What are the roles of amino acid transporters B^0AT1 and ASCT2 in kidney and intestine?

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In both kidney and intestine neutral amino acids are absorbed by a major transport activity specific for this class of amino acids, referred to as system B^0. Two different amino acid transporters have been suggested to mediate this activity, namely B^0AT1 (SLC6A19) and ASCT2 (SLC1A5). B^0AT1 (SLC6A19) is an apical neutral amino acid transporter in mammalian kidney and intestine. Amino acid transport mediated by B^0AT1 is sodium dependent, chloride independent and pH sensitive (Bröer *et al.*, 2004). Further studies revealed the transport mechanism as a cotransport of Na^+ and substrate with a stochiometry of 1:1 (Bohmer *et al.*, 2005). It has been shown that dysfunction of B^0AT1 is responsible for Hartnup disorder, an autosomal recessiv disorder of neutral amino acid absorption (Kleta *et al.*, 2004; Seow *et al.*, 2004).

ASCT2 (SLC1A5) (Avissar *et al.*, 2001; Kekuda *et al.*, 1996) also mediates transport of neutral amino acids except those with aromatic side chains. ASCT2 is a Na^+ dependent, electroneutral antiporter. At low pH, ASCT2 also accepts glutamate and aspartate. Expression of ASCT2 has been reported in the apical membrane of kidney proximal tubules and the intestine. These localization results indicate that both ASCT2 and B^0AT1 could contribute to neutral amino acid absorption in kidney and intestine. In the acidic microclimate of the intestine ASCT2 could also contribute to glutamate uptake, which would be absorbed in exchange for neutral amino acids. B^0AT1 could then recapture the neutral amino acids constituting a tertiary active transport system. The aim of this study is to determine the role of the two amino acid transport B^0AT1 and ASCT2 in kidney and in intestine.

To investigate the contribution of the two transporters, renal and intestinal brush border vesicles from mice were generated. Alkaline phosphatase enrichment suggested an 8-9-fold enrichment of the apical membrane. This was supported by Western Blots showing enrichment of the apical transporter B^0AT1. However, significant amounts of the basolateral marker 4F2hc were observed as well. Uptake of leucine was studied in the presence of phenylalanine, glutamine and alanine to discriminate between the two transporters. Competition of leucine transport was observed with all three amino acids. The data obtained from vesicle studies were compared with the properties of B^0AT1 and ASCT2 when expressed in *Xenopus laevis* oocytes.This comparison showed that leucine uptake was nearly completely inhibited by the B^0AT1 substrate phenylalanine in kidney.

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