Distribution of the amino acid transporters B^0AT1, B^0AT2 and ASCT2 in kidney and intestine

N. Tietze,[1] J.M. Vanslambrouck,[2] J.E.J. Rasko[2] and S. Bröer,[1] [1]School of Biochemistry and Molecular Biology, The Australian National University, Canberra, ACT 0200, Australia and [2]Gene and Stem Cell Therapy Program, Centenary Institute of Cancer Medicine and Cell Biology, University of Sydney, NSW 2050, Australia.

Dietary protein is almost completely absorbed in the intestine with the aid of proteases, peptidases, amino acid and peptide transporters. Plasma amino acids are filtered in the kidney and subsequently reabsorbed in the proximal tubule of the kidney. Neutral amino acids are transported in these tissues mainly by an amino acid transports activity referred to as System B^0. Three different amino acid transporters have been suggested to be member of this transport activity, namely B^0AT1 (SLC6A19), B^0AT2 (SLC6A15) and ASCT2 (SLC1A5). B^0AT1 is a Na^+ dependent, Cl^- independent and pH sensitive transporter, mediating transport of all neutral amino acids with low affinity (Bröer *et al.,* 2004). Further studies revealed a cotransport stoichiometry of 1 Na^+ together with a substrate (Bohmer *et al.,* 2005). ASCT2 mediates transport of neutral amino acids with the exception of aromatic amino acids with high affinity. It is a Na^+ dependent, electroneutral antiporter (Kekuda *et al.,* 1996; Bröer *et al.,* 2000; Avissar *et al.,* 2001). B^0AT2 has been characterized as a Na^+ dependent neutral amino acid transporter preferring branched-chain amino acids and proline with high affinity via the same mechanism as B^0AT1 (Takanaga *et al.,* 2005; Bröer *et al.,* 2006). In early studies B^0AT 2 was only detected in the brain but was subsequently also reported in kidney (Bröer *et al.,* 2006). However, its specific localisation in the kidney still needs to be elucidated and could give conclusion about function and possible compensation for other transporter malfunction. While low affinity transporters for neutral amino acids are found in the early (S1-S2) segments of the kidney, high affinity transporters have been reported in the later (S3) segments. Localisation of the B^0AT2 transporter would thus contribute to the understanding of amino acid reabsorption in the kidney.

In this study, the distribution of the neutral amino acid transporters B^0AT1, B^0AT2 and ASCT2 were investigated in kidney and intestine. Specific antibodies against these amino acid transporters were analysed in Western Blots, showing specific bands for brush border membrane vesicles and oocyte membrane preparations expressing the transporters. Immunofluorescence studies localised B^0AT1 in the apical membrane of the intestine and the proximal tubule of the kidney. B^0AT2 was found to be localised in a different part of the proximal tubule than B^0AT1. ASCT2 appears to be located in the distal tubule or in parts of the proximal tubule of the kidney.

Avissar NE, Ryan CK, Ganapathy V, Sax HC. (2001). *American Jounal of Physiology*, **281:** C963-71.

Bohmer C, Brer A, Munzinger M, Kowalczuk S, Rasko JE, Lang F, Bröer S. (2005). *Biochemical Journal*, **389:** 745-51.

Bröer A, Klingel K, Kowalczuk S, Rasko JE, Cavanaugh J, Bröer S. (2004). *Journal Biological Chemistry*, **279:** 24467-76.

Bröer A, Tietze N, Kowalczuk S, Chubb S, Munzinger M, Bak LK, Bröer S. (2006). *Biochemical Journal*, **393:** 421-30.

Bröer A, Wagner C, Lang F, Bröer S. (2000) *Biochemical Journal*, **346:** 705-10.

Kekuda R, Prasad PD, Fei YJ, Torres-Zamorano V, Sinha S, Yang-Feng TL, Leibach FH, Ganapathy V. (1996). *Journal Biological Chemistry*, **271:** 18657-61.

Takanaga H, Mackenzie B, Peng JB, Hediger MA. (2005) *Biochemical and Biophysical Research Communications*, **337:** 892-900.