BIOCHEMISTRY

Biological funcions of new 3,6 disubstituted derivatives of acridines.
supervisor: doc. RNDr. Mária Kožurková, CSc. (maria.kozurkova@upjs.sk)
study form: full time
Annotation: In the thesis, we will deal with an interaction of novel derivatives of 3,6 disubstituted derivatives of acridines with nucleic acids. The spectroscopic characteristics, hydrophibicity, stability in water solution and reactivity of the newly synthesized compounds will be studied. We will determine the mode of interaction; calculate binding constants and neighbor exclusion parameters. Inhibition effects of these compounds on topoisomerase I and II will be examined. The potential antitumor effects of these compounds will be tested against both human and mice leukemia cell lines and HeLa cell. The effect of substances on cells will be studied using flow cytometry analysis and the mode of cellular death will be determined. The localization of derivatives in cells will also be analyzed using confocal microscopy.

The influence of ligands binding recognizing non-canonical structural motifs of nucleic acids
supervisor: doc. RNDr. Viktor Víglaský, PhD. (viktor.viglasky@upjs.sk)
study form: full time
Annotation: The occurrence and location of non-canonic structural motifs in nucleic acids, e.g. DNA hairpins, triplexes and G-quadruplexes, are non-random. These motifs, and not mutation in structural genes, are crucial control elements influencing various biological processes including a gene expression of regulating proteins. There are responsible for example for the loss of cell proliferation control, induction of neoplasms formation, inefficiency in DNA repair and recombination, unexpected cell differentiation and senescence. The main task will be to determine condition of non-canonic motifs formation and their stabilization by specific ligands and their influence to cell viability.

Development of tageted contrasting DNA- aptamer-nanoconjugates for dignostics
supervisor: doc. RNDr. Viktor Víglaský, PhD. (viktor.viglasky@upjs.sk)
study form: full time
Annotation: Nanoparticles are commonly used for bioimaging and drug delivery in cancer diagnostics and treatment. Their use can be substantially improved when they are modified with DNA aptamers, artificial nucleic acid ligands, recognizing various molecular targets with high selectivity and sensitivity. Binding of the aptamer to its target “anchors” the aptamer nanoparticle conjugate at its site of action. The goal of investigation will be focused on development of targeted nanoparticle-aptamer bioconjugates. The main goal of research will be to find universal procedure for low cost production of conjugated receptor molecules which could be used for diagnostics of wide scale of molecular targets.

Design of flavoproteins as inducible producers of ROS
supervisor: doc. RNDr. Erik Sedlák, PhD. (erik.sedlak@upjs.sk)
consultant: RNDr. Nataša Tomášková, PhD.
study form: full time
Annotation: Flavin mononucleotide (FMN) is an effective photosensitizer that upon illumination with light of a suitable wavelength generates reactive oxygen species (ROS). As a result, in order to avoid uncontrolled ROS production in the cell, the FMN molecule is usually firmly bound to the protein molecule. On the other hand, such a flavoprotein can be considered as a carrier of a reactive FMN molecule that can be released into solution in a controlled manner. In this project

we will show that by appropriate mutations at the isoaloxazine ring binding site in various flavoproteins (LOV2 domain, flavodoxin, NADH oxidase), it will be possible to achieve dissociation of FMN into solution after illumination, and thus to initiate ROS production.

Nanobodies as a platform for a interactions with biological molecules
supervisor: RNDr. Gabriel Žoldák, PhD. (gabriel.zoldak@upjs.sk)
consultant: prof. Ing. Marián Antalík DrSc.
study form: full time
Annotation: Nanobodies are a group of proteins with a high potential for developing new therapeutic strategies in biomedicine. Nanobodies are a relatively small, monomeric antigen-binding proteins that are derived from the variable domain of the heavy chain of antibodies. Their main advantage over classical monoclonal antibodies is their high stability, solubility, and ease of preparation using standard techniques of biochemistry and molecular biology. This dissertation will focus on the purification of nanobodies in E. coli, understanding the structure - function-stability relationship, and on the development of experimental approaches for the identification of suitable candidates, which bind selected target molecules.

Study of DNA/BSA binding properties of newly synthesized low-molecular ligands.
supervisor: RNDr. Danica Sabolová, PhD. (danica.sabolova@upjs.sk)
study form: full time
Annotation: Uv-Vis and fluorescence spectrophotometric methods were used to determination of ct DNA/ BSA binding with newly synthesized low-molecular ligands. The Stern-Volmer and binding constants were calculated. CD spectra were measured to establish the mode of binding (intrecalation /or groove binding) of investigated compounds. The nuclease activity test and topoisomerase I/II inhibitory assay were performed using electrophoretic methods.

Extracellular electron transport for reduction of iron deposits.
supervisor: prof. Ing. Marián Antalík, DrSc. (antalik@saske.sk)
study form: full time
Annotation: Electron transfer from the cytoplasm to extracellular space for reduction of oxide iron minerals requires a sophisticated transport system involving multiple low molecular compounds and soluble multi-heme cytochromes in the periplasm as well as protein agregates made of multi-heme cytochromes that transport electrons across the outer membrane and outside of the cells. Much progress has been made very recently to obtain insight into the nature of these interesting structures and mechanism of electron transfer. However, many fundamental properties of these interesting mechanisms and multiheme proteins agregates are still not well under- stood.

New conjugates of acridines and anthracenes with nucleosides.
supervisor: doc. RNDr. Ján Imrich, CSc. (jan.imrich@upjs.sk)
study form: full time
Annotation: Nucleosides are contained in many antiviral and antibacterial compounds. Acridines and anthracenes are known as DNA intercalators and antitumor compounds. The thesis will be based on long-term expertise in the field of acridines and anthracenes at the Department of Organic Chemistry of ÚCHV PF UPJŠ, where nucleoside chemistry will represent a new element in this research. It is envisaged to prepare several tens of new acridine / anthracene conjugates with both known and novel nucleosides by methods of modern organic synthesis. The chemical, spectral and biological properties of the products will be extensively investigated. Combining

these classes of pharmacophoric precursors into one unit can yield new biologically active substances that will be tested in different types of tests in collaboration with internal and external partners. The project fits into the current world effort to find new antivirals.