In silico prediction of P-glycoprotein binding: Insights from molecular docking studies

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The P-glycoprotein is an efflux transporter that expels substances out of the cells and has an important impact on the pharmacokinetic and pharmacodynamic properties of drugs. The study of the interactions between ligands and the P-glycoprotein has implications in the design of Central Nervous System drugs and their transport across the blood-brain barrier. Moreover, since the P-glycoprotein is overexpressed in some types of cancers, the protein is responsible for expelling the drug therapies from the cells, and hence, for drug resistance. In this review, we describe different P-glycoprotein binding sites reported for substrates, inhibitors and modulators, and focus on molecular docking studies that provide useful information about drugs and P-glycoprotein interactions. Docking in crystallized structures and homology models showed potential in the detection of the binding site and key residues responsible for ligand recognition. Moreover, virtual screening through molecular docking discriminates P-glycoprotein ligands from decoys. We also discuss challenges and limitations of molecular docking simulations applied to this particular protein. Computational structure-based approaches are very helpful in the study of novel ligands that interact with the P-glycoprotein and provide insights to understand the P-glycoprotein molecular mechanism of action.

ANP

Blood-brain barrier

Drug resistance

Homology modeling

Molecular docking

P-glycoprotein

ABC transporter subfamily B

ligand

organic compound

protein binding

Article

binding site

computer model

crystallization

molecular docking

protein interaction

protein structure

animal

binding site

chemistry

human

metabolism

molecular docking

Animals

ATP Binding Cassette Transporter, Subfamily B, Member 1

Binding Sites

Humans

Ligands

Molecular Docking Simulation

Organic Chemicals

Protein Binding