Membrane complexes involved in protein digestion and nutrient signaling

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Neutral amino acid transport across intestinal epithelia is mainly mediated by the B^0AT1 transporter, additional transporters, such as PAT1 and IMINO serve to transport proline and glycine. Mutations in B^0AT1 cause Hartnup disorder, while mutations in proline and glycine transporters cause iminoglycinuria. B^0AT1 requires angiotensin converting enzyme 2 (ACE2) to be trafficked to the plasma membrane. In the intestine, larger complexes are formed including aminopeptidase N, B^0AT1 and ACE2. These complexes allow optimal digestion of short peptides. Expression of B^0AT1 in the intestine is regulated by the interplay between transcriptional activators such as HNF4α and transcriptional repressors SOX9. A mouse model of B^0AT1 deficiency replicates Hartnup disorder and demonstrates the role of B^0AT1 in neutral amino acid transport. With the exception of proline and glycine, Na^+-dependent uptake of neutral amino acids is completely abolished in the intestine. In the mouse the remaining glycine transport is mediated by PAT1, and the remaining proline transport is mediated by IMINO. In addition the mouse model demonstrates an important role of B^0AT1 in the regulation of body weight. B^0AT1-deficient mice lose body weight when the protein composition of the diet is changed. On a 6% protein diet weight loss mainly reflects loss of muscle, while on a 40% protein diet it is caused both by reduction of muscle mass and adipose tissue. Lack of B^0AT1 causes a complex change of transcription in the intestinal mucosa, allowing adaptation to protein restriction.