EXPRESSION OF THE GSK3β, BDNF, ENO2, AND HDAC6 GENES IN PATIENTS WITH MACHADO-JOSEPH DISEASE

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Machado-Joseph disease/spinocerebellar ataxia type 3 (MJD/SCA3) is an autosomal dominant genetic disease caused by CAG expansions in the ATXN3 gene. MJD/SCA3 is characterized by neurodegeneration with progressive gait ataxia and additional neurological signs. Although the ATXN3 gene is the main contributor of age of onset (AO) and severity of symptoms, other genes can interfere. The aim of this study was to evaluate whether expression of GSK3β, BDNF, ENO2, and HDAC6 genes can be associated with phenotype in MJD/SCA3 patients. The sample consisted of MJD/SCA3 patients (n=63) of both genders and different CAG expansions length (patient group) and healthy volunteers (n=8) (control group). Total RNA was extracted from leukocytes using LeukoLOCK® kit, mRNA was converted to cDNA, and relative quantification of expression of GSK3β, BDNF, ENO2, and HDAC6 genes was performed. Those genes were selected due to previously published data to be associated to other neurodegenerative diseases. Analysis of the patient group showed no statistically significant difference in the expression of any of the four genes evaluated when compared to controls (p>0.05; median test for independent samples) and no correlation with the expanded CAG allele or AO. Analysis of patients’ groups according to AO of symptoms (early, middle, and late onset) did not reveal differences in patterns of expression (p>0.05; median test independent samples). Results of this study indicate, however, that majority of the outliers patients in the curve may be identified by this approach, when analyzed individually. This study demonstrated no effect of disease into expression levels of GSK3β, BDNF, ENO2, and HDAC6 genes in MJD/SCA3 in peripheral material. We cannot rule out variation in neuronal cells. This approach has never been used before in this group of patient and it will be a guide for further studies.

Key-words: Machado-Joseph disease, Biomarkers, gene expression

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