paper in *JCI Insights*, researchers, led by Kumar Sharma, MD, professor of medicine at UC San Diego School of Medicine, revealed that the protein MDM2 was consistently down-regulated and played a key role in diabetic kidney disease progression. The researchers used the new "MetBridge Generator" bioinformatics framework to identify the relevant enzymes and bridge proteins that link human metabolomics data to the pathophysiology of diabetic kidney disease at a molecular level.

"MetBridge Generator allows for efficient, focused analysis of urine metabolomics data from patients with diabetic kidney disease, providing researchers an opportunity to develop new hypotheses based on the possible cellular or physiological role of key proteins," said Sharma, senior author and director of the Institute for Metabolomic Medicine and the Center for Renal Translational Medicine at UC San Diego School of Medicine. "The framework may also be used in the interpretation of other metabolomic signatures from a variety of diseases. For example, MDM2 is also involved in regulating tumor protein p53, which is a target for cancer treatments."

In a previous study, the authors identified 13 metabolites that were found to be altered in patients with diabetic kidney disease. Combining this information and publicly available data on metabolic pathways, the researchers tested an hypothesis that some proteins act as bridges creating less well-defined pathways. The framework then created a map of metabolic and protein-protein interaction (PPI) networks. This allowed the team to look deeper into relevant bridges with the greatest number of interactions with enzymes that regulate the 13-metabolite signature of diabetic kidney disease.

The authors already identified protein-RNA interactions as possible sources for additional key pathways underlying disease progression that could be added to the MetBridge Generator network. This growth will continue to add to possible therapeutic targets for disease treatment.

Study co-authors include: Rintaro Saito, Young-Hyun You, Manjula Darshi, Benjamin Van Espen, Satoshi Miyamoto, Jessica Pham, Minya Pu, Loki Natarajan, Keiichiro Ono, Trey Ideker, UC San Diego; Anaïs Rocanin-Arjo, Simone Romoli, Dana Thomasova, Shrikant R. Mulay, Hans Joachim Anders, Klinikum der Universität München, LMU Munich; Wenjun Ju, Matthias Kretzler, University of Michigan; Robert Nelson, National Institute of Diabetes and Digestive and Kidney Diseases; Vivette D'Agati, Columbia University; Ergin Beyret, and Juan Carlos Izpisua Belmonte, Salk Institute for Biological Studies.

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Disclosure: Sharma is the co-founder of ClinMet, Inc. He was on the board of directors, a scientific adviser and held an equity interest. Sharma's spouse is co-founder and was the president and chief operating officer and also held an equity interest.

MEDIA CONTACT

Yadira Galindo, 858-249-0456, ygalindo@ucsd.edu