Biomarkers: The Neurodegenerative Disease Game Changer

UNIVERSITY OF HELSINKI | Medix Biochemica

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Featured Speakers

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BIOMARKERS: THE NEURODEGENERATIVE DISEASE GAME CHANGER

Timo Myöhänen

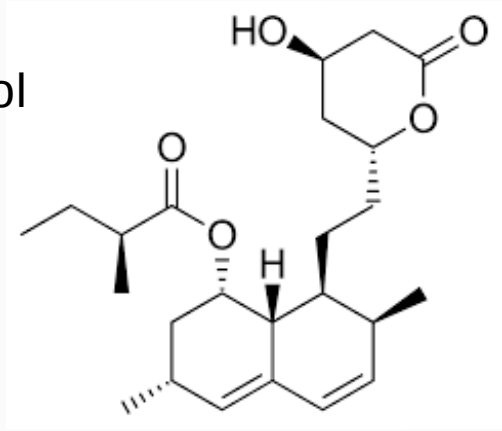
Professor of Pharmacology

Faculty of Medicine / University of Helsinki, FINLAND

HELSINGIN YLIOPISTO
HELSINGFORS UNIVERSITET
UNIVERSITY OF HELSINKI

High cholesterol

Statins



Reduced risk for infarcts and other cicrulation problems

Risk for Alzheimer's

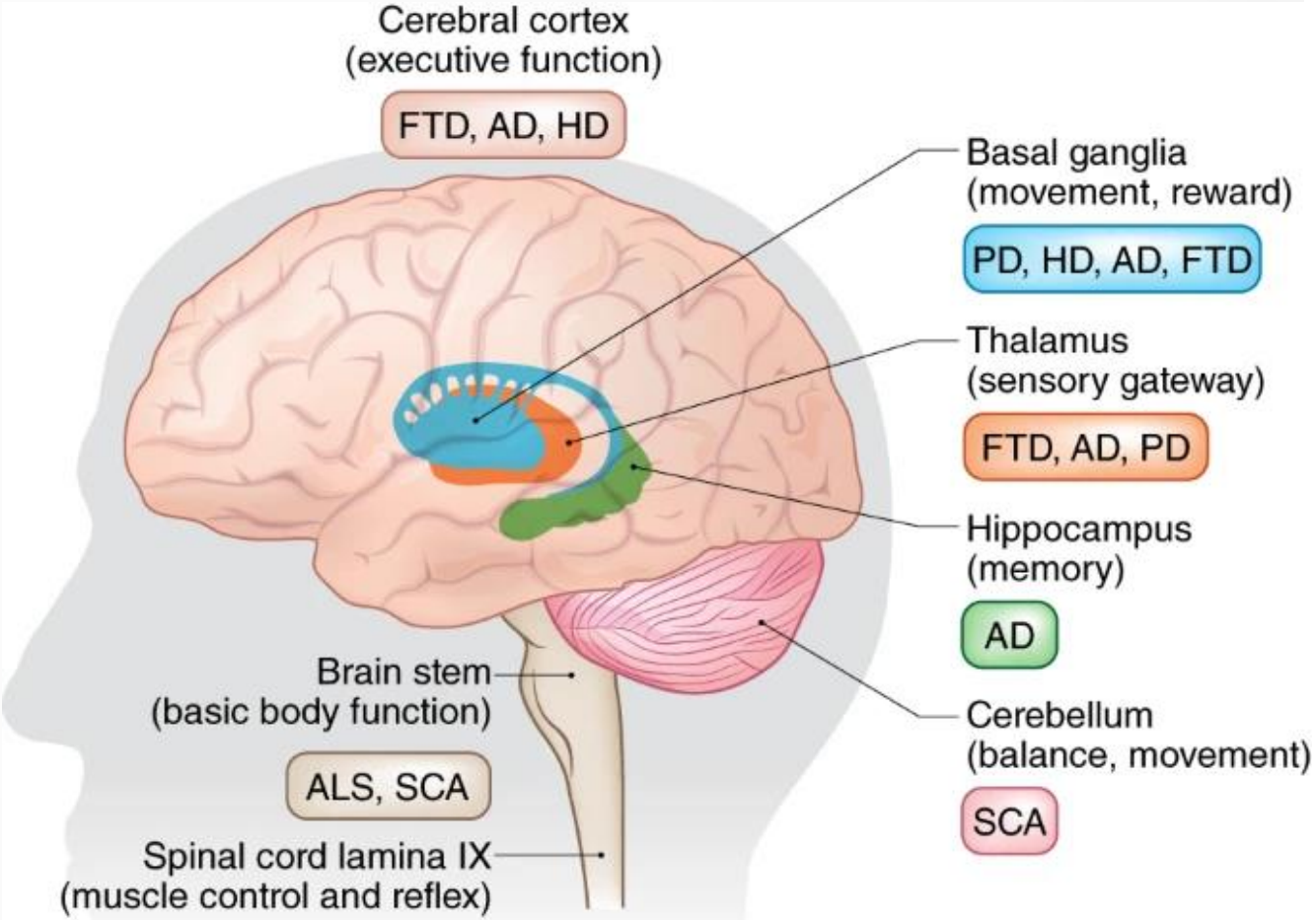
Therapy

?

No Alzheimer's disease

NEURODEGENERATIVE DISEASES

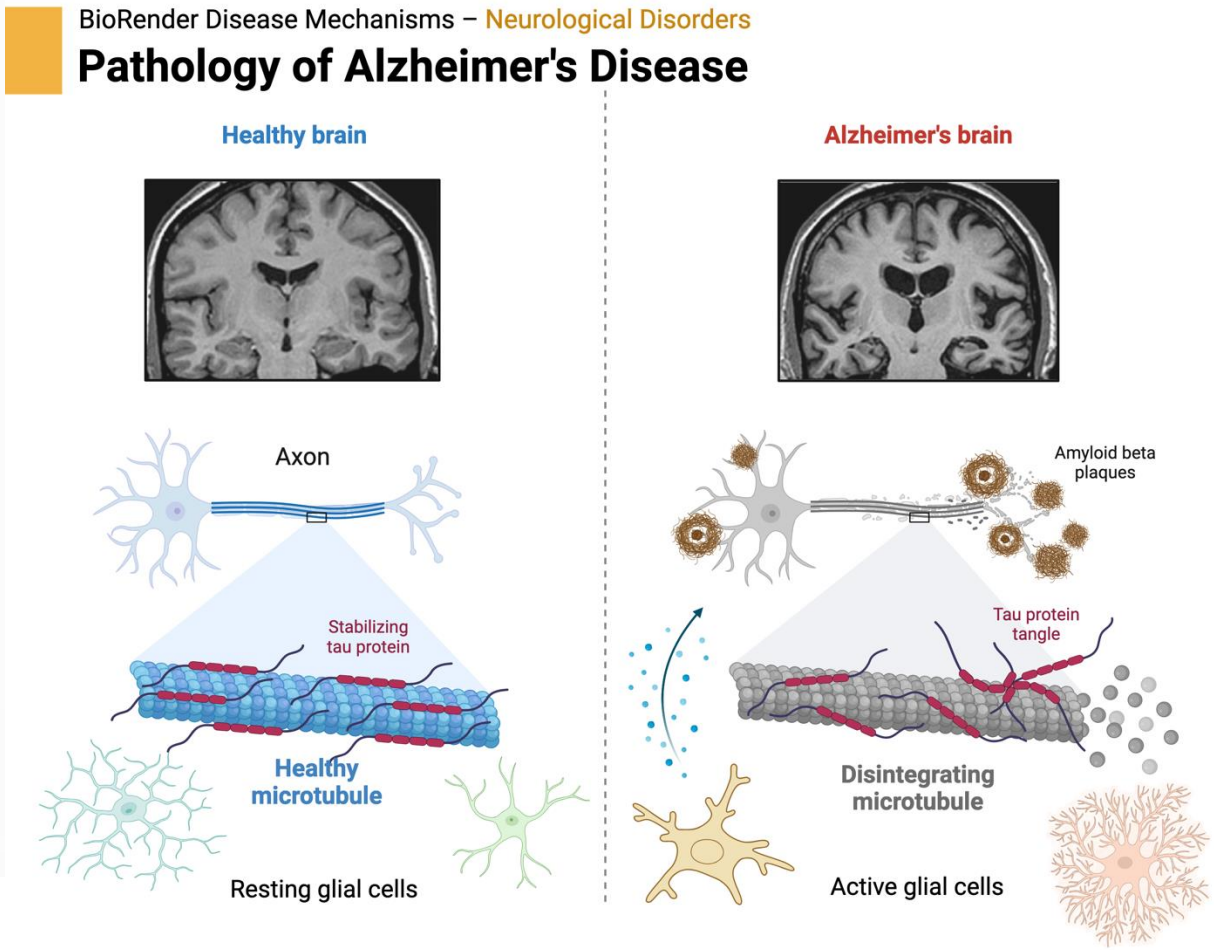
- Heterogenic group of diseases, affecting CNS
- **Alzheimer's disease** is the most common (> 50 million patients)
- Several other dementias, such as **frontotemporal dementia**
- Parkinson's disease is the most common movement disorder (>6 million patients)
- Amyloid lateral sclerosis (ALS), rapidly progressing degenerative motor neuron diseases



Gan et al. Nat Neurosci 2018

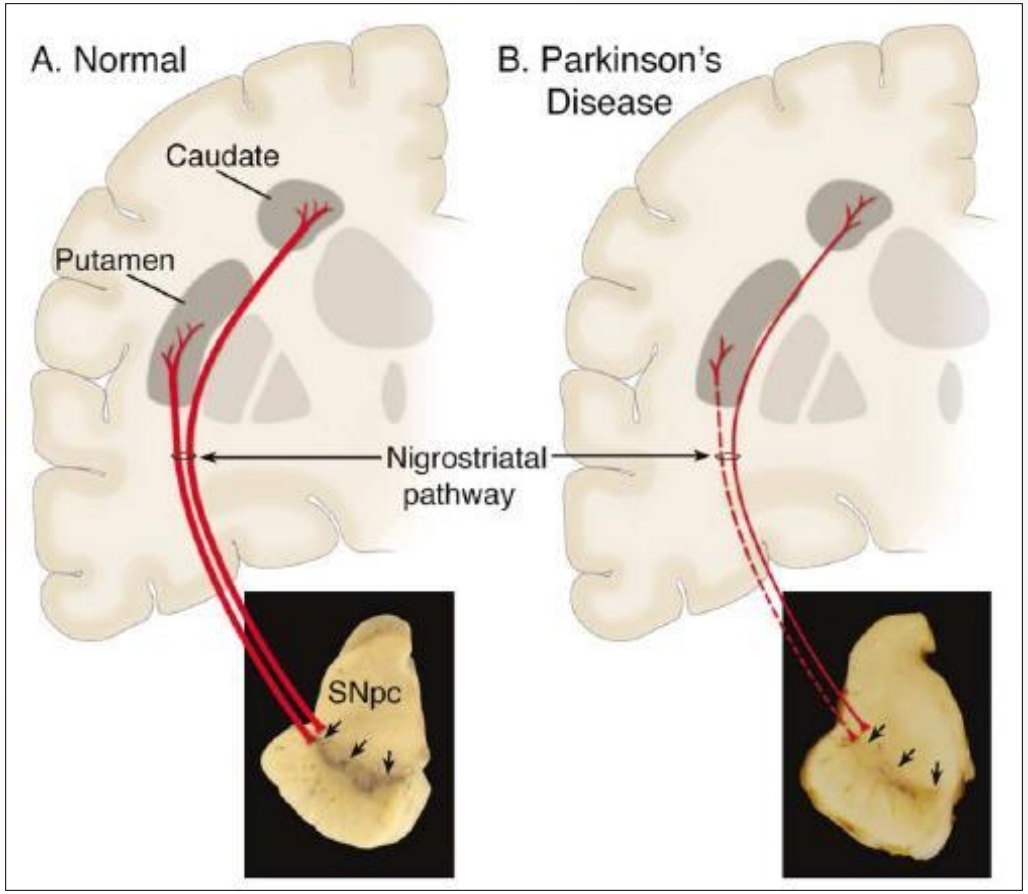
ALZHEIMER'S DISEASE AND OTHER DEMENTIAS

- Dementia is progressive cognitive decline and memory loss, atrophy in brain
- Alzheimer's disease is the most common disease behind dementia (70%)
  - Amyloid-beta plaques and Tau protein tangles in patient brain
  - Intensive microglial and astrocyte (glial cells) activation (neuroinflammation)
  - Current therapies have **poor or no efficacy on disease progression**
- Frontotemporal dementia (FTD) is another dementia, lacks amyloid-beta pathology
  - **No specific treatments**



