Upgrading multiplex panels for neurobiology with Neurofilament-Light as a reliable biomarker for neurodegeneration and brain injury

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Introduction

Neurological disorders comprise highly complex, multifaceted diseases that affect the central nervous system (CNS) and/or the peripheral nervous system. They are among the main causes of disability and mortality worldwide and can impair the brain, the spinal cord, peripheral nerves, or neuromuscular function¹⁻³. Additionally, as the global population ages, health issues related to aging, like dementia, have become significant public health concerns. Neurodegenerative diseases like Alzheimer's disease (AD) result in the most prevalent type of age-related dementia, characterized by neuronal death, cognitive decline, and loss of motor function. Neuronal loss in neurodegenerative diseases is supposed to be attributed to the formation and deposition of pathogenic protein aggregates forming "incidental" plaques, tangles, and Lewy bodies, which can arise either spontaneously or due to inherited mutations.

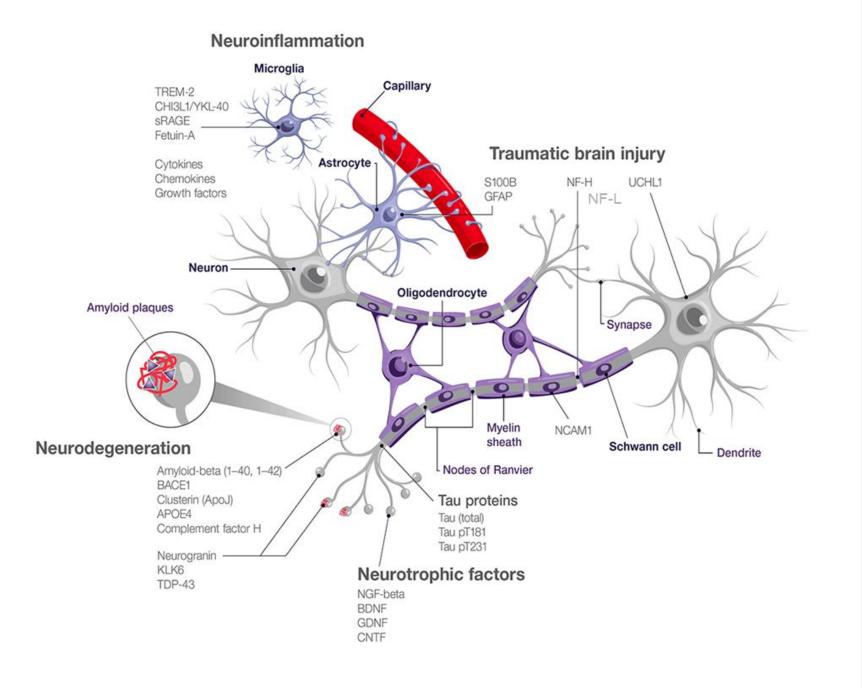
Being able to measure and track multiple biomarkers over time speeds up research, providing a deeper understanding of neuroinflammation and neurodegenerative diseases. Multiplex immunoassays enable researchers to detect biomarkers that help differentiate between diseased and non-diseased states, as well as between various neurodegenerative conditions.

Aim

Help provide comprehensive multiplex assay panels based on the established Invitrogen™ Luminex® xMAP® technology for the investigation of biomarkers for neurobiology including neuroinflammation, neurodegeneration, blood-brain-barrier integrity and neurotrophic factors.

Biomarkers for neurobiology

Figure 1. Major neuronal and non-neuronal cell types of the CNS and candidate biomarkers for neuroinflammation, brain injury and neurodegeneration.



This schematic depicts possible origins of biomarkers for neuroinflammation, traumatic brain injury, and neurodegeneration.

