Shaping the Future of Neurology: The Role of Laboratory Medicine

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PLMS 2026 Medical Laboratory Week
April 13th, 2026


Picture from: https://academic.ubc.ca/brain-health

Presentation Overview

Blood based biomarkers for brain health: from research to care

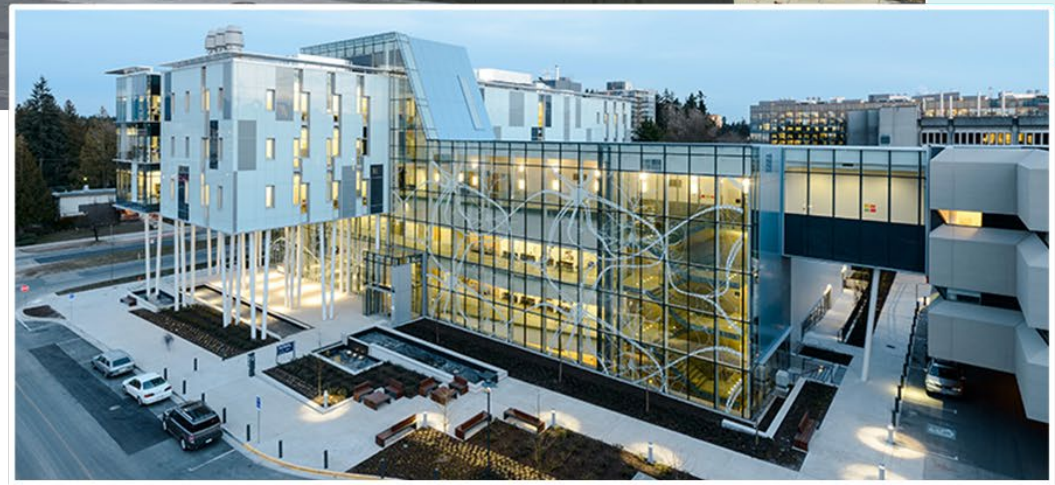
1. Discuss how technological evolution has launched the rapidly growing **field of neurological biomarker testing** and establishment of the UBC Core Facility for Neurology Biomarker Innovation (**CFNBI**)

2. Biological **diagnosis of Alzheimer's disease**: Considerations for implementation in Canada and additional research required

3. Repurposing technology: **Point-of-care testing** for remote, rural, and critical care settings

4. Establishing a **framework for clinical implementation** of blood biomarker testing: Multidisciplinary approach

Wellington Laboratory & CFNBI



We respectfully acknowledge that the UBC Vancouver academic campus is located on the traditional, ancestral, unceded territory of the xʷməθkʷəy̓əm (Musqueam), Skwxwú7mesh (Squamish) and səl̓ilwətaʔɬ (Tsleil-Waututh) peoples

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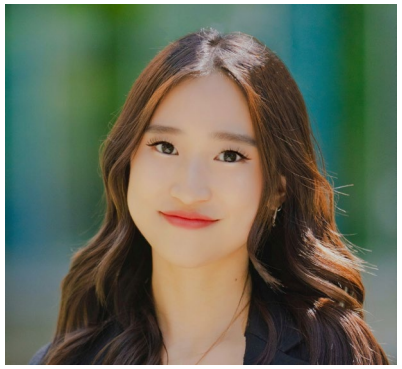


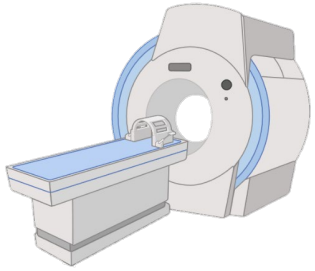
Dana Go
MSc Student
COVID-19

Alumni: Megan Harper, Tali Romero, Chloe Allen, Johnny Huang, Nyra Ahmed, Jasmine Gill, Dr. Colin Wallace

