Summary

Circulating tumor cells (CTC) have showed great potential to become both prognostic and predictive biomarker in various types of oncological diseases. CTC can help detect patients in higher risk of shorter overall survival, progression-free survival or relapse. They can be also helpful in therapy selection as in current clinical practice treatment is chosen based on primary tumor characteristics. Regular CTC counts and features monitoring can be real-time indication of therapy response and can be used to guide-targeted treatment. This information can be implemented to personalized medicine and each cancer patient can be treated based on individual profile.

However, patients' sample with CTC is easily accessible, their detection has remained challenge due to low CTC number in the circulation and heterogeneous nature. CTC can circulate in blood in the form of single cells or in clusters that usually represent minority in comparison with single CTC but their metastatic potential is significantly greater than of single CTC. Apart from CTC count, the molecular character showed dynamic development and heterogeneous nature not only between patients but also within the individual patient's tumor tissue itself. Character of primary tumor, CTC and metastasis are not always consistent and has been changing during treatment process which can significantly impact response to therapy.

In this work, we used size-based CTC enrichment in various cancer diagnoses and monitored both CTC count and molecular character in regular intervals during treatment process. Cytomorphological and genes-expression analyses revealed dynamic disease development through whole treatment process. Fluorescent microscopy found count changes not only single CTC but also in CTC clusters presence. CTC behaviour also varied during withdrawals. While some of the CTC were able to survive only days during cultivation, there were enriched CTC fractions with aggressive growth and long-term cultures were established from them. Gene-expression CTC analyses of genes associated with tumor, epithelial-mesenchymal transition, stem cells-like features and chemoresistence revealed their presence and dynamic change in expression levels. We found CTC character does not correlated to corresponding primary tumor features. The outcomes of the CTC research are summarized in publications that are part of this doctoral thesis.