

A common feature of most tumors is lowered level of oxygen. Such non-physiological level of oxygen is called hypoxia. This state is a consequence of an imbalance between the supply and consumption of oxygen. The supply of oxygen is insufficient due to inefficient blood vessel formation in fast growing neoplastic tissues. In addition, hypoxia could promote tumor invasion and metastasis as well as the resistance of tumor cells to therapy (both chemotherapy and radiotherapy). Advanced hypoxia is a prognostic for poor patient outcome.

Nowadays the evaluation of hypoxia in clinical studies is based on oxygen needle electrode, immunohistochemistry assays or PET (positron emission tomography) imaging using radiopharmaceuticals. Currently, there is an urgent need for the development of sensors, which have an increased response to subtle variations in oxygen concentration, increased kinetic stability, and which accumulate only in the hypoxic cancer tissues, avoiding the necrotic or normoxic ones and have a detection system which is relatively cheap, portable and easy to operate. To fulfill all these requirements we have designed a group of sensors based on the conjugation of bioreductive compounds with fluorescent units to form a new type of hypoxia-selective optical imaging sensors. Our preliminary studies have confirmed the excellent fluorescent properties of such conjugates. The studies will be carried out on three levels: in-solution, in vitro and in vivo.

The general aim of this project is to select the compounds which allow for the optical identification/detection of the hypoxic tissue including oxygen evaluation within it. As an outcome, the collected information should allow for a rational selection of compound/s which might be further tested for its/their clinical application and can be used as a probe in molecular biology studies.

We believe that the results from this project will turn the attention of scientists toward searching for new, better sensors for optical imaging, in particular, devoted to specific features of cancer tissues like hypoxia or lower pH. Such sensors, as non-invasive tools can provide an easy way of monitoring the disease during and after treatment. This might bring new solutions, beyond typical patterns in the application of drugs, which might be beneficial in case of combating with cancers of different origin and displaying huge diversity from patient to patient. Cancer has a substantial impact on society in terms of premature death, lower productivity and higher cost of medical care as well as emotional and psychic costs for cancer victims, their family and friends. Therefore, even a small breakthrough in the field that leads to clinical achievements in cancer therapies will have a tremendous impact.