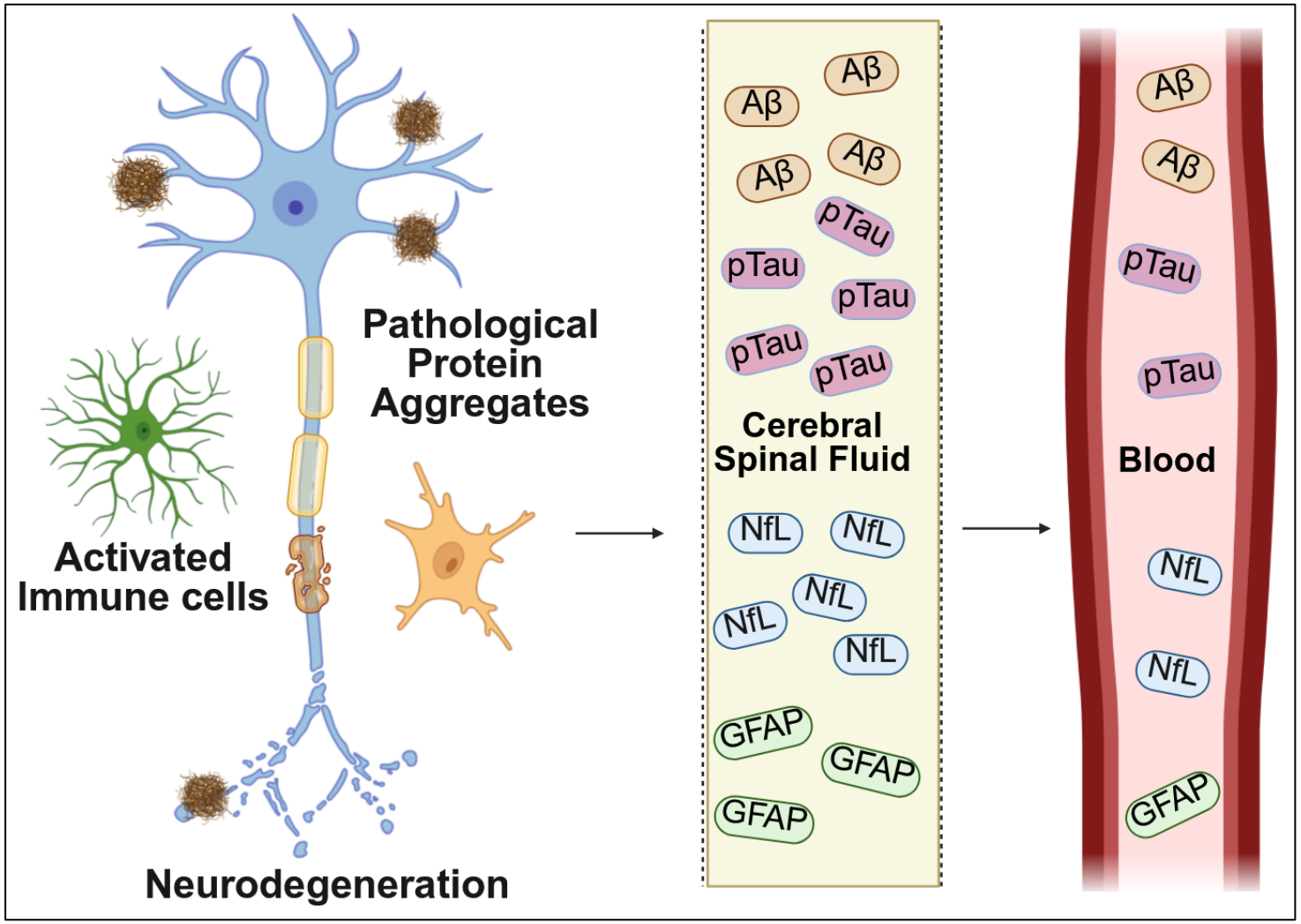
Why Do We Measure Fluid Biomarkers?

Traditional diagnostic methods for neurology:

Cognitive and Neuropsychiatric Tests



Neuroimaging (PET & MRI)



Teunissen CE, et al. Lancet Neurol. 2022 Jan;21(1):66-77

Blood biomarkers that can detect underlying pathology can provide **earlier and more accurate diagnosis**

Context of Use

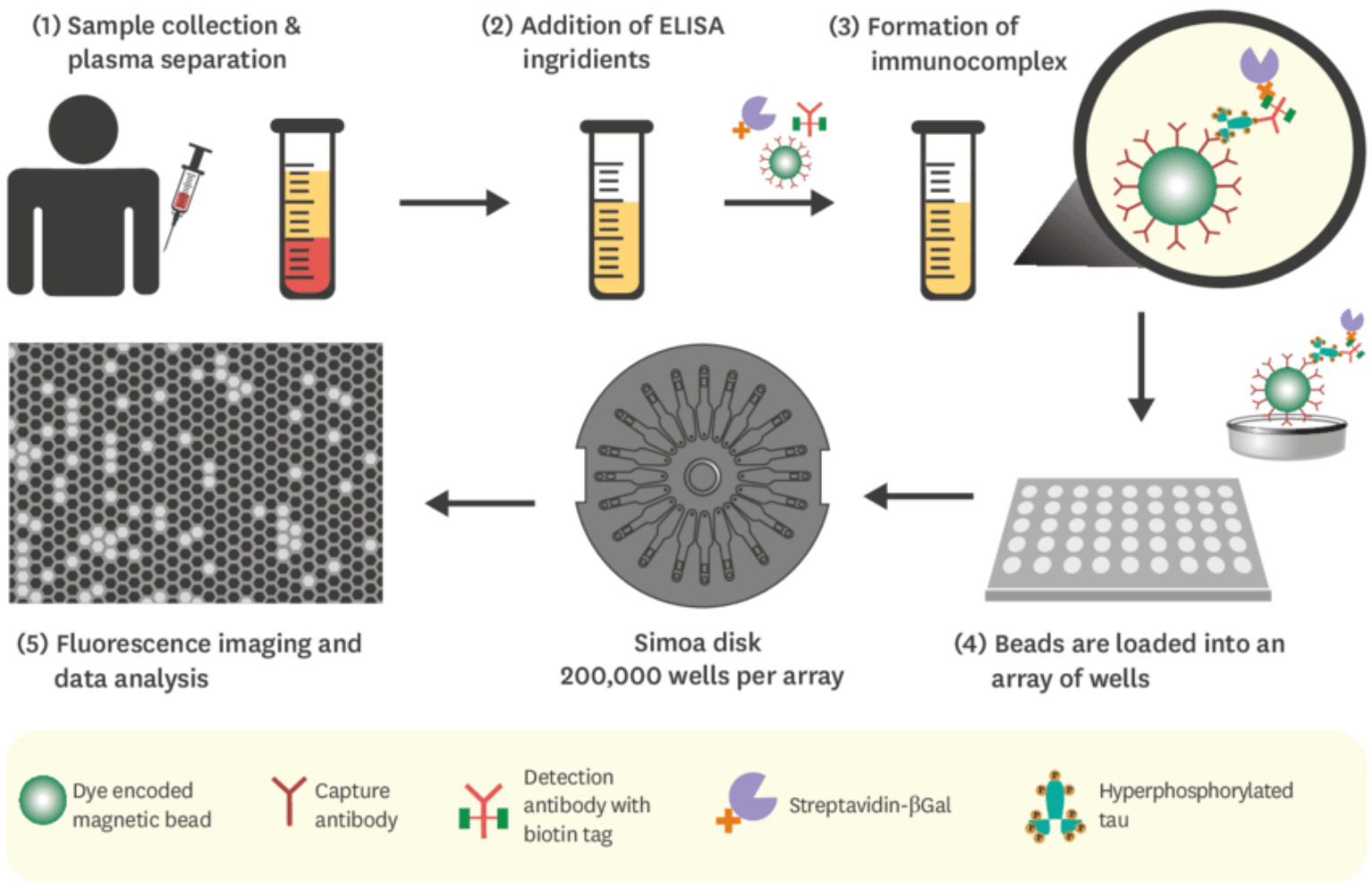
What is the condition the biomarker will be used it and what will it inform on?

