

TGM6 is a potential biomarker in MS and its expression by reactive astrocytes in the murine spinal cord during EAE correlates with disease course

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INTRODUCTION

Transglutaminase 6 (TGM6) is a member of the transglutaminase enzyme family. It is found predominately in the central nervous system where it is expressed mainly by neuronal cells under physiological conditions. TGM6 has been proposed as the autoimmune target in gluten-sensitive patients with neurological symptoms such as cerebellar ataxia and has been linked to other neurological conditions such as schizophrenia. Its relative transglutaminase 2 is the primary auto-antigen in celiac disease and has been found to exacerbate MOG-induced experimental autoimmune encephalomyelitis (EAE) in mice through positive regulation of T cell differentiation and inflammation.

OBJECTIVE

To investigate the involvement of TGM6 protein and antibodies raised against it in multiple sclerosis (MS) and EAE.

DESIGN AND METHODS

- ELISA to detect TGM6 IgG in CSF and serum of MS patients and control individuals. IHC for TGM6 in postmortem MS brain sections.
- MOG 35-55 EAE in C57BL/6J mice followed by ELISA, WB, IF, and IHC.

RESULTS

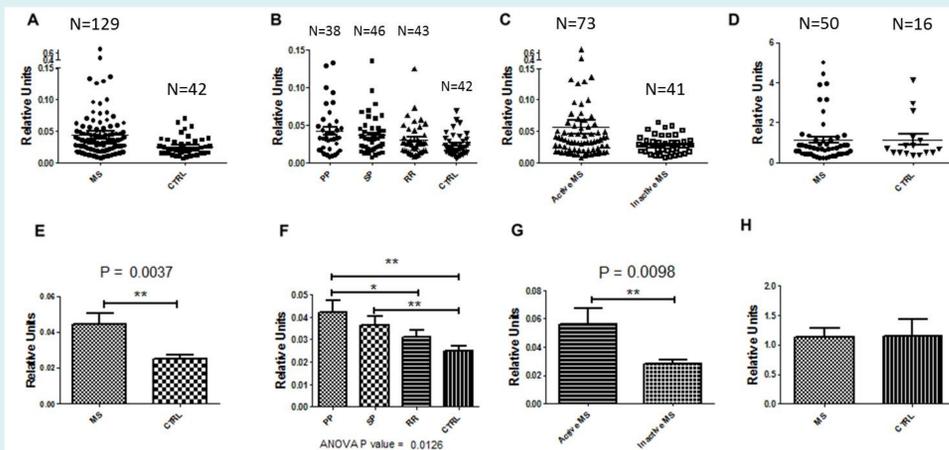


Figure 1. CSF levels of IgG against TGM6 are higher in MS vs. Controls and in active vs. inactive MS
A-C and E-G CSF levels. D and H serum levels.

