

The process of protein biosynthesis (translation) carried out in the cell by specialized organelles referred to as ribosomes is the leading topic of scientific research conducted in the Department of Molecular Biology (ZBM), Maria Curie-Skłodowska University in Lublin. Particular attention has been devoted to the key, and so far most mysterious, functional element of the ribosome, i.e. the so-called GTPase center, which determines the speed and accuracy of the translational machinery. The research team of ZBM has long been involved in investigations of the ribosomal structure and function and has contributed significantly to the elucidation and understanding of the function of the GTPase center at both the molecular and physiological levels. The proposed research project is focused on an exhaustive, multi-level explanation of the role of GTPase center modification consisting in phosphorylation of its key protein component, i.e. the ribosomal P protein complex. Although the phenomenon of P protein phosphorylation has been described more than 30 years ago, the role of this post-translational modification is still unclear. The results of our preliminary research clearly indicate that such a modification has a significant impact on the interaction of the ribosome with protein factors involved in the translation process, the so-called translational GTPases (trGTPases), which is reflected in alterations in the function of the translational machinery. Based on preliminary results, the proposed research hypothesis assumes that phosphorylation of the ribosomal P protein complex reduces the trGTPase affinity for the ribosome, which can change the profile of synthesized proteins in response to the changing environmental conditions. The implementation of the project is divided into three main parts. The first part will consist of a panel of *in vitro* studies focused on analyses of the interaction of P proteins and trGTPases using 'Bio-Layer-Interferometry' and 'Microscale-Thermophoresis' analyses as well as investigations of the translation process in an isolated system based on *in vitro* reconstitution of the translational machinery. This will allow precise determination of the effect of P protein modifications on the interaction of the ribosome with the entire range of trGTPases involved in translation and will allow tracing how this is reflected in the direct functioning of the ribosome. The subsequent part of the investigations will consist in functional analyses using eukaryotic experimental model of the yeast *Saccharomyces cerevisiae*, which will result in a description of the function of the translational machinery in a eukaryotic cell, including the role of phosphorylation of ribosomal P proteins. Various aspects of *in vivo* ribosome functioning in terms of the speed and accuracy of the translation process will be investigated. The research will include so-called high-throughput methods for gene expression analysis - transcriptomics and translomics, which will help to identify changes in the gene expression profile at the genome global level. The last group of experiments will yield a functional description of the role P protein phosphorylation in cells of higher eukaryotic organisms - mammals (including humans). As shown by the results of our preliminary research, the regulatory mechanism observed by us may constitute a yet undescribed metabolic pathway regulating cell stress response and participate in adaptation to changing environmental conditions. Defects in this pathway have been described as one of the etiological factors in a number of human diseases, e.g. neurodegenerative disorders such as Parkinson's disease and Alzheimer's disease or metabolic defects, i.e. diabetes. The discovery of a new, previously unknown branch of this metabolic pathway will provide understanding of the complex metabolic relationships in the eukaryotic cell and knowledge of the molecular background of many diseases, which may be a starting point for development of new diagnostic methods and effective strategies of treatment of civilization diseases.