Some examples of conditions: Alzheimer's disease and related dementias, traumatic brain injury, multiple sclerosis

Screening	Earlier detection of at-risk patients or pathology prior to symptom onset
Diagnosis	Detects the presence of a disease or identifies a specific disease subtype
Monitoring	Assesses the status of a disease or evidence of exposure to a treatment
Pharmacodynamic	Indicates biological response to treatment has occurred
Prognosis	Predicts the likelihood of a clinical event, disease recurrence, or progression

Methodological challenge: How do we accurately quantify ultra-low abundant analytes?

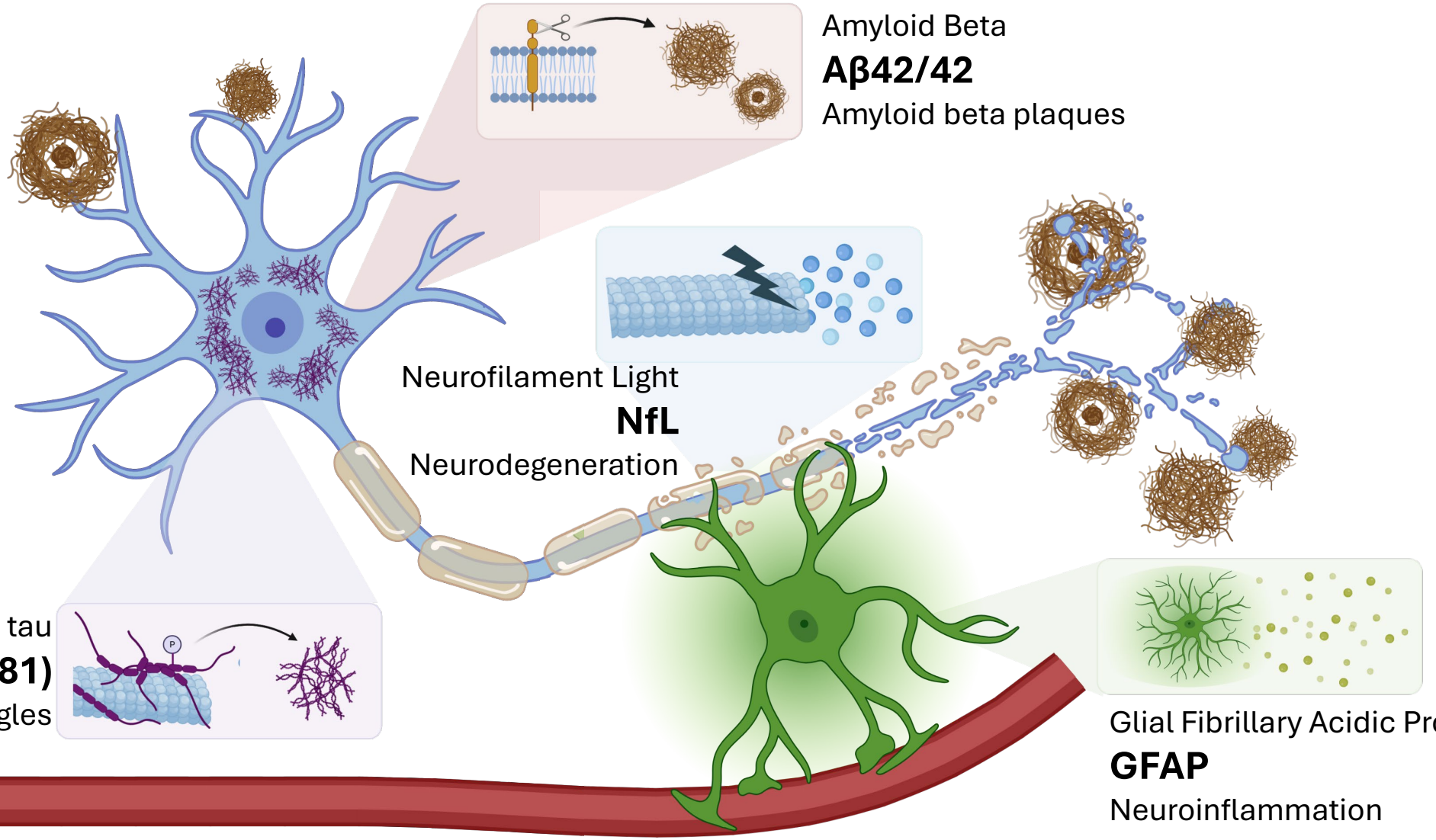
Simoa: Advent Of Ultra Sensitive Technology



Quanterix HD-X Platform

Launched in the early 2010s, Simoa technology launched the field of neurological blood biomarkers