PARKINSON'S DISEASE

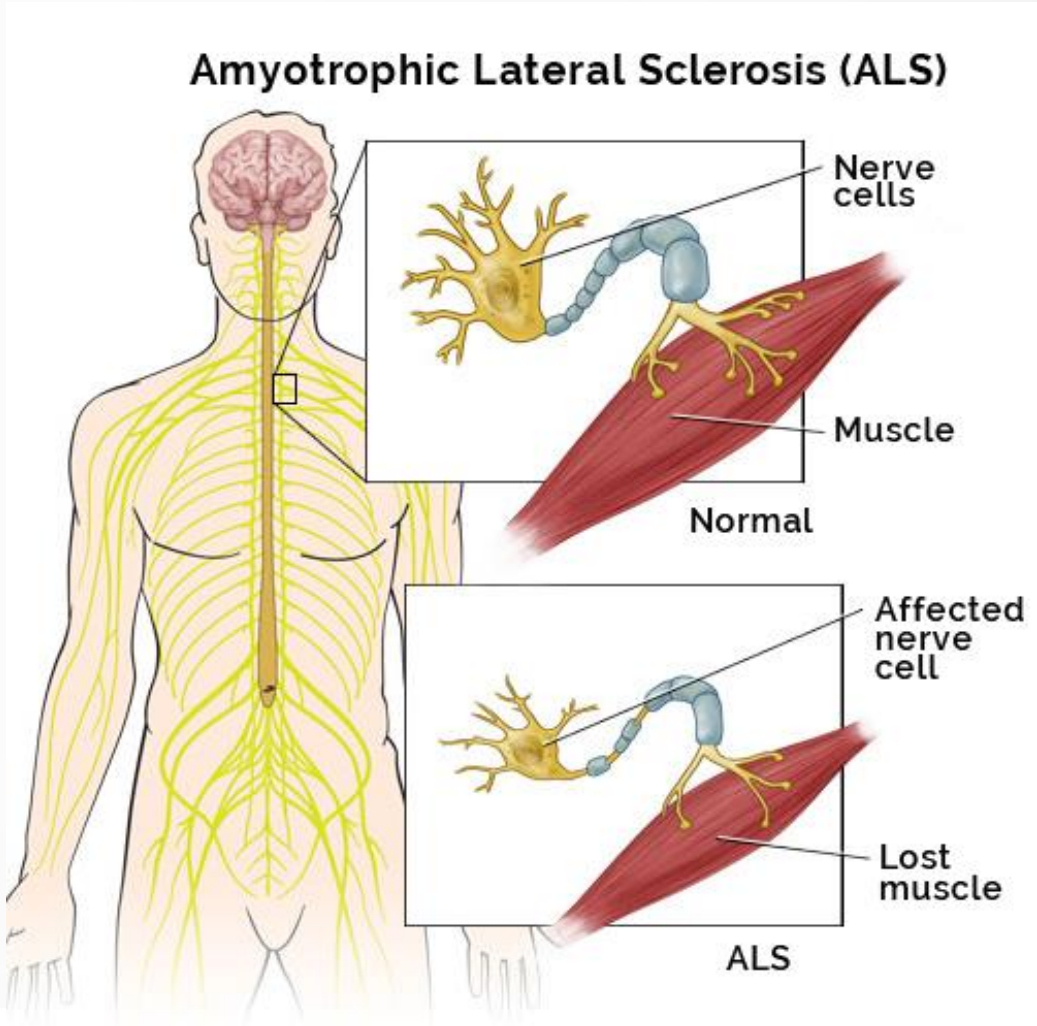
- Progressive neurodegenerative motor disorder
- Starts usually with tremor, rigidity and reduced movements
- Several non-motor symptoms, may progress to dementia
- Neuronal cells using dopamine degenerate in *substantia nigra*
  - Current medications are based **on dopamine replacement**
  - Cannot delay the neuronal death or progress of the disease



Dauer and Przedborski 2003

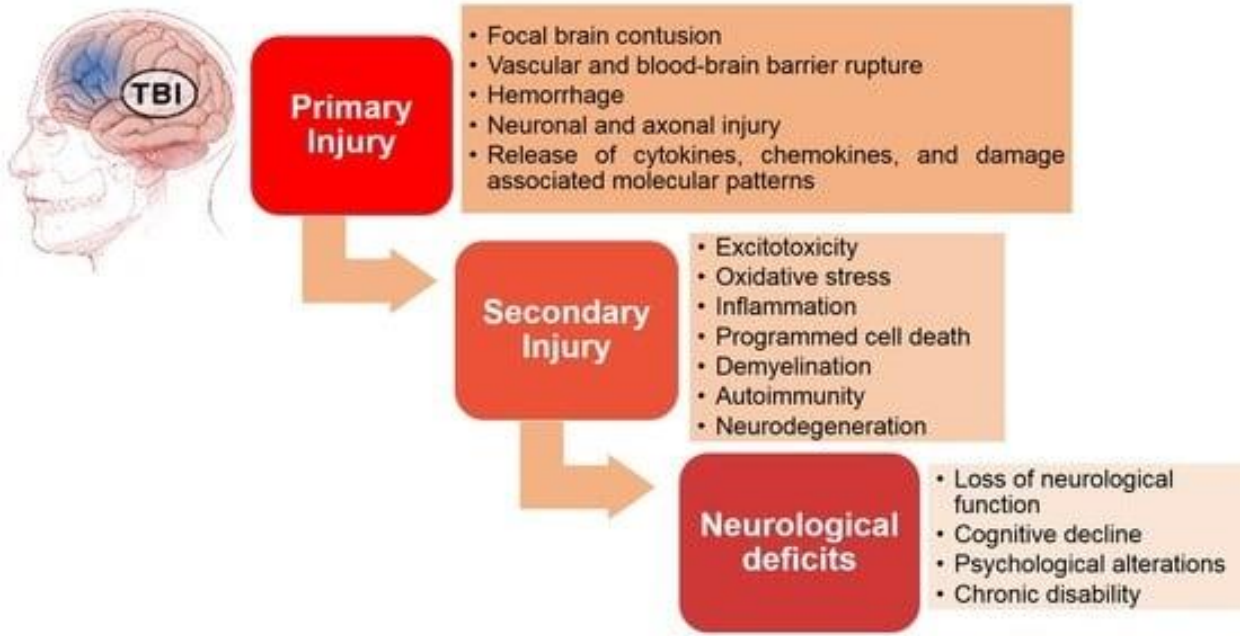
AMYLOID LATERAL SCLEROSIS (ALS)

- Motoneuron disease, neurons regulating muscles degenerate
- Starts with muscle weakness, progresses and leads to severe muscle weaknesses around the body
- Finally respiratory muscles are weakened
- Disease duration ~ 3.5 years
- No disease-modifying treatment
  - Minor effect by riluzole, a compound against excitotoxicity



TRAUMATIC BRAIN INJURY (TBI)

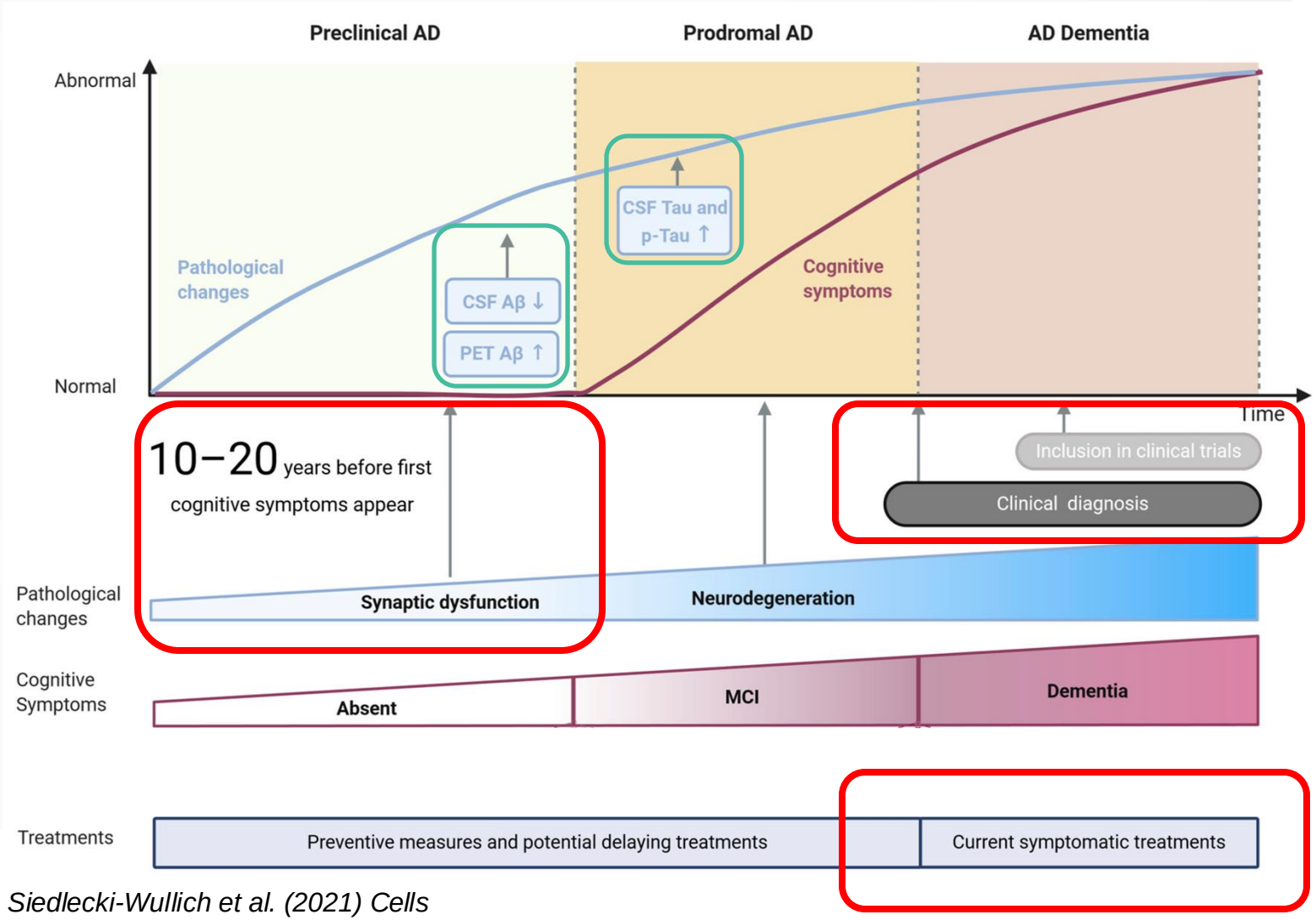
- TBI is impact on head that causes damage for brain tissue
- Can vary from mild concussion to piercing injury, affects 50-60 million people annually
- Moderate-to-severe and repeated mild TBIs are a risk factor for long-term neuronal deficits
  - After primary damage (direct tissue damages) secondary injuries (inflammation, neurodegeneration
  - May lead to neuronal deficits and even to neurodegeneration
- No effective therapies available to prevent long-term effects of TBI



Jarrahi et al. (2020) Biomedicines

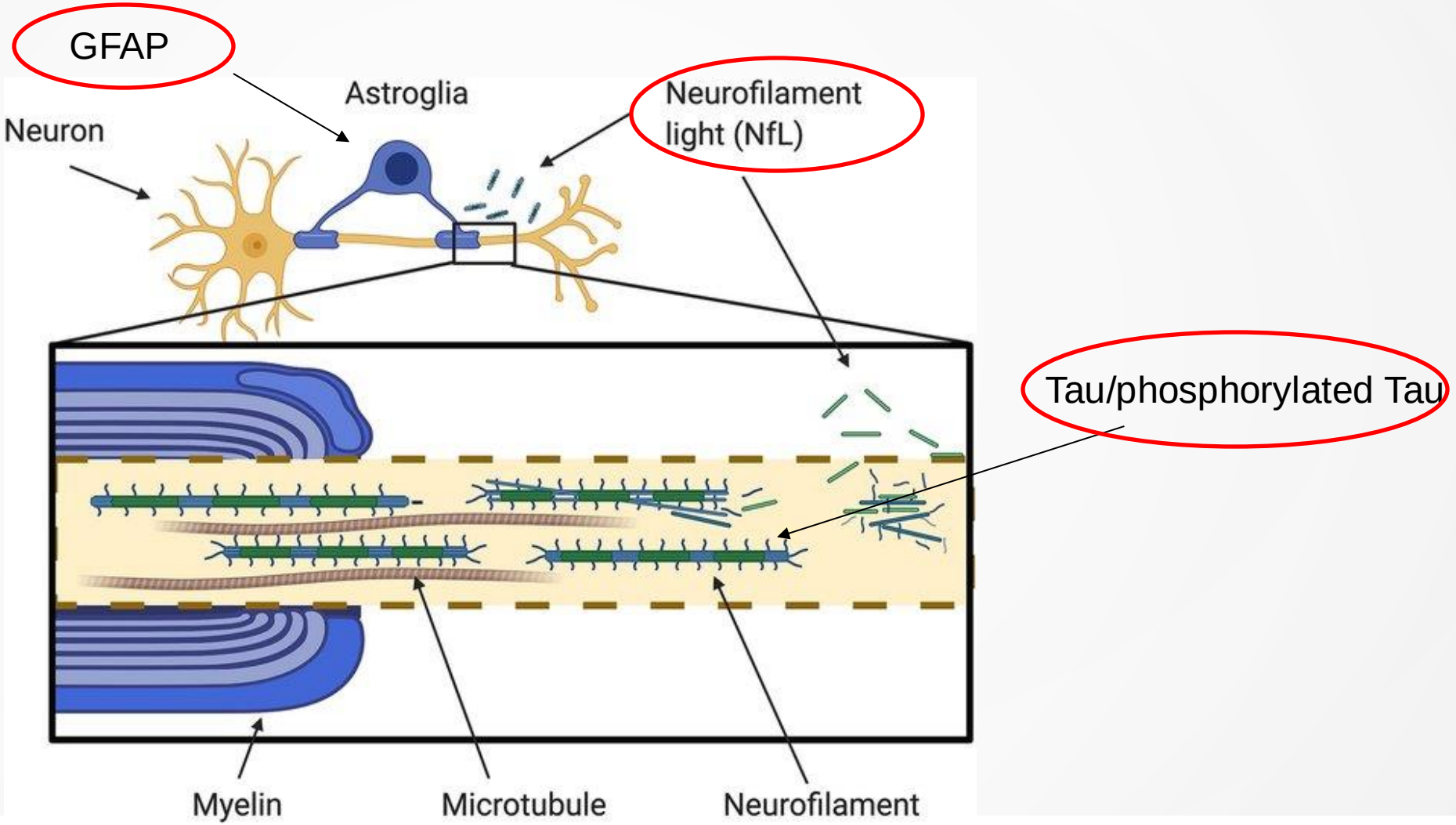
BIOMARKERS IN NEURODEGENERATIVE DISEASES – WHY?

