Structural Insights into the Substrate Transport Mechanisms in GTR Transporters through Ensemble Docking

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Abstract

Glucosinolate transporters (GTRs) are part of the nitrate/peptide transporter (NPF) family, members of which also transport specialized secondary metabolites as substrates. Glucosinolates are defense compounds derived from amino acids. We selected 4-methylthiobutyl (4MTB) and indol-3-ylmethyl (I3M) glucosinolates to study how GTR1 from Arabidopsis thaliana transports these substrates in computational simulation approaches. The designed pipeline reported here includes massive docking of 4MTB and I3M in an ensemble of GTR1 conformations (in both inward and outward conformations) extracted from molecular dynamics simulations, followed by clustered and substrate–protein interactions profiling. The identified key residues were mutated, and their role in substrate transport was tested. We were able to identify key residues that integrate a major binding site of these substrates, which is critical for transport activity. In silico approaches employed here represent a breakthrough in the plant transportomics field, as the identification of key residues usually takes a long time if performed from a purely wet-lab experimental perspective. The inclusion of structural bioinformatics in the analyses of plant transporters significantly speeds up the knowledge-gaining process and optimizes valuable time and resources.

Author keywords

Ensemble docking; Glucosinolates; GTRs; Membrane protein modeling; Phytocompounds transport mechanism