**DESCRIPTION FOR THE GENERAL PUBLIC**

The aim of the project is to develop improved methods of analysis of antisense oligonucleotides and its application in the study of their metabolites, which occur in the body. Oligonucleotides are short nucleic acid fragments, which in turn are responsible for the inheritance of traits from our ancestors. Antisense oligonucleotides, however, differ from those present in the human body - they have a different structure. Some of these compounds are used in antisense therapy as drugs. Most of them are in clinical trials, due to the possibility of their utilization during cancer treatment. Their structure is modified, so that after drug administration it would not undergo complete digestion and was able to reach the site of action in the body.

The project will test different types of modifications of antisense oligonucleotides to be able to determine which of the changes made in the structure of these compounds will be the most durable and resistant to degradation by enzymes after their administration to human body.

A method for isolating antisense oligonucleotides from plasma samples and samples after incubation with enzymes will be developed during the study. For this purpose new generation methods will be used, which would provide a high recovery of test substances from biological samples. In the next stages of experiments there will be developed method for the separation of oligonucleotides and their metabolites, which are the products of transformation of oligonucleotides in the body. In addition to the separation of mixture of these compounds, the selective and sensitive analysis is also needed. Therefore, a new generation of analytical techniques and apparatus will be applied during studies. It will allow to obtain a complete separation of antisense oligonucleotides and detection of very small quantities in e.g. serum samples.

All investigations performed within the project will be used in the final stage of the experiment, when developed methods will be applied in determining the metabolic products of antisense oligonucleotides. This is the main aim of the project and will be the most important step. Due to their use in medicine, it is necessary to know their fate in the body. This is possible due to study of oligonucleotides changes induced by enzymes. The research will make possible to determine what metabolites are formed in the body depending on structural modifications of oligonucleotides. The study will also evaluate whether the metabolic products will exhibit biological activity or if they are harmful to the body, how and when they are expelled from the body.

All stages of research conducted within the project are essential during investigation on new drugs or compounds that are drug candidates.
The project will develop new, reliable, accurate and sensitive methods for analysis of antisense oligonucleotides. They will find application in medical diagnostics, where they will have a significant impact on human health during the therapy. These methods will also be used for routine analysis of antisense oligonucleotides in the different samples. In addition, they enable understanding of the metabolic pathway of these compounds in living organisms.