The expression of all traits encoded in the genome is regulated on many levels: from the modifications of chromatin affecting transcription of DNA into RNA, through regulation of the stability and activity of RNA, which is then translated into the final product - protein. Some proteins function as enzymes – proteins that enable chemical reactions to happen in a cell. Enzymes are very important components of the regulatory pathways of all cellular processes, as they have the ability to modify other proteins, RNA or DNA and its packaging – chromatin. The cumulative outcome of all those multifactorial relationships results in a complex regulatory network. In a physiological situation, this network has inner, inherent flexibility resulting in a state of adaptive balance, which is called homeostasis.

Recently, much of the scientific attention has been paid to understanding the role of RNA in the global regulation happening in a cell. There is a plethora of different enzymes that modify RNA molecules, process or decay them affecting their activity, concentration and their half-life - the time that RNA molecules persist in a cell and fulfill their function.
The enzyme that we are heading out to study is responsible for the RNA degradation in the central compartment of the cell – nucleus. Interestingly, inhibition of its activity leads to the accumulation of RNA species, which in a normal situation are very lowly abundant in the cell. This accumulation perturbs the homeostasis, leading to an inability of the cell to divide properly. Intriguingly, if the mutation is subtle, impairment in the cell divisions can be detected, even though there is no detectable change in the abundance of any known protein-coding RNA. The only observed change is the accumulation of those very lowly abundant RNA species, which up to very recently were considered “junk RNA”. Moreover, genomic regions of these transcripts are more loosely packed in their chromatin. It is well established that the compaction of DNA is essential for its proper segregation into the two daughter cells during cell division.

The aim of this project is to understand how the accumulation of physiologically very lowly abundant RNA can interfere with the complicated regulatory network required for cell homeostasis, and eventually result in defective cell divisions. Importantly, understanding of why those cells do not divide properly may enable the design of drugs for cancer patients, who have mutations in the enzyme of our interest.