DESCRIPTION FOR THE GENERAL PUBLIC

Reactive oxygen species (ROS), including singlet oxygen, are generated in the cell as a result of naturally-occurring metabolic processes. Furthermore, various types of ROS can be generated by exogenous factors including smoking, consumption of large amounts of fats rich in saturated fatty acids or an increase in the rate of breathing during increased physical activity. The normal cell in its natural state is characterized by the balance between the formation of ROS and their removal by well-functioning antioxidant system (antioxidant defense system), which can be enhanced by antioxidants, like vitamin C and E. Imbalance between the formation and removal of ROS in the oxidation reaction is known as oxidative stress, which has the adverse effects of the cell functioning. The role of ROS in the pathogenesis of civilization diseases, i.e. diabetes, hypertension, atherosclerosis, as well as in the induction of neurodegenerative disorders, including Parkinson's disease, Alzheimer's disease or multiple sclerosis, is very well documented. A variety of different tests allows the assessment of the effects of ROS on selected cellular components and compartments, which is based on the detection of biomarkers of oxidative stress, for example malonic aldehyde or modification of thiol groups in proteins. Despite the high sensitivity, none of the available tests can monitor the level of intracellular ROS and their particular location within the cell.

Such analysis is possible thanks to the use of fluorescent probes, which, in reduced form has low fluorescence intensity, while the oxidation causes its significant increase. Flavins are examples of such molecules. Flavins are abundant in cells, where they participate in a wide range of biological processes thanks to the unique combination of their redox and optical properties. As they can be reversibly switched between the reduced, inactive (“off”) form and oxidized, “on” form in natural redox environment of the cells.

Our experience with describing spectroscopic and photophysical properties of flawin for years and inspired by the literature we hypothesize that by an appropriate modification of the flavin scaffold they can be rationally optimized to favor either fluorescence (molecular probes for redox), or light-induced singlet-oxygen generation (potential photodynamic therapeutic drug candidates).

This project meets this demand because its ultimate goal is the design, synthesis and characterization of fluorescent probes based on flavin derivatives.

The advantage of the project is the experience of the authors in this type of design, which is confirmed by results of preliminary study, including the use of human cells in vitro. Redox probes obtained in this research will allow a precise intravital study of changes of ROS level in the cell and its environment through the use of advanced microscopic techniques, flow cytometry and advanced spectrofluorimetric methods. Additionally, flavin derivatives will be used not only as a tool for assessing the level of ROS, but also as generators of singlet oxygen.

Comparison of the results of intravital study with the results of standardized tests to evaluate biomarkers of oxidative stress, will allow comprehensive characterization of the effects of ROS on the cell. Among the most exposed to the ROS cells are human erythrocytes due to the functions of oxygen transporters. Comparison of the results obtained for the analysis of human erythrocytes and selected cell lines will allow a comprehensive assessment of ROS in a variety of cell types and under various conditions of incubation in the presence and absence the reference antioxidants. This project covers the issues at photochemistry, natural products chemistry, and cell and molecular biology, both in the experimental and theoretical sphere.