DESCRIPTION FOR THE GENERAL PUBLIC (IN ENGLISH)

DNA is a molecule which is responsible for genetic information transfer in eukaryotic cells. On the basis of this information the fundamental elements for organism functioning (proteins) are produced. The process of protein production (so called protein biosynthesis) consists of two minor ones: transcription and translation. During transcription the genetic information is transcribed from DNA on mRNA molecule. On the mRNA matrix, during translation process, the proper protein is synthesized. mRNA, same as DNA, is a catenary molecule, built of elements called nucleotides. Just after mRNA synthesis it is treated properly in the process of mRNA matriculation. During this process mRNA ends (5' and 3') are modified. Especially interesting modification is located on 5' end and is called cap.

Cap structure is an unusual nucleotide connection containing 7-methylguanosine. Due to the presence of the positive charge on 7-methylguanine ring cap can interact specifically with proteins and is involved in many crucial biological processes. An example of such interactions with a protein is a cap-eIF4E complex, which forms during translation initiation process (eIF4E is also a tumor marker). The cap-forming process is no less important with its crucial part – methyl group transfer into N7 position within guanine ring. For this process, which is called methylation, RNA guanosine-N7-methyltransferase (N7MTase) protein is responsible. During some virus infections the genetic information of the virus is expressed as mRNA and one of the steps of mRNA creation is methylation process. Therefore studying methylation is also therapeutically relevant.

The main aim of this project is to develop new tools and a method for N7MTase activity monitoring based on fluorescence measurements. In the first step new fluorescently labelled guanosine nucleotide analogues and their N7-methylated equivalents (cap analogues) will be synthesized. Such systems are called molecular probes. Afterwards the best molecular probe, which fluorescence of N7-methylated and non-methylated form differs strongly, will be selected. **The difference with the fluorescence properties of methylated and non-methylated probe is the basis of the proposed method working as well as analytic signal.** The method for monitoring of the RNA N7MTase catalysis methylation process will be optimized and then applied for searching of substances, which inhibits this process (inhibitors). Such methods allowing for very fast determination of the interaction parameters for a lot of compounds are known as HTS methods (*high-throughput screening*). In this project two compounds libraries will be screened in order to find N7MTase inhibitors: small molecule commercially available LOPAC library and guanosine nucleotide analogues library (synthesized in our Laboratory). Hence the most potent RNA N7MTase inhibitors, which are potential antiviral agents, will be selected.

The proposed studies are relevant for RNA N7MTase activity studies. Moreover obtained fluorescently labelled nucleotide analogues are universal tools, which can be applied also for other protein classes studies.