Table 1. A comprehensive selection of Neuronal Biomarkers for a flexible combination to customize specific Invitrogen™ **ProcartaPlex™ multiplex panels**

Human Neuroscience Markers						
Alpha-Synuclein(pS129)	Alpha-Synuclein (total)	Amyloid beta 1-40	Amyloid beta 1-42			
BDNF	BLC (CXCL13)	CNTF	FGF-21			
GDNF	GFAP	IL-34	Kallikrein-6 (KLK6)			
NCAM-1	Neurogranin (NRGN)	NF-H	NF-L			
NGF beta	NSE	RAGE	S100B			
Tau (Total)	Tau [pT181]	Tau [pT231]	TDP-43			
TRFM-2	UCHI -1	YKI -40 (CHI3L1)				

Table 2. Preconfigured Invitrogen™ ProcartaPlex™ multiplex panels for neurobiology

paneis for neurobi	lology					
ProcartaPlex Human Neurodegeneration Panel 1, 9plex						
Cat. No.: EPX100-15836-901						
Amyloid beta 1-40	Kallikrein-6 (KLK6)	TAU (total)				
Amyloid beta 1-42	NCAM-1	TAU[p181]				
FGF-21	Neurogranin (NRGN)	TDP-43				
ProcartaPlex Human Neurodegeneration Panel 2, 10plex						
Cat. No.: EPX100-15851-901						
Amyloid beta 1-42	Neurogranin (NRGN)	S100B	UCHL-1			
BDNF	NF-H	TAU (total)				
GFAP	NF-L	TAU[p181]				
ProcartaPlex Human Neuroscience Panel, 21plex						
Cat. No.: EPX210-15839-901						
Alpha-Synuclein (total)	GFAP	NGF beta	TREM-2			
Amyloid beta 1-42	Kallikrein-6 (KLK6)	NSE	UCHL-1			

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FGF-21	NF-H	TAU[p181]				
GDNF	NF-L	TDP-43				
ProcartaPlex Human Neuroinflammation Panel, 21plex						
Cat. No.: EPX210-15852-901						
Amyloid beta 1-42	IL-13	Neurogranin (NRGN)	TNF alpha			
BDNF	IL-2	NF-H	TREM-2			
GFAP	IL-6	NF-L	UCHL-1			
IFN gamma	IL-8	S100B				

S100B

TAU (total)

TAU (total)

TAU[p181]

Neurogranin (NRGN)

