



DAREMUS

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Navn Maia Møllgaard **Institution** RH Glostrup **Alder** 30år (hvis deltagelse i konkurrence)

Cerebrospinal fluid chitinase-3-like 2 and chitotriosidase are potential prognostic biomarkers in early multiple sclerosis

M. Møllgaard¹, M. Degn^{1,2}, F. Sellebjerg³, J. L. Frederiksen¹ and S. Modvig^{1,4}

¹MS Clinic, Department of Neurology, Rigshospitalet Glostrup, Copenhagen; ²Department of Diagnostics, Rigshospitalet Glostrup, Copenhagen;

³Danish MS Research Centre, Department of Neurology, Rigshospitalet, Copenhagen; and ⁴Department of Clinical Immunology, Rigshospitalet, Copenhagen, Denmark

Purpose: The role of chitinases and chitinase-like proteins in multiple sclerosis (MS) is currently unknown; however, cerebrospinal fluid (CSF) levels of chitinase 3-like 1 (CHI3L1) predict prognosis in early MS. Whether this applies to other chitinases and chitinase-like proteins is yet to be established. Our objective was to investigate the potential of chitinase 3-like 2 (CHI3L2) and chitotriosidase as prognostic biomarkers in optic neuritis (ON) as the first demyelinating episode and to evaluate the ability of CHI3L2 to predict long-term MS risk and disability.

Methods: In a prospective cohort of 73 patients with ON as a first demyelinating episode and 26 age-matched healthy controls levels of CHI3L2 and chitotriosidase in CSF were explored by enzyme-linked immunosorbent assay. Associations with magnetic resonance imaging white matter lesions, CSF oligoclonal bands, immunoglobulin G index and leukocyte count were investigated. Long-term MS risk and disability (Expanded Disability Status Scale, Multiple Sclerosis Functional Composite components) were examined in a retrospective cohort of 78 patients with ON as the first demyelinating episode (mean follow-up 14 years). The predictive ability of CHI3L2 was compared with CHI3L1.

Results: Cerebrospinal fluid levels of CHI3L2 and chitotriosidase were significantly elevated in patients with ON and were associated with MS risk measures. CHI3L2 levels predicted MS development after ON (hazard ratio 1.95, $P = 0.00039$, Cox regression) and cognitive impairment by the Paced Auditory Serial Addition Test ($P = 0.0357$, linear regression) at follow-up. In a multivariate analysis of MS risk, CHI3L2 performed better than CHI3L1.

Conclusions: CHI3L2 and chitotriosidase are promising biomarkers in patients with a first demyelinating episode. Our findings thus support a role for these proteins as biomarkers in early MS.