

Circulating tumor cells (CTC) were observed for the first time in XIX century in a postmortem blood analysis, but their isolation, let alone analysis, were for a long time impossible due to technical limitations. Last years brought a breakthrough, with a flurry of new methods enabling efficient CTC isolation and analysis on the molecular level. These research have flourished recently, producing a lot of quite exciting data, but the accumulated knowledge concerning markers, heterogeneity and phenotype of CTCs in different types of tumors is still very limited.

Gaining more information is crucial to elucidate the biology of metastasis.

CTCs detection in the blood is also called "liquid biopsy". This is a very attractive alternative, since the analysis of a blood sample is much less invasive than standard biopsy. The presence of tumor cells circulating in the bloodstream indicates that they were released from primary site and have a potential to metastasize. Additionally, liquid biopsy can help to establish if the disease is advanced and to select optimal therapy.

In the proposed project we plan an isolation and subsequent analysis of breast cancer CTCs, including single cell heterogeneity, mutational status of selected markers' important for hormonal dependence of the cancer and CTC clusters enumeration and characteristics. Most of breast cancers are estrogen-dependent at the beginning, but secondary lesions often display hormonal independence, which precludes adjuvant treatment. In the proposed project we plan to test if the mutations leading to estrogen-independence can be detected in CTCs. The results should contribute to our knowledge of metastatic process in breast cancer and might be important for designing novel diagnostic procedures. We also expect that they may shed a new light on a known issue of a different frequency and time of metastases in luminal vs. basal breast cancers, with a long dormancy period observed in luminal cancers.