Key Neurological Plasma Biomarkers



Amyloid Beta

Aβ42/42

Amyloid beta plaques

Neurofilament Light

NfL

Neurodegeneration

Phosphorylated tau

p-tau(217 or 181)

Neurofibrillary tangles

Glial Fibrillary Acidic Protein

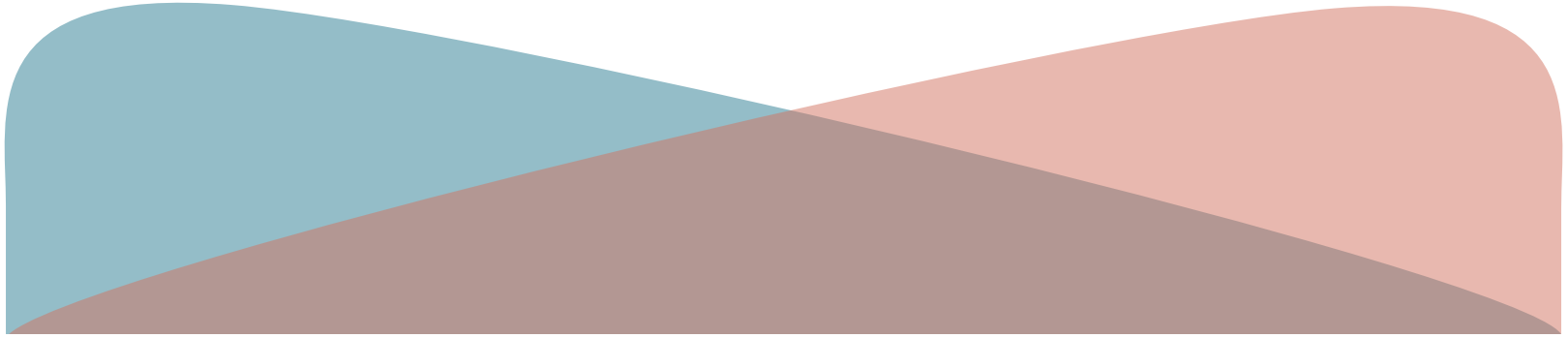
GFAP

Neuroinflammation

Expansion of Technology

Number of candidate markers

Number of biospecimens used



Marker Discovery → Analytical Validation → Clinical Validation → Regulatory Approval

ALAMAR BIOSCIENCES

Olink

somalogic

Quanterix
Discovery Fueled by Ultra-Sensitivity

Roche

SIEMENS

FUJIREBIO

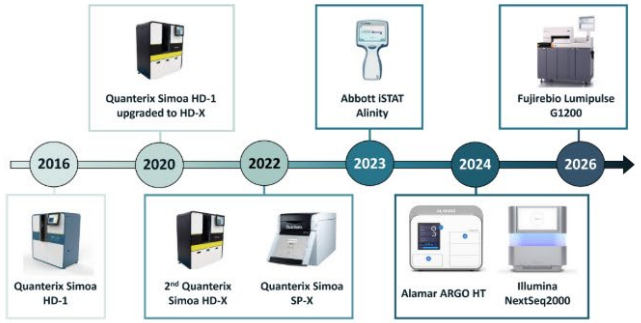
BECKMAN COULTER

Abbott

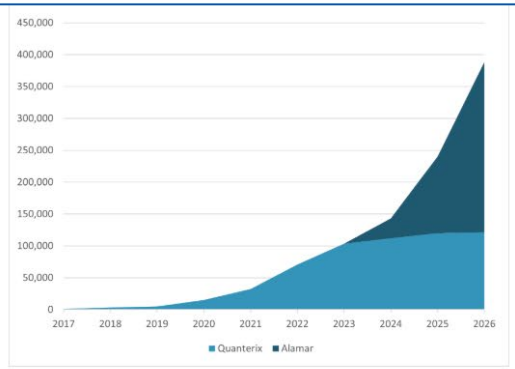
Core Facility for Neurology Biomarker Innovation

Our goal is to improve the diagnosis, prognosis, and treatment for individuals with neurological conditions by advancing fluid biomarker research

