Immune activation in Fragile X Mental Retardation 1 (FMR1) premutation carriers: Levels of IL-10 as a prognostic marker for Fragile X-associated Tremor/Ataxia Syndrome (FXTAS) progression


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ABSTRACT

Fragile X-associated Tremor/Ataxia Syndrome (FXTAS) is an inherited late onset neurodegenerative disorder, caused by premutation expansions (CGG repeats ranging from 55 to 200) in the non-coding region of the Fragile X mental retardation 1 (FMR1) gene. It is characterized by both neurological and systemic abnormalities.

We investigated the immune status of FXTAS patients, not assessed prior to this study, since abnormal immunological patterns are often associated with neurodegenerative disorders and implicated in their etiology. Peripheral blood mononuclear cells (PBMC) were collected from 15 FMR1 premutation carriers and 20 age-matched control individuals. Concentrations of three immune molecules (IL-6, IL-8, IL-10) were measured in PBMC supernatants with classical ELISA and multiplex assays.

We found a significant increase in the concentration of the major anti-inflammatory cytokine interleukin-10 (IL-10) in supernatants of PBMC derived from premutation carriers when compared to controls (p-value= 0.019). This increase correlated significantly with the number of CGG repeats (p-value = 0.002) and it was observed in all premutation carriers, even before appearance of disease symptoms. Therefore, IL-10 may be the first biomarker to follow the onset and progression of FXTAS.

Keywords: Fragile X mental retardation 1 (FMR1) gene, Fragile X-associated Tremor Ataxia Syndrome (FXTAS), immune activation, cytokines, interleukin-10.