Project title: Deciphering malignancy of cancer cells outside the primary tumors through molecular characterization of single circulating tumor cells from breast cancer patients

Breast cancer is the most frequent tumor in women worldwide and the cause of over half a million of deaths. Development of distant metastases is linked with especially poor prognosis of patients, however the mechanism of metastases formation has not been fully understood. In order to improve treatment outcomes new factors informing about the disease course are needed; for this reason tumor cells outside the primary started to be investigated, as these cells were already able to move through several steps of metastatic cascade. Circulating tumor cells (CTCs) present in blood of cancer patients are therefore a selected population of cancer cells, which might differ in its molecular profile from the heterogenous tumor bulk and bring additional information about possible disease course. Because of low number of CTCs in single blood sample, precise characterization of CTCs molecular profile is at best achieved at a single cell resolution, without any contaminating non-cancerous cells which might bias the gene expression profile. Moreover, CTCs in one patient might comprise a heterogenous population, differing in their ability to form distant metastases, thus it is not the number but molecular profile of CTCs, which might carry the most important, and clinically relevant information.

The aim of the project is to uncover CTCs molecular profiles linked to increased invasiveness/aggressiveness, stemness and escape from the control of the immune system. Within the project we will also analyze if CTCs use the mechanism of clusters formation with stromal cells during hematogenous dissemination and if this is specific to a particular type of CTCs. Obtained data will be correlated with clinico-pathological characteristics of the patients, in order to reveal how CTCs molecular profile is related to the disease course. In mouse model of breast cancer we will check if inhibition of cellular pathway linked to aggressiveness of cancer cells decreases CTCs dissemination and distant metastases formation.