

Cancer is one of the most serious diseases at present in the world. Effective methods of therapy, despite significant scientific and technological development, are still limited. This involves, among others with no obvious differences between normal and cancer cells. Moreover, classical chemotherapy is often associated with the distribution of highly toxic effects, at dosages that may cause non-specific drug effects. To reduce the side effects and increase the specificity of chemotherapeutics to cancer cells, new methods of their delivery to tumors are being sought. Lung and prostate cancers are one of the most frequent malignancies with a high mortality rate. So far, no effective and selective therapy of cancer with reduced activity towards normal cells have been developed.

Unsymmetrical bisacridines (UAs) are a new class of compounds developed in the Department of Pharmaceutical Technology and Biochemistry at the Gdańsk University of Technology. UAs exhibit high cytotoxic *in vitro* and antitumor *in vivo* activity, preferentially against human lung, colon, prostate, breast, and pancreatic cancer. These compounds were patented in Europe and the USA. Our recent results indicated that depending on the cancer cell line, UAs conjugated with QDs improved cytotoxicity of these drugs in lung cancer cells (H460), but not in colon (HCT116) cancer cells, and protects normal cells from drugs action.

One of the strategies for selectively delivering the studied chemotherapeutics to cancer cells is the use of targeting linkers, e.g., folic acid (FA) or transferrin (Tf), due to their high affinity of overexpressed receptors on the membrane surface of cancer cells. The use of folic acid and/or transferrin as a linker in QD-UAs conjugates may increase their selectivity to tumor cells with overexpression of FA and Tf receptors on the surface of the cell membrane and increase the cytotoxic activity of UAs in cells. At the same time, the effect of QD-UAs conjugates in normal cells may be weaker (protective effect) because of the much lower number of FA and Tf receptors on the membrane surface of these cells.

This project aims to **assess the ability of folic acid (FA) and/or transferrin application as a linker between conjugates of quantum dots with unsymmetrical bisacridines (UAs) to enhance their selectivity and cytotoxicity against lung (H460) and prostate (Du-145 and LnCaP) cancer cells.** The project includes synthesis and *in vitro* characterization of QD-FA-UAs conjugates. Mechanism of internalization, cellular fate, as well as cellular response induced by these conjugates in cancer and normal (MRC-5 and RWPE-1) cells will be also examined.

The results of the presented project will extend the basic knowledge about the biological activity of UAs conjugated with QD, as well as the effect of using folic acid and/or transferrin as a targeting linkers in QD-TM-UAs conjugates to cancer cells with overexpression of FA receptors on the membrane surface. Moreover, the planned research will help to design the individual scheme of anticancer therapy with QD-UAs with a different linker, as a drug delivery system to cancer cells.