No. 0723

Expression and Functional Analyses of Na^+/Monocarboxylates Co-Transporters in the Intestine

Toshihiko Iwanaga [1], Seiji Miyauchi [2]

[1] Hokkaido University Graduate School of Medicine
[2] Hokkaido University Graduate School of Pharmaceutical Sciences

Summary

Expression analysis of transporters selective for monocarboxylates such as lactate and ketone bodies in the intestine and kidney contributes to understanding the energy metabolism and the role of sodium in the transport of monocarboxylates. Distribution and expression intensity of a sodium-dependent monocarboxylate transporter (SMCT) and proton-coupled monocarboxylate transporters (MCT) were examined in the mouse intestine and kidney. Short-chain fatty acids (SCFA) are monocarboxylates produced by bacterial fermentation that play a crucial role in maintaining homeostasis in the large intestine. Two major transports for SCFA exist in the digestive tract. The expression of mucosal MCT1 in the mouse was most intense in the cecum, followed by the colon, but low in the stomach and small intestine. Among other MCT subtypes, only MCT2 was detected in the parietal cell region of the gastric mucosa. SMCT had predominant expression sites in the distal half of the large bowel and in the most terminal ileum. The mucosal MCT1 was localized in the basolateral membrane of enterocytes, while SMCT was restricted to the apical cell membrane, suggesting the involvement of SMCT in the uptake of luminal SCFA, and of MCT1 in the efflux of SCFA and monocarboxylate metabolites towards blood circulation. The large intestine expressed both types of the transporter, but their distribution patterns differed along the longitudinal axis of the intestine and along the perpendicular axis. *In situ* hybridization survey in the kidney detected significant mRNA expressions of SMCT and MCT-1, 2, 5, 8, 9, 10, and 12. Among these, signals for SMCT, MCT2 and MCT8 were predominant; transcripts of SMCT were restricted to the cortex and the outer stripe of outer medulla, while those of MCT2 and MCT8 gathered in the inner stripe of outer medulla and the cortex, respectively. Immunohistochemically, SMCT was present at the brush border in S2 and S3 of proximal tubules, suggesting the active uptake of luminal monocarboxylates here. MCT1 and MCT2 immunoreactivities were respectively found baso-laterally in S1 and thick ascending limbs of Henle's loop. The cellular localization of transporters suggests the involvement of SMCT in the uptake of filtrated lactate and ketone bodies and that of MCTs in the transport of monocarboxylate metabolites between tubular cells and circulation, but the different distribution patterns do not support the notion of a functional linkage between SMCT and MCT1/MCT2.