Analyzer Evolution



Data Points



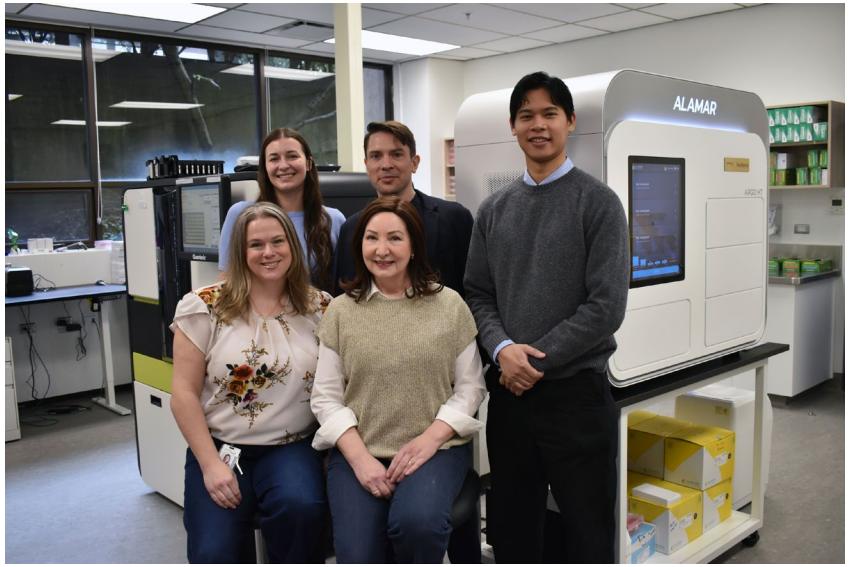
Our Collaborative Network

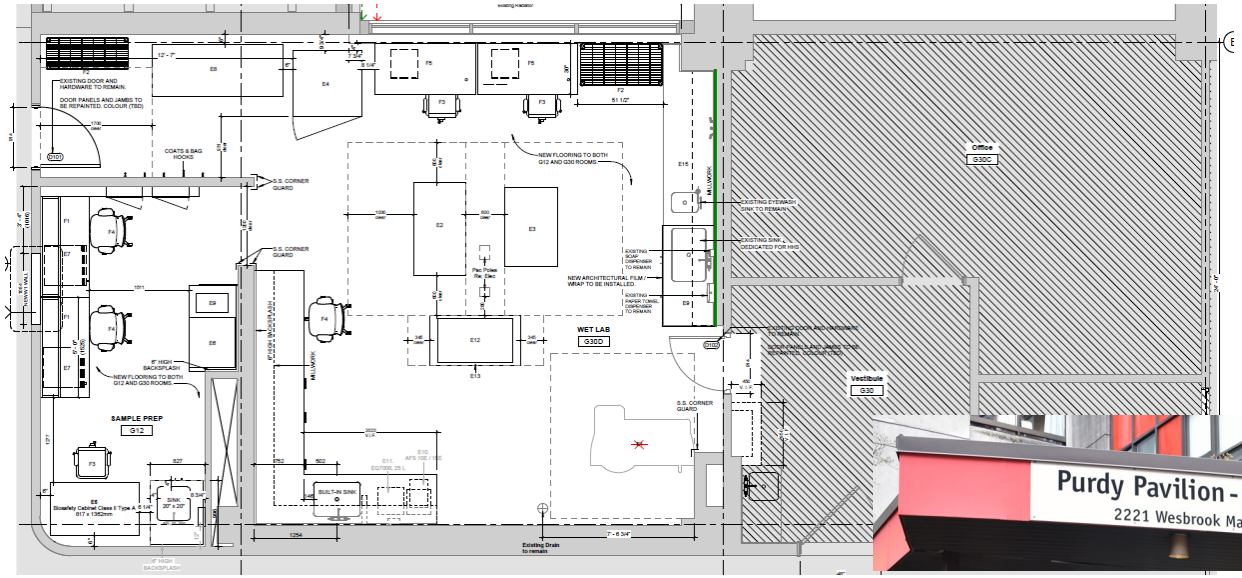
>140 Investigators Engaged

National	International
116 investigators	24 investigators

From >39 Institutions

23 across Canada

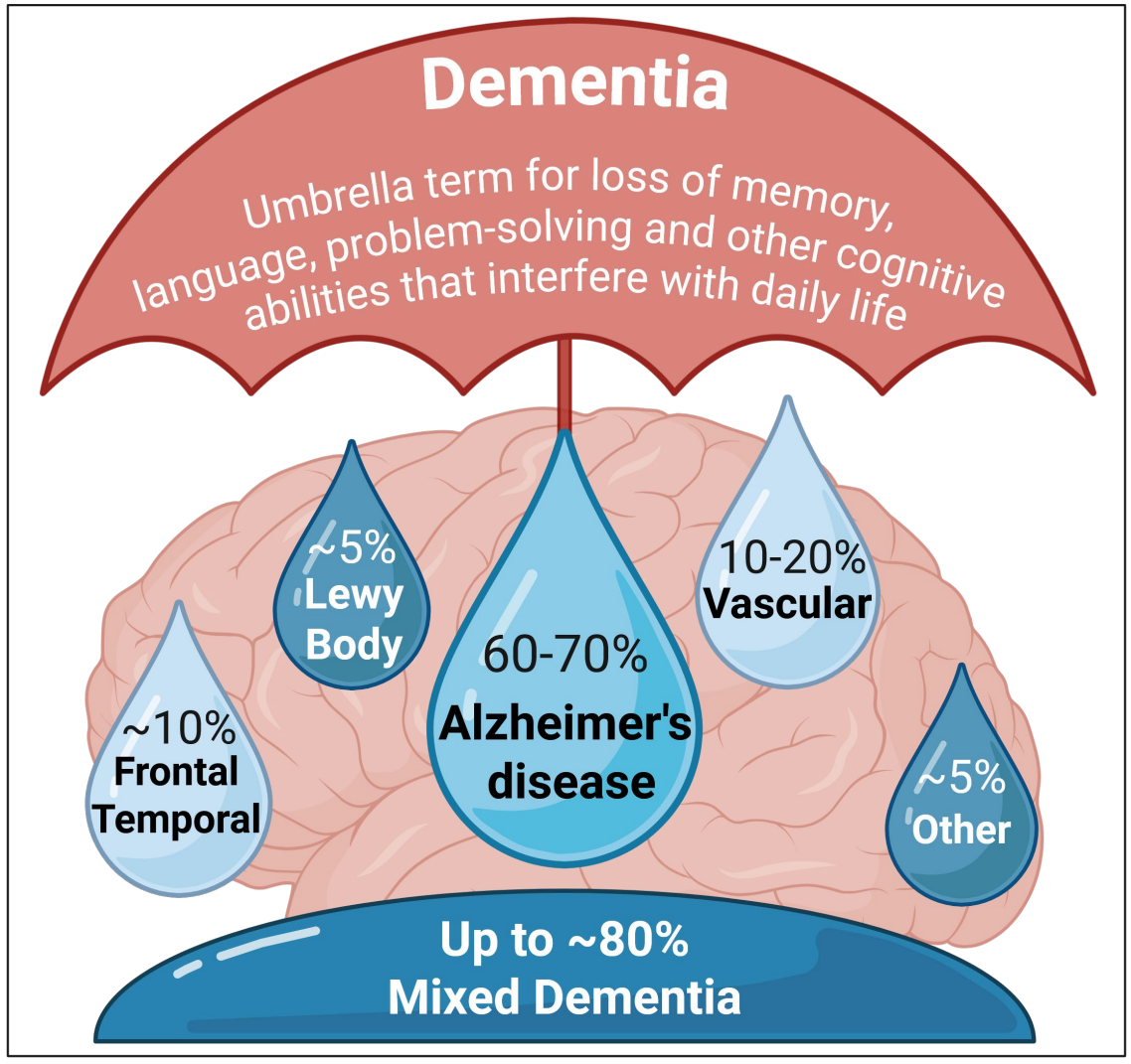




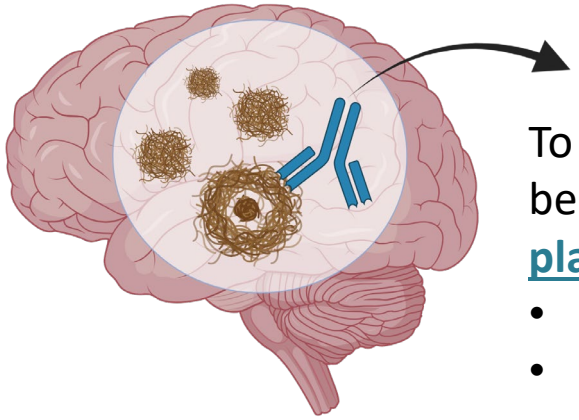
Blood Biomarkers for Alzheimer's Disease: Considerations and Implementation

Closer Look at Alzheimer's Disease

What does it mean to diagnose Alzheimer's disease?



When we talk about diagnosis AD with a blood test, we mean **detecting AD pathology**, not diagnosis AD dementia



To date most blood tests for AD have been focused on detecting **amyloid plaques**

- Pathological hallmark
- New disease modifying therapies

To fully implement and integrate blood tests into the clinical care pipeline, we need to consider:

- **Who** are we testing
- **How** are we testing them
- **What** questions remain unanswered