- Neurogenerative diseases develop approx. 10-20 years before the symptoms
  - → **large number of neurons is lost by the time of diagnosis**
- Markers would be important for;
  - → Diagnosis
  - → Potential risk
  - → Treatment
  - → Drug development



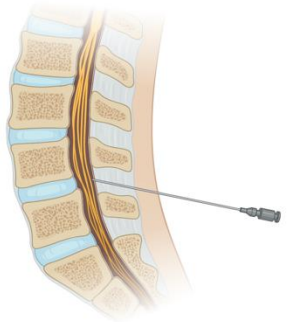
Siedlecki-Wullich et al. (2021) Cells

BIOMARKERS – WHAT WE CAN DETECT?

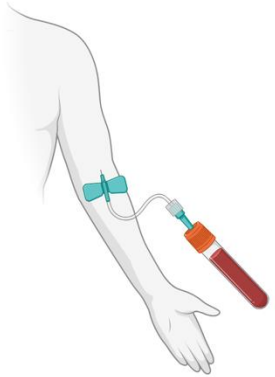


Tjensvoll et al. (2021) J Neurol

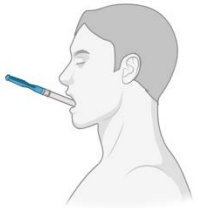
BIOMARKERS – HOW THEY ARE COLLECTED AND MEASURED?



CSF
+ more accurate
- invasive

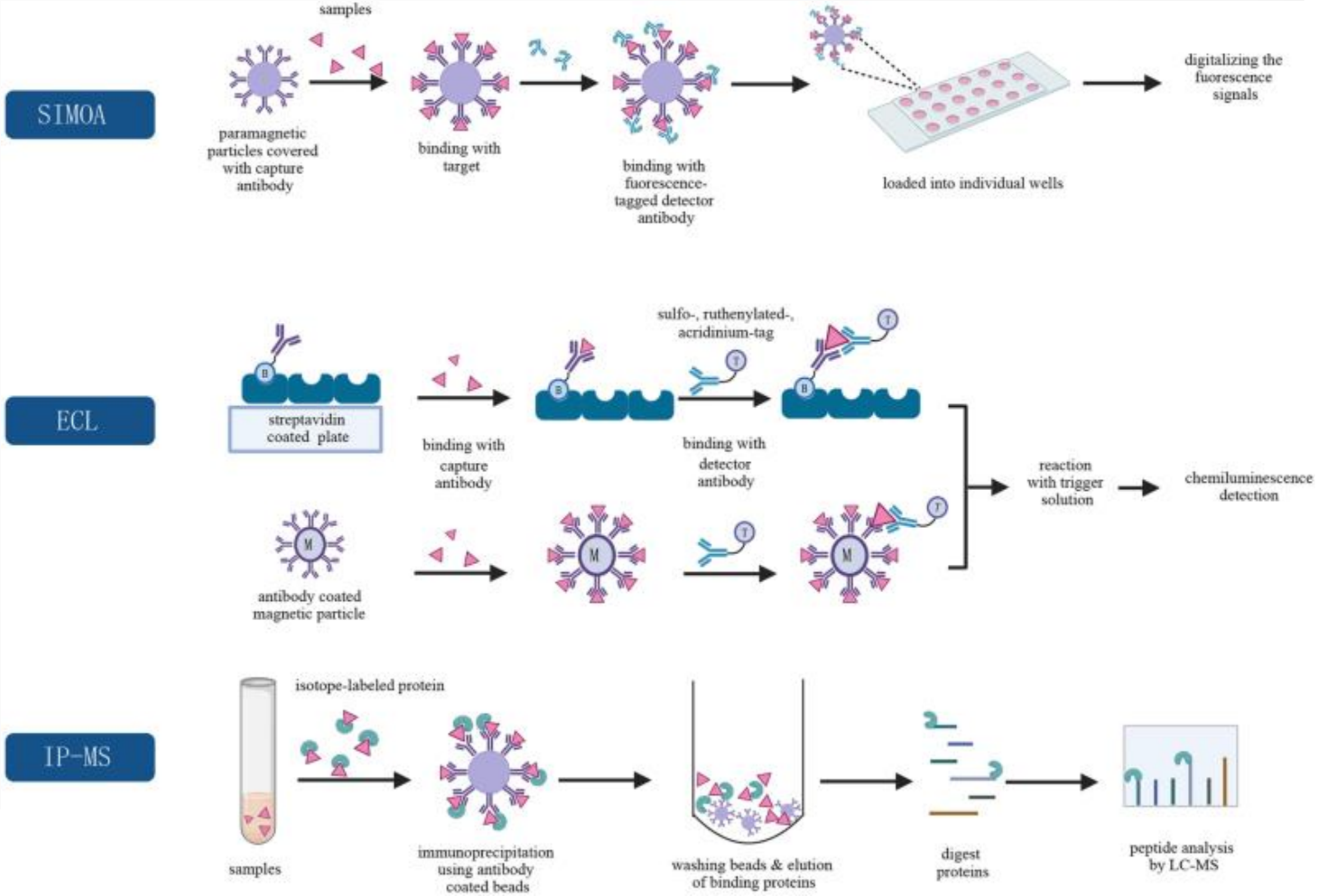


Blood sample
+ easier sampling
- less accurate



Saliva

Skin biopsy

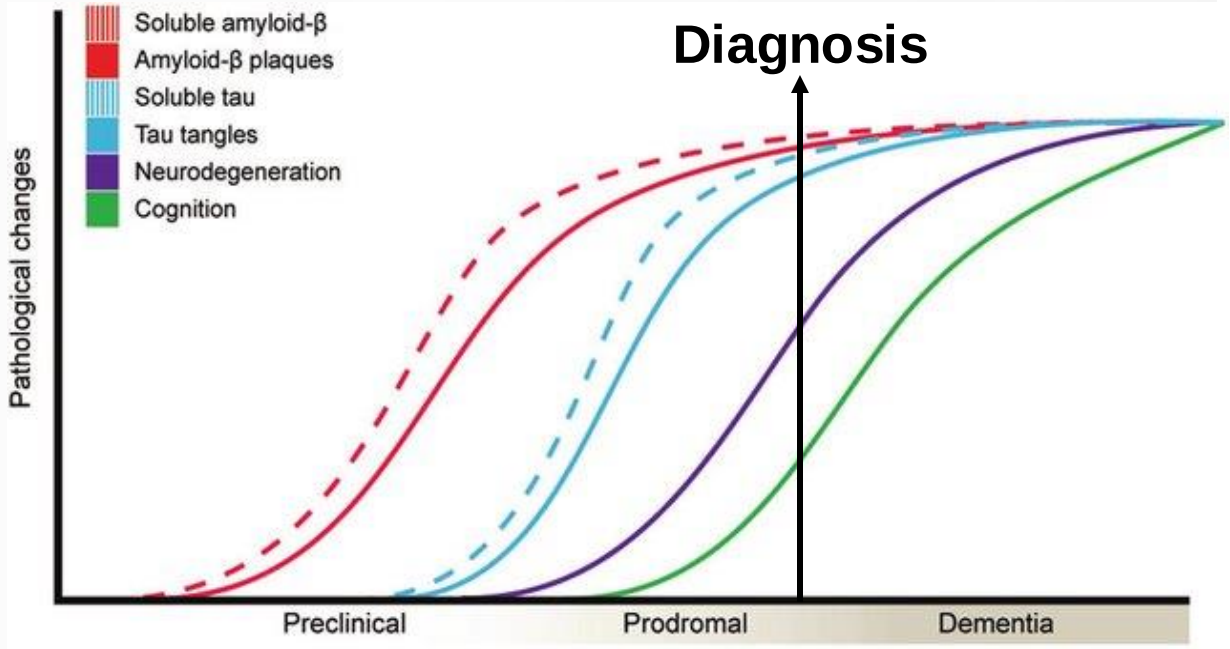


Created by Biorender

An et al. (2021) Med Rev

BIOMARKERS IN ALZHEIMER'S DISEASE

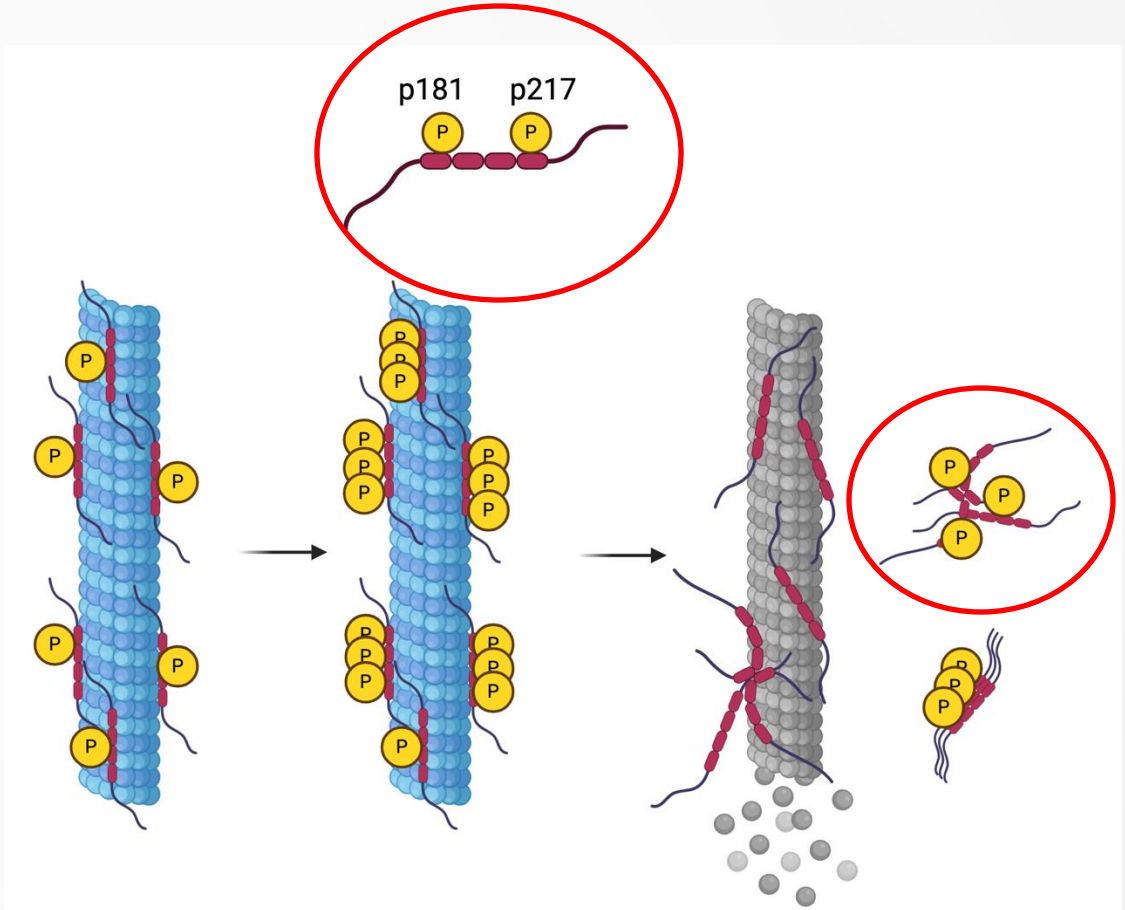
- Role of amyloid-beta
  - Can be detected as reduced **amyloid-beta 1-42 peptide or changed ratio** in the CSF
  - To verify Alzheimer's disease diagnosis
- Changes in plasma are modest compared to CSF
- Predictive value in the plasma?
- Tau, and different phosphorylated forms of Tau protein have shown better efficacy



Leuzy et al. (2019) Mol Psych Time course of Alzheimer's disease

BIOMARKERS IN ALZHEIMER'S DISEASE – TAU AND PHOSPHORYLATED TAU

- Tau hyperphosphorylation leads to its disintegration from microtubules
- Initiates Tau aggregation, microtubule disintegration and toxicity
- Released Tau can be detected from cerebrospinal fluid (CSF) and blood
- **Total Tau** and **181 and 217 phosphorylated Tau** has been used as a biomarker for Alzheimer's disease