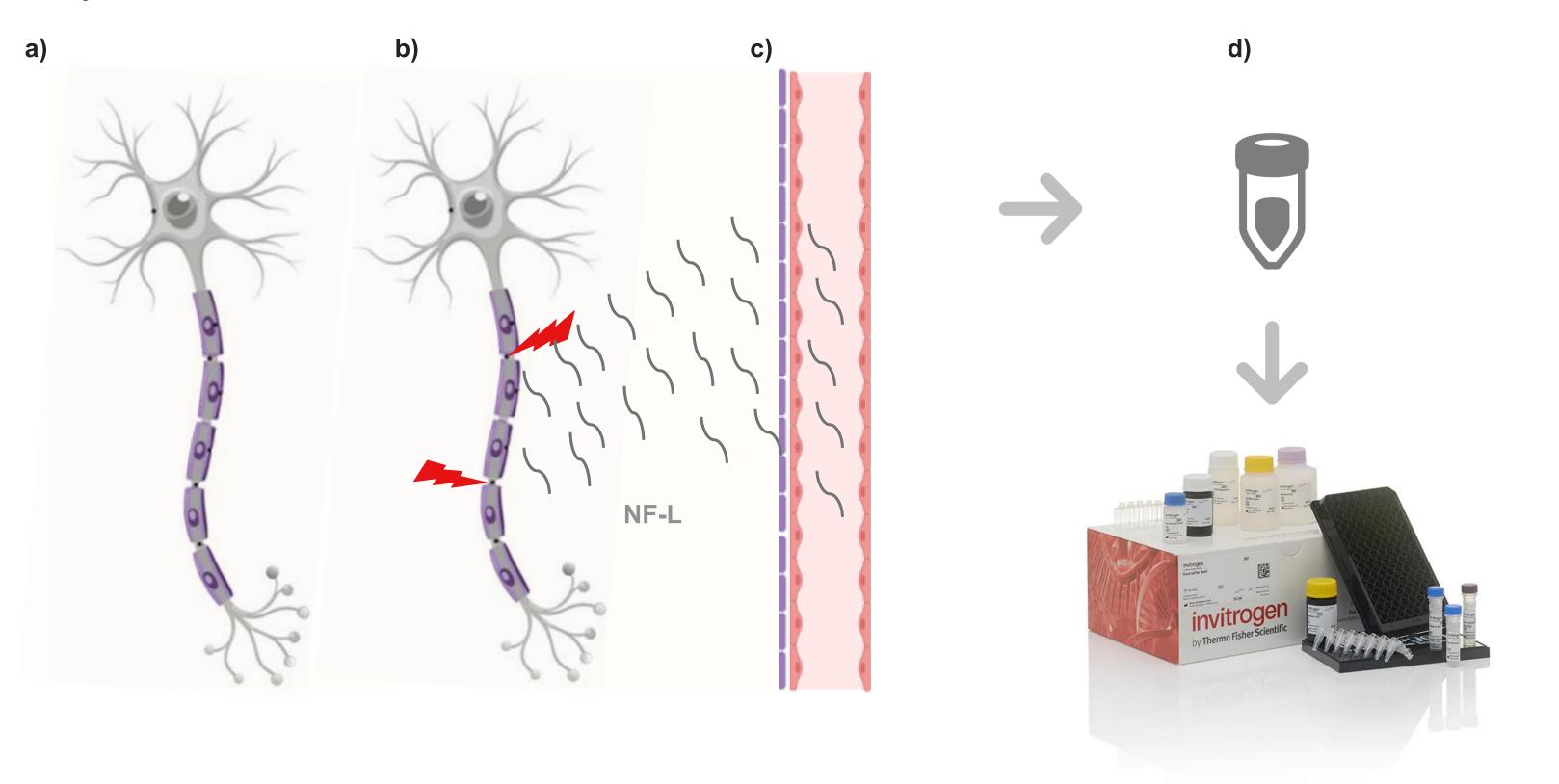
IP-10

MCP-1

Neurofilament-Light (NF-L) – Filling the neuronal biomarker gap

Neurofilament-Light (NF-L) chains are subunits of the neurofilament scaffolding protein of neurons. Neuronal damage can cause the release of neurofilament and its subunits into the interstitial fluid and subsequently into the cerebrospinal fluid (CSF) and the blood. The Neurofilament-Light chain is described as particularly suitable for diagnostic purposes⁴. Highly sensitive immunoassays enable the quantitative analysis of NF-L not only in CSF, but also in serum or plasma.

