Paper highlight: Signaling hope for polycystic kidney disease

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Autosomal Dominant Polycystic Kidney Disease (ADPKD) is a common genetic disease that results in chronic kidney failure.

Although the genes responsible for ADPKD have been identified (PKD1, PKD2), relatively little is known about how mutations in these genes promote cyst growth molecularly.

In this paper, scientists at Children's Hospital in Boston, lead by Jordon Kreidberg, investigated the signaling pathways that go awry in the disease using mouse kidney epithelial cells in which Pkd1 was genetically deleted.

They found that the protein c-Met was hyperactive in Pkd1-deficient cells, resulting in increased mTOR signaling, a pathway that had previously been linked to cyst formation. The increase in c-Met activity was related to sequestration of the protein c-Cbl in a cellular compartment known as the golgi, which increased c-Met protein stability.

In support of a critical role for c-Met activity in disease progression, pharmacological inhibition of c-Met decreased mTOR activity and blocked cyst formation in a mouse model of ADPKD, leading the authors to suggest that c-Met is a potential therapeutic target in patients with ADPKD.

More information: Failure to ubiquitinate c-Met leads to

hyperactivation of mTOR signaling in a mouse model of autosomal dominant polycystic kidney disease: www.jci.org/articles/view/4153 … 07331a5bc3d8a1998c3f