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Renal outer medullary potassium channel knockout models reveal Bartter's syndrome and dysfunction of potassium homeostasis

The renal outer medullary potassium channel (ROMK) is an ATP-sensitive inward-rectifier potassium channel (Kir1.1 or KCNJ1) highly expressed in the kidney. We have demonstrated that ROMK-/- mice show a similar phenotype to Bartter's syndrome of salt wasting and dehydration due to reduced Na-K-2Cl-cotransporter activity in the thick ascending limb (TAL). Patch clamp studies showed that ROMK is required to form both the small-conductance (30-pS, SK) K and the 70-pS (IK) K channels in the kidney. At least three ROMK isoforms have been identified in the kidney; however, unique functions of any of the isoforms in nephron segments are still poorly understood. We have generated a mouse deficient only in ROMK 1 by selective deletion of the ROMK 1-specific first exon using an ES cell Cre-LoxP strategy and examined the renal phenotypes, ion transporter expression, ROMK channel activity and localization under normal and high K intake. Unlike ROMK -/- mice, there was no Bartter's phenotype with reduced NKCC2 activity and increased NCC expression in ROMK1-/- mice. The SK activity showed no difference of channel properties or gating in the collecting tubule (CCD) between ROMK1+/+ and ROMK1-/- mice. High K intake increased SK channel number per patch and the ROMK channel intensity in the apical membrane of the CCD in ROMK1+/+, but such regulation was diminished with significant hyperkalemia in ROMK1-/- mice. These results are consistent with previous studies that ROMK1 does not localize in the TAL, and that ROMK1 is a key target of PTK-mediated ROMK trafficking in response to K+ intake.

Biography

Tong Wang has completed her MD and Clinical Trainings at Beijing University, School of Medicine in China. She then spent two Postdoctoral training period at the University of Illinois at Chicago and Yale University School of Medicine with Dr. Gerhard Giebisch. Currently, she is a Full Professor, Director of the Small Animal Physiology Core in the Department of Cellular and Molecular Physiology and Co-Director of the Renal Physiology Core in the George M O'Brien Kidney Center at Yale University. She has published more than 100 papers in reputed journals and has been serving as an active member of NIH KMBD study section.

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