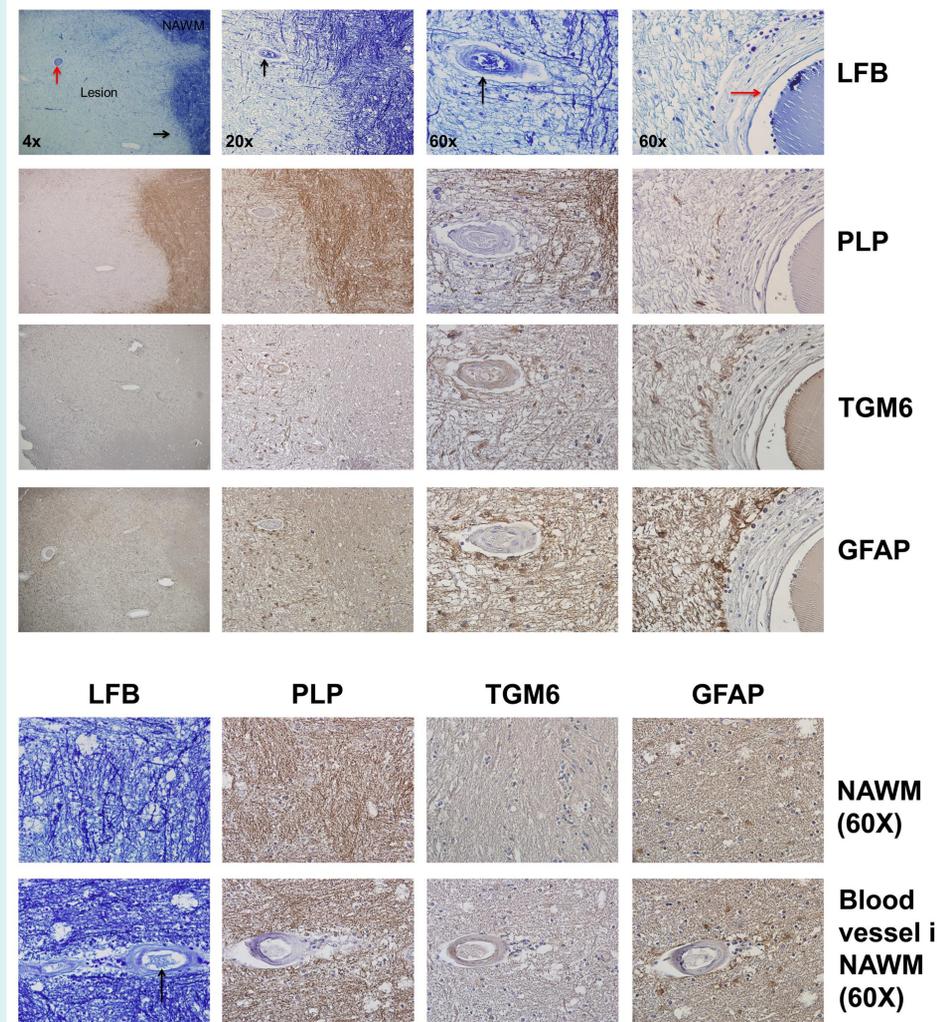


Figure 2. TGM6 is highly expressed in MS plaques
Black arrows = small blood vessels. Red arrow = large blood vessel.
NAWM = normal-appearing white matter.

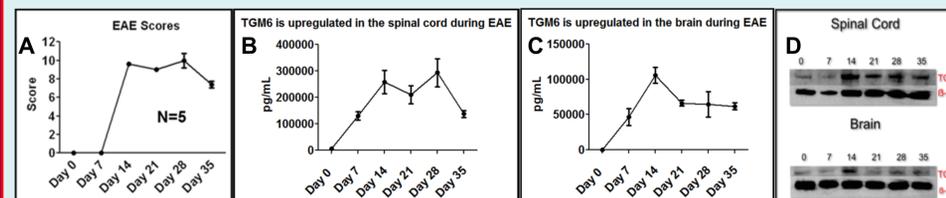


Figure 3. TGM6 is upregulated in mouse CNS during EAE
A EAE score. B-C ELISA for TGM6 during EAE. C western blot for TGM6 during EAE.

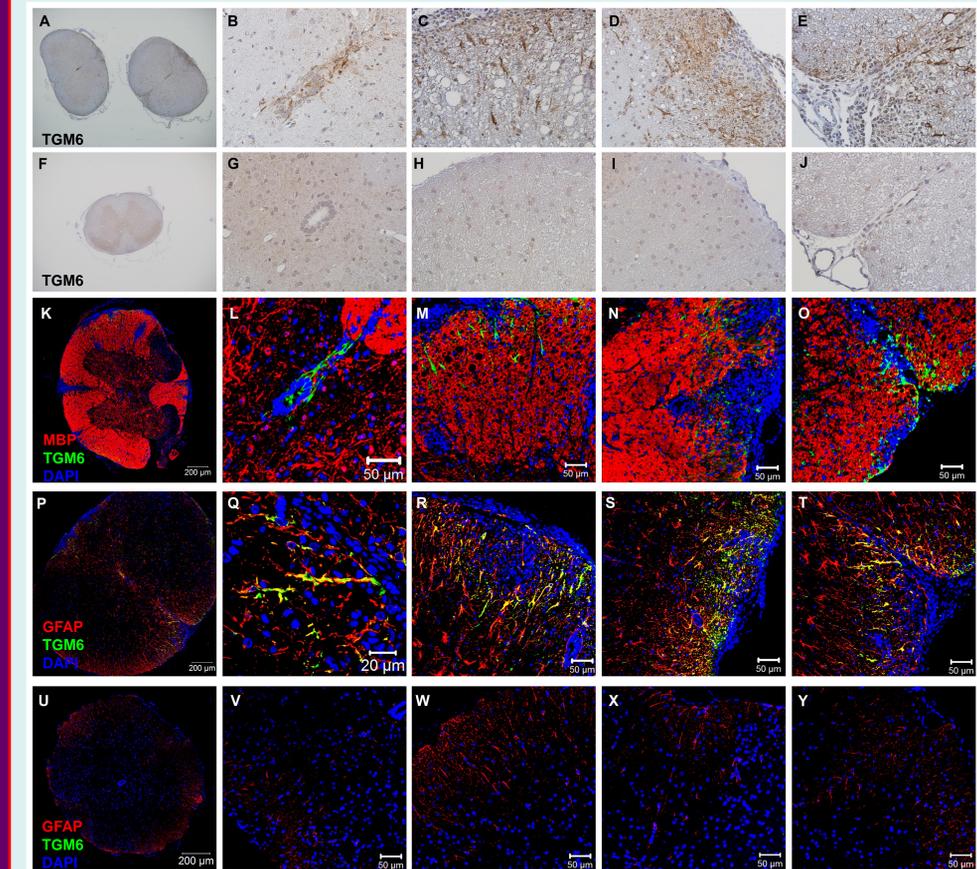


Figure 4. TGM6 is highly expressed by reactive astrocytes infiltrating spinal cord lesion during EAE
A-E, K-O, and P-T spinal cord from day 14 EAE mice. F-J and U-Y spinal cord from naive mice.

CONCLUSIONS

- CSF levels of IgG against TGM6 could be a useful biomarker to differentiate between MS subtypes and to determine disease activity and progression.
- TGM6 is strongly expressed in reactive astrocytes during EAE suggesting a potential role for this protein in the mechanism of glial scar formation in MS.