Questions and considerations for clinical validation

Who are we testing?

Are we testing symptomatic (dementia, cognitive impairment), or asymptomatic individuals?

- Currently anti-amyloid therapies are only approved for use in symptomatic people

- Testing prior to symptoms could halve pros or cons
  - Pros: early screening could lead to earlier more effective treatment
  - CON: ~20-30% of people >70y old have Aβ plaques in their brain, but not all develop AD dementia
    - A further prognostic test for development of symptoms would be required

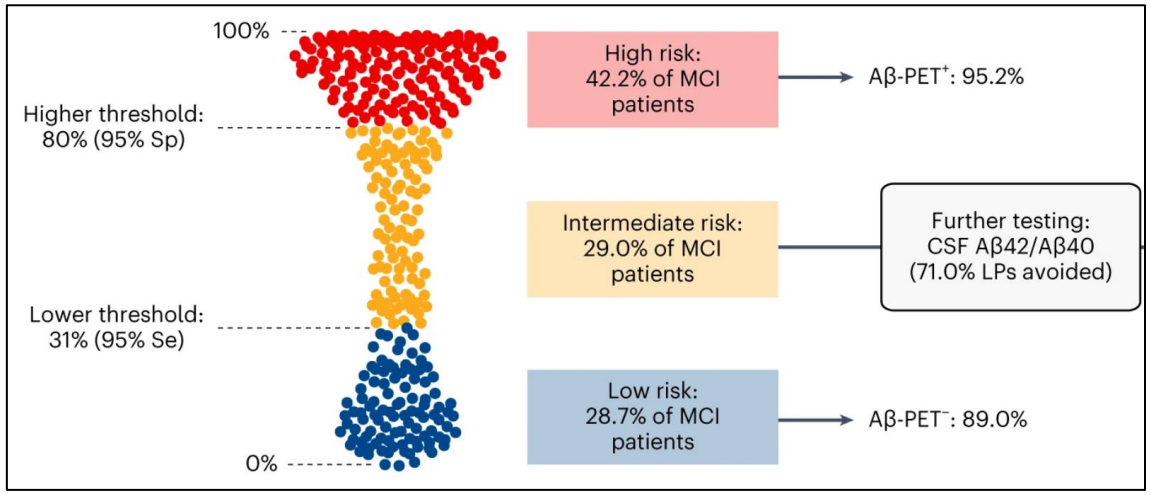
- In 2025, both Fujirebio and Roche gained FDA approval (breakthrough device) for their plasma tests, but with slightly different approaches:
  - Fujirebio (pTau217/Aβ42): symptomatic adults > 55 years of age in specialized care settings; used to predict the presence of amyloid (AD+)
  - Roche (pTau181): symptomatic adults > 55 years of age in primary care setting; used to rule out AD during initial assessments