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BIOMARKERS IN ALZHEIMER'S DISEASE – TAU AND PHOSPHORYLATED TAU

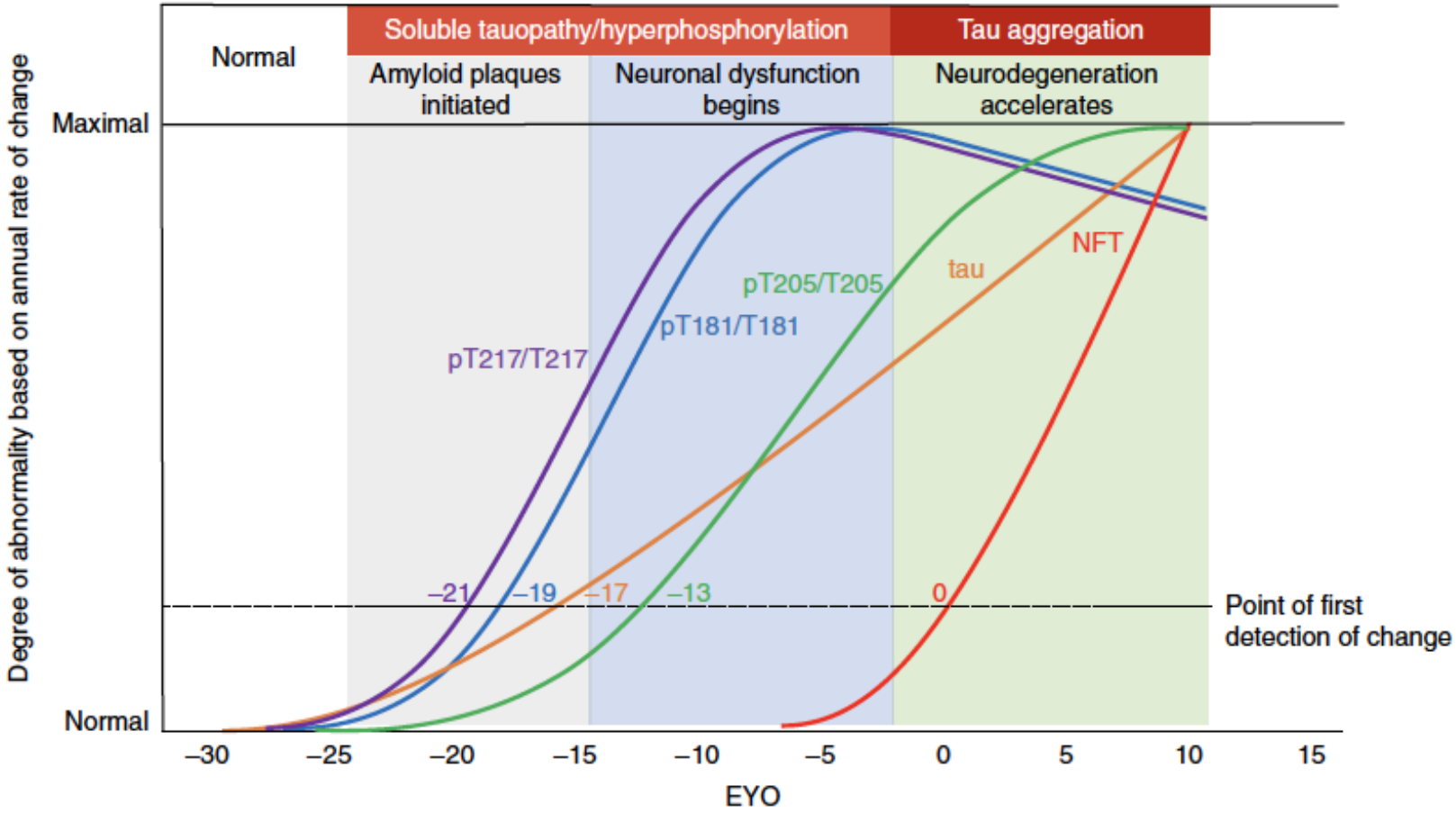
Tau p181

- First phosphorylated Tau biomarker
- FDA approved as CSF marker
- Detects more aggregated Tau
- Good sensitivity particularly with amyloid-beta positivity
- Can be used to verify the diagnosis together with amyloid-beta
- Plasma and CSF levels correlate
- **Increased in the CSF and plasma even 8 years before symptom onset**

Tau p217

- FDA approved as plasma marker
- Detects earlier forms of Tau aggregation than p181
- Better detection between non-AD and AD compared to p181
- Clearer signal with or without amyloid beta positivity
- More significant increase with Tau aggregation than p181
- **Increased levels in CSF and plasma predict symptom onset at over 8 years before**

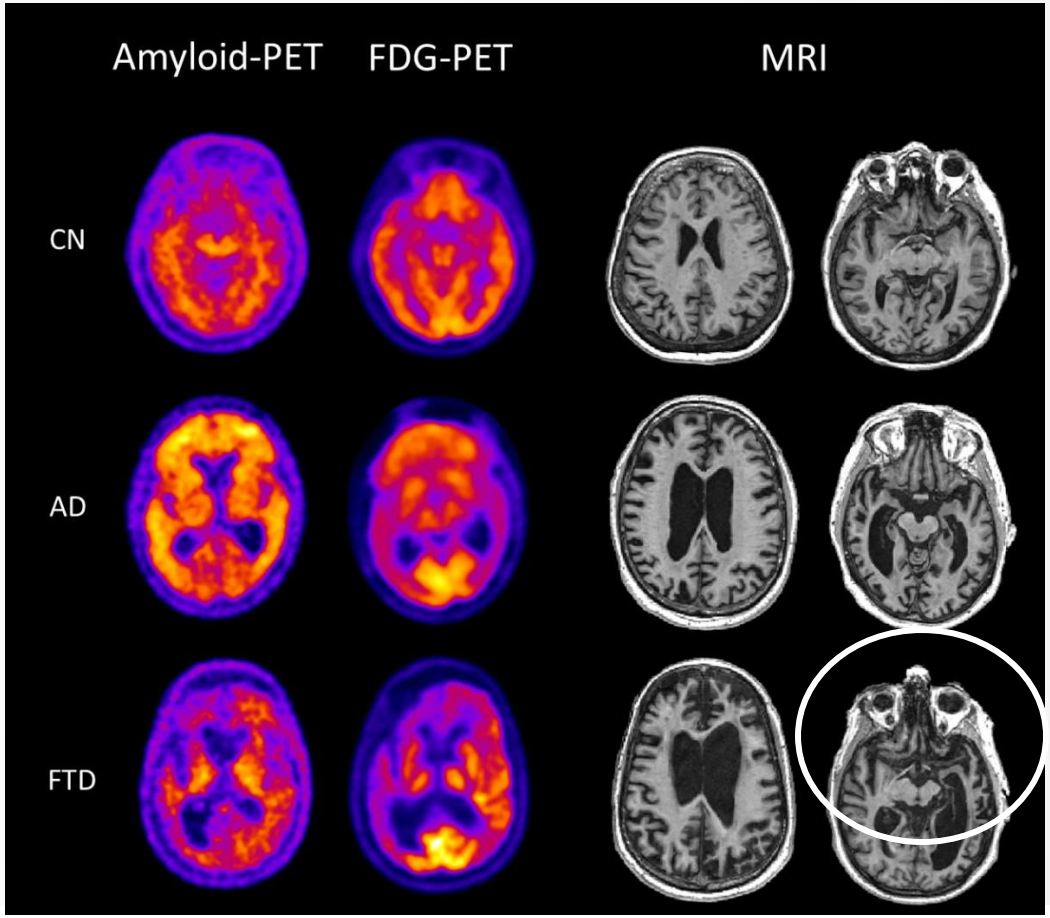
BIOMARKERS IN ALZHEIMER'S DISEASE – TAU AND PHOSPHORYLATED TAU



Barthelemy et al. (2020) Nat Med

TAU AND PHOSPHORYLATED TAU IN OTHER DEMENTIAS?

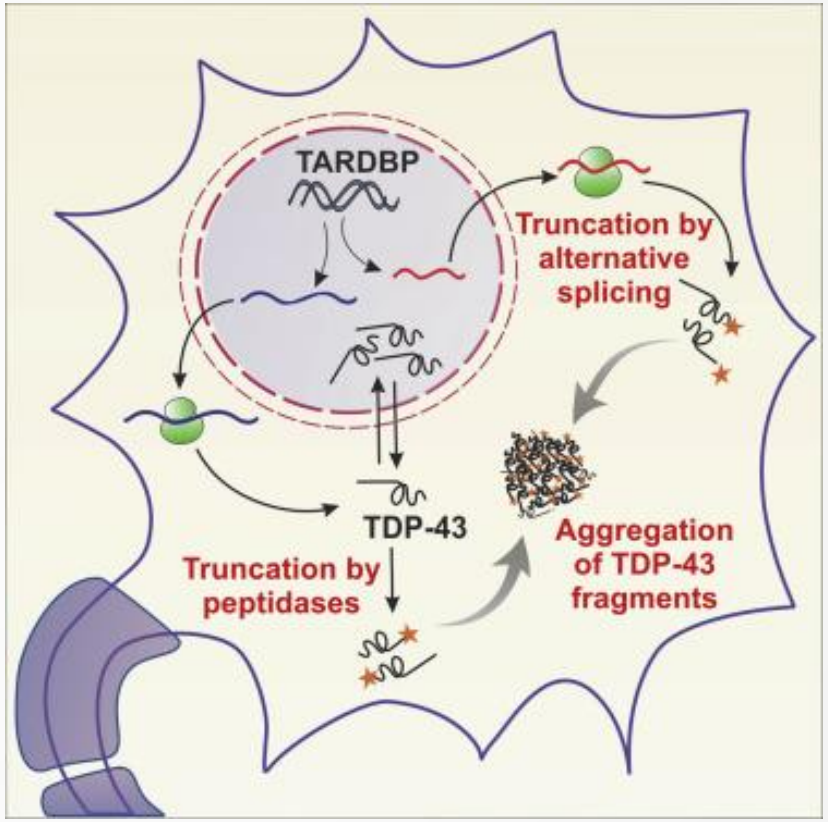
- Other dementias, like frontotemporal dementia, have Tau pathology without amyloid-beta pathology
- **Interestingly p181 and p217 Tau** seem to be specific for Alzheimer's disease
- CSF total Tau increases in FTD
- Can be used for diagnosis if amyloid-beta is excluded
- Increased CSF total Tau predicts worse symptoms and faster disease progression



Murray et al. (2014) Alz Res Ther

TDP-43 – A BIOMARKER FOR FTD AND ALS?

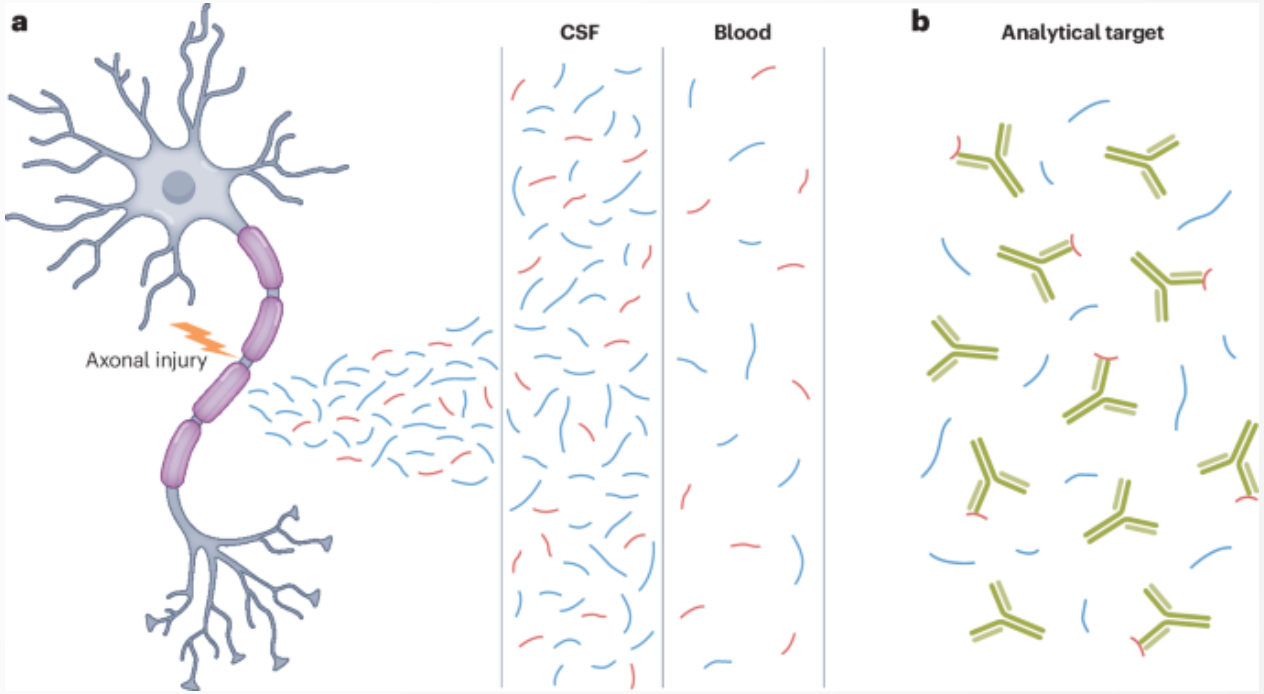
- TDP-43 (TAR DNA-binding protein 43)
- Protein that regulates several functions in nucleus
- In ALS and also other neurodegenerative diseases, particularly ALS, exists nucleus and forms aggregates in the cell
- Disturbs cellular functions, leading to neuronal death
  - Generally increased in the CSF and plasma in ALS
  - Cannot differ FTD and ALS without imaging or other markers
  - A marker for TDP-43 targeted drug discovery



