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Title

Comparison of mechanistic transport cycle models of ABC exporters

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Abstract

ABC (ATP binding cassette) transporters, ubiquitous in all kingdoms of life, carry out essential substrate transport reactions across cell membranes. Their transmembrane domains bind and translocate substrates and are connected to a pair of nucleotide binding domains, which bind and hydrolyze ATP to energize import or export of substrates. Over four decades of investigations into ABC transporters have revealed numerous details from atomic-level structural insights to their functional and physiological roles. Despite all these advances, a comprehensive understanding of the mechanistic principles of ABC transporter function remains elusive. The human multidrug resistance transporter ABCB1, also referred to as P-glycoprotein (P-gp), is one of the most intensively studied ABC exporters. Using ABCB1 as the reference point, we aim to compare the dominating mechanistic models of substrate transport and ATP hydrolysis for ABC exporters and to highlight the experimental and computational evidence in their support. In particular, we point out *in silico* studies that enhance and complement available biochemical data.

Keywords:
ABC transporter, ABCB1, P-glycoprotein, molecular dynamics simulations, transport cycle, mechanistic models