

## Preparation and physico-chemical characterization of transfection carriers based on polycationic surfactants

One of the greatest challenges of today medicine, is to develop effective treatments for a broad spectrum of diseases so far incurable. To this group belong not only all the diseases of genetic origin, such as: phenylketonuria, cystic fibrosis, myotonic dystrophy, cancer, but also diseases caused by bacteria, viruses, etc. The diversity of their causes, symptoms and course causes significant problems in finding a satisfactory therapeutic methods. The answer seems to be developed in recent years, gene therapy, which consists of treatment with the therapeutic nucleic acid<sup>1</sup> fragments. Its main objective is to provide to a diseased body cells short siRNAs (ie. *transgene*). Currently distinguished transgenes with different mode of action. It may rely on:

- replacement of the defective gene by introduced molecule (nucleic acid fragments),
- modification of processes leading to "read" of the genetic information which will be visualize in the form of organism characteristics,
- blocking of the formation in the diseased cells abnormal proteins (ie. *RNA interference*).

Despite a series of well-defined assumptions gene therapy for us is still a huge challenge. Its implementation faces natural barriers in which in the way of evolution have equipped themselves living organisms. Omission the processes of the immune response that would result in such to destroy of transgene, or even scale death of normal cells is very difficult. The main problem becomes in this case is carried out a successful transfection, or introduction of a nucleic acid molecule into the diseased cells. Still used for this purpose methods are not effective because the cells most often reject introduced therapeutic molecules treating them as foreign bodies, pathogenic, leading to the natural defense of the body by the immune system as it is with any disease. To prevent this, it is necessary to develop suitable carriers, which are able to transport the transgene into the cell without inducing immune processes. The only possibility is therefore to create such factors that thanks to its structure and physico-chemical properties would be treated by the cell as "their". The promising class of compounds having such properties are "*surfactants*".

This project focuses on producing and thorough investigation in terms of the physico-chemical properties of selected transfection systems from polycationic surfactants. For this purpose, will be used advanced research techniques in the field of microscopy, spectroscopy<sup>2</sup>, electrokinetics<sup>3</sup>, scattering methods<sup>4</sup> and cell studies<sup>5</sup>. By using these methods will be specified among others: stability (durability) designed siRNA-surfactant complexes, their morphology (shape, size, weight, texture at the micro and macro scale) and changes in the spatial structure of nucleic acid molecules, which is located in the complex. It will also be investigated same process of formation of the lipoplexes (connecting to siRNA molecules with surfactant), the effects (toxicity) of these complexes for the selected cell types, eg. tumor, to examine the viability of the cells in the presence of a complex, and the process of transfection using the obtained factors. All this will determine the suitability of the test compounds for therapeutic purposes.

The expected result of planned in this project research is to develop new, stable and non-toxic transfection systems and also, what is most important, determine the method of conducting the process of siRNA transfection using these systems.

<sup>1</sup>*nucleic acid* - high molecular weight organic compound (biopolymer) occurring in all cells and viruses encoding genetic information relating to the organism and participating in the production of the proteins; built from nitrogenous bases, whose order determines the variability of the characteristics of the individual, eg. color of hair, eyes, character, etc.; among several kinds of nucleic acids most important is deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). The gene therapy use of the so-called siRNAs (small-interference RNA).

<sup>2</sup>*spectroscopy* - section of physics concerning issues of creation and analysis of radiation emitted or received by the various types of chemicals, solutions, etc.

<sup>3</sup>*electrokinetics* - section of physics concerning the characterization of chemical compounds in terms of size, shape, weight, etc. on the basis of the way its move in artificially induced electric field.

<sup>4</sup>*scattering methods* - research methods involving the characteristics of the compounds on the basis of the way in which its dispersed various types of radiation.

<sup>5</sup>*cellular studies* - the experiments conducted in laboratory conditions on various types of cells.