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MIF and HTRA1 – new potential biomarkers for MS?

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Multiple sclerosis (MS) is the most common chronic inflammatory disorder of the CNS and affects 2.5 million people worldwide. The pathogenesis of MS remains poorly understood and the clinical representation very heterogeneous. The current diagnostic tools are therefore far from ideal and there has been great efforts to identify new biomarkers for MS.

One of the proteins that recently has been suggested as a biomarker for MS is Macrophage Migration Inhibitory Factor (MIF). MIF has been identified as an important regulator of inflammatory responses and have been extensively studied in immune system. In the CNS, MIF has been identified in most cells and several studies suggests that MIF can regulate inflammatory responses in both astrocytes and microglia, including modulating the expression of pro-inflammatory cytokines. However, the exact function of MIF in the adult brain is not clear. It has been implicated in several neurological diseases, including Alzheimer’s, Parkinson disease, and MS.

We have recently found a new binding partner to MIF; High Temperature Requirement Serine Protease A1 (HTRA1). It belongs to the trypsin-like serine protease family and carries out both extra- and intracellular functions. Within the cells HTRA1 co-localizes with microtubules and controls both proliferation and migration of several cell types. In the extracellular space HTRA1 digest ECM, as well as proteins belonging to the TGFβ, FGF, Wnt and Notch family, thereby regulating several signaling pathways.

In this study, we show that the level of MIF in CSF from RRMS patients is significantly reduced compared to CSF control levels, while the levels of MIF in CSF from patients diagnosed with SPMS is similar to that seen in CSF from healthy controls. We also show that the levels of MIF are unaffected by treatment in both patient groups (Tecfidera or Mitoxatrone). We further, demonstrate that the CSF levels of HTRA1 is significantly increased in CSF from both RRMS and SPMS and that HTRA1 levels in CSF from RRMS return to levels comparable to that seen in healthy controls after treatment with Tecfidera.