Abstract

Cancer, group of diseases characterized by an uncontrolled cell growth, represents one of the great challenges of modern clinical research. Currently, the standard treatment of the cancer disease relies mainly on the whole body exposition to various factors, which targets the dividing cells, combined with surgical resection of the tumor. Unfortunately, this treatment is sometimes accompanied by numerous severe side-effects (e.g., nausea, loss of hair, infertility etc.). Therefore, in the past 40 years enormous resources and effort have been invested into finding a way how to specifically target and destroy the cancerous cells. This goal has been primarily addressed by the search for molecules, mainly proteins, which are predominantly expressed in the cancerous tissues compared to the healthy cells.

Glutamate carboxypeptidase II (GCPII), also known as prostate specific membrane antigen (PSMA), represents such a target since it is highly expressed in a prostate carcinoma as well as in a solid tumor neovasculature. Additionally, GCPII is widely used as a model target molecule for proof-of-principle studies on targeted drug delivery. GCPII thorough biochemical characterization is essential for its appropriate use. Therefore, our laboratory has been investigating GCPII from various perspectives for more than 15 years.

The studies presented in this thesis aim to introduce new advanced methodologies for GCPII expression, purification and characterization. These methodologies should enable more simple and reliable study of GCPII and facilitate its application as a specific address for targeted drug delivery. In order to achieve this goal, we established a one-step reliable and versatile affinity purification protocol for GCPII. Subsequently, we performed a thorough comparative study characterizing majority of currently used monoclonal antibodies (mAbs) against GCPII in both quantitative and qualitative manner. Finally, we characterized one of the closest GCPII homolog, *N*-acetylated alpha-linked acidic dipeptidase-like (NAALADase L) protein in terms of its tertiary structure, expression profile, and enzymatic activity.