ACID-BASE DISORDERS

Paracrine regulation of acid–base balance

Paracrine communication between different parts of the renal tubule is required for the maintenance of systemic acid–base balance, say researchers. “We demonstrate that the kidney regulates acid–base balance through a paracrine mechanism in which α -ketoglutarate, an intermediate of the citric acid cycle, acts as a paracrine mediator between the proximal and distal parts of the renal tubule,” explains researcher Dmitri Firsov.

The researchers initiated the current study to investigate the role of the α -ketoglutarate receptor, OXGR1. Earlier work had shown that urinary levels of α -ketoglutarate vary in response to systemic changes in acid–base balance, leading Firsov and colleagues to hypothesize that OXGR1 is involved in maintaining acid–base homeostasis.

“Previous studies demonstrated that changes in dietary acid–base load reversed the direction of apical α -ketoglutarate transport in the proximal tubule and loop of Henle from reabsorption (with acid loading) to secretion (with base

loading),” says Firsov. “Now we show that the resulting changes in the luminal concentrations of α -ketoglutarate are sensed by OXGR1 expressed in the type B and non-A-non-B intercalated cells of the connecting tubule and cortical collecting duct.” The researchers found that luminal activation of OXGR1 by α -ketoglutarate resulted in the increased secretion of HCO_3^- and reabsorption of NaCl, processes that are involved in maintaining acid–base equilibrium. “Using *in vivo* experiments we also showed that this paracrine signalling is functionally important since mice devoid of *Oxgr1* exhibit a reduced capacity to maintain acid–base equilibrium,” notes Firsov.

The researchers say that OXGR1 could be a target for the treatment of acid–base disorders or tubular disorders associated with kidney stones.

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