Chhangani et al. (2021) iScience

BIOMARKERS IN OTHER DEMENTIAS - NFL

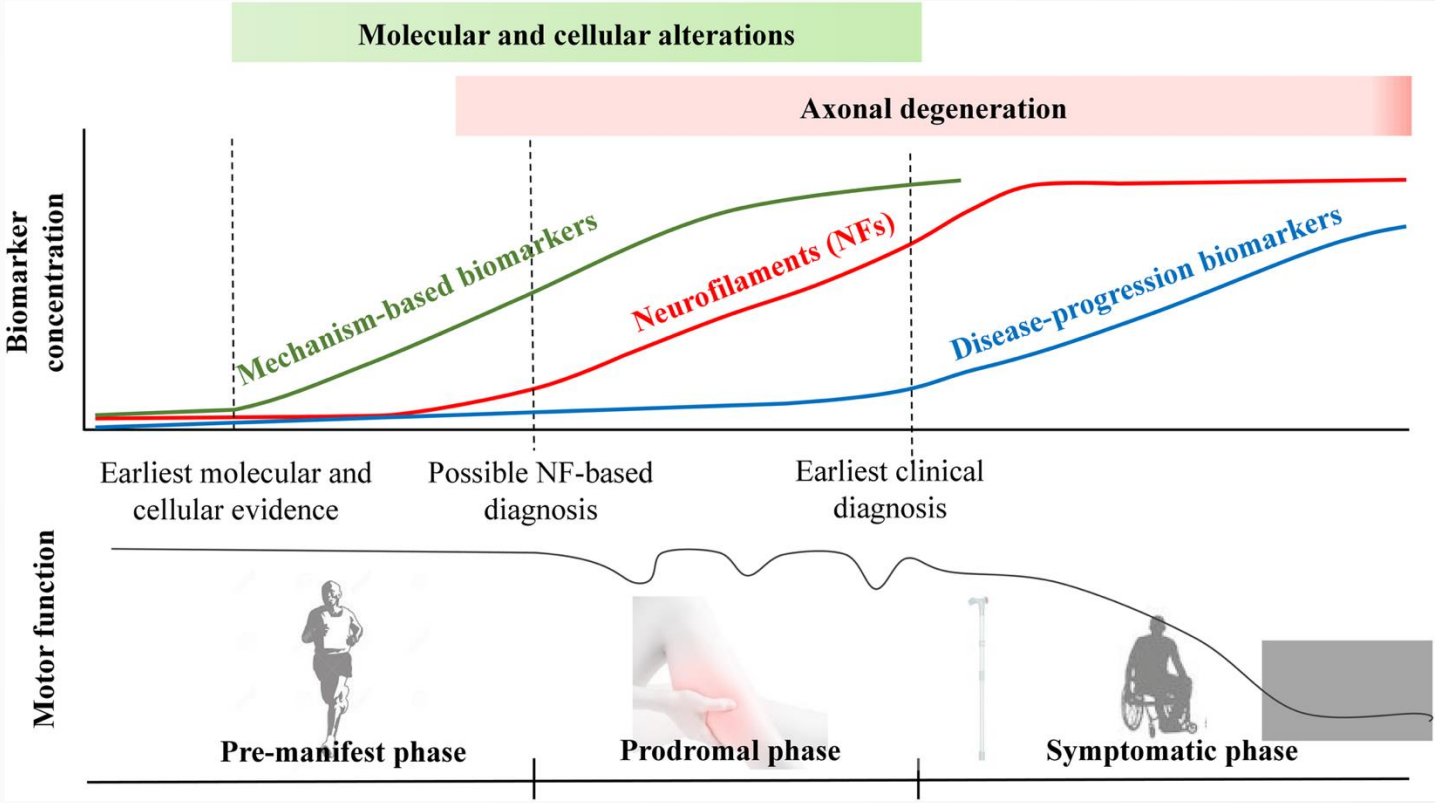
- Neurofilament light is a neuron structural protein
- When neuron is damaged, it leaks easily to circulation
- Increases in FTD both in serum and plasma
- Indicates faster progression of the disease even when measured from plasma
  - Correlates with cognitive decline
- Can be used part of diagnosis (Alzheimer or different variants in FTD), maybe as a biomarker in clinical trials?
- Increases also by age



Khalil et al. (2024) Nat Rev Neurol

NFL IN OTHER NEURODEGENERATIVE DISEASES

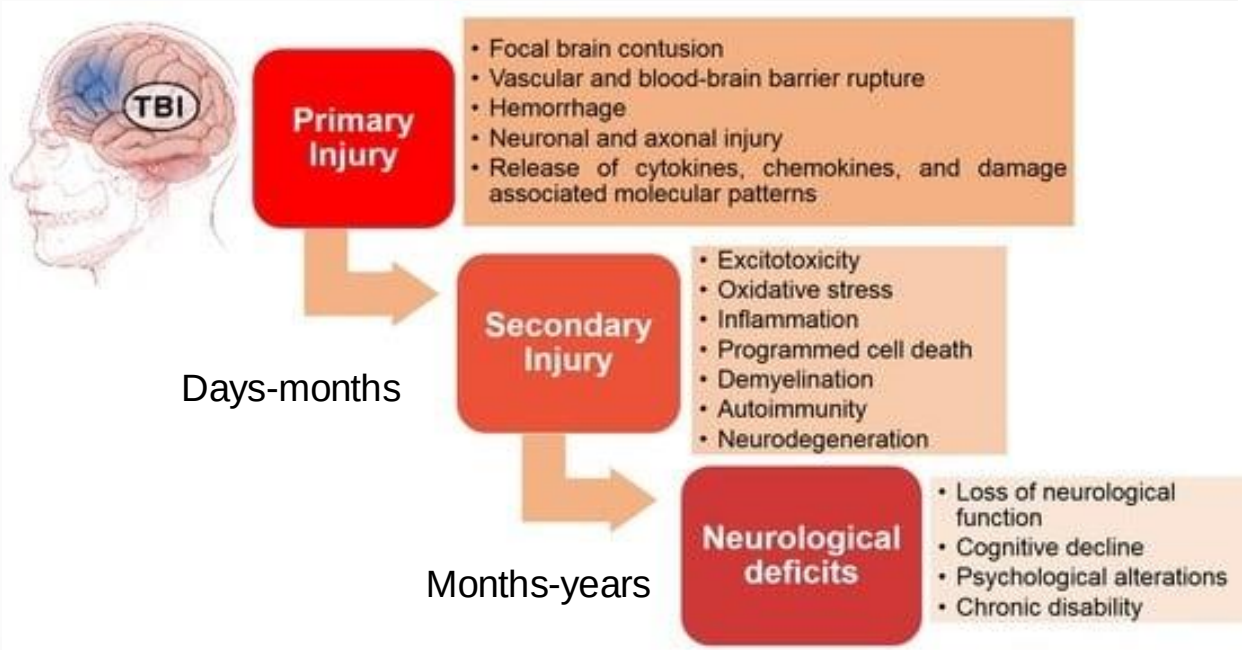
- **ALS**
  - Nfl is highly elevated in serum and CSF in ALS, particularly in early phase
  - Indicative for neuronal degeneration
  - Can be even used to classify ALS from other neurodegenerative diseases
  - Good marker for disease progression
  - Other biomarkers still under investigation
- **Alzheimer's disease**
  - Correlates well with axonal degeneration → clinical trials?
  - Can predict disease onset and progression particularly in genetic forms



Zucchi et al. (2020) Mol Neurodeg

BIOMARKERS IN TRAUMATIC BRAIN INJURY

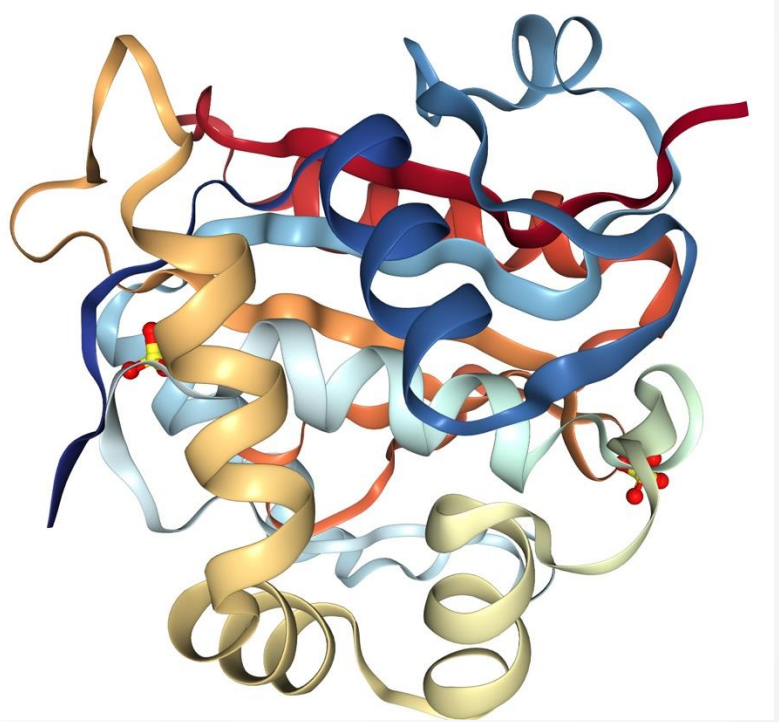
- Axonal damages, neuroinflammation and in long term even Tau accumulation after TBI
- Use of biomarkers to:
  - Assess severity of the TBI or predict secondary outcomes of TBI?
  - Who are in high risk for long-term effects and neurodegeneration?
- **Plasma/CSF Nfl** is good marker for:
  - Outcome prediction (higher Nfl after TBI, more probable secondary damages)
  - Acute mild TBI vs. more severe TBI, need for a CT imaging?
  - Late identification, developing neurodegenerative disease (higher)



Jarrahi et al. (2020) Biomedicines

UCHL-1 IN TRAUMATIC BRAIN INJURY

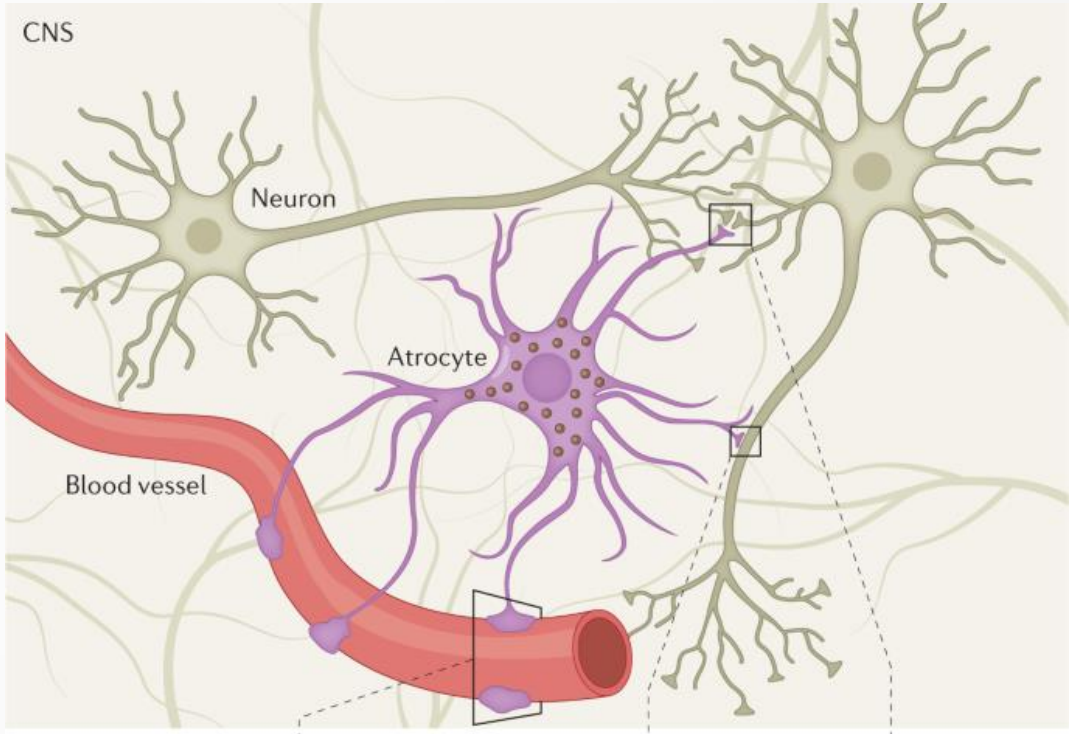
- Ubiquitin C-terminal hydrolase L1 (UCHL1)
- Involved in protein degradation process and metabolism
- Neuronal specific marker
- Indicates for neuronal damage in TBI whereas Nfl and GFAP are more related to axonal damage and glial cells
- Elevated 5-7 h after TBI
- Increased UCHL-1 and GFAP may predict poor outcome after the TBI



Sino Biological

GLIAL FIBRILLARY ACIDIC (GFAP) PROTEIN AS TBI MARKER

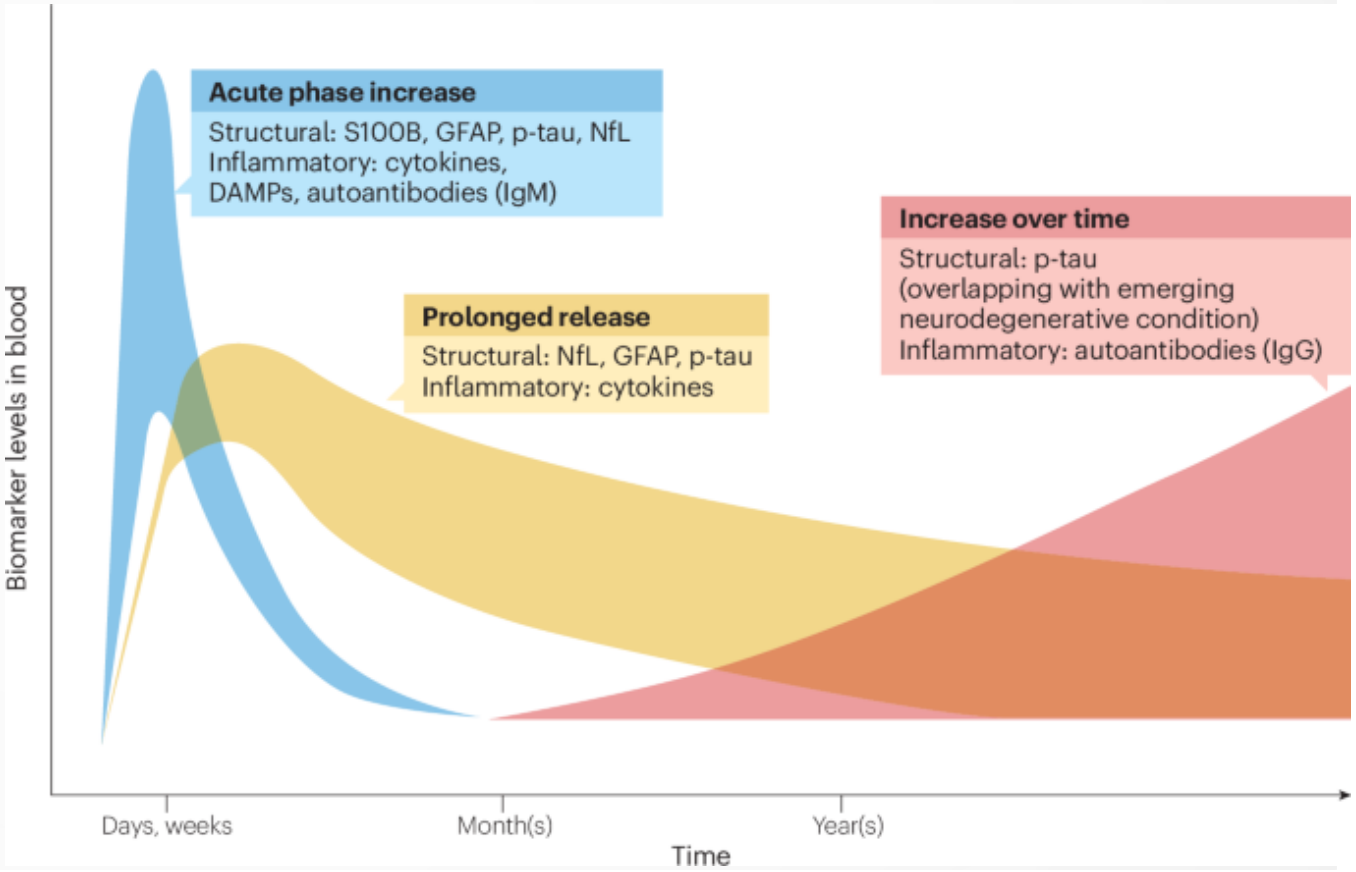
- GFAP is an essential part of astrocyte cells
- Astrocytes support neurons, blood vessels and blood-brain barrier
- Important for brain tissue structure
- Reactive to the damage, part of neuroinflammation but also important for repair process
- Damages in the blood vessels and axons during the TBI
- Indicative also for repair process (=larger damage)?



