„Molecular determinants behind the selective transport of phenylpropanoids fulfilled by ABCG46 from *Medicago truncatula*”

Konrad Mateusz Pakuła

Although ABC (ATP Binding Cassette) transporters form one of the largest protein family present in all of the known organisms, the molecular details of their functioning are still not fully understood. Historically the research concerning ABC proteins was focused on the context of the so called multidrug resistance phenomena, in which certain ABCs contribute as a membrane pumps extruding wide range of chemically diverse drugs outside the cell. Notably plants are especially rich in ABC transporters comparing to other organisms, which is postulated to be a consequence of adaptation to the sessile life style. In order to fulfill their role in various physiological processes, such as growth or response to biotic and abiotic stresses, some plant ABC transporters exhibit higher selectivity towards translocated molecules. An example of such is ABCG46 from *Medicago truncatula*, which is involved in distribution of highly specific precursors from the medicarpin pathway, namely liquiritigenin and *para*-coumaric acid. The aim of this work was identification of molecular determinants behind the MtABCG46 transport selectivity.

Combination of phylogenetic analyses and *in silico* modeling of the MtABCG46 structure enabled the rationally designed site directed mutagenesis. Next, based on the biochemical evaluation and molecular dynamics of MtABCG46 variants, amino acids and structural features crucial for selective transport of liquiritigenin and *para*-coumaric acid were successfully identified.

An additional aim of the work was to investigate the potential correlation between transport and ATPase activity stimulation of the full size ABCG transporters by translocated molecules. Such correlation could be potentially used as a method for identification of theirs endogenous substrates.