Neurocan is a new substrate for the ADAMTS12 metalloprotease: Potential implications in neuropathies

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Background/Aims: The composition of the extracellular matrix (ECM) in the central nervous system (CNS) has several features that make it unique. For instance, it is remarkable for the presence of proteoglycans such as versican, brevican, and neurocan, some of which have been identified as substrates of different members of the ADAMTS family of secreted metalloproteases. Previous studies have associated ADAMTSs with the repair of the CNS, including recovery following degradation of glial scar tissue and the stimulation of axonal growth after brain injury. However, the involvement of ADAMTSs in diseases of the CNS is complex and not understood fully, and a current challenge is unraveling the precise roles of these metalloproteases in the brain. Methods: ADAMTS12 and neurocan gene expression was examined by quantitative PCR. Western blot analysis was employed to detect ADAMTS12 and neurocan protein expression in cell lines, and immunostaining techniques were used to detect neurocan in mouse brain tissues. Neurocan cleavage using recombinant ADAMTS1, ADAMTS4, ADAMTS5, and ADAMTS12 metalloproteases was evaluated by western blotting. Cell adhesion and migration were assessed using uncoated culture dishes or dishes coated with Matrigel or ECM components. Results: We identified neurocan

as a novel component of brain ECM that can be cleaved by ADAMTS12. In addition, we showed that neurocan cleavage by ADAMTS12 altered the adhesive properties of the human neuroglioma H4 cell line. Moreover, immunohistochemical analysis of Adamts12-deficient mice revealed the significant accumulation of neurocan in the brain of neonatal mice. Conclusion: Overall, our results suggest that ADAMTS12 could be involved in the repair of the CNS through its ability to degrade neurocan. Moreover, it can be inferred that alterations in neurocan degradation processes could be associated with the pathogenesis of neurological disorders.

ADAMTS

Extracellular matrix

Metalloprotease

Neurocan

Neurocanase

ADAMTS protein

ADAMTS12 protein

neurocan

unclassified drug

ADAMTS protein

ADAMTS12 protein, human

Adamts12 protein, mouse

lectin

NCAN protein, human

Ncan protein, mouse

nerve protein

proteochondroitin sulfate

proteoglycan

adult

animal cell

animal tissue

Article

bioaccumulation

brain

cell adhesion

controlled study

embryo

extracellular matrix

H4 cell line

human

human cell

immunohistochemistry

mouse

neuropathy

newborn

nonhuman

priority journal

protein cleavage

animal

biosynthesis

cell motion

cranial neuropathy

gene expression regulation

genetics

metabolism

pathology

protein degradation

tumor cell line

ADAMTS Proteins

Animals

Cell Adhesion

Cell Line, Tumor

Cell Movement

Chondroitin Sulfate Proteoglycans

Cranial Nerve Diseases

Gene Expression Regulation

Humans

Lectins, C-Type

Mice

Nerve Tissue Proteins

Proteoglycans

Proteolysis