Transport metabolons in the apical membrane

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Protein absorption in the small intestine is an efficient process, assimilating 95% of protein amino acids. To achieve complete digestion, pancreatic and brush-border peptidases work together with a variety of amino acid and peptide transporters. The aim of this project was to identify whether peptidases and transporters form complexes in the membrane to optimize protein absorption. The major transporter for neutral amino acids in the intestine and kidney is called B0AT1 or SLC6A19 (Broad neutral (0) Amino acid Transporter1). Expression of B0AT1 at the cell surface requires coexpression of the carboxypeptidase angiotensin-converting enzyme 2 (ACE2). Coexpression of B0AT1 together with ACE2 increases transport activity more than 20-fold. ACE2 preferentially hydrolyses neutral amino acids from the carboxyterminus of small peptides, which then become substrates of B0AT1. However, kinetic properties of B0AT1 remain unaltered in the presence of ACE2 and both proteins could not be coimmunoprecipitated suggesting that they do not form a tight complex. Coexpression of B0AT1 with aminopeptidase N, by contrast, increased surface expression and changed the kinetic parameters of the transporter. Similarly, ACE2 increased surface expression and the kinetic parameters of the related transporter B0AT3 (SLC6A18), which is coexpressed together with ACE2 in the kidney. Thus, members of the SLC6 family require brush-border membrane peptidases for surface expression and to optimize transport of neutral amino acids. A model is proposed whereby peptidases act as binding proteins for neutral amino acid transporters. Binding proteins are known to be involved in bacterial ABC transporters, but have not been demonstrated in higher cells.