ABSTRACT

The Huntington disease (HD) is a hereditary neuro-degenerative disorder caused by a mutation of the huntigtin gene that codes a protein of the same name. The mutated form of the huntigtin gene plays its part in many pathological interactions and influences a number of cellular mechanisms, including the immune system that could serve as a modifier of the neuropathology of the disease. The cells of the monocyte-macrophage system express cytokines whose production changes in relation to the activation of the cell. The presence of the mutated huntingtin protein in these cells renders them hyper-responsive to immunity incentives leading to changes in the production of cytokines. These differences are discernible a few years prior to the appearance of the symptoms. Therefore, the changes in the levels of certain cytokines could serve as appropriate biomarkers for monitoring of the onset of the disease and its progression.

The HD pathogenesis includes an inflammation of the central neutral system. Inflammatory changes in peripheral tissues could reflect inflammatory processes in the central neural system. A miniature TgHD pig could represent an appropriate model organism for studying of the impact of the mHtt on the immune system. This model enables to observe a slow progression of the disease. Changes in the production of cytokines in the cerebrospinal fluid and of microglia secretome have been detected in miniature pigs. Given the difficulty of isolation of these body samples, a question should be asked whether inflammatory processes found in the central neural system of these miniature pigs will correspond to those in the periphery with regard to the less invasive isolation of peripheral tissues and fluids.

Using the high-sensitive quantitative proteomic analysis Luminex xMAP, we have detected several changes in the production of cytokines (especially IL-1β, TNFα, IL-4, IFNα) in peripheral tissues. These cytokines could be used as promising HD biomarkers. At the moment, there is no cure for the disease. Available treatment focuses solely on the symptoms of the disease. A detailed characterization of transgenic HD miniature pigs is necessary in order to find an appropriate therapeutic approach and prospective treatment of the Huntington disease.

Key words:

Huntington´s disease, huntingtin, monocytes, macrophages, cytokines