Quanterix™
The Science of Precision Health

Simoa® Nf-L
Neurofilament light

What is Nf-L?

Neurofilament light (Nf-L) is a 68 kDa cytoskeletal intermediate filament protein that is expressed in neurons. It associates with the 125 kDa Neurofilament medium (NfM) and the 200 kDa Neurofilament heavy (NfH) to form neurofilaments.

Neurofilaments are major components of the neuronal cytoskeleton, and are believed to function primarily to provide structural support for the axon and to regulate axon diameter.
Neurofilaments are released into the extracellular space and further into the cerebrospinal fluid (CSF) and blood following neuro-axonal damage or neuronal degeneration. CSF and blood Nf-L has been shown to be increased in people with traumatic brain injury (TBi), multiple sclerosis, frontotemporal dementia, amyotrophic lateral sclerosis and other neurodegenerative diseases.

How to Measure Nf-L?

The Simoa● NF-light™ assay is a digital immunoassay for the quantitative determination of Nf-L in serum, plasma and CSF. The antibodies (Uman Diagnostics, Umeå Sweden) also cross react with murine, bovine, and macaque Nf-L epitopes, and the assay can be used for research with these species.

What is the Simoa Difference?

Simoa is a powerful new technique that is up to 1000 times more sensitive than standard sandwich-based immunoassay techniques. Traditional ELISA measurements are limited to pg/ml levels of detection. Quanterix can achieve sensitivity as low as femtogram (fg/ml) levels, allowing the detection and quantification of biomarkers at concentrations previously difficult or impossible to measure.

Simoa is based upon the isolation of individual immunocomplexes on paramagnetic beads using standard ELISA reagents. The main difference between Simoa and conventional immunoassays lies in the ability to trap single molecules in femtoliter-sized wells, allowing for a "digital" readout of each individual bead to determine if it is bound to the target analyte or not

Neurological conditions, from TBIs to Alzheimer's disease, continue to be among the greatest health mysteries of our time. Unlike "visible" illnesses, brain injury and neurodegeneration can be overlooked or mistaken for other conditions. The subtlety of symptoms and subjective nature of today's assessments also make it difficult to identify these diseases early. There are still no definitive tests for early detection of conditions like Alzheimer's disease or Parkinson's disease. Doctors can only conclusively diagnose them once symptoms start to present. As a result, many patients may wait years for a diagnosis or clear treatment pathway.

Biomarkers, like neurofilament light (Nf-L) and tau proteins, are turning this on its head. Since we acquired the rights to the Nf-L antibodies from UmanDiagnostics last year, we've seen applications for the biomarker take off . More than hundred of studies using Simoa have demonstrated the potential of Nf-L as a critical tool for early detection, prognosis and monitoring treatment for a range of neurodegenerative conditions. Moreover, combining Nf-L with other biomarkers, such as Aβ and tau has been shown to hold promise for better understanding pathophysiological mechanists of neurodegeneration and early detection of associated conditions.

Nf-L in action

Blood neurofilament light levels sefregate treatment effects in multiple sclerosis

The study was designed to determine the factors (including the role of specific disease modulatory treatments [DMTs]) associated with (1) baseline, (2) on-treat-ment, and (3) change (from treatment start to on-treatment assessment) in plasma neurofilament light chain (pNfL) concentra-tions in relapsing-remitting multiple sclerosis (RRMS). Data including blood samples analyses and long-term clinical follow-up information for 1,261 Swedish patients with RRMS starting novel DMTs were analyzed using linear regressions to model pNfL and changes in pNfL concen-trations as a function of clinical variables and DMTs (alemtuzumab, dimethyl fumarate, fingolimod, natalizumab, rituximab, and teriflunomide).

