English abstract

Glutamate carboxypeptidase II (GCPII, EC 3.4.17.21) is a type II transmembrane glycoprotein which has been discovered in nervous system as an enzyme responsible for the hydrolysis of neuropeptide N-acetyl-L-aspartyl-L-glutamate to N-acetyl-L-aspartate and L-glutamate and that has been hypothesized to influence glutamatergic signaling processes. Except for brain, GCPII was mainly found in prostate, kidney, and small intestine. In small intestine, GCPII cleaves terminal glutamates from polyglutamylated folates facilitating thus absorption of dietary folates. In prostate, this enzyme is known as prostate-specific membrane antigen and is used as a cancer marker.

Mus musculus is an important model for studing GCPII and its homologs as a therapeutic target. While human GCPII and its paralog GCPIII are relatively well characterized, no biochemical study of their mouse orthologs is available. That is why mouse glutamate carboxypeptidase III (mGCPIII) was cloned, prepared by recombinant expression in insect cells and characterized.

We show that pure mouse GCPIII possesses α-glutamate carboxypeptidase activity which is effectively inhibited by specific inhibitor GCPII, 2-PMPA. We also analyzed sensitivity and specifity of monoclonal antibodies against mouse GCPIII. Immunoblots demonstrate that antibody GCP-04 recognizes human GCPII as well as human GCPIII and mouse GCPIII, but antibody GCP-3-02 recognizes only human GCPIII.

Key words: GCPII, GCPIII, 2-PMPA, glutamate, homologs