Characterization of Humane Autoantibody Response to Brain Proteins in Multiple Sclerosis Patients

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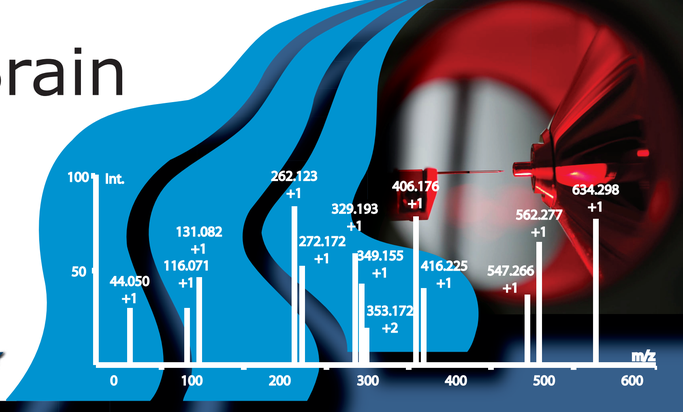

Introduction

Multiple sclerosis (MS) is a neurodegenerative disease, where chronic inflammation plays a central role in the pathology. MS has been described as an autoimmune disease due to the nature of inflammation, which has shown similarities to other autoimmune diseases such as rheumatoid arthritis. A key shared feature present in MS is the induction of autoantibodies stimulated by altered peptide ligand responses and progression by epitope spreading causing loss of tolerance for native peptides. In numerous studies, the idea concerning involvement of autoantibodies in pathogenesis have been suggested to initiate and drive the inflammatory progression in autoimmune diseases, however the etiology is not fully understood. In this pilot study, we test a novel method for annotation of potential autoantigens, which could be relevant for diagnostic and prognostic discovery.

AIM

Test the usabilityof antibodies from Multiple Sclerosis patient's serum and cerebrospinal fluid (CSF) to immunoprecipitate potential autoantigens for epitope pattern annotation and biomaker discovery.

Conclusion

This pilot study using antibodies from MS patient sera and CSF to immunoprecipitate potential autoantigens revealed brain related proteins indicating autoantibody reactivity.

Perspectivation

In future experiments we will collect serum and CSF from a large population of specific MS disease stages and compare these to healthy control and in-between the different disease groups.

Potentially this could reveal both diagnostic and prognostic biomakers. These could not only explain the biological difference between disease stages, but also lead to discovery of new drug targets.

Methods

Oligoclonal bands, which reflect presence of antibodies, have been identified and correlated with disease progression in MS patients. However, previously studies have not been able to identify the antigens recognized by the autoantibodies.
We have observed autoantibody responses in diseased animals in both rat experimental autoimmune encephalomyelitis models of MS. In addition, potential autoantigens recognized by the autoantibodies were identified utilizing mass spectrometry based proteomics. Based on these observations in animal models we now analyzed serum and CSF of patients suffering from relapsing-remitting and secondary progressive MS using immunoprecipitation of brain proteins recognized by these antibodies. Thereby, we mapped potential antibody response in human MS patients against human brain proteins using proteomics.

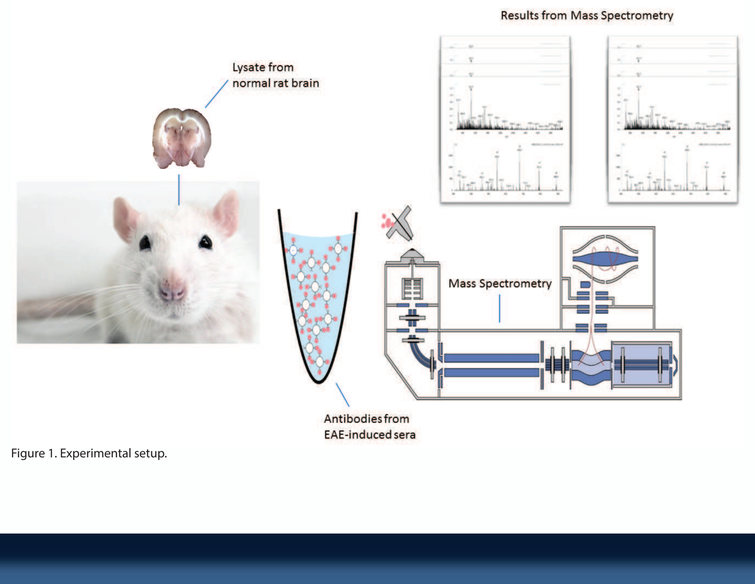

Figure 1. Experimental setup.

Results and Discussion

The results showed 11 proteins in total, which were targeted by autoantibodies in the MS patients.

Figure 2. Venn Diagram showing the similarities between potential autoantigens involved in MS targeted by autoantibodies in plasma and CSF.

Potential Autoantigenic Proteins
Apolipoprotein A-I
Complement component 1, q subcomponent, C chain, isoform CRA_a
Complement C1q subcomponent subunit B
Complement component 1, q subcomponent, A chain, isoform CRA_a
Transthyretin
cDNA FLJ37971 fis, clone CTONG2009958, highly similar to CERULOPLASMIN
Tubulin alpha chain
cDNA FLJ50830, highly similar to Serum albumin
cDNA FLJ58286, highly similar to Actin, cytoplasmic 2
Full-length cDNA clone CS0DD006YL02 of Neuroblastoma of Homo sapiens

Tabel 1. Potential autoantigens targeted by autoantibodies.

All 11 proteins were identified in plasma, and 7 of them were also identified in CSF.

Poster

Acknowledgements

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