

Cellular processes are complicated pathways that depend on interaction between different proteins, which may also be parts of many, various complexes. Despite years of research many of intracellular pathways, because of their complexity, have not been fully understood. Nowadays, numerous scientific studies all over the world focus on characterization of protein complexes and their role in complicated mechanisms that regulate all cell functions. In our primary research we have shown that one of the well-known protein hDpy30 forms complex with srGAP2 protein, which has not been described yet. The main aim of the project is to recognize the structure and physiological function of this complex.

Both parts of the newly identified complex are very well-known, but till now, nobody have described the direct connection and features of this association. The hDpy30 is one of the basic elements (core subunits) of all known histone methyltransferase complexes which methylate lysine 4 on histone H3. They are located in nucleus where they are responsible for epigenetic regulation of genes expression. The regulatory mechanism, in which hDpy30 takes part, relies on chemical modifications of histones. Histones are proteins around which deoxyribonucleic acid is wound in nucleus. These modifications may be recognized by effector proteins, which have the ability to remodel chromatin and allow to start of transcription in this area. The hDpy30 protein plays a significant role during the epigenetic regulation of gene expression. This protein is one of important elements necessary to activate the transcription of genes important for the development of nervous system, stem cells differentiation, proliferation, migration and cells adhesion. But some studies have shown that the hDpy30 role is not limited to methyltransferase complexes. This protein is located also in the Golgi apparatus, where it is responsible for proteins intracellular transport. Moreover, decreased level of hDpy30 changes cell adhesion and migration processes. It is an effect of incorrect transport of protein that is crucial for adhesion and migration. However, the results of our research have shown that another, regulatory mechanism of cell adhesion and migration might exist, which depends on interaction between hDpy30 and srGAP2.

The second protein - srGAP2 plays also role as a regulator of cell adhesion and migration. This protein is responsible for remodeling intracellular, actin cytoskeleton and formation of membrane protrusions such as filopodia. Moreover, srGAP2 is important for the correct morphogenesis and functioning of neuronal cells as well as for the regulation of other cells types. This protein is encoded in all mammalian genomes, but only in human genome there are four non-identical copies of the srGAP2 gene. They are the result of duplication, a process of doubling chromosome regions that contains a gene. The last research has shown that duplication of srGAP2 gene took place about 3 to 1 million years ago. Probably in the same time *Homo* evolved and their cognitive skills increased. Supposedly, duplicated copies of the srGAP2 have features antagonistic to copies which human share with their ancestors. The result of these evolutionary changes is a greater human brain size with more complicated structure and higher plasticity (the ability of reorganization and formation of new neural connections as a results of adaptation changes).

The identification of the hDpy30/srGAP complex has led to great number of questions and we are going to solve these problems during realization of this project. How is the hDpy30/srGAP2 complex organized? Can hDpy30 interact with all duplicated copies of srGAP2 or only with several of them? What cellular networks may be regulated by hDpy30? In which mechanisms, except histone modification is the hDpy30 protein involved in?

Answers to these questions will give us knowledge about the structure, mechanisms and cellular processes in which proteins hDpy30 and srGAP2 take part. The importance of this project is due to the fact that both proteins have important role in the development of human cells. Protein hDpy30 is necessary for the development of embryonic cells and proper gene expression in differentiated cells and the srGAP2 is crucial for the correct development and function of nervous system cells. Moreover these studies will allow to understand in a better way cell adhesion and migration regulatory mechanisms. What is significant, these processes are crucial for lymphatic and cancer cells and developmental stages such as nervous system morphogenesis.