Abdelhak et al. (2022) Nat Rev Neurol

GFAP PROTEIN AS A TBI MARKER

- Higher acute levels of GFAP in plasma and CSF correlate with higher damage in CT imaging
- Long-term increase (months to years) predicts cognitive impairment
- Particularly with moderate-to-severe TBIs → could be used to predict outcomes and modify treatment?
- In mild TBIs, the role of GFAP levels is not that clear, some contrasting studies are found



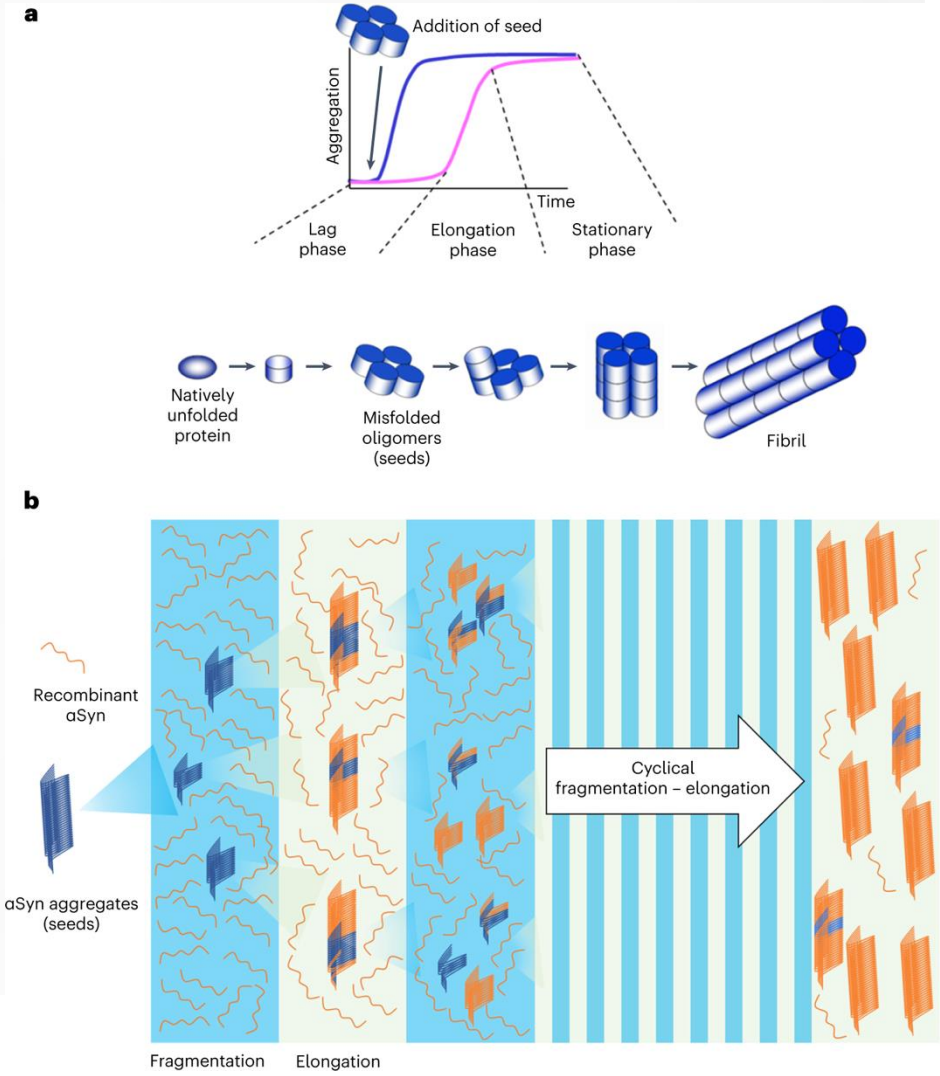
Friberg et al. (2024) Nat Rev Neurol

GFAP AS A BIOMARKER FOR OTHER NEURODEGENERATIVE DISEASES

- **Alzheimer's disease**
  - GFAP is reactive for e.g. amyloid beta and cytokines
  - Elevated already before mild cognitive impairment but increases until the diagnosis and Alzheimer's progression
  - Increase in amyloid beta positive dementia (Alzheimer's disease), can be used to differ from other dementias
  - Higher levels correlate with cognitive decline
  - Increased plasma GFAP predicts onset of Alzheimer's disease
- **ALS**
  - May predict disease progression
- **FTD**
  - May differ between disease subtypes
  - Behavioral vs. language variants, more elevated in BvFTD
- **Parkinson's disease**
  - More elevated in patients with dementia

PARKINSON'S DISEASE BIOMARKERS

- **GFAP** is generally not elevated but can be used for diagnosis between Parkinson's disease and other movement disorders like MSA and PSP
- **Nfl** is not elevated at least early in the disease but similar to GFAP can be used to discriminate other movement disorders
- Most accurate is **alpha-synuclein seed-amplification assay**
  - Based on toxic forms of alpha-synuclein that transforms normal forms as aggregated alpha-synuclein
  - Diagnostic marker, >90% accuracy with prodromal symptom (hyposmia, sleep disorder)
  - Yes-or-no, does not show the amount of alpha-synuclein
  - Only CSF sample is accurate (at the moment)



Concha-Marambio et al. (2023) Nature Protocols

OVERVIEW

Alzheimer's disease

- CSF amyloid beta to verify diagnosis
- pTau217 has the best predictive value even from plasma
- Nfl and GFAP depict disease progression and neuronal damages

FTD and other dementias

- pTau217 and 181 are not reliable for FTD
- Total Tau predicts faster progression
- Nfl and GFAP correlate with faster progession, differences between variants

ALS

- Nfl increased during the disease progression
- Diagnostic marker
- GFAP similar but not as clear as Nfl

TBI

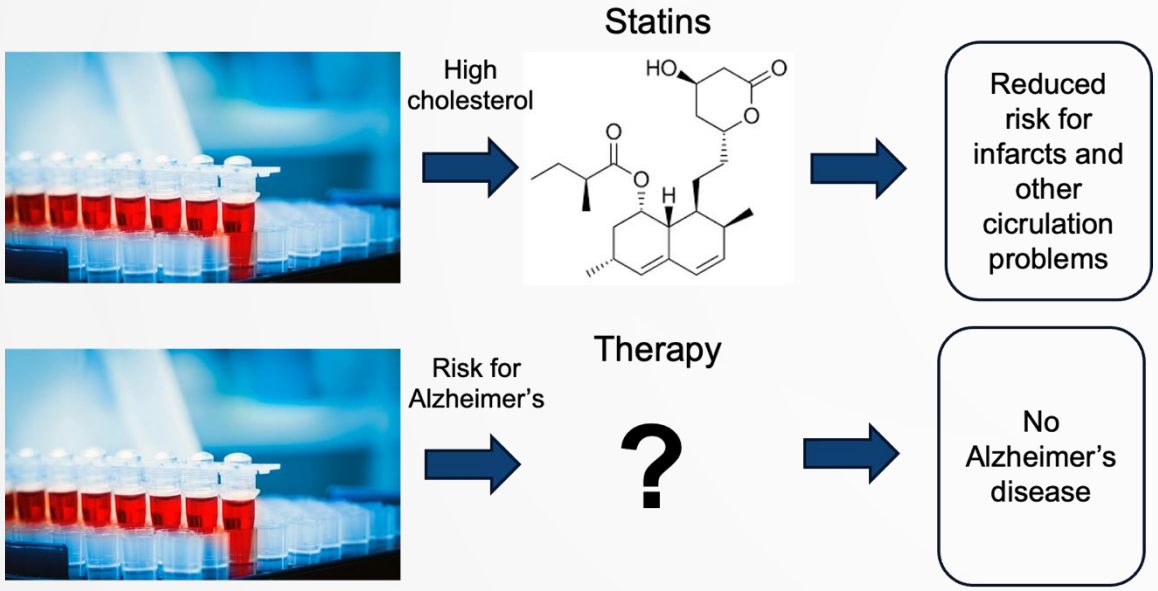
- Nfl predicting outcome and to separate mild from moderate-to-severe
- Elevated GFAP, particularly long term, predicts coginitive decline and poor recovery

PROS AND CONS OF BETTER BIOMARKERS IN NEURODEGENERATIVE DISEASES

- Pros
  - Diagnostic accuracy – correct treatment faster
    - Long diagnostic period may delay the treatment
  - Predictive diagnosis – those who are in risk
    - Possibility for pharmacological or non-pharmacological interventions
    - Routine blood test?
  - Following the disease progression
    - Particularly clinical trials

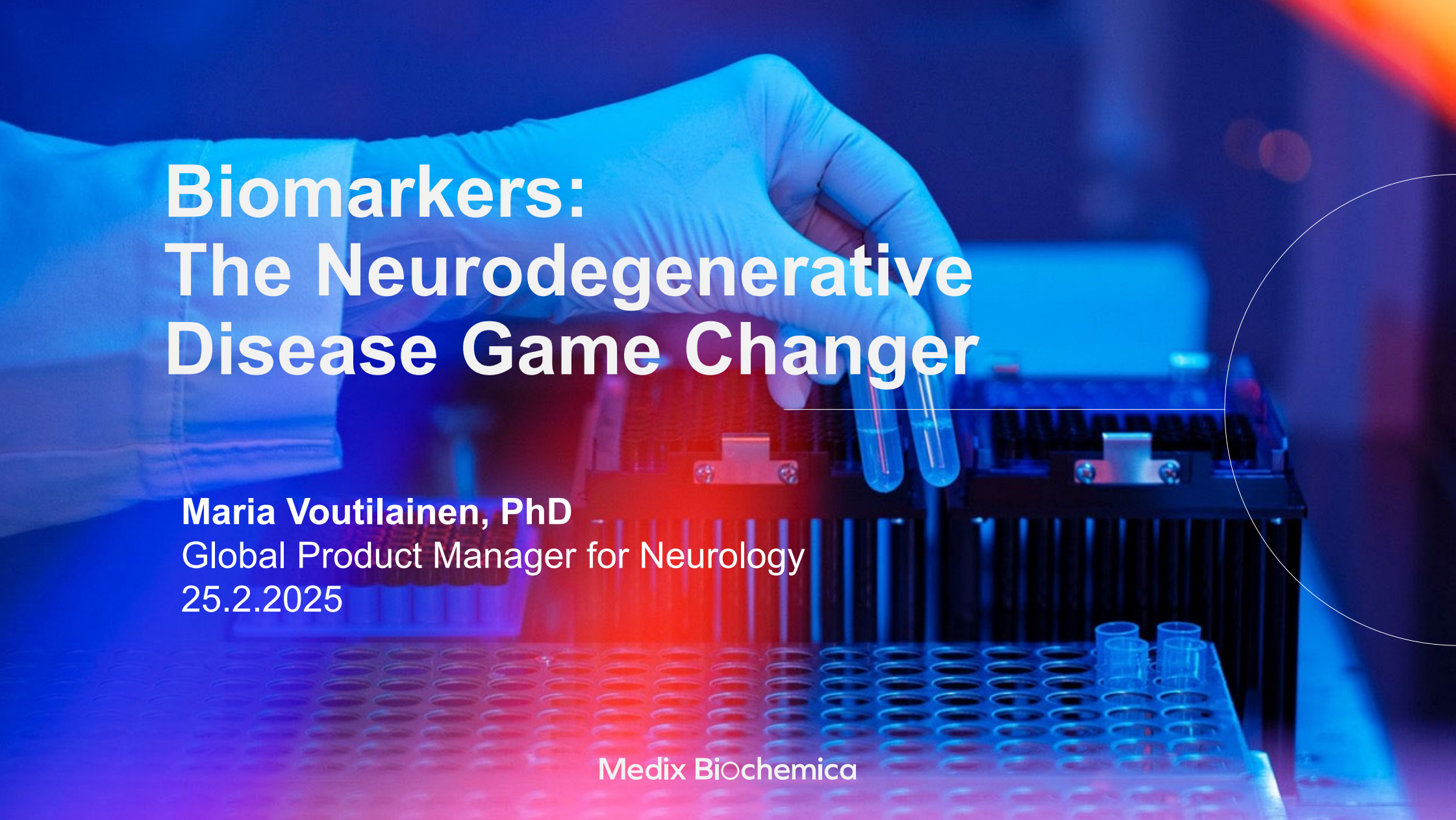
- Cons
  - Serious diseases – accuracy should be very good
    - Emotional stress of false positive diagnosis?
  - No disease-modifying therapy for most of the neurodegenerative diseases
    - How the knowledge of being in the risk affects the patient?
  - For some assays, invasive sampling needed

FUTURE DIRECTIONS



- What we need?
  - Accurate blood-based biomarkers
    - Other sampling methods are too invasive
  - Accurate enough to classify different diseases
    - No false positives
    - One marker of combination?
    - Novel markers
  - Disease-modifying therapy
    - Better biomarkers will help with this
- This will be the future

THANK YOU!



