MedicalXpress

Researchers identify promising new drug target for kidney disease

March 11 2012

Researchers from Mount Sinai School of Medicine have identified a regulator protein that plays a crucial role in kidney fibrosis, a condition that leads to kidney failure. Finding this regulator provides a new therapeutic target for the millions of Americans affected by kidney failure. The research is published in the March 11 issue of *Nature Medicine*.

Led by John Cijiang He, MD, PhD, Professor of Nephrology and Pharmacology and Systems Therapeutics; and Avi Ma'ayan, PhD, Assistant Professor of Pharmacology and Systems Therapeutics at Mount Sinai School of Medicine, the research team studied three mouse models of kidney fibrosis: one group of mice contained HIV viral proteins incorporated into their genome; the second group was injected with a high dose of folic acid; in the third mouse model, kidney filtration was blocked in one kidney. All of these factors cause kidney fibrosis.

The researchers gathered the genetic material of the mice and compared it to the genetic material of mice that did not have kidney fibrosis. Using a new computational systems biology algorithm and software called Expression2Kinases—developed by the Ma'ayan Laboratory at Mount Sinai—the results from these experiments were analyzed. They found that HIPK2, a protein kinase, or regulator, was highly active in the mice with kidney fibrosis. HIPK2 regulates the way certain genes are expressed and when HIPK2 is highly active this leads to kidney fibrosis. Drs. He and Ma'ayan also found that when they eliminated HIPK2, fibrosis was less prominent and the condition of the mice significantly

improved.

"Our findings have important implications for people with kidney diseases, patients I treat every day," said Dr. He. "Protein kinases like HIPK2 are highly effective therapeutic targets. We look forward to exploring this further."

Incorporating a systems approach allowed the Mount Sinai team to identify a target that is a regulatory protein modified during chronic disease. The high activity of HIPK2 in kidney fibrosis was not identifiable by standard methods that examine gene expression changes alone, but by modeling a network of proteins using computational systems biology, the research team was able to home in on the regulator protein, HIPK2. Now, Mount Sinai scientists can work to develop a drug intervention that inhibits the activity of HIPK2.

"This study is an important example of the translational research we are doing at Mount Sinai," said Dr. Ma'ayan. "Using algorithms and software developed here, we worked with Dr. He, who is a kidney disease physician and scientist, to better understand what causes kidney fibrosis, and we are now one step closer to finding a therapeutic solution to a complex disease that affects millions of Americans."

Provided by The Mount Sinai Hospital