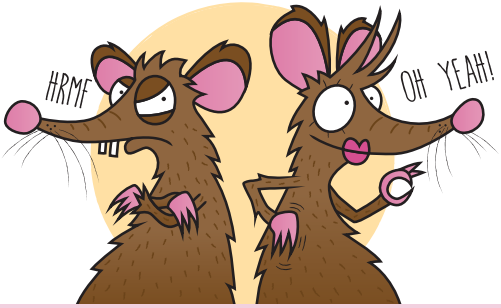
Nature Reviews Nephrology | Published online 21 Aug 2017;
doi:10.1038/nrneph.2017.122



RENAL PHYSIOLOGY

The sexually dimorphic kidney

Before the age of 60, females are protected from cardiovascular and renal disease relative to males. Alicia McDonough and colleagues show that there is a sexually dimorphic pattern of renal tranporters across the nephron and that this pattern may be associated with the 'female advantage'.

"We were doing pilot experiments on renal mechanisms of potassium adaptation in a mouse genetic model that lacks a muscle-specific sodium pump," explains McDonough. "The immunoblots of renal sodium transporter abundance exhibited uncharacteristic variability in both the wild-type and modified mice. When we analysed the results according to sex, bimodal patterns emerged". Interestingly, the researchers found that female rats had a lower rate of proximal tubule reabsorption and excreted a saline load more rapidly than male rats, which suggests that there were physiological consequences to these biomodal patterns.

To determine the renal physiology of male and female rats at baseline, the researchers examined the relative abundance of transporters in the proximal tubule, loop of Henle, distal tubule and the collecting duct, and proteins related to these transporters in homogenates of the kidney cortex and medulla, by quantitative immunoblot. They found that female rats have a lower abundance of sodium and associated transporters in the proximal tubule, but a higher abundance and activation of sodium transporters in distal nephrons, compared to male rats. "This distal activation is known to facilitate potassium secretion and, indeed, female rats exhibited a lower plasma potassium concentration set point" says McDonough. Furthermore, a potassium-rich meal increased the urinary potassium concentration in female rats compared with male rats and this meal was associated with an increased activation of renal sodium transporters, suggesting how female rats can maintain a lower potassium set point than male rats.

Notably, the nephron of female mice showed a similar transporter profile to that of female rats; however, female mice did not show substantial differences in saline or potassium clearance relative to male mice. "Determining whether humans also exhibit similar sexual dimorphisms warrants careful investigation and would provide mechanistic information relevant to the idea of a female advantage in some cardiovascular diseases and hypertension,"concludes McDonough.

Shimona Starling

ORIGINAL ARTICLE Veiras, L. C *et al.* Sexual dimorphic pattern of renal transporters and electrolyte homeostasis. *J. Am. Soc. Nephrol.* http://dx.doi.org/ 10.1681/ASN.2017030295 (2017)

> "female rats had a lower rate of proximal tubule reabsorption and excreted a saline load more rapidly than male rats"