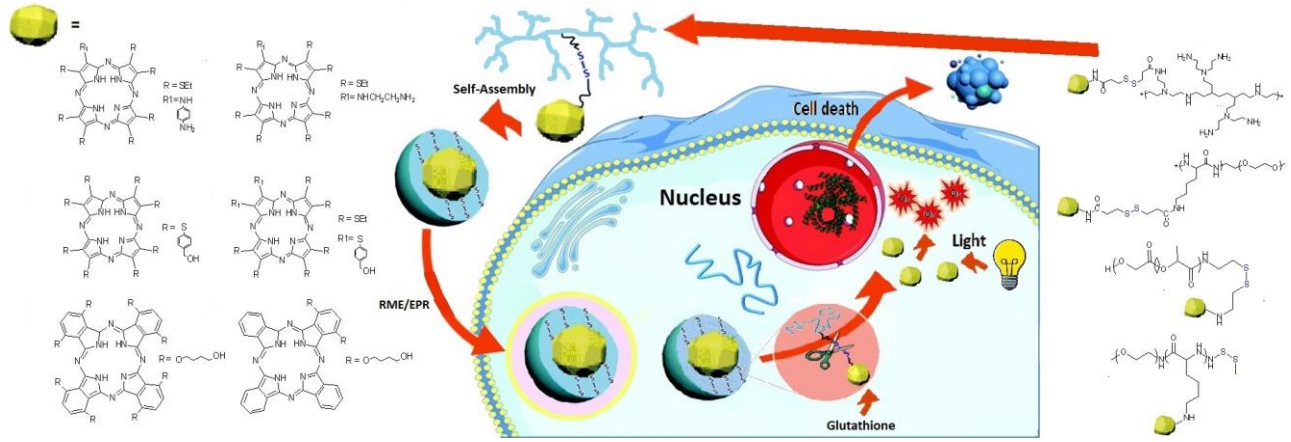
Porphyrazines are macrocyclic compounds which reveal interesting electrochemical and optical properties of importance for their potential applications in PDT, antimicrobial photodynamic therapy (PACT), and photodynamic diagnosis (PDD). PDT offers the possibility to destroy cancerous tissue *via* photochemical reactions in a selective manner without the risk of damage to healthy tissues. In PDT, a photosensitizer is administered to the tumor tissue and then activated with light. Further energy transfer from excited photosensitizer to the molecular oxygen generates reactive oxygen species - ROS, including singlet oxygen. As a consequence of macromolecular damage, cancer cell death occurs mostly by apoptosis than necrosis. **The therapeutic effect of the pharmaceutically active ingredient, which is an essential ingredient of any drug, can be improved by taking into account biopharmaceutical aspects and preparation of a proper pharmaceutical formulation and, in some cases, also preparation of drug delivery system - DDS.** API can be conjugated to or enclosed in DDS and release in the proper place in the body or tissue. This idea of using DDS is intended to ensure safe transport of active substance to the target site in the body, prevent its decomposition under the influence of specific enzymes or pH values as well as increase its solubility and permeability through dedicated biological compartments. Various types of API have been so far combined with carriers and exhibited exceptional biocompatibility and biodegradability. **A further step has been the development of a novel, and to a greater extent, improved smart drug delivery system, with its redox-responsive modalities.** In this case, glutathione - GSH is the triggering agent for the release of the intrinsic or micelle-embedded active substance within the cell. Taking advantage of the fact that the concentration of GSH in cancer cells is from 2 to 10 mM, which is 100 - 500 higher than in healthy cells, it provides an amazing selectivity for the release of APIs from their DDS. **The proposed features of novel DDS for photosensitizers, which according to PI's knowledge, has never been proposed for porphyrazines, demonstrate the first example of modern photosensitizer delivery triggered by the addition of non-toxic reagent dithiothreitol - DTT.**



The driving force of this proposal will be the synthesis, determination of physicochemical and biological properties of novel porphyrazine derivatives in their free form and after encapsulation in biodegradable polymer matrices fulfilling the role of DDS for PDT. The main tasks of the project are (*i*) **chemical synthesis** of porphyrazine derivatives and modified block polymers based on biocompatible polyethylene glycol, poly(lactide-co-glycolide), polylactide, polyethyleneimine and polypeptide polymers such as polylysine, (*ii*) **chemical conjugation of porphyrazines to biodegradable polymer matrices** and their subsequent emulsification, sonication, concentration, and lyophilization, which will be accompanied by the preparation and characteristics of poly(lactide-co-glycolide) nanoparticles with encapsulated, non-bound Pzs to polymers for comparative study, (*iii*) **physicochemical characterization of new porphyrazines as well as novel polymeric micelles with polymer-conjugated porphyrazines, and porphyrazines embedded in biodegradable polymeric nanoparticles**, including X-ray and NMR structural studies, spectroscopic (absorption, emission, singlet oxygen generation, solvatochromic), drug loading assessment, microscopic measurements, determination of critical micelle concentration - CMC, morphology and size analysis of created micelles, evaluation of obtained macrocycle containing polymers towards DDS functionalities, (*iv*) ***in vitro*** **photocytotoxicity study on a series of cancer cells** determining pharmaceutical drug-delivery and medicinal chemistry applications. **The proposed studies leading to the novel system will be performed at the Poznan University of Medical Sciences, which demonstrates 15-year experience in the medicinal chemistry of novel photosensitizers and nanoparticles, including modern dendrimers.**