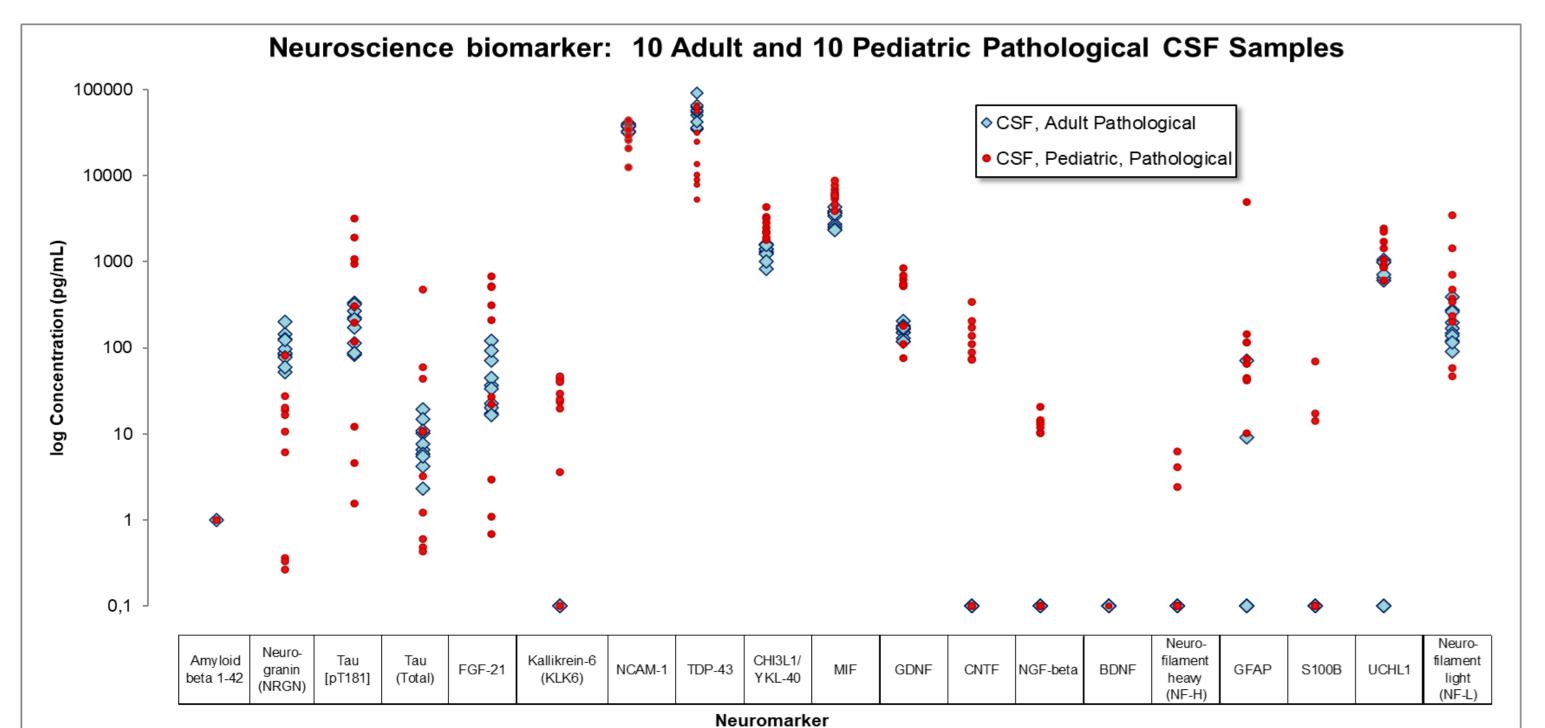
Figure 2: Neuroaxonal injury leading to Neurofilament-Light release serving as blood biomarker detectable with ProcartaPlex™ assays



In intact neurons (a) neurofilaments serve as main cytoskeletal component which is damaged during neurodegenerative diseases or brain injury (b). Neurofilament subunits like the neurofilament light chain are released and diffuse across the blood-brain-barrier into the bloodstream (c) and are detectable in serum and plasma samples using ProcartaPlex™ assays (d).

