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Keynote talk - Intestinal peptide and drug uptake – a structure perspective

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Nutrient uptake across the lipid bilayer is essential for life. Membrane transporters with specialized functions have evolved to maintain the nutrient homeostasis of cells. Many of those are energized by an electrochemical proton gradient. Prominent members of such 'secondary active transport system' are the oligopeptide transporters PepT1 and PepT2. Both belong to the Solute Carrier Family 15 (SLC15), which is highly conserved among all phyla of life. They are known to play key roles in human diseases and impact the pharmacokinetic profiles of orally administered drug molecules. I will highlight the approaches that allowed us to structurally characterize this transporter family. We studied transporter homologs (from bacteria to humans) by structural (X-ray crystallography, SAXS, and cryo-EM), biochemical and biophysical approaches, and determined the molecular basis for ligand recognition. The transporter has been captured in different conformations allowing us to obtain a molecular picture of the transport cycle.

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