The standard treatment procedures of drug dosing have several disadvantages. Mainly, the problem is related to nonspecific introduction of drugs into tissues. Consequently unwanted overall toxicity of many drugs and additional negative effects observed in healthy tissues appear. Due to these facts, a new trend appeared in the research: design of drug delivery carriers specifically dedicated for selective delivery to particular places in the organism (this is called "targeted therapy"). Development of nanotechnology- and polymer sciences give an opportunity for designing a variety of hydrogel-based nanostructures as carriers for improved delivery of various drugs. Many hydrogels possess very good biocompatibility to human tissues, that results in: a) good accumulation of water and b) phase-to-phase tension that blocks the absorption of large molecules, e.g. proteins, into the networks. Many hydrogels are environmentally sensitive and are called "smart networks" due to their ability of changing their properties under the influence of various environmental factors. This gives a possibility of application of hydrogel-based nanostructured materials for controlled storing and delivery of small molecules, including drugs to cells.

The submitted proposal is aimed at the synthesis of novel, biodegradable, multicomponent copolymer-based nanogels and optimization of their parameters for targeted delivery of two selected anticancer drugs. For improvement of selectivity of interactions of novel nanogels with particular cancer tissues, we will introduce additional active ligands: hyaluronic acid and two aptamers. Both types of molecules can selectively bind to overexpressed particular types of proteins in cancer tissues. The exploitation of the unique properties of aptamers, small single stranded ssDNA and RNA molecules called "chemical antibodies", will allow to direct the active transport of nanogels and drugs to particular cancer tissues. Thanks to this, the way of drugs to targeted places will be shorter and appropriate doses of drugs will be released by controlled way. The novel trend presented in this proposal will be the placing of aptamer-drug conjugates into the nanogel networks. Such action should be more effective from the point of view of controlled and more effective delivery of conjugates compared to unbounded drugs and should better protect the conjugates against the interaction with external environment. Other important aspect is the design of biodegradable nanosystems that will allow easy removal of the particles from the body environment. Designed nanogels will be modified with additional functional crosslinking molecules. We plan to introduce: oligonucleotide-based crosslinker with sulfide bridges (S-S), peptide-based crosslinker with selenium bridges (Se-Se) and hyaluronic acid network (HA). All molecules can dissociate, thus the nanogels can be degraded in the presence of higher concentrations of particular compounds overexpressed in cancer tissues.

Two anticancer drugs: Doxorubicin (DOX) and Symadex will be examined. Synthesis routes will be realized by copolymerization reactions of various components. We will search for the most optimal, biocompatible, biodegradable and selectively environmentally sensitive (to temperature, pH and presence of chemical compounds) carriers. A very important aspect of the investigations will be the controlled release process of drugs from novel nanosystems and selective binding of targeted molecules with overexpressed membrane proteins.

Final positive results of the work may allow to present several types of novel multicomponent nanosystems dedicated to controlled, targeted release process involving selective environmental sensitiveness and unique relation between particular membrane proteins and selected aptamers.