Sugar and amino acid symporters: common structure and mechanism

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Symporters are responsible for the active accumulation of glucose, amino acids and other solutes in epithelial cells and other cells throughout the body including neurons. Over the past twenty years considerable success has been achieved in cloning solute transporters and the human genome contains over 360 in 55 gene families, *e.g.* the sodium symporters in the glucose (SSF, SLC5) and neurotransmitter (SNF, SLC6) gene families. Although there is no amino acid sequence homology between the SSF and SNF transporters, these genes are often expressed in the same cell type, epithelia and neurons, and have very similar transport kinetics despite the fact that there is no overlap in substrate specificity. Recent progress in solving the atomic structure of transport proteins (LeuT, vSGLT, Mhp1, & BetP) has provided a dramatic new perspective on the transport mechanism. Namely, that genetically diverse transporters have a common structure that is also shared with a proton/amino acid symporter (ApcT) and a Na^+-independent amino acid antiporter (AdiC). Despite the lack of amino acid homology these structures can be aligned (RMSD <5 Å) and their substrates can be placed in a common occluded binding site. Of course the coordinating residues for each substrate are different. Despite the overlap of the six structures they are in slightly different conformations, *e.g.* open outward facing, closed outward facing with substrate, and closed inward facing with substrate. These different conformations provide the first structural basis for the alternating access mechanism of solute transport. In addition, these advances demonstrate that the structural fold of membrane proteins has to be included in the classification of transporters into families.