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Cerebrospinal Fluid Proteomics Reveals Biomarkers of Response to Anti-Nogo-A Antibody Treatment in Spinal Cord Injury Patients

Spinal cord injury (SCI) is a debilitating neurological condition resulting in partial or complete loss of motor and sensory function. Its complex pathophysiology, involving both immediate mechanical damage and secondary degenerative processes, presents major challenges for treatment. Among neuroregenerative approaches, anti-Nogo-A antibody (NG101) therapy promotes axonal regeneration and has shown promise in enhancing motor outcomes. However, clinical responses remain highly variable, emphasizing the need for biomarkers to predict treatment efficacy and support patient stratification.

To address this, we performed a large-scale, untargeted proteomic analysis of cerebrospinal fluid (CSF) samples from 133 individuals enrolled in a clinical trial: 74 SCI patients treated with NG101, 44 receiving placebo, and 15 healthy controls. CSF was collected pre-treatment and at one and three months post-treatment. Upper Extremity Motor Scores (UEMS) were used to monitor recovery. SCI induced substantial changes in the CSF proteome, involving immune response pathways and processes related to neurogenesis and axonal development. Longitudinal analysis showed largely overlapping protein expression changes in both treated and placebo groups, enriched in cytoskeletal protein binding. Notably, immunoglobulin complex components increased over time, reversing their initial downregulation post-injury.

Despite shared molecular trajectories, proteins associated with motor recovery differed significantly between groups. Using machine learning, we identified a panel of protein biomarkers capable of predicting treatment response and improving current clinical models. This study, the first comprehensive proteomic analysis of both NG101 and placebo-treated patients, provides novel insights into mechanisms of spontaneous versus treatment-mediated recovery and offers a foundation for biomarker-guided therapeutic strategies.

Research type

Clinical research

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