Reg. No: 2015/18/M/ST5/00060; Principal Investigator: prof. dr hab. inż. Janusz Edward Kasperczyk

The serious problem is the increasing new cancer cases and the fact that tumors are the leading cause of death in developed countries. The drawback of intravenous systemic chemotherapy is the unspecific targeting to the tumor and difficulties to achieve therapeutic levels of drug within or adjacent to the tumor. Furthermore, significant concentrations of drug frequently accumulate in healthy tissue, leading to severe side effects and dose-limiting toxicity. Therefore, the aim of the project is to develop a new, intelligent delivery system of anticancer drugs (Fig. 1). Polymeric micelles will be used as drug carrier. The micelles will be obtained from block copolymers consisting of hydrophobic poly(lactide) (PLA) and hydrophilic poly(ethylene glycol) (PEG). Additionally, the copolymers will be functionalized with folic acid (FA), that selectively binds to cancer cells with overexpression of FA receptors (FAR). The selected derivatives of betulin will be incorporated into micelles. The agents possess the anticancer activity, however they are poorly soluble in water, therefore it is important to develop dosage form that can effectively solubilize drug but also provides biocompatibility.

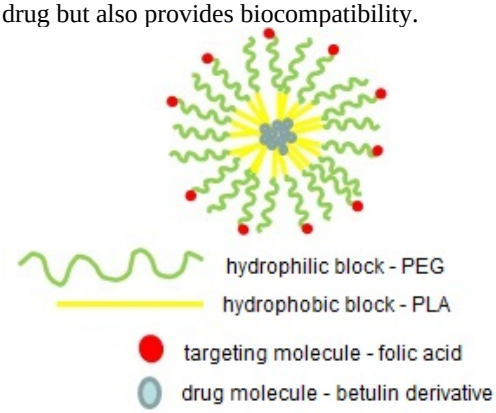

Figure 1. PLA-PEG-FA micelle with betulin derivative.

In the frame of the project biodegradable polymers with targeting moiety (PLA-PEG-FA) will be synthesized. Self-assembling properties of amphiphilic copolymers in aqueous medium will be analyzed. Acetylenic, phosphate or phosphonate derivatives of betulin will be synthesized. The incorporation method of betulin derivative to the inner core of micelles will be developed. Degradation of micelles, their stability and drug release rate and profile will be studied. Finally, the potential of the obtained controlled drug delivery systems in chemotherapy will be tested under in vitro conditions using several carcinomas derived from breast, ovaries and cervix. Based on the obtained results, the most promising micellar delivery system against examined cancer cells will be selected.

The project will be realized in cooperation between experienced scientists including chemists, biologists, pharmacists and physicists and all the partners present an excellent complementarity. The synthesis of new amphiphilic PLA-PEG-FA copolymers will be coordinated by Professor Suming Li (European Institute of Membranes, UMR CNRS, University of Montpellier, France). Professor Li has been working for more than 20 years in the synthesis, structure-properties, biodegradation and drug delivery systems of polymeric biomaterials and has got worldwide recognition because of outstanding achievements. The collaboration since 2003 via bilateral The National Center for Scientific Research in France (CNRS) and Polish Academy of Sciences (PAN) exchange programmes has been very fruitful with the publications in prestigious journals. The possibility of a joint project therefore enable a further step towards the mutual exchange of experiences and knowledge between teams of two large university centers of the Polish and France.