

EBV and *Mycobacterium avium subsp. paratuberculosis* peptides induce a diffuse immune response against myelin basic protein and human interferon regulatory factor 5 in MS patients.

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Background. *Mycobacterium avium subsp. paratuberculosis* (MAP) and Epstein-Barr virus (EBV) epitopes elicit a humoral response in MS patient's serum. The cross-reactivity against the homologous myelin basic protein (MBP) and human interferon regulatory factor 5 (IRF5) epitopes has not been examined within the Cerebral Spinal Fluid (CSF).

Materials and methods. We evaluated in serum and CSF of patients with MS and with other neurological diseases (OND), the humoral response against peptides derived from: EBV antigens BOLF1 and EBNA1; MAP antigens MAP 4027 and MAP 0106c; the human homologous from IRF5 and MBP. Relapses at sample collection time were recorded in MS group. Statistical analysis was performed using GraphPad Prism 6.0 software (San Diego, CA, USA). To compare the categories in the univariate analysis was used the Mann-Whitney U test. The diagnostic value of the indirect ELISA assays was evaluated by the receiver operating characteristic (ROC) curve. The optimal cut off values were chosen according to ROC analysis, setting specificity at 90 % (i.e., Ab + HCs 0.5 %) for the MS patients.

Results. Forty-three MS and 33 OND patients were included. The study of antigens in serum and CSF of MS and OND showed a significant frequency in MS group of: EBNA1, BOLF1, MAP 0106c, MAP 4027, IRF5. Moreover, analyzing together the homologous antigens, we found significant results for BOLF/IRF5, MAP 4027/IRF5, BOLF1/MAP 4027/IRF5. See table 1 for the details.

Table 1

Peptides	MS serum/CSF pos	OND serum/CSF neg	p value
EBNA1	33%	9%	0.025
BOLF1	37%	9%	0.007
MAP 0106c	37%	15%	0.04
MAP 4027	30%	3%	0.0024
MBP	26%	15%	0.39
IRF5	30%	6%	0.001
EBNA1/MBP	20%	9%	0.33
BOLF1/IRF5	28%	3%	0.001
MAP 0106c/MBP	19%	12%	0.53
MAP 4027/IRF5	23%	3%	0.02
EBNA1/MAP 0106c/MBP	14%	9%	0.7
BOLF1/MAP 4027/IRF5	21%	0%	0.0042

We showed in the table 2 the expression of the peptides in CSF of MS patients in relation to relapses.

Table 2

Peptides	MS with relapse	MS without relapse	p value
MBP	57%	15%	0.01
EBNA1/MBP	43%	15%	0.05
MAP0106/MBP	43%	10%	0.02

Discussion and conclusions. Our data showed that the humoral response against EBV, MAP, MBP and IRF5 was significantly higher in MS patients compared to OND both in serum and in CSF. We found a significant intrathecal immune response against MBP and their EBV and MAP homologous in patients with relapse. Our findings support the role of EBV and MAP in MS and their cross-reactivity with MBP and IRF5 in CSF too. Moreover, the higher presence of MBP and their MAP and EBV homologous in CSF during relapses suggests a role of the pathogens in enhancing inflammation. On the other hand, the great inflammation in relapses could promote general antibodies production, also against MAP and EBV.

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References:

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