Detection of neuronal markers in CSF

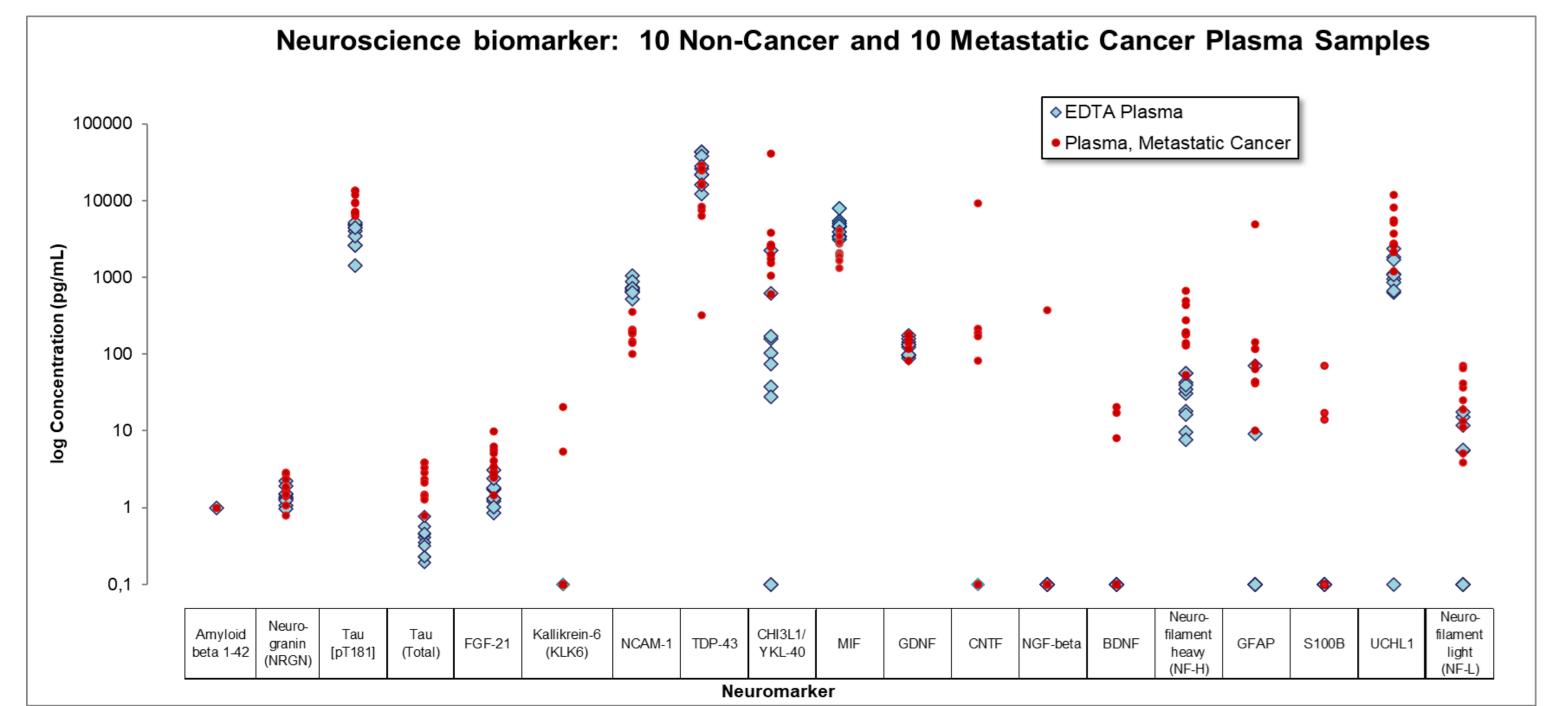
Figure 3: Quantification of neuronal biomarkers in CSF.



Levels of 19 biomarkers from 10 human adult and 10 human pediatric subject CSF samples were tested using ProcartaPlex™ Neuroscience biomarker assays. Data provided by The Washington University Bursky Center for Human Immunology and Immunotherapy Programs (CHiiPs) Immunomonitoring Laboratory.

Detection of neuronal markers in plasma

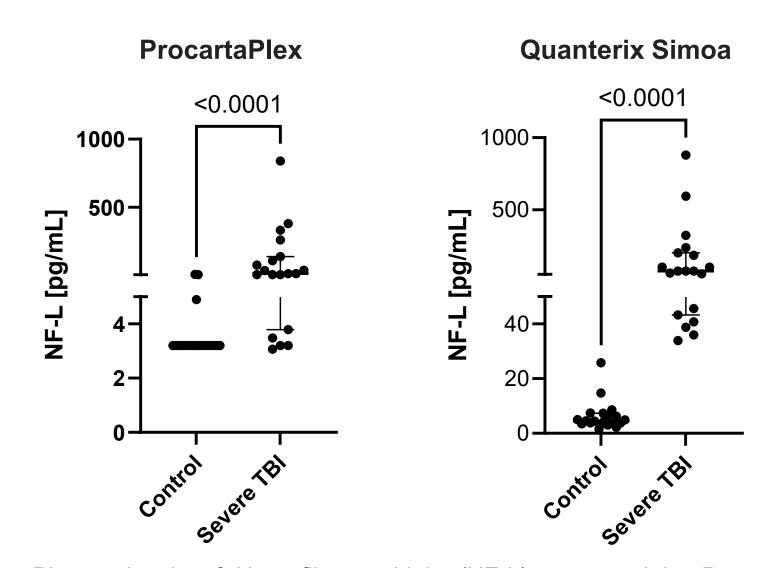
Figure 4: Quantification of neuronal biomarkers in plasma.



Levels of 19 biomarkers from 10 human adult subjects with metastatic brain cancer and 10 control plasma (EDTA) samples were tested using ProcartaPlex™ Neuroscience biomarker assays. Data provided by The Washington University Bursky Center for Human Immunology and Immunotherapy Programs (CHiiPs) Immunomonitoring Laboratory.

