The protein with two faces - characterization of a dual-activity deoxyhupusine synthase from *Trichomonas vaginalis*

mgr inż. Elżbieta Wątor

Posttranslational modifications (PTMs) influence physical and chemical properties of proteins, but also in many cases determine their functions. The most common PTMs include e.g. phosphorylation or glycosylation. However, some proteins require unique post-translational modifications to perform their functions. One of such proteins is eukaryotic translation factor 5A (EIF5A), which participates in the control of all stages of translation and, in particular, stimulates the formation of proline-rich regions. To perform its function, EIF5A requires exclusive modification of particular lysine residue to a unique amino acid: hypusine. In most of the organisms, this PTM formation consists of two steps: during the first step deoxyhypusine synthase (DHS) catalyzes the transfer of the 4-aminobutyl moiety from spermidine to lysine, following by hydroxylation of resulting deoxyhypusine to hypusine by deoxyhypusine hydroxylase (DOHH). Only hypusinated-EIF5A protein can participate in translation control and is able to ensure proper cell proliferation.

However, in 2016 in 2016 Quintas-Granados and colleagues identified, that the synthesis of hypusine in *Trichomonas vaginalis* depends on the presence of only one enzyme: deoxyhypusine synthase (tvDHS), which is capable of carrying out the full modification. Therefore, the main goal of the project is the biochemical and structural characterization of this unique, bifunctional tvDHS and its interaction with the protein substrate tvEIF5A.

During the course of the project, various molecular biology, biochemical and structural biology techniques will be implemented. This multifaceted approach will allow us to solve the crystal structures of proteins and characterize their activity and binding. In the last part of the project, we will reconstitute in vitro and characterize the protein complex formation between tvDHS and tvEIF5A.

Synthesis of hypusine in various organisms has been indicated as the potential target of anti-cancer and anti-parasitic therapies. We believe that our results will help in better understanding of hypusination and the research on the unique route of hypusine synthesis in *T. vaginalis* may enable the design of selective inhibitors to be used in the therapy of the most common sexually transmitted disease: trichomoniasis.