Basolateral Expression of the Ammonia Transporter Family Member, Rh C Glycoprotein, in the Mouse Kidney: Strain-dependent Difference

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Ammonia metabolism and transport is critical for acid- base homeostasis. Recent studies have shown that distal renal tubules critical for ammonia secretion express the ammonia transporter family member, Rh C glycoprotein (Rhcg), and that Rhcg expression is regulated in parallel with renal ammonia metabolism. However, previous studies report inconsistencies in the subcellular distribution of renal Rhcg among animal species. Both apical and basolateral Rhcg immunoreactivity were detected in rat and human kidney, whereas only apical Rhcg was found in mouse kidney. Because the membrane location of Rhcg is critical for understanding its physiologic role, this study reassesses mouse kidney Rhcg localization using refined immunolocalization methods. Immunohistochemistry demonstrated basolateral Rhcg expression in the mouse kidney, in addition to the previously identified apical Rhcg immunoreactivity. Basolateral Rhcg intensity varied in different mouse strains, and was substantially less intense in the Balb/C mouse compared to the C57BL/6 mouse strain. Immunogold electron microscopy confirmed basolateral plasma membrane Rhcg expression, and in addition, showed that Rhcg was also present both in the apical plasma membrane and in sub- apical cytoplasmic vesicles, similar to its location in rat kidney. Immunoblots and northern blots of Balb/C and C57BL/6 mouse kidney identified only single protein and mRNA bands, suggesting that basolateral Rhcg may result from alternative trafficking of Rhcg. Furthermore, less basolateral Rhcg expression in the Balb/C mouse as compared to the C57BL/6 mouse strain was associated with lower urinary ammonia excretion in response to metabolic acidosis conditions. Although basolateral Rhcg expression differed in C57BL/6 and Balb/C mice, basolateral Rhbg expression did not, either under basal conditions or in response to metabolic acidosis. These results indicate that Rhcg is present in both the apical and basolateral plasma membrane in the mouse kidney where it is likely to contribute to renal ammonia metabolism.

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