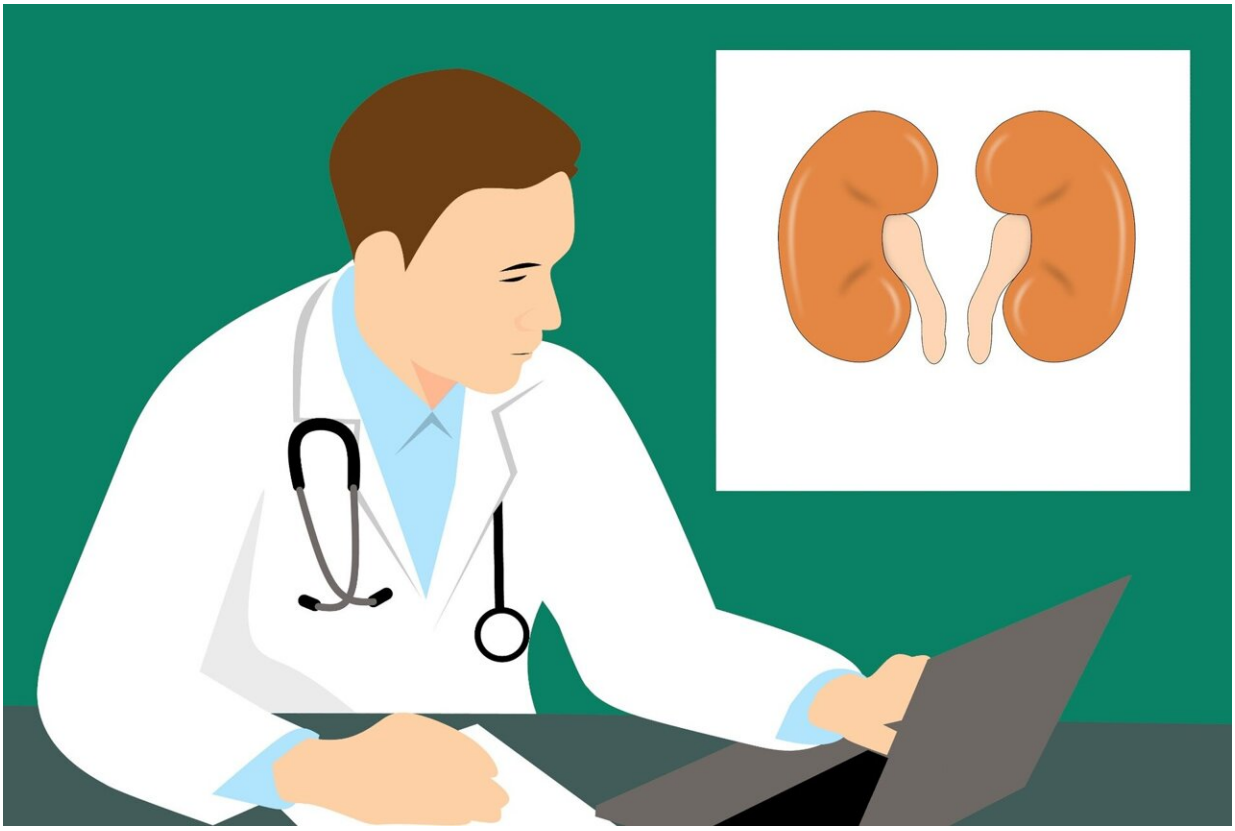
Study shines light on cause of chronic kidney disease

May 31 2023



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Fresh insights into a protein that causes damage in kidneys and hearts could open up new treatment options for chronic kidney disease, research shows.

In a study in mice, scientists found that scarring in kidneys and hearts was driven by a protein called Indian Hedgehog (IHH), which is produced and released by a subset of cells in aged and injured kidneys.

Experts say further studies are needed to explore IHH as a potential target for therapies to treat chronic kidney disease (CKD)—a condition that affects 10 percent of the world's population.

CKD is a term used to cover any form of kidney disease that continues for more than a few months. It can affect people of any age, but older people are more likely to experience some level of CKD.

While CKD primarily causes damage to kidneys, it is also a major risk factor for accelerated cardiovascular disease and premature death.

Progressive fibrosis—scarring of the kidneys—is a common feature in all CKD, but the mechanism underlying this connection is not fully understood.

A team from the University of Edinburgh identified a subset of epithelial cells—cells which make up body tissue—that produce IHH and are only present within aged or injured mouse kidneys.

They showed that these cells produced IHH in response to being activated by the protein TNF—a well-recognized driver of inflammation.

When blocking the actions of TNF or IHH in mouse models of kidney scarring, the team found that scar production in the kidney was reduced and kidney function was also better preserved. Increased levels of scarring in the heart also returned to normal levels.

In humans, the team showed that circulating IHH levels were

significantly raised in patients with CKD. Patients with cardiovascular disease also had higher levels of IHH than those without cardiac problems.

The findings offer hope that blocking the TNF/IHH signaling pathway could improve both kidney and heart fibrosis problems—the leading cause of morbidity and mortality in patients with CKD.

The study is published in the journal *Science Translational Medicine*.

Dr. David Ferenbach, MRC Senior Clinical Fellow at the University of Edinburgh and the senior author of this study, said, "There is a major unmet need for better treatments to halt the progressive kidney scarring and cardiovascular problems which affect so many patients with CKD. I'm excited at the potential of this work, and the new insights to be gained into the role of IHH as a major driver of multi-organ fibrosis, which we hope can be a first step on the road towards better treatments for patients."

More information: Eoin O'Sullivan et al, Indian Hedgehog release from TNF activated renal epithelia drives local and remote organ fibrosis, *Science Translational Medicine* (2023). DOI: 10.1126/scitranslmed.abn0736.
www.science.org/doi/10.1126/scitranslmed.abn0736

Provided by University of Edinburgh