Molecular basis of the selective transport fulfilled by plant ABCG proteins

Research hypothesis

Plant genome encodes for more than 100 ABC transporters, largely exceeding that of other organisms. It is postulated that, in plants, ABC transporter genes underwent multiplication and functional diversification/specialization, and thereby assumed the ability to transport selected compounds critical for successful adaptation to dry land. High diversification of secondary metabolites signifies importance of their biosynthesis pathways evolution but, at the same time, distribution systems of such molecules. This coevolution of complex chemical background as well as ABC transporters is somehow unique plant feature and brings a new quality/selective pressure possibly resulting in new features of these proteins. The ABCG subfamily is the largest among ABC proteins. Genes encoding the so called full-size ABCG proteins are characteristic for plants and fungi and several plant full size ABCGs have been described as being involved in response to biotic stresses. The latter response often relies on secretion/translocation of endogenous/defensive secondary metabolites. In contrast to their fungal analogues (functioning as multidrug pumps) certain plant full size ABCGs involved in secondary metabolites distribution appear to be more selective than expected. The molecular mechanisms/determinants that regulate transport fulfilled by full size ABCGs are not fully understood. Taking into account a vast array of secondary metabolites and coevolution of such compounds together with their distribution systems we propose that plant ABCGs offer matchless chance to look for determinants (single amino acids or even α helices) responsible the molecular fit between protein and a particular class of secondary metabolites/translocated molecules.

Research project methodology

Conducted initial bioinformatics analyses point towards residues which are conserved among ABCG's α-helices (forming the membrane-spanning pore and passage for translocated molecules) and those which are not. The latter provide "flexibility" and, as consequence, offer adaptation possibility towards translocated/dedicated molecules. By the use of: (i) distinct plant ABCG transporters involved in translocation of differently originated endogenous metabolites, (ii) targeted mutagenesis, (iii) heterologous expression systems, (iv) devoted transport experiments we would like to address a question if/how evolution solved the molecular fit between such proteins and translocated molecules

Expected impact of the research project

Historically in mammals and pathogenic fungi the ABC transporters have been often described as the multidrug pumps. They were identified as transporters involved in detoxification processes. Because of the so called multidrug resistance (MDR) or plejotropic drug resistance (PDR) phenomena, associated with certain ABC/ABCG proteins, the investigation/identification of the molecular determinants behind transport fulfilled by ABC proteins is of great importance. The discovered function of plant ABCGs in secondary metabolites distribution and their unique character provide a novel impetus for examining this issue. Finding a possible link between α helices composition and selective transport of secondary metabolites will be, not only, a new finding important for processes in physiological responses but also valuable for pharmaceutical or biotechnological community. This is especially truth for MDR/PDR phenomena. The results of this study might shed new light on our understanding of MDR/PDR and effective usage of plant derived drugs- especially secondary metabolites. Next to these considerations we expect the results of the proposed research can have an impact on the design of new strategies for effective drug production.