Abstract popular science

Recent years have been marked by a huge interest in the development of innovative therapeutics from the interface of chemistry and biology. Among them perhaps the most promising are therapies based on mRNA, an information-carrying ribonucleic acid constituting a cellular recipe for protein synthesis. mRNA of any chosen sequence can be easily synthesized in a test tube. However, due to its natural features such as instability and immunogenicity, the therapeutic mRNA needs to be properly designed to meet the requirements imposed on therapeutic molecules. Currently, mRNA is tested against various types of diseases, from cancers, through genetic and viral diseases, to cardiovascular diseases. However, regardless of the application, when designing such therapeutic strategy, knowledge about the properties and metabolism of mRNA in the cell is crucial. One important aspect of mRNA metabolism is the fact that at least three nucleotides at the 5' end of the mRNA may undergo a certain type of labeling by methyl group(s). This applies to both ribose residues and nucleobases. Some of these methylations are recognized by specific proteins involved in various stages of gene expression, others are a specific markers that differentiate human mRNA from pathogens such as viruses, while the role of other methylations has not yet been recognized. Some of these methylations are irreversible, others seem to be a transient regulatory mechanism. In this project, the synthesis of tools for the preparation of mRNA with various methylation states at the 5 'end is planned. These tools will be used to investigate the effect of particular methylations on the biological properties of mRNA, in particular those important from the therapeutic application perspective, i.e. the efficiency of translation in various cells, intracellular stability, or the ability to activate the immune system. Attempts will be made to select the cellular proteins responsible for the regulation of gene expression, which occurs by methylation of the 5 'end of the mRNA. The project assumes interdisciplinary studies relying on modern methods of biological chemistry, biophysics, and molecular and structural biology. We hope that the results of this project will increase knowledge about the role of RNA methylation in cells and will be useful in the design of modern mRNA-based therapies.