1. No.
   2017G028

2. Title
   Role of the ubiquitin-proteasome pathway upon acidosis in the progression of chronic kidney disease and its regulation by nicotine

3. Period
   2017-2021

4. Summary

   In the present study, we investigated the regulation and mechanisms for urinary acid excretion through Rhcg, an ammonia transporter, expressed in the intercalated cells of the renal collecting duct. We also investigated the role of aldosterone and nicotine in urinary acid excretion, focusing on the ubiquitin-proteasome system (UPS) and the regulation of Rhcg. Metabolic acidosis induced by acid loading increased the protein expression of ubiquitin in collecting duct cells. Administration of MG132, a proteasome inhibitor, resulted in the accumulation of Rhcg protein at the luminal membrane in the collecting duct together with increased acid excretion into urine, suggesting that metabolic acidosis should induce the activation of UPS and degradation of Rhcg protein. Aldosterone stabilized Rhcg protein *in vitro* and increased its accumulation at the luminal membrane *in vivo*, suggesting that aldosterone could inhibit the degradation of Rhcg protein through the UPS. We showed that short-term treatment with nicotine increased urinary acid excretion under metabolic acidosis, although the effect of its long-term treatment was obscure. Nicotine increased the protein expression of ubiquitin and the accumulation of Rhcg protein at the luminal membrane, suggesting the involvement of UPS in the regulation of Rhcg protein expression. However, nicotine did not exert a significant effect on the stability of Rhcg protein *in vitro*. Further studies are needed to define the long-term effect of nicotine administration on acid excretion *in vivo*, as well as to clarify the regulation and precise mechanisms for urinary acid excretion by aldosterone and nicotine.