BIOPHYSICS

Development of Nanosensors based on Plasmonic-Enhanced Optical Spectroscopy for molecular sensitive and selective detection
supervisor 1: prof. RNDr. Pavol Miškovský, DrSc. (pavol.miskovsky@upjs.sk)
supervisor 2: dr . Santiago Sanchez Cortes, PhD (CSIC Spain)
study form: full time, study organization: co-tutoring
Annotation: The interaction of light with nanostructure of plasmic metals, such as silver or gold, produces a large intensification of electric field on the metal surface. This is the basis of the so-called Plasmonic-Enhanced Optical Spectroscopy - PEOS (Raman, Fluorescence and IR) that leads to a huge enhancement of spectroscopic signal from molecules placed on the metal surface. PEOS techniques are based on Nanotechnology, and in the last 20 years a boom in the applications of PEOS have been noted due to the development of new and magic nanostructured metal substrates able to induce a high intensification of the electric field. In this PhD work the fabrication of new and feasible nanostructures based on plasmonic metals is intended. These new nanosensors will be prepared under specific architectures and morphologies in order to find surfaces with innovative properties to be applied in the detection of a large list of pollutants (environment), biomolecules (medicine) and colorants of interest (cultural heritage).

Mechanism of cell resistance and apoptosis in 3D spheroids: cross-correlation of protein kinase C and ABC transporters functions
supervisor: RNDr. Veronika Huntošová, PhD. (veronika.huntosova@upjs.sk)
study form: full time
Annotation: The main aim of the Thesis is to investigate cross-correlation of protein kinase C and ABC transporters during apoptosis and generally, during cell response after stimulation with different drugs. Preferentially, we will pay attention to cancer. Tumors are spherical systems. For this reason the study will be performed in 3D spheroids. The results will be compared with cell monolayers approach. Protein kinase C (PKC) phosphorylates different proteins and enzymes in cells that are active in apoptotic signaling pathways. Drug resistance is one of the main problem in cancer treatment. We will focus our study to investigate mechanism of PKC interactions with ABC transporters and other multi-drug resistance proteins. Mechanisms will be studied by the techniques available at Center for Interdisciplinary Biosciences and Department of Biophysics: steady-state and time-resolved microscopy, spectroscopy, western blotting, different isolation technique for protein expression determination in cells.

Development and characterization of lipoprotein nanoparticles for targeted drug delivery to cancer tissues
supervisor: doc. Mgr. Daniel Jancura, PhD. (daniel.jancura@upjs.sk)
consultant: RNDr. Veronika Huntošová, PhD. (veronika.huntosova@upjs.sk)
study form: full time
Annotation: Naturally occurring low-density lipoproteins (LDL) and high-density lipoproteins (HDL) are adequate vehicles for drug delivery and targeting to cancer tissues. The capacity of both types of the lipoproteins to bind hydrophobic drugs and their functionality as drug carriers has been examined in several studies. However, a difficult isolation of the lipoproteins in large quantity from a biological organism as well as a variability of the composition and size of these molecules makes practical application of LDL and HDL as drug delivery systems quite

complicated. Synthetic LDL and HDL and large unilamellar vesicles (LUV) are potentially candidates to substitute the native lipoproteins for targeted and effective drug delivery. This main goal of this thesis is to develop and characterize several types of synthetic lipid-based nano-particles (sLNP) and large unilamellar vesicles (LUV) containing various amount of cholesterol. The complex physico-chemical characterization of these systems: chemical composition, size, zeta potential, stability and the mechanisms of their interactions with hydrophobic/amphiphilic molecules with potential to be applied in cancer treatment, will be thoroughly studied. Further, cellular uptake of the constructed lipoprotein/drug complexes by several cell types will be also investigated.

Utilization of ribosome display in development of enzymes
supervisor: doc. RNDr. Erik Sedlák, PhD. (erik.sedlak@upjs.sk)
consultant: RNDr. Gabriel Žoldák, PhD. (gabriel.zoldak@upjs.sk)
study form: full time
Annotation: Techniques of protein evolution offer an efficient tool in modulation of properties of proteins and enzymes such as for example stability, solubility, affinity and specificity of binding towards selected ligand and catalytic activity. Improving of catalytic activity of enzymes belong to complex problems, which are practically unsolvable by rational design approach. In this work therefore, to "improve" properties of selected enzyme from the family of dehalogenases we apply the technique of ribosome display that we have recently established in laboratories of Center of Interdisciplinary Biosciences.

