

Description for the general public

State of the art.

Nature is a rich source of biologically active compounds which for a long time served as the only drugs available for human diseases and currently still play such an important role. Polyisoprenoid alcohols, an example of such compounds, are biopolymers present in the cells of all living organisms: bacteria, yeast, plants and animals. Although polyisoprenoids have already been identified in the 60s of the last century and are extensively studied since that time our knowledge in this field remains incomplete. It is well established that bacteria have only one polyprenol called bactoprenol, whereas in eukaryotic cells polyisoprenoids exist as mixtures ('families') of homologues with one homologue dominating. These compounds play an indispensable role in biological processes such as modifications of proteins (prenylation, glycosylation), synthesis of the polymers of bacterial cell wall and also protection of plants from adverse environmental factors. Polyisoprenoids have also been examined for their use in the treatment of many inherited (e.g. cystic fibrosis, hemophilia) and acquired (neoplastic, neurodegenerative or cardiovascular) diseases. It has been shown, that polyisoprenoids and/or their derivatives might be used as antiviral, immunomodulatory, hepatoprotective or anti-cancer agents or diet supplements. Furthermore, polyprenyl cationic derivatives have been tested as drug carriers. Recently, it has been shown that mutations in the genes from polyisoprenoid biosynthesis pathway lead in humans to Congenital Disorders of Glycosylation (CDG), which manifest as mental retardation and physical disabilities. Currently, no effective treatment may be offered to CDG-patients and dietary supplementation specific polyisoprenoids seems plausible in the future use.

Aim of the project

Recently, we have identified bacterial-like polyprenols in yeast and plant cells. Interestingly, the presence of such prenols was observed in mammalian cells already in the 70s of the last century, but so far mechanism of their formation and role in the cell are unknown. The aim of our project is to elucidate the role of bacterial-like polyprenols in eukaryotic cells. Studies will be performed with three experimental models: the plant, yeast and mammalian cells using a wide variety of biochemical and molecular biology methods and bioinformatic analysis.

Studies of bacteria-like polyprenols in eukaryotic cells will be focused on:

- ✓ The identification of the gene encoding the enzyme responsible for the formation of these compounds.
- ✓ The search of the role of these compounds in proteins glycosylation and their involvement in cells response to stress conditions.

The importance of the project

The results obtained in this project will complement the existing knowledge about the basic mechanisms regulating cellular metabolism. Identification of genes encoding enzymes responsible for the biosynthesis of Pren-11 and proteins involved in interactions with Pren-11 will provide new insights into the regulation of polyisoprenoid biosynthetic machinery and protein glycosylation. Furthermore, the results obtained in this project may appear useful for the design of CDG therapeutic strategies in future.

Results of this project will be available in public domain - they will be discussed with the specialists in field during scientific conferences and will be published in professional journals. Moreover, review articles summarizing the results of the project will be published in scientific journals as well as popular magazines focused on popularization of the recent scientific achievements (Kosmos, Postepy Biochemii). The latter seem important especially for young researchers and undergraduate students.

Implementation of the project will allow the contractors to acquire new skills and ensure their personal professional development. Published works will enable them to establish research collaborations with groups from the EU and outside, which in turn will enable preparation of joint research proposals, including applications for European funds within the Horizon 2020 frame program. Established contacts will enable young investigators involved in the project to apply for internships and post-doctoral fellowships in the top research centers in the locally and abroad.