Biomarkers: The Neurodegenerative Disease Game Changer

Maria Voutilainen, PhD
Global Product Manager for Neurology
25.2.2025

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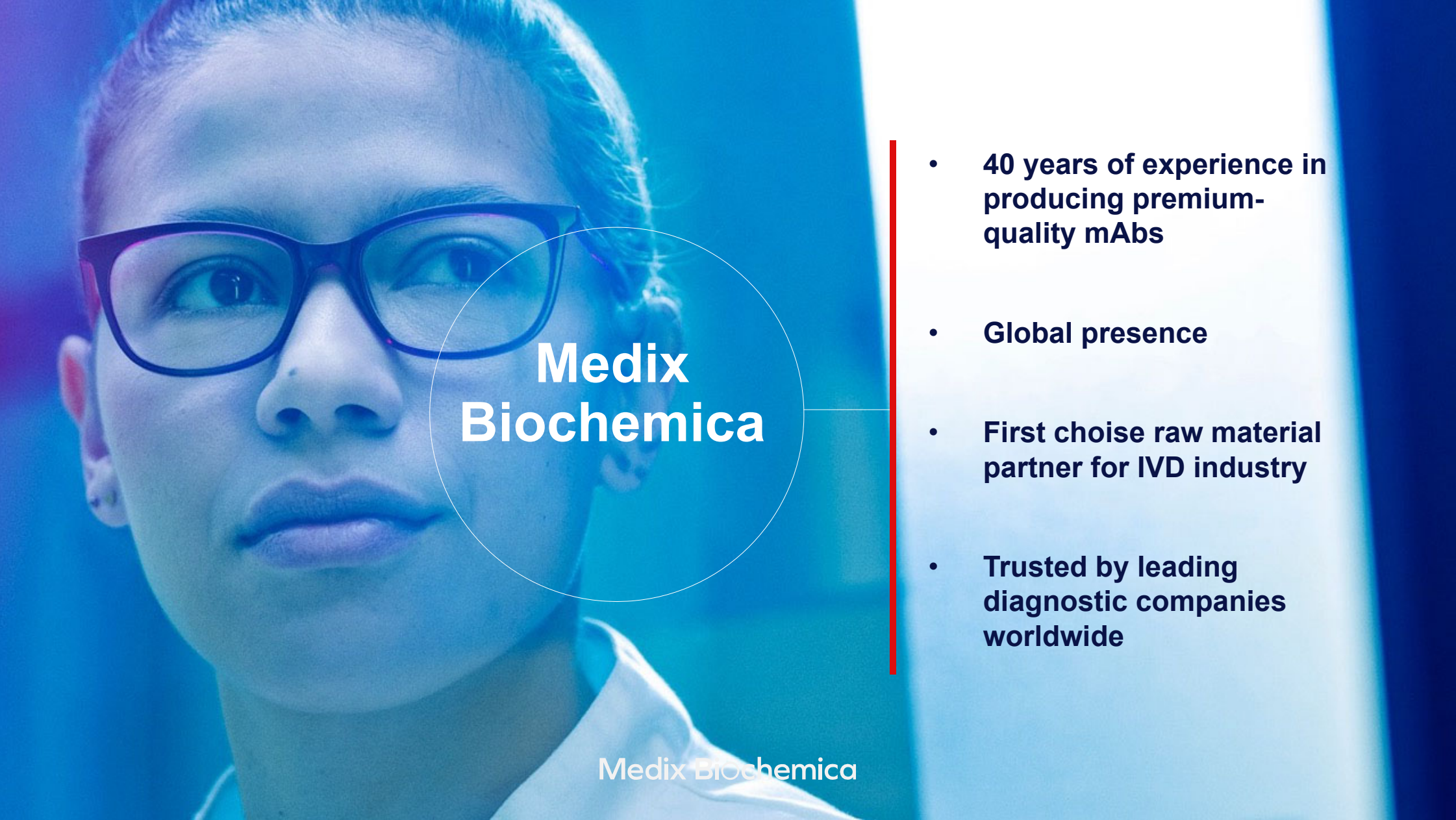

Medix Biochemica

- 40 years of experience in producing premium-quality mAbs
- Global presence
- First choise raw material partner for IVD industry
- Trusted by leading diagnostic companies worldwide

The Qualified Supplier to the IVD Industry

IVD test manufacturers across the globe trust Medix Biochemica as their partner of choice for IVD raw materials

- **Quality**
- **Supply Reliability**
- **Scientific Innovation**
- **Comprehensive Portfolio**

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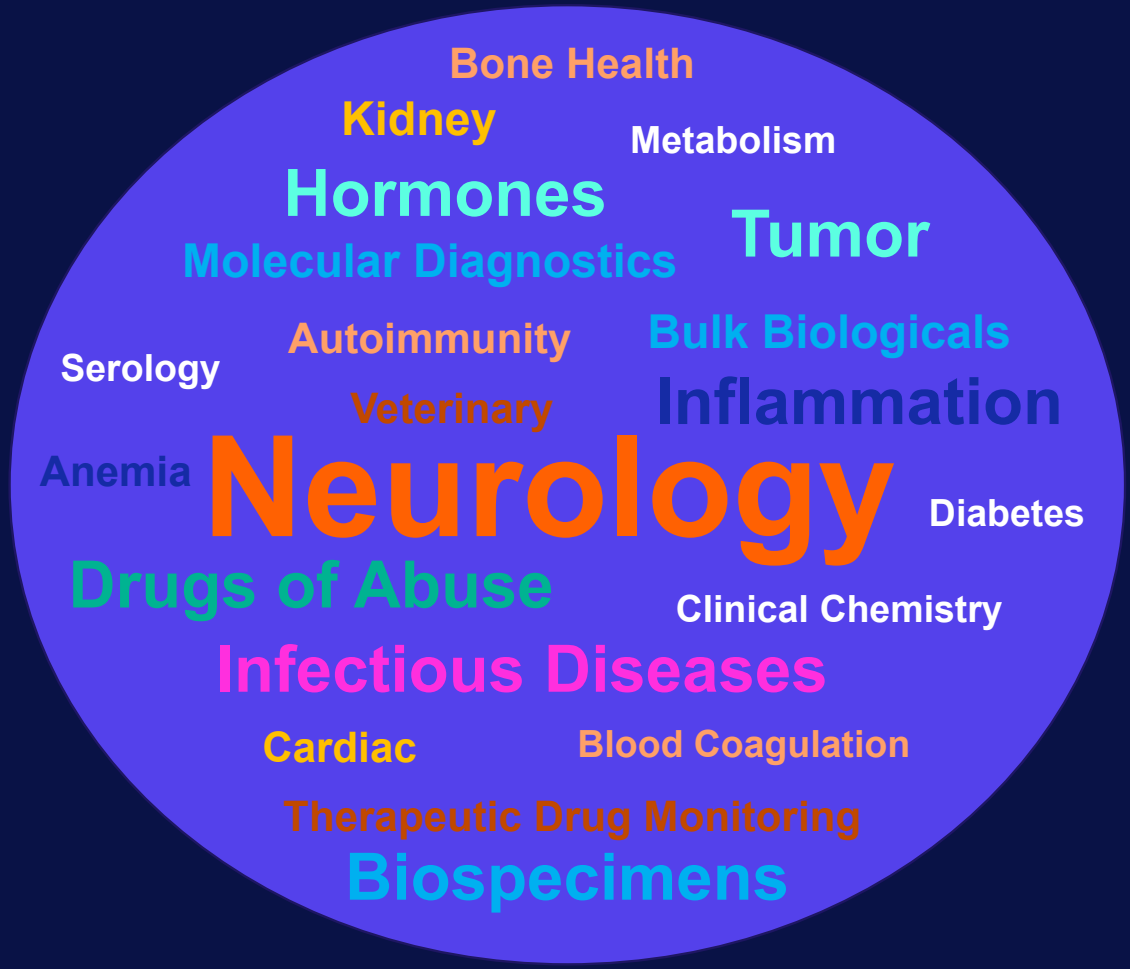
Clinical Areas Supported



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Clinical Areas Supported

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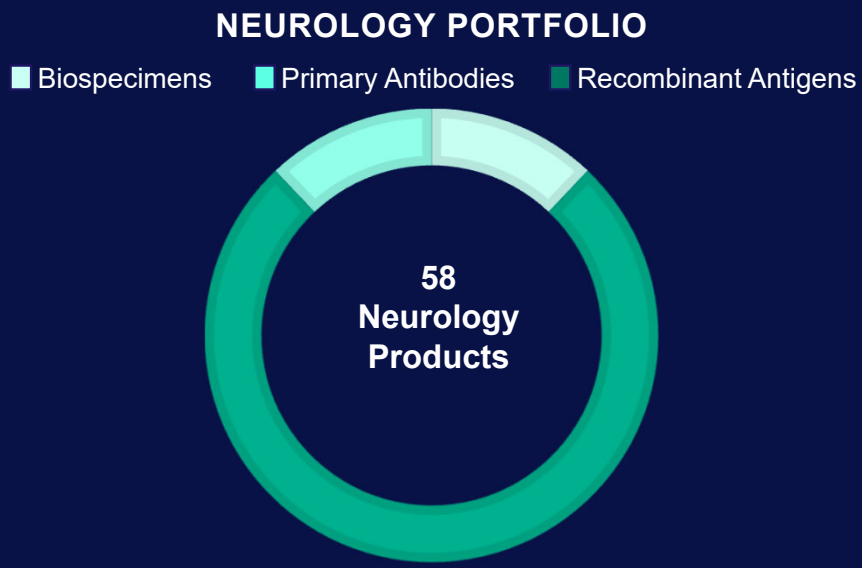
Neurology Portfolio

Antibodies & Antigens

- GFAP (Glial Fibrillary Acidic Protein)
- NfH (Neurofilament H)
- NfL (Neurofilament L)
- NSE (Neuron Specific Enolase)
- S100B
- α-Syn (Synuclein alpha)
- Tau
  - P-Tau181
  - P-Tau217
  - P-Tau231
  - Total Tau
- UCHL1 (Ubiquitin carboxy-terminal Hydrolase)

Upcoming Products:

- Amyloid beta (1-40)
- Amyloid beta (1-42)



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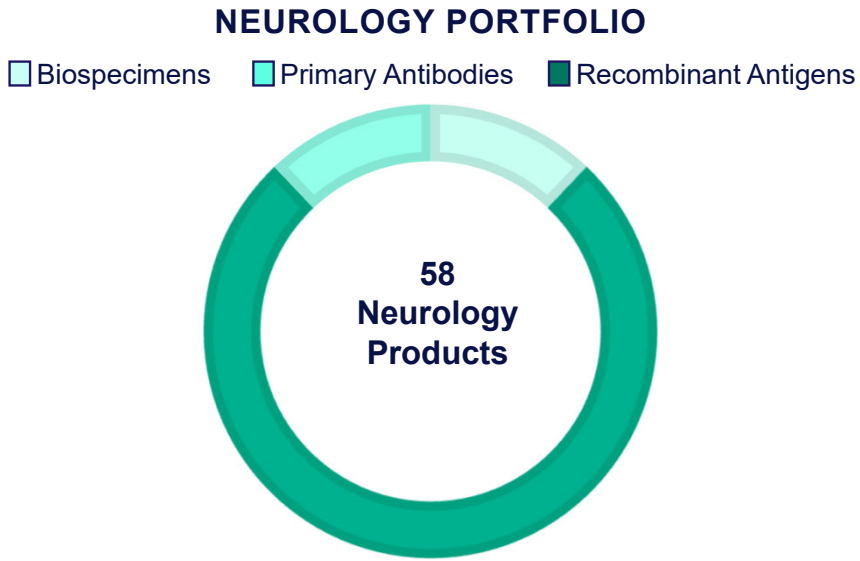
Medix Biochemica Neurology Portfolio

Antibodies, Antigens & Neuro Biospecimens

Extensive list of Neurology mAbs and Antigens

mAbs	Product Number
NSE	100388
	100408
S100B	100778
	100779
	100781
p-Tau231	140036
p-Tau181	140037
p-Tau217	140050
Total Tau	140038
	140039
	140040
GFAP	140046
	140047
	140048
	140049
Synuclein alpha	HM1089
	HM1092
	HM1093
	HM1094
NfL	100984
	100985
	100986
NfL	HM1095
	HM1096
	HM1097
	HM1098
	HM1099
	HM1100
	HM1101
	HM1184
NfH	HM1247
	HM1249
	HM1250
	HM1252
	HM1253
	HM1254
UCHL1	HM1415
	HM1416
	HM1417
	HM1418
	HM1419
	HM1420
	HM1421
	HM1422

Antigen	Product Number
NSE	430-11
	610150
S100B	LA521
Synuclein alpha	LA662
NfL	LA665
	LA666
	LA667
NfH	LA789



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Medix Biochemica Neurology Portfolio

