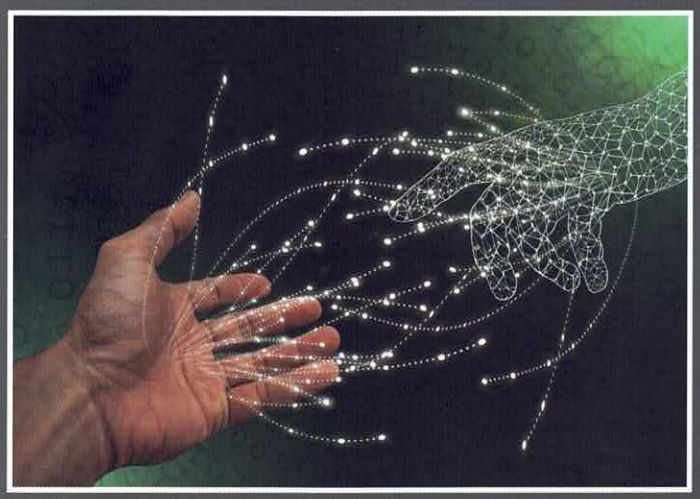
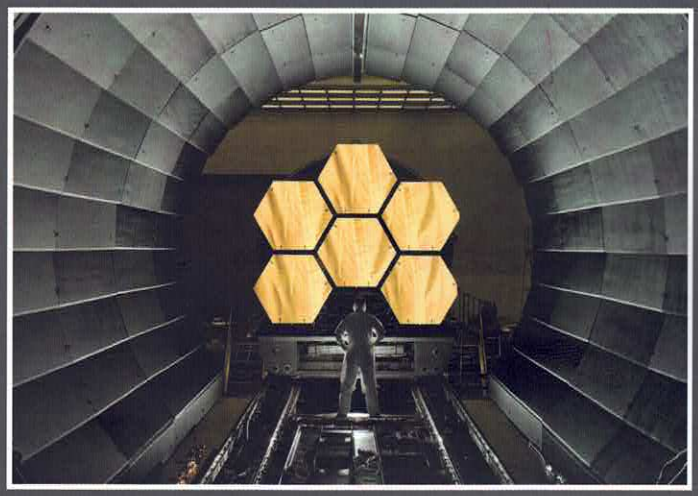
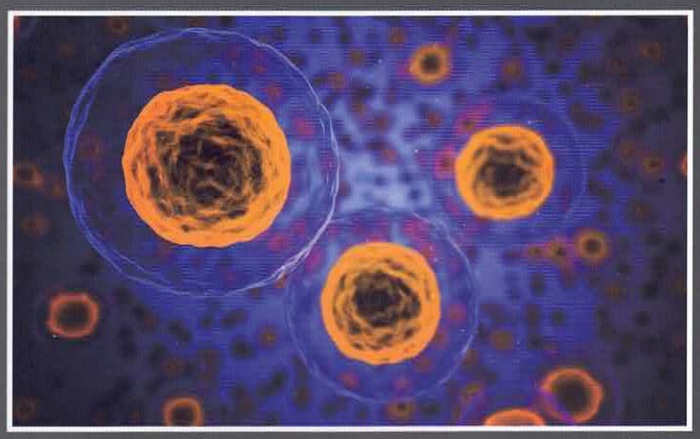
Scientific Research Centre at Sofia University "St. Kliment Ohridski"

Yearbook of Scientific Research Projects at Sofia University 2021–2022







Design and experimental validation of chimeric antisense oligonucleotides as antibacterial agents

Research area: Medical sciences

Research unit: Faculty of Biology

Funding institution: Bulgarian National Science Fund

Project duration: December 2017 – June 2022

PROJECT COORDINATOR

Prof. Robert Penchovsky, Ph.D.
Department of Genetics,
Faculty of Biology

PARTNERS

Department of Medical Microbiology, Medical University, Sofia

PROJECT OBJECTIVES

The project continues a very successful research in the field of RNA synthetic and computational biology, medicine and pharmaceutical started by the project leader Prof. Dr. Robert Penchovsky several years ago as a postdoctoral fellow at Yale University.

The main goal of this project is to design antisense oligonucleotides, which are directly binding and regulating the target bacterial pathogen's riboswitches. The riboswitches are structured RNA domains usually residing at the 5'-untranslated region of messenger RNAs that directly bind specific metabolites. They serve as logic gates regulating gene expression. As a result, riboswitches enable mRNAs to regulate their own expression without the need of any regulatory proteins. This way, the essential metabolites for the bacteria will not be synthesized by the cell or transported into the cell from the extracellular matrix. The result is the death of Staphylococcus aureus for instance. Antisense oligonucleotides show bacteriostatic effect and can be tested as novel antibacterial agents in bacterial isolates and human embryonic kidney cell lines (HEK 293) for toxicity.

