NANOSTRUCTURED LIPID LIQUID-CRYSTALLINE CARRIERS FOR CHEMOTHERAPEUTICS AND CORPUSCULAR RADIATION EMITTERS IN TARGETED CANCER THERAPY

Apart from cardiovascular diseases, one of the main reasons of deaths in Poland and Europe are malignant tumors. The number of cases in the last three decades has radically increased and the perspectives for the next years are not optimistic. In Poland, mortality from malignant tumors is even still higher than in European Union countries. Despite the use of advanced diagnostic and therapeutic techniques many aggressive cancers such as glioma or cervical/endometrial carcinoma cannot be effectively cured. The life expectancy of patients diagnosed with GBM is 12 to 15 months displaying the worst median overall survival among all human neoplasms. The present therapies of malignant tumours are frequently palliative and sometimes the relapses occur even several years after the treatment. Unfortunately, chemotherapy acting on the rapidly dividing cancer cells causes also damage of healthy tissues leading to adverse side effects. Additionally, many tumors exhibit resistance for chemotherapeutic drugs or radiation therapy. Recently, cancer stem cells (CSC) have been proposed to play a significant role in oncology, since they seem to be responsible for the initiation and propagation of tumor cells. Satisfied results in the treatment of cancers can be achieved by using targeted radionuclide therapy (TRT) employing radiotherapeutic agents, which being attached to biomolecules selectively accumulate in cancer cells, destroy them and don't cause the damage in healthy tissues. Another promising method is chemotherapy where drug is transported to cancer cells by drug carriers. An advantageous system to use for drug delivery should have a high drug loading capacity to reduce quantity of matrix material needed and a controlled release drug delivery to achieve the correct dose of drug. Of special interest to this proposal are the non-toxic, biodegradable lipidic non-lammelar liquid crystalline structures (LCP) and especially their nanoparticles (LCNP) and their application for drug immobilization. Their internal nanostructures hold potential for accommodating hydrophobic, hydrophilic, and amphiphilic drugs (or drug combinations). A diverse range of compounds may be added to functionalize the LC mesophase. The release rate from liquid crystalline systems can be manipulated by changing variables such as temperature, pressure, pH or composition.

Therefore, in our project we propose new chemotherapy that in combination with radiopharamceuticals could represent an attractive route for the treatment of cancer. We will try to answer the question if the combination of two therapeutics methods: chemotherapy and radionuclide therapy based on the new lipidic liquid crystalline nanostructures doped with chemotherapeutics and labeled with β and α radionuclides (^{177}Lu/^{225}Ac) could increase the efficiency of cancer treatment. To provide selective targeting, biomolecules having affinity to receptors on cancers cells (glioma/cervical/endometrial cancers), will be attached to the carriers. Within the same dosage it will be possible to target the delivery of drugs to the site of disease and reducing unwanted side effects.

In contrary to standard radiotherapy which causes damage in normal tissues, the use of liquid-crystalline nanostructures conjugated to biomolecules having affinity to receptors on glioma and cervical/endometrial cancer cells and labelled with radionuclides, will allow to obtain new class of nanoparticles for targeted therapy. We expect that these compounds will enhance the therapeutic effect through their synergy. Furthermore, based on literature data, the use of α emitting radionuclide – ^{225}Ac can have an impact on the damage of cancer stem cells which are responsible for initiation of tumor formation *in vivo*, sustains its growth and creates metastatic lesions.