Antibodies, Antigens & Neuro Biospecimens

Extensive list of Neurology mAbs and Antigens

mAbs	Product Number
NSE	100388
	100408
S100B	100778
	100779
p-Tau231	140036
p-Tau181	140037
p-Tau217	140050
Total Tau	140038
	140039
	140040
GFAP	140047
	140048
	140049
Synuclein alpha	HM1089
	HM1092
	HM1093
	HM1094
NfL	100984
	100985
	100986
NfL	HM1095
	HM1096
	HM1097
	HM1098
	HM1099
	HM1100
	HM1101
	HM1184
NfH	HM1247
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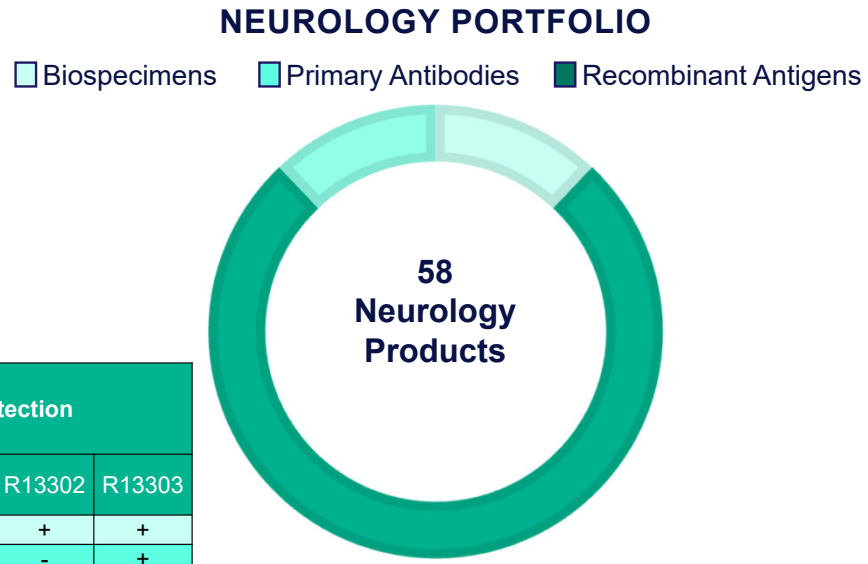
	HM1250
	HM1252
	HM1253
	HM1254
UCHL1	HM1415
	HM1416
	HM1417
	HM1418
	HM1419
	HM1420
	HM1421
	HM1422

Antigen	Product Number
NSE	430-11
	610150
S100B	LA521
Synuclein alpha	LA662
NfL	LA665
	LA666
	LA667
NfH	LA789

			Detection		
			R13301	R13302	R13303
Capture	(t-Tau)	R13301	-	+	+
		R13302	+	-	+
		R13303	+	+	-
	(p-Tau181)	R13321	+	+	+
	(p-Tau231)	R13322	+	+	+
	(p-Tau217)	R13323	+	+	+



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Biomarker Indications

Amyotrophic Lateral Sclerosis (ALS)
- NfL (Neurofilament L)
- UCHL1 (Ubiquitin carboxy-terminal Hydrolase)

Parkinson's Disease
- α-Syn (Synuclein alpha)

Alzheimer's Disease
- Amyloid beta (1-40) (Upcoming)
- Amyloid beta (1-42) (Upcoming)
- Tau
  - P-Tau181
  - P-Tau217
  - P-Tau231
- Total Tau
- GFAP (Glial Fibrillary Acidic Protein)
- NfL (Neurofilament L)

Traumatic Brain Injury (TBI)
- GFAP (Glial Fibrillary Acidic Protein)
- NfH (Neurofilament H)
- NfL (Neurofilament L)
- UCHL1 (Ubiquitin carboxy-terminal Hydrolase)

General Neuronal Injury
- NSE (Neuron Specific Enolase)

Multiple Sclerosis
- GFAP (Glial Fibrillary Acidic Protein)
- NfH (Neurofilament H)
- NfL (Neurofilament L)
- S100B
- UCHL1 (Ubiquitin carboxy-terminal Hydrolase

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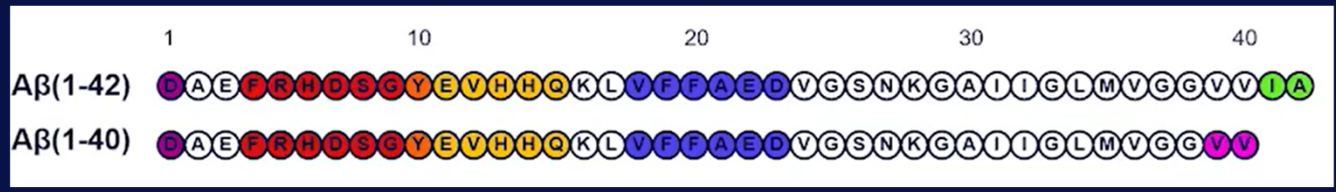
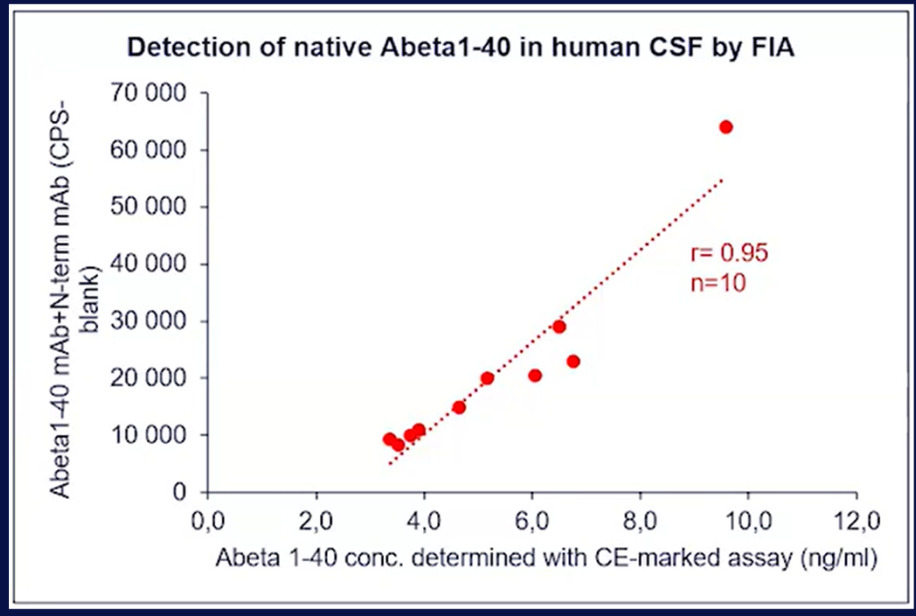
NEW Launch: Amyloid Beta (1-40) & (1-42)



- Monoclonal antibodies (mAbs) for the specific detection of the C-terminus in Aβ42 and Aβ1-40, and mAbs for the N-terminus.
- For Aβ1-40, the detection of the native protein in cerebrospinal fluid (CSF) has been verified with correlation to known concentrations measured using a CE-marked assay.

Amyloid β 1-40 available in March 2025 and
Amyloid β 1-42 in summer, 2025



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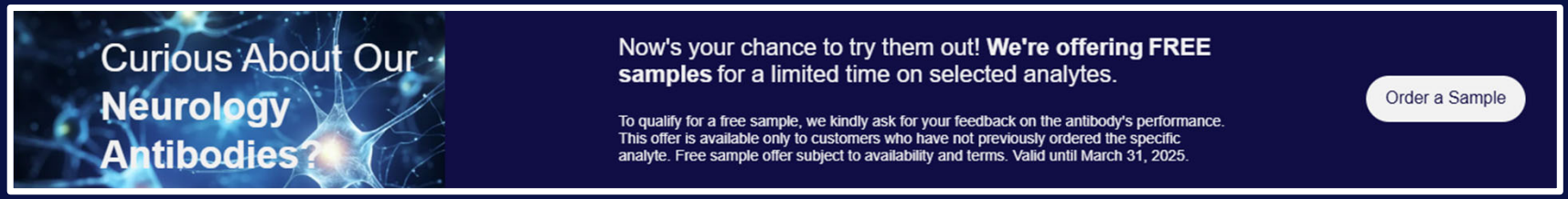
Exclusive Offer of Free Neurology Samples



Exclusive Offer: Free Samples

We are offering free samples of our selected neurology antibodies for a limited time. Test our products and provide feedback!

List of Free Samples

Analyte	Product Number
NSE	100388
	100408
S100B	100778
	100778
	100781
NfL	100984
	100985
	100986
p-Tau231	140036
p-Tau181	140037
p-Tau217	140050
Total Tau	140038
	140039
	140040
GFAP	140046
	140047
	140048
	140049

Not seeing your analyte of interest? Let us know which ones below and we'll be in touch on what we can offer:

- NfH
- UCHL1
- Synuclein alpha
- Other

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Biospecimens for Neurology

Capabilities

- Custom collection criteria or selection
- Demographic and disease/severity selection, infectious testing of samples/donors
- Clinical remnants/single samples
- Bulk, pooled volumes
- Target analyte testing and reporting
- Individual lot testing, selection, hold, and acceptance

Product Code	Matrix	Indication	Donor Data Available	Volumes Offered per Donor
991-19-S	CSF	Single Donor	Age, Gender, Collection Date	1-5 mL
991-19-S-PED	CSF	Pediatric Donors (<18 years old)	Age, Gender, Collection Date	1 mL
991-19-P	CSF	Pooled Donors	Custom pooling abilities	1-1000 mL
991-58-S-ALZ	Plasma	Alzheimer's Disease	Age, Gender, Race, MMSE Score	1-10 mL, paired sets available
991-58-S-MS	Plasma	Multiple Sclerosis	Age, Gender, Race, EDSS Score	1-10 mL, paired sets available
991-58-S-PD	Plasma	Parkinson's Disease	Age, Gender, Race	1-10 mL, paired sets available
991-58-S-MCI	Plasma	Mild Cognitive Impairment	Age, Gender, Race	1-10 mL, paired sets available
991-24-S-ALZ	Serum	Alzheimer's Disease	Age, Gender, Race, MMSE Score	1-10 mL, paired sets available
991-24-S-MS	Serum	Multiple Sclerosis	Age, Gender, Race, EDSS Score	1-10 mL, paired sets available
991-24-S-PD	Serum	Parkinson's Disease	Age, Gender, Race	1-10 mL, paired sets available
991-24-S-MCI	Serum	Mild Cognitive Impairment	Age, Gender, Race	1-10 mL, paired sets available


Thank you
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Questions and Answers

Professor Timo Myöhänen

Professor in Pharmacology
Faculty of Medicine, University of Helsinki

Dr. Maria Voutilainen

Global Product Manager
Medix Biochemica

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Thank you
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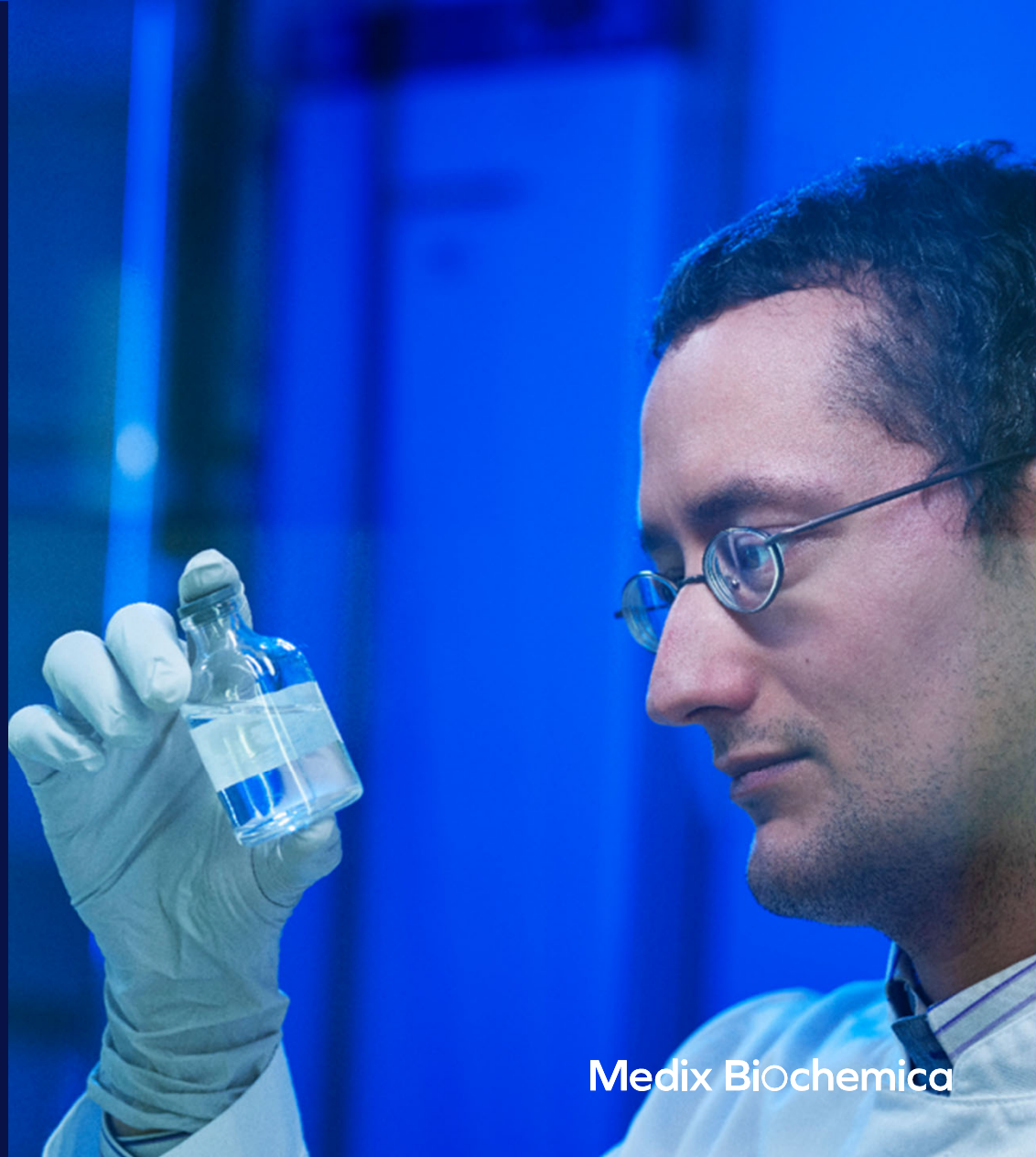

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