OUTCOMES

The results of the research under the project are published in 20 publications (with an impact factor of 84 points and Q1-4 of 274 points, and 86 citations so far). Their list is available here: https://penchovsky.atwebpages.com/research.php?page=13.

During the period of the project, doctoral students and young scientist have participated in 3 international conferences with 2 presentations and 4 posters in Bulgaria and Austria (14th National Congress of Microbiology with international participation and German Bioinformatics Conference, Vienna, Austria).

Sixteen pieces of software have been written and now are available for free hare: https://penchovsky.atwebpages.com/applications.php.

Four Ph.D. students and 1 master student defended successfully their theses, all under the guidance of the project coordinator – Prof. Dr. Robert Penchovsky. The grant received the highest possible rating. This research grant was funded with only €61,000.

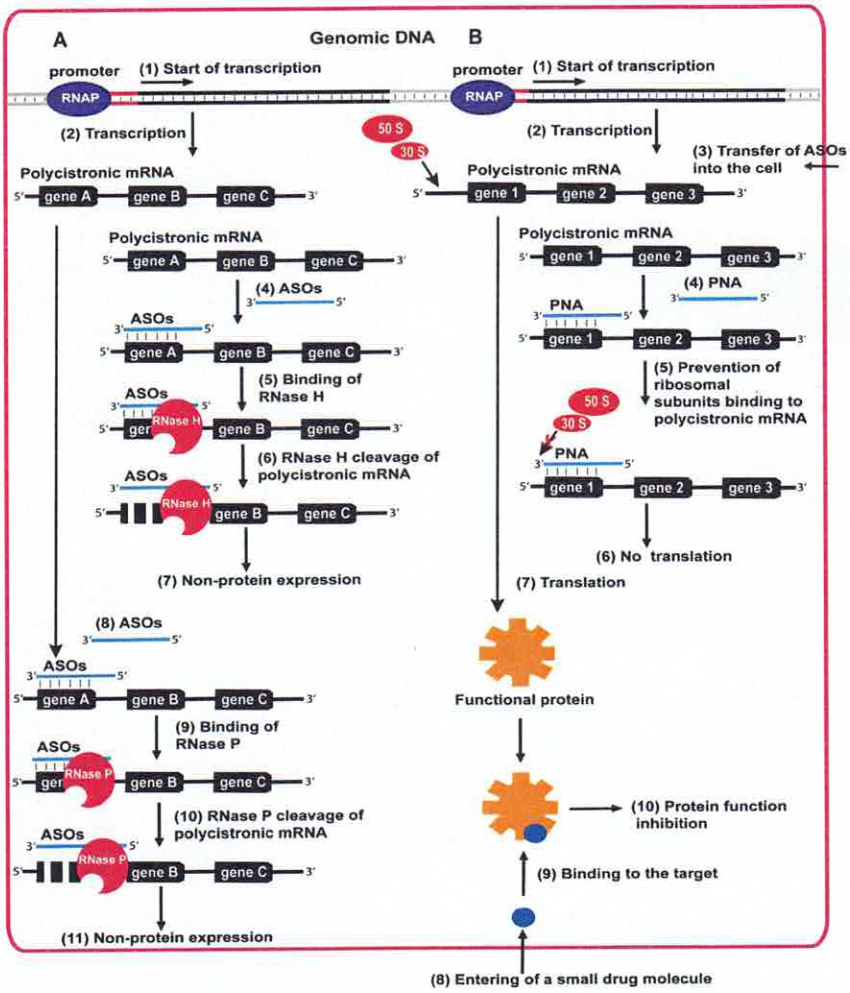
Project team members (from left to the right): Dr. Katya Popova, Dr. Nikolet Pavlova, Dr. Martina Traykovska and Dr. Lozena Otcheva

APPLICATION AREAS

The developments achieved by the project are applicable in a very wide range of fields. Those of greatest importance are human healthcare, pharmaceuticals and medicine, due to the possibility of antisense oligonucleotides being used as potential drug candidates to counter the enormous social and global problem of antibiotic resistance in bacteria.

PROJECT BENEFITS

Our main contributions are in the development of a method for the precise design of chimeric antisense oligonucleotides, which allows their specific targeting to a region (riboswitch or other mRNA) of a specific human pathogenic bacterium or group of bacteria, including multi-drug resistant bacteria, with a shown antibacterial effect without affecting the probiotic bacteria of the human microbiome.



Mechanisms of actions of ASOs

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