

## ABSTRACT

Glutamate carboxypeptidase II (GCPII), also known as prostate-specific membrane antigen (PSMA), is a membrane metallopeptidase overexpressed on most prostate cancer cells. Additionally, GCPII also attracted neurologists' attention because it cleaves neurotransmitter *N*-acetyl-L-aspartyl-L-glutamate (NAAG). Since NAAG exhibits neuroprotective effects, GCPII may participate in a number of brain disorders, which were shown to be ameliorated by GCPII selective inhibitors. Therefore, GCPII has become a promising target for imaging and prostate cancer targeted therapy as well as therapy of neuronal disorders.

Globally, prostate cancer represents the second most prevalent cancer in men. With the age, most men will develop prostate cancer. However, prostate tumors are life threatening only if they escape from the prostate itself and start to spread to other tissues. Therefore, considerable efforts have been made to discover tumors earlier at more curable stages as well as to target aggressive metastatic cancers that have already invaded other tissues and become resistant to the standard treatment. Since patients undergoing a conventional therapy (a combination of chemotherapy and surgery) suffer from severe side effects, more effective ways of treatment are being searched for. Novel approaches include selective targeting of tumor antigens overexpressed on tumor cells. GCPII represents such a target that may be used either for imaging of advanced cancers or as an address for prostate-targeted drug delivery.

The studies presented in the thesis focused on GCPII as a potential diagnostic and therapeutic target as well as development of novel molecular tools for studying physiological and pathological role of GCPII in various tissues. Therefore, we evaluated GCPII potential to become a serum marker of prostate cancer and determined its concentration in the blood plasma among healthy population. Since the development and testing of novel therapeutics and methods require a model organism, we characterized mouse GCPII as mice represent most widely used model animals. Finally, we developed polymer conjugates decorated with GCPII inhibitors that might become a tool for an active drug delivery to cells expressing GCPII. These conjugates might also serve as antibody mimetics enabling selective targeting of desired proteins, their isolation and visualization *in vitro* and *in vivo*. Therefore, this novel chemical-biological tool, called iBodies, also has the application outside of the area of GCPII.