Prostate cancer is the second most frequent cancer affecting males. It accounts for an estimated 142,000 deaths in the industrialized countries each year. Metastases are the major cause of all cancer-related deaths (>90% of cases). In prostate cancer, they occur mainly in distant lymph nodes and bones, but also less frequently in liver, lungs, kidney or even central nervous system. Metastases are incurable. Patients suffering from metastasis receive hormonal therapy, which always leads to resistance to this therapy, or palliative treatment.

Therefore, this study is designed to challenge early enough identification of metastatic progression and provide hints for metastasis-targeted therapy, in particular in case of bone metastases. Despite of many worldwide attempts to address those ambitious goals, still little is known about prostate cancer dissemination and metastases formation, and no successful treatment is offered to patients suffering from (bone) metastases. Thus, the proposed project is yet a pioneering study and carries the potential to pave the way for precision oncology. We plan extensive screening for putative markers associated with metastases and their multi-layered validation in different clinical setups and *in vitro* experiments in order to support early detection of metastasis-initiating cells, and in turn improve patients diagnostics. Of note, the project will take an advantage of i) big data analysis using different publicly available datasets, and ii) our own previously and newly generated data on unique material incl. disseminating tumors and metastatic samples using modern and powerful tools such as NanoString^{TM} technology and single cell RNA sequencing, respectively. To the best of our knowledge, there are only a few studies investigating public datasets towards site-specific profiling of metastases oriented towards druggable markers, and studies working on metastatic samples are still very scarce due to the lack of clinical material. Last but not least, this project will aim not only to improve understanding of metastatic cascade but also to evaluate the therapeutic potential of the selected markers using both two- (2D) and three-dimensional (3D) culture systems. In particular, 3D system might be worth to be introduced in translational research as it mimics *in vivo* 3D organization of cells and extracellular matrix within tissues and organs in a better way. It is very challenging approach, but if successful, patients-derived prostate cancer organoids might provide preclinical models to perceive precision medicine by drug screening of individual patient sample.

Of note, it is difficult to study during the project all steps of tumor progression, whereas this project will enable work on the unique clinical material covering all those steps and incl. primary tumors, circulating tumor cells and metastases. The collection of prostate cancer samples is already in a large part available for study, whereas samples collection for liquid biopsy has been already initiated and will be continued in order to add bone metastasis samples from local wards.

This project has the chance to improve understanding metastatic cascade in prostate cancer and even improve patients' treatment.