MS05-3 The role of PCFT/SLC46A1 in intestinal absorption of folates

◯Katsuhisa INOUE[1], Hiroaki YUASA[1]

[1]Nagoya City Univ. Grad. Sch. of Pharm. Sci.

Folates (folate and its several derivatives) are essential cofactors that are required for the provision of one-carbon moieties in key biosynthetic and epigenetic processes. Mammals cannot synthesize folates and, hence, dietary sources must meet metabolic needs, necessitating an efficient intestinal absorption mechanism. Absorption of folates occurs primarily in the duodenum and upper jejunum, and involves a carrier-mediated process with a low-pH optimum that operates efficiently within the acidic microclimate of the intestinal surface. Although specific carriers for folates such as reduced folate carrier 1 (RFC1) and folate receptors had been identified and known for more than a decade, there was controversy about the involvement of these carriers in intestinal absorption of folates. Thus, the molecule entity of the carrier-mediated intestinal transport system had long been unclear. It was only recently that proton-coupled folate transporter (PCFT/SLC46A1), which was originally cloned as a heme transporter, heme carrier protein 1 (HCP1), was redefined as a transporter that mediates the translocation of folates across the cellular membrane by a proton-coupled mechanism. Since this discovery, studies on SLC46A1 have been progressing rapidly, accumulating evidences for its role as the major folate transporter in the intestine. In this presentation, we summarize up-to-date information on this newly identified transporter, and discuss its significance in exploring therapeutic strategies to overcome the malabsorption of folates and antifolate drugs such as methotrexate and in developing antifolate drugs.