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GROWTH AND DEVELOPMENT

Determinants of kidney size

Kidney size increases with increasing body mass and in response to the loss of a single kidney but the mechanisms behind these changes are unclear. Recent data reveal context-dependent roles for PTEN-dependent class I PI3K/mTORC2/Akt signalling and PTEN-independent class III PI3K/mTORC1/S6K1 signalling in determining kidney size.

To investigate the role of mTOR signalling in kidney growth, Raymond Harris, Jian-Kang Chen and colleagues selectively deleted Pten—a negative regulator of the class I PI3K/AKT signalling pathway—from proximal tubules of mice. Pten deletion resulted in greatly enlarged kidneys, with activation of the class I PI3K/mTORC2/Akt pathway. Unilateral nephrectomy induced further hypertrophy of the remaining kidney in Pten-knockout mice. "Unilateral nephrectomy did not activate the class I PI3K/mTORC2/AKT pathway, but proximal-tubule-specific Pten-knockout mice exhibited persistent activation of this pathway and kidney hypertrophy, which could be reversed by administration of the mTORC1 inhibitor rapamycin or by proximal-tubule-specific deletion of EGFR," explains Chen.

Exogenous delivery of amino acids to mimic the increased metabolic requirements after unilateral nephrectomy activated the class III PI3K/mTORC1/S6K1 pathway. "These findings demonstrate context-dependent roles for EGFR-regulated PTEN-dependent class I PI3K/mTORC2/AKT signalling in the adaptation of normal kidney size, and PTEN-independent nutrient-dependent class III PI3K/mTORC1/S6K1 signalling in the compensatory enlargement of the remaining kidney following unilateral nephrectomy," explains Harris.

Susan J. Allison

Original article Chen, J.-K. *et al*. Phosphatidylinositol 3-kinase signaling determines kidney size. *J. Clin. Invest.* doi:10.1172/JCI78945