Epithelial-stromal interactions play a key role in prostate carcinogenesis. However, the underlying molecular and cellular mechanisms remain largely unknown. I hypothesize that carcinoma associated fibroblasts (CAFs), one of the most abundant non-malignant cell type in the tumor microenvironment, communicate with neighboring prostate cancer cells via secretion of extracellular vesicles to regulate prostate carcinogenesis.

To investigate the mechanisms of stromal cell-cancer cell interactions in the prostate tumor microenvironment, primary cell cultures of patient-derived prostate stromal cells will be established from prostatectomy samples; cellular heterogeneity of such cultures will be assessed by immunofluorescent stainings and methylation-specific real-time PCR. Then, exosomes will be isolated from human-derived prostatic normal fibroblasts and CAFs. Exosomes will be characterized by western blotting and transmission electron microscopy, followed by deep microRNA profiling. To validate the microRNA profiling data, the impact of differentially expressed selected microRNAs overexpression on cellular proliferation and migration in prostate cancer cells will be investigated.

Overall, the project will provide new insights into mechanisms regulating heterotypic cell-cell interactions in the prostate tumor niche and may result in identification of novel biomarkers of the prostate tumor microenvironment. It is expected that this project will result in a discovery of those exosomal microRNAs, that originate from CAFs. Such a discovery can lead to unravelling whether prostatic CAFs can be a cell of origin of exosomal microRNAs in body fluids of patients with prostate cancer.