Closer Look at Alzheimer's Disease

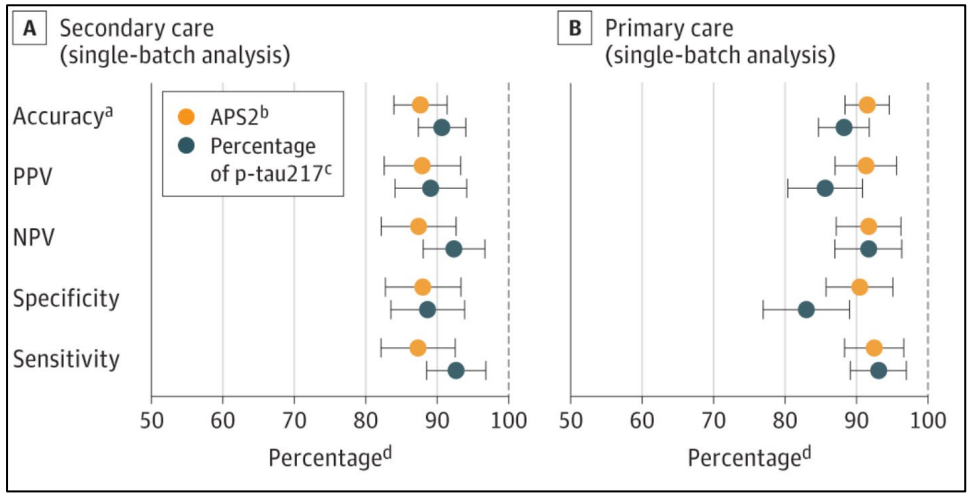
Questions and considerations for clinical validation

What cut-off(s) are we using?

Use one marker or multiple? Single cut-off or more? What balance of sensitivity and specificity should we aim for?



A two-step workflow based on plasma p-tau217 to screen for amyloid β positivity with further confirmatory testing only in uncertain cases
https://www.nature.com/articles/s43587-023-00471-5



Blood Biomarkers to Detect Alzheimer Disease in Primary Care and Secondary Care https://jamanetwork.com/journals/jama/fullarticle/2821669

Alzheimer's Association Clinical Practice Guideline on the use of blood-based biomarkers in the diagnostic workup of suspected Alzheimer's disease within specialized care settings
https://alz-journals.onlinelibrary.wiley.com/doi/10.1002/alz.70535
(1) BBM tests with ≥90% sensitivity and ≥75% specificity can be used as a triaging test and (2) BBM tests with ≥90% sensitivity and specificity can serve as a substitute for amyloid PET imaging or CSF AD biomarker testing in patients with cognitive impairment presenting to specialized care for memory disorders.

Closer Look at Alzheimer's Disease

Challenges of moving into clinical practice (Canada)

Regulatory approval is different in every country. In Canada a test can be approved as a lab developed test (LDT) or an in vitro diagnostic test (IVD).

- IVDs are regulated by Health Canada, while LTDs are not
  - LTDs are therefore easier to move forward, but can be harder to standardize or publicly fund

- Each province has a different method of approving tests
  - Both in terms of its use and its coverage

- As of fall 2025, Life Labs started to offer an array of AD blood tests (pTau217, pTau181, Aβ, NfL, APOE4)
  - ~300-$600 out of pocket for the patient per biomarker
  - All physical analysis being done out of Canada (we currently lack infrastructure)
  - Extensive economic analysis is required to determine public funding for test → will it be possible to complete this prior to a larger scale role out of disease modifying therapies for AD?

