Description for the general public

Breast cancer is one of the most commonly occurring malignancy in women worldwide. It is predicted that one in eight women will develop breast cancer in her lifetime. However, it is the metastasis that is a major clinical problem. Despite major advancements in the treatment of breast cancer, the biology of this disease is still not entirely understood which justifies the necessity of basic research in the field of oncology.

In recent years it has become clear that cancer cells do not work autonomously, but they closely interact with the components of the surrounding environment. The tumour microenvironment consists of many different cell types, including stromal cells, blood vessels and tumour-infiltrating immune cells. Various processes have been identified by scientists showing the involvement of the tumour microenvironment in oncogenesis. The components of tumour microenvironment are critical for the initiation of cancer, progress towards malignant phenotype and metastasis. In addition, despite the presence of immune cells in the tumour, cancer cells effectively avoid the immune response. This process is called immunosuppression and is largely associated with the induction of an immunosuppressive events in the tumour milieu. The network of the communications between cancer cells and tumour microenvironment is very dynamic and it changes according to the stage of oncogenesis and in response to the treatment. Understanding the molecular basis of these interactions is a key for the development of better anti-cancer therapies, which highlights the need for new discoveries in basic biology of cancer.

The main objective of this project is **to describe the role of MLK4-dependent communication between breast cancer cells and macrophages, which are the most abundant immune cells in tumour microenvironment**. MLK4 is a serine/threonine kinase that plays an important role in various cellular processes including proliferation, differentiation, migration of cells. We have recently proven that MLK4 is highly expressed in breast carcinoma and that it contributes to invasive phenotype of breast cancer cells. During the process of invasion, cancer cells communicate with tumour microenvironment in order to guarantee the most tumour-promoting conditions. **We therefore assume that high expression of the MLK4 is also important in the interaction between tumour microenvironment and breast cancer cells.** In our research, we will evaluate the role of MLK4 on the abundance and behaviour of immune cells, macrophages, in tumour surroundings. In addition, our previous studies have shown that the MLK4 kinase is involved in the production of cytokines, which are often immunosuppressive factors. In the proposed project, we plan to examine in detail the molecular mechanisms responsible for these processes.

The results obtained in this project will deepen our knowledge about the complex network of interactions that take place in the tumour microenvironment. We anticipate that the data generated by us will be of interest to scientists as well as clinicians and pharmaceutic companies. The long-term goal of this research is to contribute to the field of personalised medicine by uncovering the molecular basis of breast cancer progression.