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Functional analysis of organic cation transporter OCTNs in mouse renal brush border membrane

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In the kidney, tubular secretion and reabsorption of cationic drugs are performed by transcellular transport. The epithelial cells of renal tubules possess two kinds of membrane regions that are important for vectorial transport of drugs, i.e., brush-border membrane and basolateral membrane. Gene knockout analyses showed that OCT1 and 2 are responsible for the uptake of cationic drugs at basolateral membrane. On the other hand, at brush-border membrane, the existence of H^+/organic cation antiporters has been suggested by kinetic analysis although their molecular identification has not yet been performed. OCTN1 identified in our laboratory has such H^+/organic cation antiport activity and is expressed on renal apical membranes. The purpose of this study was to characterize the transport function of mouse OCTN1 and OCTN2, with an aim to identify the transporters responsible for cationic drug transport in mouse renal brush-border membrane. Membrane vesicles were prepared from both renal cortex and HEK293 cells stably expressing each OCTN family. Effect of pH, membrane potential and inhibitors on the uptake of [14C]TEA or [14C]carnitine was compared between the two vesicles. Effects of pH gradient and most of the inhibitors examined were principally similar between both vesicles although some differences were observed in the effect of membrane potential and the inhibitory effect of carnitine and guanidine. In addition, no significant differences were observed between cation transport activities in BBMVs of wild mice and jvs mice lacking OCTN2 gene, suggesting that OCTN2 is not majorly involved in H^+/organic cation antiport system. These results indicate that OCTN1 is, at least partially, responsible molecule for H^+/cation antiport systems at renal brush-border membrane.

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