Cancer is the main cause of human mortality in developed countries. For a long time it has been thought that tumours consist of only cancer cells. Currently it is known that cancer cells are surrounded by other cells, such as fibroblasts, immune cells and endothelial cells, which together form the tumour microenvironment. Cancer cells reprogram the cells in the tumour microenvironment in order to support tumour growth and invasion. **Therefore, a better understanding of the interaction between the microenvironment and the tumour cells might be crucial for the development of new methods of treatment.**

Insufficient blood supply in rapidly growing tumours and anti-cancer therapies induce hypoxia and metabolic depletion, which are inherent stress factors of the tumour microenvironment. Cancer cells respond to the cytotoxic effects of such metabolic stresses either by activating adaptive processes to survive or by undergoing cell death. Cancer cell death occurs mostly by necrosis because apoptosis is limited during carcinogenesis. Unlike tumour-suppressive apoptotic cell death, necrosis may paradoxically support tumour growth and progression. In support of this, development of a necrotic core in cancer is associated with poor prognosis for patients.

For many years it was thought that necrosis is an accidental and genetically unprogrammed form of cell death. Currently, it is known that there are many types of non-apoptotic cell death, for example oncosis, necroptosis and ferroptosis, which are controlled by specific genetic mechanisms and which morphologically resemble necrosis. In my research, I plan to focus on ferroptosis and its role in cancer development. Ferroptosis is a form of cell death caused by excessive oxidation of cell membrane lipids in an iron-dependent process due to oxidative stress. The role of ferroptosis in cancer development and progression remains unclear. Based on the recent findings, ferroptosis may have a tumour suppressor function, and interestingly, invasive cancer cells, cancer stem cells and chemotherapy-resistant cancer cells are particularly susceptible to ferroptosis. Thus, the induction of ferroptosis in tumours seems to be an interesting strategy for cancer therapies. However, cancer cells that die as a result of ferroptosis secrete a number of molecules into the extracellular space that may potentially promote tumour development by modulating immune cells, inducing angiogenesis and activating live cancer cells. **We suspect that ferroptosis, induced for example by anti-cancer therapies, may potentially contribute to cancer development and recurrence through phenotypic modulation of the tumour microenvironment. Furthermore, we believe that hypoxia may play an essential role in this phenomenon, as it enhances expression of some of the secreted molecules.** Thus, further research is needed to elucidate how ferroptotic cancer cells impact various cells in the tumour microenvironment and to identify the molecular mechanisms of these interactions.

In our project, we will perform a number of experiments and analyses that will be aimed at verifying our hypothesis. These will include experiments using both *in vitro* cell cultures and animal models. We are convinced that the results of this project will lead to a deeper understanding of cancer biology, and in the future may contribute to the development of more effective anti-cancer therapies.