Complete article, published in Neurology is available at www.quanterix.com

Serum neurofilament light chain in genetic frontotemporal dementia: a longitudinal, multicentre cohort study

Neurofilament light chain (NfL) is a promising blood biomarker in genetic frontotemporal dementia, with elevated concentrations in symptomatic carriers of mutations in GRN, C9orf72, and MAPT. Findings show the value of blood NfL as a disease progression biomarker in genetic frontotemporal dementia and suggest that longitudinal NfL measurements could identify mutation carriers approaching symptom onset and capture rates of brain atrophy. The characterization of NfL over the course of disease provides valuable information for its use as a treatment effect marker.

Complete article, published in The Lancet Neurology is available at www.quanterix.com

Reference interval and pre-analytical properties of serum neurofilament light chain in Scandinavian adults

The study establishes the serum NfL reference interval, provide estimated upper reference inteval limits in 10-year intervals to increase the clinical applicability and uncover pre-analytical properties that make serum NfL feasible for clinical use.

Complete article, published in Scandinavian Journal of Clinical and Laboratory Investigation is available at www.quanterix.com

Customer Case Study:

Disarm Therapeutics, a biotechnology company creating a new class of disease-modifying therapeutics for patients with axonal degeneration, recently announced preclinical data demonstrating that small molecule inhibitors of SARM1 protect axons in both *in vitro* and *in vivo* models of axonal degeneration.

The data shows that SARM1 inhibitors protect axons, including human iPSC-derived motor axons, in vitro from multiple causes of degeneration, including traumatic, chemotoxic, and mitochondrial insults. In addition, pharmacologic inhibition of SARM1 via oral, small molecule inhibitors prevented axonal degeneration and preserved axonal structure and function in a rodent model of chemotherapy-induced peripheral neuropathy (CIPN). Protection from axonal degeneration was measured using neurofilament light chain (Nf-L), a downstream biomarker of axonal degeneration that can be detected in blood.

To view the full case study visit www.quanterix.com

Blood neurofilament light as a potential endpoint in Phase 2 studies in MS

To assess whether neurofilament light chain (NfL) could serve as an informative endpoint in Phase 2 studies in patients with relapsing–remitting multiple sclerosis (RRMS) and estimate the sample size requirements with NfL as the primary endpoint. Using data from the Phase 3 FREEDOMS study, we evaluated correla-tion of NfL at Month 6 with 2-year outcomes: relapses, confirmed disability worsening (CDW), new or enlarging T2 lesions (active lesions), and brain volume loss (BVL). We compared the proportion of treatment effect (PTE) on 2-year relapses and BVL explained by 6-month log-transformed NfL levels with the PTE explained by the number of active lesions over 6 months.

Complete article, published in Annals of Clinical and Translational Neurology is available at www.quanterix.com

Serum neurofilament light chain at time of diagnosis is an independent prognostic factor of survival in amyotrophic lateral sclerosis

The prognostic value of serum neurofila-ment light chain (sNfL), a biomarker of neurodegeneration, compared to other prognostic factors of amyotrophic lateral sclerosis (ALS) at the time of diagnosis, remains unclear. Sera from ALS patients were prospectively collected at the first diagnostic visit in our centre. sNfL levels were determined by single molecule array in 207 ALS patients and in 21 healthy controls. The prognostic value of sNfL was compared with that of other known clinical prognostic factors using a Cox regression model and multivariate analysis.

Complete article, published in European Journal of Neurology is available at www.quanterix.com

Serum neurofilament dynamics predicts neurodegeneration and clinical progression in presymptomatic Alzheimer's disease

This study leverage the unique characteristics of the Dominantly Inherit-ed Alzheimer Network and ultrasensitive immunoassay technology to demonstrate that NfL levels in the cerebrospinal fluid (n = 187) and serum (n = 405) are correlat-ed with one another and are elevated at the presymptomatic stages of familial Alzheimer's disease. Serum NfL was predictive for both the rate of cortical thinning and cognitive changes assessed by the Mini-Mental State Examination and Logical Memory test.

Complete article, published in Nature Medicine is available at www.quanterix.com

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