Small nucleolar ribonucleoprotein (snoRNP) complex consists of RNA molecule (snoRNA) and core proteins. It is involved in the modification of other noncoding RNAs in the cell. Interestingly, snoRNA can be also further processed into shorter functional form, with the length of ~25 nucleotides, called sdRNA (snoRNA-derived RNA). The role of sdRNAs in the regulation of gene expression, by affecting different molecular pathways (splicing, editing, transcripts stability or translation), was exemplified. However, the mechanism of sdRNAs generation is still not completely understood.

Our research showed, that the FUS protein binds, and negatively regulates the level of selected snoRNAs in human cells. Further results suggested, that FUS induces the production of sdRNAs that, in turn, leads to decreased level of mature snoRNAs. Therefore, the main goal of this project is **to identify all FUS-dependent sdRNAs**, describe their determinants, and finally **to elucidate the molecular mechanisms underlying the biogenesis of sdRNAs, mediated by FUS**. We also want **to investigate the localization within the cell and biological function of the FUS-dependent sdRNAs**. According to our preliminary experiments, they can play a role in the regulation of gene expression by stabilizing the protein coding transcripts, and protein synthesis on the ribosomes.

Interestingly, in 2009, mutations in the *FUS* gene were identified in patients with an inherited form of amyotrophic lateral sclerosis (ALS) disease. The mutations cause a cytoplasmic mislocalization of FUS in neurons and glial cells, that impairs its nuclear function. However, the downstream consequence(s) of this mislocalization on cellular pathways still remains largely unknown. Based on our results, we hypothesize, that one of **the consequences of the ALS-linked FUS mutations, that leads to neurodegeneration, might be the defect in the sdRNA production, followed by the deregulated expression of particular transcripts** in neuronal cells. Moreover, the FUS proteins, assembled into cytoplasmic aggregates, were also observed in response to various cellular stresses. Therefore, **the effect of biological stresses** (oxidative or hyperosmolar stress) **on sdRNAs localization, synthesis and function** will also be tested.

The snoRNA processing to shorter, stable RNA species, is a wide-spread phenomenon, however, the sdRNAs biogenesis and function is poorly described. The following questions will be addressed in the proposed project: how many sdRNAs depend on FUS? How are the FUS-dependent sdRNAs generated? What is the mechanism of sdRNAs action? What is their role in the cells? Is the sdRNAs synthesis/production affected in ALS disease? Whether stress induces or inhibits sdRNAs production? The continuation of already started research, that brought us to the conclusion of the FUS involvement in sdRNA processing, is very important for a broader understanding of all sdRNAs biogenesis. We are convinced that answering the questions asked in this project, will also make a significant contribution to understanding the function of the FUS-dependent sdRNAs, in the regulation of gene expression, and will shed new light on the biological consequences of this kind of regulation. Moreover, it will help to describe fundamental processes, implicated in the etiology of ALS, and the basis of the cellular response to stresses.