Title: The impact of cytoplasmic polyadenylation on local translation in neurons

Neurons communicate with each other through synapses, specialized contact sites that enable electrical impulses to be transmitted between cells. Synapses are small, but partly independent compartments of the neuron because they contain the molecular machinery indispensable for protein synthesis. This process of protein production on the basis of mRNAs transported to distant synapses from the cell body is called "local translation". Local protein synthesis is essential for the proper functioning of the synapse, and its dysregulation is the cause of severe neurodevelopmental disorders. In recent years, thanks to the development of new technologies, we have learned more about these essential processes taking place in synapses. However, the precise molecular mechanisms by which synaptic translation is regulated is still far from being understood.

The ends of mRNA molecules are specifically modified in order to enhance their stability and ability to serve as a template for proteins synthesis at ribosomes: at the beginning, they contain so-called cap structure, while at the end, there is a poly(A) tail. The poly(A) tail is a homopolymeric tract of adenosine nucleotides added by specific enzymes. Nearly all mRNAs in the cell are polyadenylated in the nucleus right after being transcribed from DNA and before the transport to the cytoplasm. However, there is growing evidence that the process of polyadenylation can also take place in the cytoplasm and is therefore called cytoplasmic polyadenylation. In neurons, cytoplasmic polyadenylation of synaptic mRNAs plays a significant role in the regulation of protein synthesis. However, until now it was studied only for a few mRNAs, and the global impact of this phenomenon and the specific enzymes carrying out the reactions are unknown. We aim to answer these questions in the proposed project.