The aim of the project is to establish whether and, if so, to what extent gut microbiota metabolites of ellagitannins, urolithins, and flavan-3-ols, 5-(3',4',5'-trihydroxyphenyl)-γ-valerolactone (M4 vaerolactone), may contribute to health effects of polyphenol rich diet or products supplementation in prostate cancer.

The effects of these metabolites and their combinations with drugs used in conventional prostate cancer therapy, an anti-androgen bicalutamide and a chemotherapeutic docetaxel, on prostate cancer cells proliferation and survival will be examined during realization of this project. The prostate cancer cell lines differing in sensitivity to both drugs –LNCaP and DU-145- will be used as *in vitro* models of malignant cells and immortalized PZ-HPV-7 line as model of normal prostate cells. In the first stage of the study, cells proliferation and apoptosis after incubation with tested compounds and combinations will be examined. The results of proliferation studies will be used to determine whether pharmacodynamic interactions exist between gut microbiota metabolites of polyphenols and the drugs and, if so, what type they are (synergistic, additive, antagonistic). The second stage of the project will focus on establishing, whether and how tested compounds and combinations affect pre-selected signalling pathways and molecular targets playing important role and often disrupted in prostate cancer development: androgen receptor, STAT3, Akt kinase and NF-κB signalling and expression of proteins regulating cell survival (Bcl-2, Bax, survivin).

Prostate cancer is one of the most common cancers and cancer death causes in men worldwide. About 30% of prostate cancer patients use supplements, often plant derived, to manage their cancer. Moreover, prostate cancer patients with more advanced disease are significantly more likely to use complementary and alternative medicine (CAM). Among most popular supplements are preparations of pomegranate fruit and green tea polyphenols. Depending on individual patient situation, such interventions may be considered as elements of chemoprevention or complementary therapy. While use of phytotherapeutics is usually safe for general population, it may be not so during pharmacological cancer therapy. Quite a large number of phytochemicals interacts with cancer therapies either diminishing their effectiveness or increasing toxicity. Although *in vivo* studies of pomegranate and green tea preparations in animal prostate cancer models had encouraging results, it is hard to explain these observations as direct effects of pomegranate and green tea polyphenols. These polyphenols are poorly bioavailable after oral administration. In contrast, their gut microbiota metabolites are readily absorbed after formation in intestines and present in biological fluids in concentrations at least several folds higher than their parent compounds. Establishing the role of gut microbiota metabolites in systemic biological effects of orally administered polyphenols will provide useful information about combined effects of gut microbiota and phytotherapeutics and may throw new light on mechanisms of health benefits of polyphenol rich diet/supplements.