Description for the general public

Our studies are focused on the elucidation of the role and biosynthesis mechanisms of polyisoprenoid lipids in the eukaryotic cells and regulation of their formation. Polyisoprenoids (polyprenols and dolichols) have been found in all living organism, from bacteria to mammals. These linear polymers are built from five to more than 100 isoprene units (i.u.). Dolichols are involved in protein glycosylation process where they serve as sugar carriers. The key enzymes responsible for biosynthesis of these lipid compounds are *cis*-prenyltransferases (CPTs) that elongate polyisoprenoid chain. The size of dolichols is variable and depends on the species. Arabidopsis – our model plant – accumulates in the roots 3 families of dolichols with dominating dolichol containing 13, 16 and 21 i.u., respectively. In human cells only one family of dolichols is accumulated with dominating dolichol containing 19 i.u. A characteristic shortening of dominating dolichol by one isoprene unit to 18 i.u. has been observed in patients with retinitis pigmentosa. Moreover, any disruption of the dolichol production pathway results in Congenital Disorders of Glycosylation type I (CDG I) which manifest as mental retardation and physical disabilities. Currently, no effective treatment is offered to CDG-patients. Previous studies indicated that dietary dolichol accumulated by the liver might play a role in protein glycosylation in human body. Thus, supplementation of the human diet with specific dolichol-enriched plant tissues seems plausible in the future use as treatment of CDG I. Our research planned in this proposal will concentrate on the identification of mechanisms determining the final length of the polyisoprenoid chain to be used in the future for large-scale production of humanized dolichols in plants.

Moreover, polyisoprenoids also protect plants from adverse environmental conditions. Clarification of the regulatory mechanisms of polyisoprenoid biosynthesis might appear important to obtain crop plants with increased adaptive capacity.

The other interesting topic related to this proposal is formation of natural rubber (NR) in plants. Similarly to polyisoprenoids, the molecules of NR are built from isoprene units (approx. 10000 i.u.) by *cis*-prenyltransferases too. The major commercial source of natural rubber is the Amazonian rubber tree (*Hevea brasiliensis*). Despite the foundation of large plantations of rubber trees, the economic cost of obtaining natural rubber is still high and intimately linked to the enormous threat to the environment. Therefore the alternative ways of obtaining this polymer are explored. Recent literature data show novel mechanism regulating the activity and subcellular localization of rubber producing CPT by interaction with REF (Rubber Elongation Factor) and SRPP (Small Rubber Particle Protein). The homologues of REF/SRPP proteins are present in non-rubber producing plants e.g Arabidopsis however their role in polyisoprenoid lipid biosynthesis has never been characterized. In this grant application studies will be focused on explaining this phenomenon. Obtained results will be important for building up of the biotechnological platforms aiming at generation of natural rubber – a critically important raw material for industry especially in the light of its limited/decreasing natural resources and strong demand for sustainable sources.

Furthermore, results obtained in this project will complement the existing knowledge about the basic mechanisms regulating cellular metabolism. They will be discussed with the specialists in field during scientific conferences and will be published in professional journals. Implementation of the project will allow the contractors to acquire new skills and ensure their personal professional development. The latter seem important especially for newly recruited young researchers and undergraduate students participating in this project.