Drug tansport in biological systems
supervisor: doc. Mgr. Gregor Bánó, PhD. (gregor.bano@upjs.sk)
study form: full time
Annotation: Drug treatment optimization requires the knowledge of the pharmacokinetic properties of the used drug molecules. The concentration time course of active substances in the organism is greatly influenced by their transport in the blood stream, in tissue, and inside cells. The passage of substances across biological membranes plays an important role here. Membrane transport can be monitored using model systems (vesicles or various artificial lipid bilayers) or directly on live cell cultures. The project is focused on experimental study of drug transport in solutions and membranes using a modular micro-Raman apparatus in combination with optical tweezers. The project comprises development of new experimental techniques for monitoring drug movement dynamics in biological systems.

Photobiomodulation effect on damaged neuronal cells.
supervisor: doc. RNDr. Katarína Štroffeková, PhD. (katarina.stroffekova@upjs.sk)
consultant: doc. Mgr. Gregor Bánó, PhD. (gregor.bano@upjs.sk)
study form: full time
Annotation: The civilization diseases common denominator, including cardiovascular and neurodegenerative ones, is increased oxidative stress and mitochondrial dysfunction, which result into cell dysfunction or apoptosis. Traumatic brain and spinal cord injury also result in increased ROS production, Ca2+ overload and mitochondrial dysfunctionNear-infrared (NiR) photobiomodulation (PBM) has the potential to fulfill protective and regenerative functions for cells. The emphasis will be to study PBM effects and their optimization at the molecular and cellular level. We will use interdisciplinary approach of metabolic fluxes measurements, confocal fluorescent microscopy, molecular biology and spectroscopy.

Hypericin as potential BH3 sensitizer and its role in apoptosis and autophagy.
supervisor: doc. RNDr. Katarína Štroffeková, PhD. (katarina.stroffekova@upjs.sk)
consultant: RNDr. Gabriela Fabriciová, PhD. (gabriela.fabriciova@upjs.sk)
Annotation: Members of the Bcl2 family of proteins are key regulators of apoptosis. The intricate network of protein-protein interactions between multi BH domain anti- and pro-apoptotic Bcl2 proteins, and/or BH3-only proteins control cell survival or death via regulation of mitochondria function and fission/fusion processes. The BH3-only proteins has been shown to fulfill role of either sensitizer or direct activator of pro-apoptotic Bax and Bak. The importance of interaction between pro-survival Bcl2 proteins and BH3 motifs of either pro-apoptotic or BH3 only proteins for cell death or survival decisions makes this interaction an appealing target for cancer therapy and at the present, more than 20 small molecule inhibitors of pro-survival Bcl2 proteins, termed as BH3 mimetics, were explored. We have shown evidence that Hypericin (Hyp) may be another naturally occurring BH3 mimetic. The goal of this study will focus on Hyp interaction with anti-apoptotic Bcl2, Bcl_{XL} and Mcl1 in apoptosis and autophagy pathways in cancer cells. We will use interdisciplinary approach of confocal fluorescent microscopy, molecular biology and spectroscopy.

New reconstruction approaches for 2.5 and 3D reconstruction of single-shot multiple projection data from X-ray experiments.
supervisor: doc. RNDr. Jozef Uličný, CSc. (jozef.ulicny@upjs.sk)
study form: full time
Annotation: Structural dynamics of biomedical and technological objects can be revealed using short intense X-ray pulses. Within few tens of femtoseconds, the sample is completely destroyed, so that only few simultaneous projections are available for 2.5D or even 3D reconstruction. For such underdetermined system, the reconstruction is possible only for systems with fair amount of structural *a priori* information. The task of PhD student will be to design 3D models of fibrillar structures with optimized placement of sequence-specific fiducial markers for imaging experiment at European XFEL. Subsequently, to design and implement reconstruction algorithms for obtaining structural information with gradually increasing realism of experiment. The PhD work assumes active participation on experiments utilising 3rd and 4th generation coherent X-ray sources in international collaboration comprising of scientists from Institute of Physics of Czech Academy of Sciences, University of Lund, European XFEL and CFEL – Center for free electron laser science.