

Pancreatic cancer is the deadliest tumor type (5-year survival applies to only 9% of patients) and the incidence is steadily increasing worldwide. Late diagnosis, limited surgical and therapeutic options stand behind the high mortality rate of pancreatic cancer patients. Therefore, new methods of pancreatic cancer detection and novel therapeutical approaches (especially targeted medicine with limited side effects) are urgently needed.

Cancer cells are characterized by uncontrolled and enhanced cell proliferation, intensive cell migration and avoidance of apoptosis. Proteoglycans (HSPGs) are cell surface proteins that orchestrate the action of growth factors and their receptors, facilitating proliferation and migration of cancer cells. Importantly, elevated levels of HSPGs were found in pancreatic cancer cells compared to normal pancreatic cells. The differences in HSPGs levels between tumor and healthy pancreatic tissue and the involvement of HSPGs in oncogenic cellular processes make these proteins attractive molecular targets for development of precise medicines.

In the frame of this project, we will develop novel macromolecules recognizing HSPGs, which will serve as HSPGs blocking agents and drug carriers to precisely eliminate pancreatic cancer cells. We will use fibroblast growth factor 1 (FGF1), which has a natural ability to bind HSPGs. FGF1 will be re-programmed to lose its affinity for FGFRs and mitogenic activity, and will display improved HSPGs binding. The modified FGF1 will be combined with several protein oligomerization scaffolds, resulting in FGF1 oligomers of distinct architecture, HMLAs, characterized by enhanced SPGs binding. By binding HSPGs on the surface of pancreatic cancer cells, HMLAs will block pro-oncogenic effects of HSPGs-dependent growth factors and will serve as drug vehicles to selectively kill pancreatic cancer cells overproducing HSPGs.