

Sperm-associated antigen 16 is a novel target of the humoral autoimmune response in MS.

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Research question and background

Using a high-throughput cDNA phage display-based approach, we previously identified eight potential autoantibody targets in the CSF of MS patients. One of the identified targets was sperm-associated Ag 16 (SPAG16) isoform 2, which had never been linked to MS. Two SPAG16 isoforms exist: isoform 1 (SPAG16-1; 71 kDa) and isoform 2 (SPAG16-2; 20.4-kDa). In sperm cells SPAG16-1 is part of the axoneme and plays a role in sperm motility. The function of SPAG16-2 is unknown. In the current study, we further investigated SPAG16 - a protein with unknown function in the central nervous system - in MS pathology

Methods and tissues used

SPAG16 expression was determined in brain tissue of 7 MS patients and 5 non-demented controls (both plaque tissue and normal appearing white matter). In addition, SPAG16 expressing cells were identified in these tissues.

Results and conclusion

Immunohistochemical analysis showed low SPAG16 expression levels in the white matter of control brains and in neurons in the gray matter. In MS lesions, SPAG16 was upregulated compared with normal appearing white matter of MS patients and normal white and gray matter in controls. Most intense staining was demonstrated in astrocytes in the center of active lesions. At the lesion edge, SPAG16 expression was still detectable in astrocytes but less intense. Double-staining for SPAG16 and glial fibrillary acidic protein (GFAP) confirmed SPAG16 expression in astrocytes.

Additional experiments revealed that SPAG16-specific oligoclonal bands were present in 22% MS patients' cerebrospinal fluid. Further, significantly elevated anti-SPAG16 antibody levels were found in 21% MS patients with 95% specificity. The pathologic relevance of anti-SPAG16 antibodies was underlined by disease exacerbation in EAE mice injected with the antibodies. Together, these results indicate that SPAG16 is a novel autoantibody target in a subgroup of MS patients with pathologic relevance.