World Health Organization (WHO) declares that, 1 in 6 deaths are the result of neoplastic changes in the human body. The main efforts of scientists are focused on early diagnosis, prevention and inhibition of tumor growth in the place where the tumor arose. Less attention is, however, paid to the neoplasms in advanced stages, in which the process of cell metastasis is observed, during which secondary tumors are often formed in other, often distant, organs, even though this process is actually responsible for approximately 90% of all cancer-related deaths. The latent process of metastasis occurs parallel to the development of the primary tumor or later, when tumor cells with the potential for metastasis enter the bloodstream from the primary tumor site during surgery causing metastasis to distant organs. These cells are called circulating tumor cells (CTCs). They can be considered the important indicators of metastasis in malignant tumors and represent the main focus of the proposed project.

In our project we plan to use magnetic particles coated with charged polymers to capture CTC. Due to their composition and extremely small size these particles have exceptional magnetic properties and are known as superparamagnetic iron oxide particles (SPION). Once SPION bind to cancer cells, they may serve as a magnetic label for diagnostic purposes (Magnetic Resonance Imaging (MRI) contrast). They may also be used to bind and magnetically capture CTC. In both cases SPION must first selectively bind cancer cells, which means that they should not attach to normal cells. To achieve that selectivity we plan to decorate SPION with antibodies (anti N-cadherin, anti-VCAM-1) and chemokine CXCL12. These proteins were designed by nature to selectively bind specific to groups (antigens or receptors) present on the surface of cancer cells, in a way similar to the way key fits the lock hole. Such SPION-antibody or SPION-chemokine systems are known as targeting systems, as they can selectively target cancer cells.

These targeting systems may be further developed into theranostic systems when anti-cancer drug (e.g. pioglitazone) is also attached to SPION surface. Then, once such nanoparticles find and selectively bind to CTC, they may 1) be visualized using magnetic methods (MRI) and 2) prevent cells from multiplying or even kill them. We plan also to use another compound, phycocyanin, instead of the drug. This dye, derived from marine plants, can prevent cancer growth and metastasis. It also emits intense reddish light which can be used for the optical visualization of CTC in the patient's body.

Targeting SPION systems may also be used without further modification to magnetically capture CTC - either in the blood sample or, in more advanced set-up, in the bloodstream (similarly to haemodialysis). While the first approach would allow to establish the source of metastasis (primary tumor), the latter may allow to remove CTC from bloodstream before secondary tumors are formed, preventing or at least slowing down cancer invasion to other organs. The magnetic removal of the CTC cells will also be tested using surfaces with attached antibody-modified magnetic nanotubes (HNTs filled with SPION particles).

In this project chemists will prepare SPION, make them stable in bloodstream by coating with especially synthesized polymers, decorate with antibodies/chemokine CXCL12, and some of them also with drugs and labels for visualization. Biochemists will then study different cancer cell lines able for metastasis in order to verify if these cells may be captured and killed using SPION systems. Safety of these SPION systems for normal cells (and thus the safety of the therapy) will also be tested. Finally, a group of physicists will analyse magnetic properties of SPION systems and will develop the best stationary and flow conditions for effective magnetic capture of SPION-decorated CTC.

This multidisciplinary project aims at the development of a new, advanced SPION-based system for effective capture of CTC cells, which may provide means for a better diagnosis, and preventing, limiting or at least slowing down the metastasis in the patients with advanced cancer, significantly improving their prognosis. As in the case of some cancers, for example, in the case of pancreatic cancer, there are no early symptoms or successful screening tests, we hope the proposed study, using a variety of neoplasms, will result in offering patients a tool for early detection and uptake of CTC cells, significantly improving patients' prognosis.