The human Solute Carrier (SLC) transporters are important targets for drug development. Structure-based drug discovery for SLC transporters requires the description of their structure, dynamics, and mechanism of interaction with small molecule ligands and ions. The recent determination of atomic structures of human SLC transporters and their homologs, combined with improved computational power and prediction methods have led to an increased applicability of structure-based drug design methods for human SLC members. The utility of these methods will be illustrated by presenting case studies in which rational integration of computation and experiment was used to characterize SLC members that transport key nutrients such as the amino acid transporters ASCT2 and LAT1.