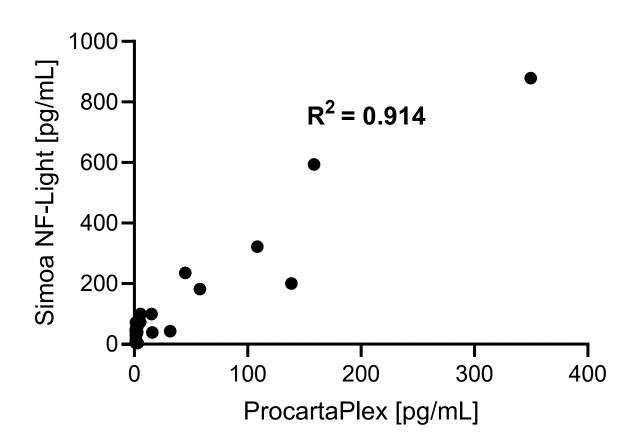
NF-L benchmark analysis

Figure 5: Analysis of plasma samples from severe traumatic brain injury (TBI) vs. control subjects



Plasma levels of Neurofilament-Light (NF-L) measured by ProcartaPlex™ (left) and Quanterix Simoa® (right) in 19 human subjects with severe traumatic brain injury (TBI) and 19 human age- and gender-matched controls. Each datapoint represents an individual subject analyzed. Lines in scatterplots represent the median with interquartile range. P-value of significance < 0.0001.

Figure 6: Correlation between ProcartaPlex™ and Simoa® platform



Expand your analysis

Cytokines, chemokines and growth factors are also involved in CNS tissue homeostasis and neuroinflammation. . Their impact on tissue injury, repair, and the identification and stratification of neurodegenerative diseases can now be investigated. We have tested and evaluated the Invitrogen™ ProcartaPlex™ Human Cytokine/Chemokine/Growth Factor Panel 1, 45plex (Cat No: EPX450-12171-901) alongside neurobiology markers to help provide a comprehensive selection of highly relevant biomarkers.

ProcartaPlex™ Human Cytokine/Chemokine/Growth Factor Panel 1, 45plex					
Cat No: EPX450-12171-901					
BDNF	Eotaxin/CCL11	EGF	FGF-2		
GM-CSF	GRO alpha/CXCL1	HGF	NGF beta		
LIF	IFN alpha	IFN gamma	IL-1 beta		
IL-1 alpha	IL-1RA	IL-2	IL-4		
IL-5	IL-6	IL-7	IL-8/CXCL8		
IL-9	IL-10	IL-12 p70	IL-13		
IL-15	IL-17A	IL-18	IL-21		
IL-22	IL-23	IL-27	IL-31		
IP-10/CXCL10	MCP-1/CCL2	MIP-1 alpha/CCL3	MIP-1 beta/CCL4		
RANTES/CCL5	SDF-1 alpha/CXCL12	TNF alpha	TNF beta/LTA		
PDGF-BB	PLGF	SCF	VEGF-A		
VEGF-D					

Explore all available targets and build your custom panel at thermofisher.com/order/luminex/



Conclusion

The Invitrogen™ ProcartaPlex™ assays for neurobiology enable an exceptional tool for measuring novel and established CNS-specific markers in conjunction with other factors involved in neuroinflammation and neurodegeneration.

Adding the Neurofilament-Light (NF-L) assay to the Invitrogen™ ProcartaPlex™ neurobiology marker portfolio significantly increases the value of multiplexing in neuroscience.

References

- 1. World Health Organization, "Fact sheet N° 362: Dementia," WHO, Geneva, 2015.
- 2. World Health Organization, "Chapter V(F): Mental and Behavioral Disorders" in The ICD-10 Classification, WHO, Geneva, 2013.
- 3. World Health Organization, "Fact sheet N° 396: Mental disorders" WHO, Geneva, 2015.
- 4. Khalil, M. et al. Neurofilaments as biomarkers in neurological disorders — towards clinical application. Nat Rev Neurol (2024).

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CNTF

IL-1 beta

IL-10

YKL-40 (CHI3L1)