The serine protease HTRA1 increases in the brain and CSF in Multiple Sclerosis

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**Title:** The serine protease HTRA1 increases in the brain and CSF in Multiple Sclerosis


**Hypotese:** High Temperature Requirement Serine Protease A1 (HTRA1) is an enzyme involved in extracellular matrix (ECM) degradation, proliferation, migration and phagocytosis. HTRA1 is present in the central nervous system (CNS), where it has been suggested to support neural outgrowth and astrocyte development while modulating the immune system. HTRA1 has been implicated in CNS diseases, such as the small vessel disease CARASIL and Alzheimer’s disease. We hypothesized that HTRA1 may be implicated in MS.

**Metoder:** The HTRA1 levels were investigated in spinal fluid from patients with relapsing remitting (RRMS) and secondary progressive MS (SPMS) using ELISA before and after treatment. The cellular distribution of the protein was also studied in the human brain by immunohistochemistry. The tSNE expression of HTRA1 was investigated in the oligointernode database (https://ki.se/en/mbb/oligointernode).

**Resultater:** We found that HTRA1 is expressed in several different cell types in the human brain, and the cellular distribution and expression was increased in the MS. The CSF levels of HTRA1 was also increased in patients with MS. In RRMS, HTRA1 was significantly elevated compared to healthy controls and increased further with disease progression. Treatment of both subtypes of MS patients significantly decreased the HTRA1 levels, though the effect were more pronounced in the Tecfidera treated RRMS patients.

**Diskussion:** We suggest that HTRA1 may be a good diagnostic marker for MS. The reason for the elevated levels of HTRA1 in CSF are still unknown but HTRA1 may be connected to both the immune system response, ECM breakdown and remyelination in MS.