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Identification of a driver of fibrosis in chronic kidney disease

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Chronic kidney disease can develop in response to a variety of insults and is characterized by progressive renal fibrosis and atrophy of kidney tubule. Therapeutic options are limited and the disease is often not detected until later stages. A new study in the inaugural issue of *JCI Insight* identifies the Wnt pathway modulator Dickkopf-3 (DKK3) as a driver of kidney fibrosis.

A team led by Bernd Arnold and Hermann-Josef Gröne at the German Cancer Research Center in Heidelberg, Germany determined that DKK3 expression is elevated in tubular epithelia upon stress and associates with profibrotic T cell responses.

In mouse models of CKD, genetic loss of Dkk3 or antibody blockade of DKK3 mitigated interstitial fibrosis and improved kidney function. DKK3 was secreted in the urine of mice following renal injury and associated with the extent of damage. Importantly, in patients with CKD of various etiologies, DKK3 levels in urine were elevated and correlated with the extent of fibrosis and tubular atrophy.

The results of this study identify DKK3 as a driver of renal fibrosis and as a potential biomarker of disease severity.

More information: Giuseppina Federico et al. Tubular Dickkopf-3 promotes the development of renal atrophy and fibrosis, *JCI Insight* (2016). DOI: 10.1172/jci.insight.84916