Control of the expression of cell genetic information, or "deciphering" the data stored in DNA, largely takes place at the RNA level. The amount of RNA molecules present in the cell is essential for its functioning and is primarily determined by the rate at which two processes, *i.e.* RNA synthesis and degradation, occur. An extremely important aspect that guarantees the correct functioning of the cell is also the recognition and removal of aberrant RNA, *i.e.* RNA quality control. One of the most important factors responsible for RNA decay both in the nucleus and in the cytoplasm of eukaryotic cells is the so-called exosome complex. Exosome is targeted to specific RNA molecules by auxiliary factors – in the cytoplasm this function is fulfilled by the SKI complex. While the exosome complex itself and the SKI have been very extensively studied for years and have been fairly well understood in the yeast *Saccharomyces cerevisiae* cells, the knowledge about the cooperation between these two machineries in human cells is quite fragmentary. In the case of yeast, the interaction between the exosome and the SKI complex is mediated by the Ski7 protein. Ski7 and the homologous Hbs1 factor participate in different decay and quality control pathways of mRNA, *i.e.* protein-coding RNA. Of these two proteins, only Ski7 has the ability to interact both with the exosome and the SKI complex. It is known that in human cells, SKI complex is composed of proteins homologous to the subunits of an analogous yeast complex, and mutations in the genes encoding its components lead to systemic disease of the childhood, termed THE syndrome. This demonstrates an important role that SKI complex plays in cell physiology. Until recently, however, there was a lack of molecular data that would explain the functions of the SKI complex in the regulation of RNA metabolism in human cells. The results of our research, published at the beginning of year 2017, showed that the interaction between exosome and SKI complexes in humans is mediated by a newly identified isoform of HBS1L protein, *i.e.* homologue of the yeast Hbs1 factor, named HBS1LV3. The second HBS1L variant – HBS1LV1 – does not interact with the exosome. Interestingly though, both HBS1LV1 and HBS1LV3 interact with the SKI complex. The network of interactions between the primary factors involved in the regulation of RNA metabolism pathways is therefore different in the two evolutionarily distant eukaryotic organisms – yeast and humans. It is thus essential to accurately characterize the mode of action of the SKI complex, the HBS1LV1 and HBS1LV3 proteins, and to precisely describe the mechanisms of RNA degradation in which these factors participate, which is the purpose of the proposed project. This will be achieved through proposed biochemical and structural studies, combined with experiments carried out with the use of human cell line models, as well as global analyses performed using high-throughput RNA sequencing. It is planned to carry out co-purification of the components of the complex under investigation, and to map the sites of their interactions. An attempt will be made to determine the structure (shape) of the SKI complex and HBS1LV1/HBS1LV3 proteins, as well as their mutual spatial distribution, using crystallography and electron microscopy. The aspect of SKI complex interaction with ribosomes will be investigated, since most mRNA degradation and quality control processes occur during protein synthesis, *i.e.* translation. Experiments carried out in specially engineered cellular models, using so-called reporter plasmids, *i.e.* externally introduced DNA molecules – in our case capable of producing mRNAs containing various types of sequence or structure errors, should allow to elucidate the role of interactions between SKI complex, HBS1LV1/HBS1LV3 and ribosome in the elimination of defective transcripts. Transcriptomic analyses will be also carried out to determine the pool of natural SKI complex substrates on a global scale, based on studying changes in the repertoire of mRNA molecules in the cell upon impairing the network of interactions between proteins under investigation, as well as a large-scale, direct identification of transcripts physically binding to the key subunit of the SKI complex. In addition, we will analyze the impact of possible SKI complex dysfunction, resulting from mutations found in THE syndrome patients, on various aspects of RNA metabolism. The information obtained in the course of all above-mentioned analyses should significantly enhance the basic knowledge of the essential RNA degradation pathways, indispensable for the proper functioning of human cells. In particular, the proposed research will deepen the knowledge of mechanisms, by which cells remove incorrect, and therefore dangerous, RNA molecules.