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MOLECULAR BIOMARKERS AS A PROGNOSTIC TOOL FOR CLINICAL COURSES OF EXPERIMENTAL AUTOIMMUNE ENCEPHALOMYELITIS IN RATS IMMUNIZED WITH SPINAL CORD HOMOGENATE

Goran Stegnjaić,[1] Milica Lazarević,[1] Bojan Jevtić,[1] Suzana Stanisavljević,[1] Neda Nikolovski,[1] Miljana Momčilović,[1] Marija Mostarica Stojković,[2] Đorđe Miljković,[1] Mirjana Dimitrijević[1]

[1]Institute for Biological Research "Siniša Stanković" - National Institute of Republic of Serbia, University of Belgrade, Belgrade, Serbia; [2]Institute of Microbiology and Immunology, School of Medicine, University of Belgrade, Belgrade, Serbia

Introduction: Experimental autoimmune encephalomyelitis (EAE) in inbred rodents commonly shows different clinical courses, so that the diseased animals can be clustered into four groups: mild, moderate, severe, and lethal. Our aim was to determine biomolecular markers in the preclinical phase of EAE that allow the prediction of clinical course.

Methods: Female Dark Agouti rats were immunized with spinal cord homogenate without adjuvant and examined for four weeks for clinical signs of EAE. Cells and sera from blood collected on days 0, 3, and 7 after immunization were processed for detection of proinflammatory cytokines (IL-1, IL-6, TNF-α, and IFN-γ) by "real-time" RT-PCR and ELISA, respectively.

Results: Induction of EAE resulted in the downregulation of *ifng* and *tnfa* in the preclinical phase of disease, whereas *il1* and *il6* expression levels were unaffected. However, there was no correlation between the relative expression of *ifng* or *tnfa* and the cumulative clinical score (sum of daily clinical scores), suggesting that they are not predictive markers of EAE severity. Our preliminary results that suggest a negative correlation between *il1* expression level before EAE induction and cumulative score require further justification.

Conclusion: The proinflammatory cytokines investigated so far in our study cannot be considered as good biomarkers of EAE severity. However, the downregulation of *ifng* and *tnfa* in the blood cells during the asymptomatic phase of EAE suggests that they enter the central nervous system early from the bloodstream, which argues for the study of chemokine and/or chemokine receptors expression as potential biomarkers for the clinical courses of EAE.

Keywords: biomarkers; cytokines; experimental autoimmune encephalomyelitis; multiple sclerosis; neuroinflammation

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