

Effects of Interferon-beta Therapy on Proteasome Gene Expression Levels in Patients with Multiple Sclerosis

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Abstract: Multiple sclerosis (MS) affects around 2.3 million patients worldwide. It is a neurodegenerative and autoimmune inflammatory disease that damages central nervous system, causes breakdown of insulating layer of nerve fibers – myelin – and eventually leads to neurological disabilities. Ubiquitin-proteasome system (UPS) is responsible for degradation of intracellular proteins and it is one of the key factors in regulation of the immune system. Accumulation of toxic protein aggregates can be observed in MS patients, indicating dysfunction of UPS. Interferon β (IFN β) is the first class of disease modifying therapies for MS. As a member of a family of cytokines it possesses immunomodulatory properties and it is associated with beneficial health effects in MS patients. The aim of the current study was to investigate association of IFN β therapy with expression levels of several proteasomal genes in patients with MS. Peripheral blood samples were acquired from 54 MS patients treated with IFN β therapy, 44 MS patients without the treatment (NT) and 17 control individuals. Isolation of RNA was followed by synthesis of cDNA. PSMA3, PSMA6, PSMA7 and PSMC6 gene expression levels were analysed with qPCR. The expression levels of all four genes were not changed between NT and the control groups. IFN β therapy showed tendency to increase the expression of PSMA3, PSMA6 and PSMA7 genes compared both to the control and NT groups, reaching statistical significance in case of PSMA6 gene ($p=2.14 \times 10^{-2}$ vs. control and $p=3.65 \times 10^{-2}$ vs. NT). Expression of PSMC6 gene did not differ significantly among groups. Results suggest that IFN β therapy increases transcription of genes of 20S proteasome α type subunits. This might indicate stimulation of proteasome de novo synthesis and it is in accordance with data of increased proteasome concentration after IFN β therapy and improved clinical course of MS

Keywords: autoimmune disease, mRNA, peripheral blood, ubiquitin-proteasome system

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