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METABOLISM

Energy-efficient transport in the kidney

> inherited or acquired defects in proximal tubular paracellular transport might predispose patients to AKI

The transmembrane protein claudin-2 mediates paracellular sodium reabsorption in the proximal tubule, but given the versatility of transcellular epithelial transport, the paracellular pathway seems dispensable. Now, Alan Yu and colleagues report that paracellular sodium transport increases the energy efficiency of the kidney.

To investigate the importance of paracellular sodium reabsorption in the proximal tubule, the researchers analysed urinary sodium excretion in claudin-2-knockout mice on a very low sodium diet. "We thought that under this dietary challenge, these mice might be unable to maximally reabsorb salt so would become salt-depleted and dehydrated," says Yu. "However, they were perfectly fine and maximally reabsorbed sodium from the urine." Further investigations showed that the knockout mice were able to compensate for defective paracellular sodium transport by upregulating transcellular sodium transport in the thick ascending limb of the loop of Henle. "This finding raised an even more interesting question," says Yu. "If paracellular transport in the proximal tubule is not needed, why did it evolve? Or more generally, why does paracellular transport in the epithelia exist?"

Neil Smith/NPG

The researchers hypothesized that paracellular transport might increase the energy efficiency of the epithelia by enabling the movement of solutes and water without the consumption of energy and oxygen. Consistent with this theory they found that the kidneys of claudin-2-knockout mice consume more oxygen than those of wild-type mice, resulting in increased hypoxia in the outer medulla. Under normal conditions this reduced efficiency of renal oxygen utilization did not seem to have adverse effects, but when exposed to mild kidney ischaemia the knockout mice were much more susceptible to acute kidney injury (AKI) than were normal controls. "An analogy might be a hybrid electric vehicle," explains Yu. "Without its energy-efficient electric motor it would just be a regular gas-guzzling vehicle. Both can get you to your destination and you would only know the difference if you looked at the amount of gas being consumed. However, if gasoline prices become prohibitively expensive, you might not be able to run the regular vehicle."

The researchers now plan to investigate whether inherited or acquired defects in proximal tubular paracellular transport might predispose patients to AKI. They are also interested in the potential role of paracellular transport in increasing energy efficiency in non-renal epithelial tissues.

Ellen F. Carney

ORIGINAL ARTICLE Pei, L. *et al.* Paracellular sodium transport maximizes energy efficiency in the kidney. *J. Clin. Invest.* http://dx.doi.org/10.1172/JCI83942 (2016)