Analysis of substrate specificity in the ABC transporter ABCG36/PDR8/PEN3 from *Arabidopsis thaliana*

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ABCG36/PDR8/PEN3 belongs to the pleiotropic drug resistance (PDR)-type ABCG subfamily ATP-binding cassette (ABC) superfamily, only found in fungi and plants. Recently, the *abcg36-5/pen3-5*, but not the *abcg36-6/pen3-6* allele, was reported to uncouple several ABCG36 functionalities from ABCG36 activity in extracellular defense.

Structure modelling and molecular dynamics analyses revealed that *abcg36-5* and *abcg36-6* are part of the putative substrate translocation chamber facing putative exit and entry points of transmembrane helices 4 and 10, respectively. Transport studies in Arabidopsis and tobacco indicated that underlying mutations of A1.357V (*abcg36-6*) but not of L704A (*abcg36-5*) abolishes transport of both recently identified ABCG36 substrates, IBA and 4MeOI3M. This provides a molecular explanation for the uncoupling of IBA-mediated root growth from ABCG36 function in cellular defence found for the *abcg36-5* allele. In summary, we provide new insights in the mechanism of multiple substrate specificities in ABCG transporters.

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