

We have recently identified a new RNase involved in the degradation of transcripts called ZC3H12B. It is located in the cytoplasm and forms small, granular structures typical for proteins involved in the RNA turnover. We have found that ZC3H12B not only controls the level of proinflammatory mRNAs, but also inhibits cell proliferation. The highest expression of ZC3H12B is observed in the brain. In high-grade gliomas, in which inflammation is one of the hallmarks of their pathology, the level of ZC3H12B is reduced. Therefore, we decided to study the biological role of ZC3H12B in human neural progenitor cells and in differentiated astrocytes and confirm the obtained results in tumors derived from patients with astrocytoma. We will also analyze the role of ZC3H12B using mouse model of glioma. To identify ZC3H12B substrates we performed RNAseq analysis of transcriptomes isolated from human astrocytoma cell lines with different levels of ZC3H12B expression. Among identified potential ZC3H12B substrates were transcripts encoding proteins involved in the regulation of inflammation and proteins involved in the regulation of cell proliferation or differentiation. Surprisingly, among potential ZC3H12B-targets are also long non-coding RNA (lncRNA). This observation is very interesting because lncRNAs seem to play a particularly important function in the brain. Brain-specific lncRNAs exhibit the highest signals of evolutionary conservation compared to lncRNAs found in other tissues. Furthermore, the highest amount of lncRNA was found in the brain. To better understand the role of ZC3H12B in the regulation of pathophysiology of cells which are involved in glioma development, we plan to answer the following questions:

1. What mechanisms underlie the inhibition of brain cell proliferation by ZC3H12B?
2. Which lncRNAs are substrates of ZC3H12B and what is their function during inflammation in the central brain system?
3. Which inflammation-related mRNAs are regulated by ZC3H12B?
4. Is there a correlation between expression levels of ZC3H12B, its substrates and the tumor malignancy?