

### Disorders of Carbohydrate Metabolism: Sucrase-Isomaltase Deficiency

- brush border membrane of the small intestine is endowed with seven glycosidases that are responsible for splitting dietary disaccharides into free monosaccharides
  - \* glucoamylase complex: two maltases
  - \* sucrase-isomaltase: two maltases
  - \*  $\beta$ -glycosidase: lactase and glycosylceramidase
  - \* trehalase
- these enzymes are stalked intrinsic proteins of the membrane with the bulk of the peptide protruding out towards the lumen of the intestine
- both primary (genetic) and secondary deficiencies of these enzymes occur in humans, with adult-type hypolactasia being the most common (in fact, it occurs in the majority of humans and all other mammals)

- sucrase-isomaltase (SI) is synthesized as a single large polypeptide of about 200 kDa (pro-SI); after maturation, the protein is roughly 250 kDa due to the addition of multiple sugar chains within the ER and Golgi
- the isomaltase portion is attached to the membrane in the SI complex
- once the protein is sorted to the apical surface of the intestinal cells, it is cleaved by trypsin into two separate enzymes that remain associated
- O-linked glycans in the stalk region have been shown to play a role in the apical sorting of the enzyme; interaction of lectin-like protein with SI glycans allows protein to associate with detergent resistant membranes at apical surface
- clinically, loss of SI is manifested as an osmotic-fermentative diarrhea; colonic flora normally salvage inadequately absorbed carbohydrates by fermentation to gases and organic acids that are easily metabolized in the colon
- multiple mutations have been identified in the SI gene that affect its activity, processing and sorting