

# **Biomarkers in Blood and Cerebrospinal Fluid for Monitoring and Differentiating Demyelinating Inflammatory Central Nervous System Disorders**

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentlig försvaras i lokal Förmaket, Sahlgrenska Universitetssjukhuset, Blå stråket 5, Göteborg, den 24 april 2026, klockan 9.00

av Magnus Johnsson

Fakultetsopponent:

Professor Trygve Holmøy

Oslo Universitet, Norge

## **Avhandlingen baseras på följande delarbeten**

- I. Johnsson M, Farman HH, Blennow K, Zetterberg H, Malmeström C, Axelsson M and Lycke J. *No increase of serum neurofilament light in relapsing-remitting multiple sclerosis patients switching from standard to extended-interval dosing of natalizumab*. Mult Scler 2022 Vol. 28 Issue 13 Pages 2070-2080
- II. Johnsson M\*, Stenberg YT\*, Farman HH, Blennow K, Zetterberg H, Malmeström C, Sandgren S, Rosenstein I, Lycke J, Axelsson M and Novakova L. *Serum neurofilament light for detecting disease activity in individual patients in multiple sclerosis: A 48-week prospective single-center study*. Mult Scler 2024 Vol. 30 Issue 6 Pages 664-673 \* Shared first authorship
- III. Johnsson M, Eriksson K, Rosenstein I, Novakova L, Malmeström C, Lycke J, Sandgren S, Zetterberg H, Blennow K, Johansson K, Axelsson M. *The value of CSF diagnostic and prognostic biomarkers in NMOSD and MOGAD in real-life use*. Mult Scler Relat Disord 2025 Vol. 94:106302
- IV. Johnsson M\*, Meda FJ\*, Lycke J, Novakova L, Rosenstein I, Johansson K, Malmeström C, Zetterberg H, Kvartsberg H, Axelsson M. *Cerebrospinal fluid alpha-internexin is increased in patients with multiple sclerosis and correlates strongly with neurofilament light protein*. Mult Scler Relat Disord. 2025 Dec;104:106805. \* Shared first authorship
- V. Johnsson M, Lycke J, Novakova L, Rosenstein I, Hafsteinsdottir B, Malmeström C, Axelsson M. *Calprotectin Reveals Distinct Innate Immune Signatures in NMOSD, MOGAD, and Multiple Sclerosis*. 2026 Jan Manuscript – Submitted.

# Biomarkers in Blood and Cerebrospinal Fluid for Monitoring and Differentiating Demyelinating Inflammatory Central Nervous System Disorders

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## Abstract

Inflammatory demyelinating disorders of the central nervous system (CNS) are characterized by immune-mediated myelin injury and neuroaxonal damage. This thesis focused on multiple sclerosis (MS), neuromyelitis optica spectrum disorder (NMOSD), and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), which share clinical features but differ in immunopathology, prognosis, and treatment response. The aim was to evaluate soluble cerebrospinal fluid (CSF) and serum biomarkers reflecting neuroaxonal and astrocytic injury, blood-brain barrier dysfunction, and innate immune activation across these disorders.

The first two studies investigated serum neurofilament light (sNfL) concentrations in patients with relapsing-remitting MS (RRMS). In a prospective cohort (**Paper I**) of clinically stable patients switching from standard to extended-interval natalizumab dosing (n = 45), sNfL concentrations remained stable over 12 months, supporting maintained therapeutic efficacy without evidence of increased axonal injury. In a second prospective study (**Paper II**) including patients with active disease (n = 44), repeated sNfL measurements demonstrated moderate sensitivity and specificity for detecting inflammatory disease activity at the individual level, supporting its role as a complementary monitoring tool. In **Paper III**, soluble biomarker data from patients with NMOSD and MOGAD were retrospectively retrieved from medical records. CSF glial fibrillary acidic protein (GFAP), particularly when combined with albumin quotient, robustly discriminated AQP4-IgG-positive NMOSD from the combined MS, seronegative NMOSD, and MOGAD groups. In **Paper IV**, a newly developed method for quantifying the intermediate filament protein alpha-internexin in CSF was applied, demonstrating elevated concentrations in MS and a strong correlation with NfL, supporting its role as a marker of axonal injury. In **Paper V**, elevated serum calprotectin distinguished NMOSD and MOGAD from RRMS, indicating distinct patterns of innate immune activation across these disorders.

In conclusion, biomarker profiles differ across inflammatory demyelinating disorders and reflect disease-specific pathobiology. Integrated biomarker assessment may improve diagnostic precision and individualized monitoring of disease activity.

**Keywords:** multiple sclerosis, neuromyelitis optica spectrum disorder, MOGAD, neurofilament light, calprotectin, alpha-internexin

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