The search for potential anticancer drugs leading in our laboratory developed recently new promising compounds, unsymmetrical bisacridines (UAs), which exhibited high cytotoxic and antitumor activity, preferentially against human pancreatic cancer. The preliminary results also indicated that human colon and lung cancers were sensitive toward some bisacridines. Our preliminary studies on the mechanism of action of UAs (unpublished data) showed that these compounds expressed the specific mechanism on the DNA level with the participation of *KRAS* as well as *c-Myc* protein promoters. It is the crucial mechanism as it influences the cell proliferation and cell cycle progression. Our studies also suggested that UAs may induce apoptotic cell death in pancreatic cancer. Beside the studies on the cellular level another aspects of drug treatment should be considered in the process of the new antitumor drug development. The major clinical obstacle that limits the efficacy of anticancer therapy is the problem of appropriate delivery of the therapeutic agent to the target in tumor cells. The promising strategy for overcoming the antitumor drug resistance seems to be nanoparticle-based drugs. They act as a drug vehicle able to target tumor tissue and protect the drug from undesired degradation during its transport.

Taking into account the general knowledge presented above and our current results we suggest in this project that the observed specific mechanism of bisacridines on DNA levels would participate in the cytotoxic effects of these compounds and in the specific cellular response induced by them. We will study these effects in human colon and lung cancer after drug treatment. We also intend to show that bisacridines conjugated with core-shell nanoparticles of magnetic and luminescence properties will express higher activity and better pharmacological properties than the native compounds.

To verify the above hypothesis the proposed investigations will consider two aspects: the first one relates to biological effects of bisacridines in tumor cells and in the specific kind of mice with natural immunodeficiency transplanted with human tumors. The second aspect relates to antitumor effects, which would induce bisacridines conjugated with nanoparticles. Therefore, the proposed studies will be performed in two steps.

Studies of the I step will include the following tasks:

- the examination of the type of cellular response and the changes in the cell cycle progression induced by the selected bisacridines derivatives in human colon and lung cancer cells as well as in normal cells;
- the research concerning antitumor activity of UAs derivatives against colon or lung cancer transplanted in mice with natural immunodeficiency;
- the detection and characteristic of cancer stem cells population (CSCs);

Studies of the II step will consider the following tasks:

- ❖ the synthesis of the bisacridine conjugates with core-shell nanoparticles of magnetic and luminescence properties;
- ❖ the studies on the uptake processes, cytotoxicity and the cellular effects of nanoparticles conjugated with UAs derivatives in human colon and lung cancer cells as well as in normal cells.

To realize the above strategy, a wide spectrum of experimental methods will be applied in the project. The majority of the studies proposed here require maintaining the cell culture, which is in our direct disposal. The impact of studied compounds on the cell cycle progression and on cellular response in tumor cells will be investigated using flow cytometry, fluorescence and light microscope as well as western blots. Antitumor *in vivo* testing of UAs will be conducted on human cancer cells transplanted in mice with immunodeficiency. The synthesis of nanoparticles and their conjugates with bisacridines will be performed according to the method developed at the Chemical Faculty of Warsaw University.

The proposed studies will extend the knowledge about molecular mechanisms responsible for the action of the new promising, patented, highly active antitumor unsymmetrical bisacridines, which are developing currently by our group. The studies will also improve the pharmacological properties of new potent antitumor bisacridines and will influence the development of pharmacology and biology of cancer. Therefore, it will impact significantly the society and will be strongly involved in the development of civilization.