Most of the cancer patients die not because of the local tumor growth but as a result of the process of metastasis, when tumor cells are breaking away and spread into vasculature and then into other tissues and organs. For colon cancer patients removal of tumor confined to the bowel wall results in survival of 80-95% cases. Once the tumor becomes metastatic, the chance of survival is very low. We are focusing on colorectal cancer cells in this project as this is one the most common cancers with the lowest survival rate with metastatic tumors.

Chemotherapy, the use of drugs to kill cancer cells unfortunately also kills normal cells. Thus, the alternative interventions are needed to stop cancer cells from moving. Cancer cells consist of similar structures and are using similar methods of moving as normal cells do. Once in vasculature cancer cells are interacting with other circulating blood cells. Some blood cells are removing cancer cells but some are helping them to spread. Small cells circulating in vasculature called platelets, made mostly of protein particles, are important for stopping bleeding after injury but also are detrimental in cancer. There is a poor prognosis for colon cancer patients if platelet number in blood is higher than normal. Also animal research shows that removing platelets helps in stopping of cancer spreading. The treatment is complicated because platelets and their proteins are physiologically needed to stop bleeding. Research focused on intervention with the mechanism by which platelets interact with cancer cells is under way. Gene therapy as well as the use of small molecules targeting this interaction have been proposed. However, because of the similarity of cancer cells function to those of normal, the side effects exist and clinical trials are rare.

Surgery to treat cancer patients leads to blood loss. Also post-surgery chemotherapy and radiation therapy affect bone marrow that produces blood cell so cancer patients frequently need blood transfusion. Transfusion delivers platelets and their proteins that are needed to stop bleeding but also platelets and a very small particles formed by platelets in circulation, called platelet microparticles that consists of some platelet proteins.

Platelet microparticles were also found to be harmful for cancer patients. The question in this proposal addresses the mechanism of how platelet microparticles affect the colon cancer cells in metastasis. They can fuse with cancer cells and increase their possibility to migrate, survive and form tumors in distant organs during called metastasis. In order to find out how the platelets can be changed to be less harmful, in this project we will look what is the protein content of microparticles when colon cancer cells interact with them in the vasculature. We will isolate the microparticles from blood of healthy people and examine their fusion with cancer cells isolated from patients on different stage of colorectal cancer progression. Such cells are commercially available for researchers. Then we will compare the ability of colon cancer cells without and with incorporated platelet microparticles to attach to blood vessel wall, travel through vasculature and invade other tissues. We will also examine the mechanism(s) by which microparticles modulate cancer cell invasion and how we can stop this process. Further, we will examine the effect of platelet microparticles in the animal models of cancer progression and metastasis.

Once we find out which proteins of platelet microparticles are most important for colorectal cancer cells invasion properties, we can, outside the human body, make a modified platelets lacking this proteins. Production of platelets *in vitro* is already under investigation in many laboratories worldwide but is still on the basic research stage. Our next goal will be to make platelets that are less detrimental for cancer but still working as a part of clot that stops bleeding and to check its activity in animal models. Such modified platelets can in the future be transfused to cancer patients as they need it, without risk of increasing the pool of platelet microparticles that help survival and migration of cancer cells and are harmful for patients.