PLASMA TDP-43 LEVEL AS PUTATIVE BIOMARKER FOR INCLUSION BODY MYOSITIS AND AMYOTROPHIC LATERAL SCLEROSIS

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Introduction: In 2006, TDP-43 was identified as a major component of inclusions in the brain of patients with frontotemporal lobar degeneration with ubiquitin-positive inclusions (FTLD-U) and amyotrophic lateral sclerosis (ALS). Since then, several disorders were identified with TDP-43-positive inclusions, including Alzheimer's disease (AD) and the inflammatory myopathy inclusion body myositis (IBM).

Aims: To develop a sensitive ELISA to quantify TDP-43 in body fluids, and to investigate whether TDP-43 can function as a biomarker to diagnose disorders with TDP-43-positive protein inclusions.

Methods: We developed a sandwich ELISA to quantify TDP-43, and used this assay to measure TDP-43 levels in plasma of 1) patients with IBM and other inflammatory myopathies, 2) patients with ALS and 3) healthy controls.

Results: TDP-43 levels were significantly increased in patients with IBM, but also in patients with other inflammatory myopathies. TDP-43 levels were non-significantly increased in patients with ALS, with a trend towards increased TDP-43 levels in patients with shorter disease duration versus patients with a longer disease duration ($p=0.068$).

Conclusions: Plasma TDP-43 levels do not serve as a diagnostic biomarker for IBM or ALS. Future research should include the measurement of phosphorylated TDP-43 (for IBM and ALS), and measurement of TDP-43 in the cerebrospinal fluid (for ALS). A biomarker assay for phosphorylated TDP-43 may aid in the diagnosis of diseases with TDP-43-containing protein aggregates, like ALS and IBM, but also AD and FTLD-U.