In addition to implementation, more research is required to answer key questions

Generation of Reference Curves

Canadian Health Measures Survey – Statistics Canada

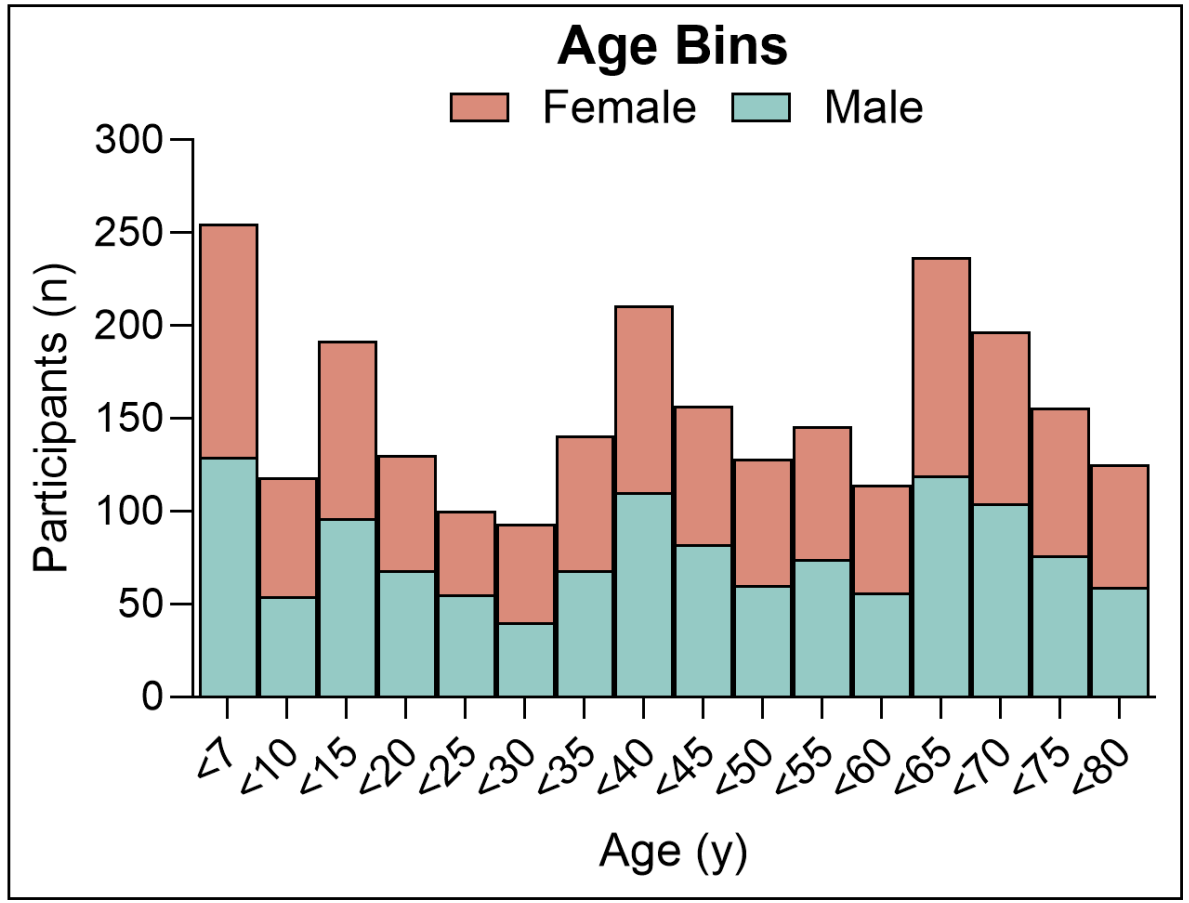
Statistics Canada

National observational epidemiological study to improve the prevention, diagnosis and treatment of illnesses

Normative population = Representative of full population *NOT* purely healthy

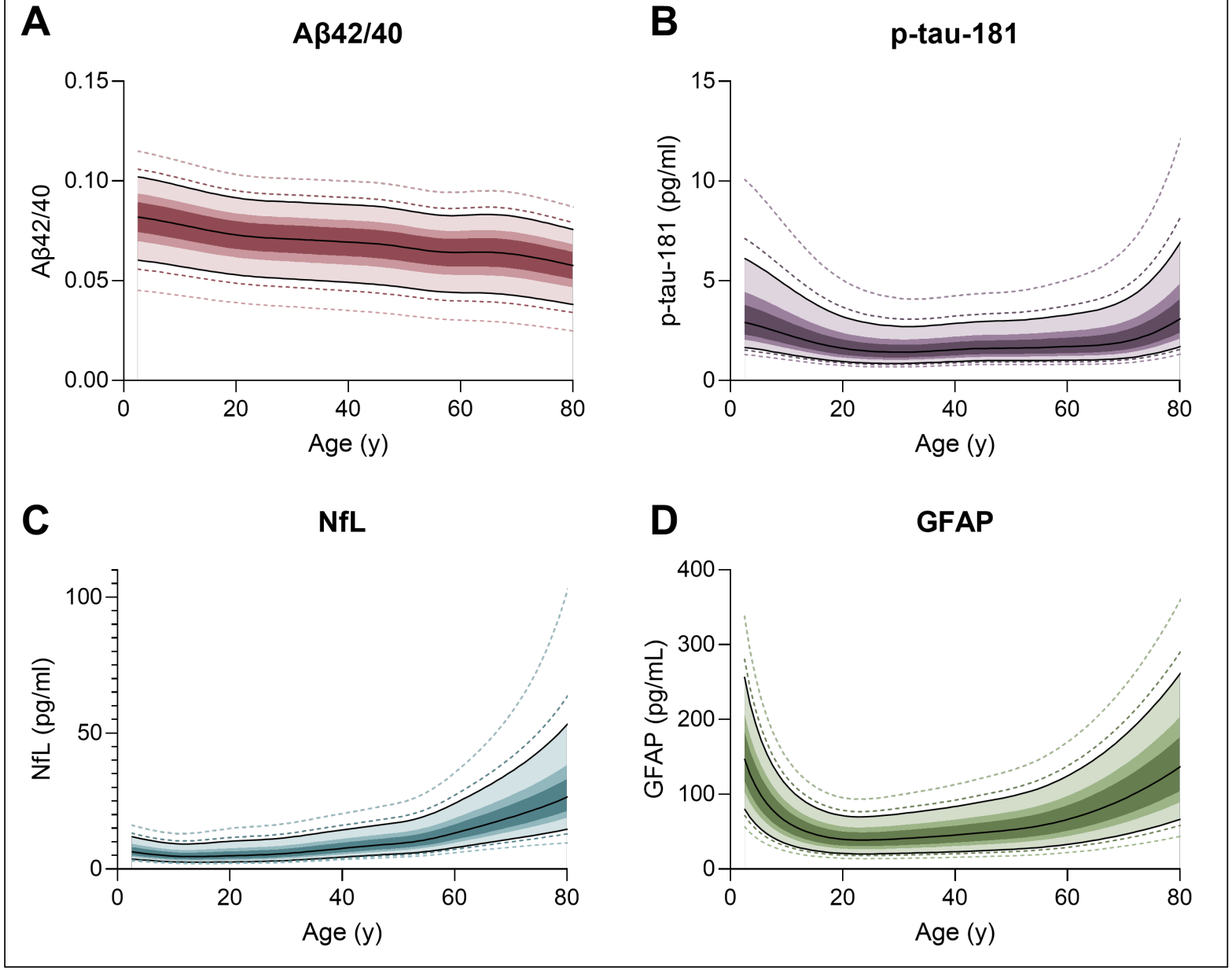
Cross sectional study repeated every ~2 years that collects data on ~6,000 Canadians

- Socio-demographic factors
- Chronic health conditions and medications
- Lifestyle and environmental exposures
- Clinical lab tests



Key Question: Do we need age-specific reference intervals for plasma biomarkers?

Plasma Reference Curves



GAMLSS regression was used to determine smoothed percentiles: 1st, 3rd, 5th, 15th, 25th, 50th, 75th, 85th, 95th, 97th, 99th.

5th to 95th percentiles would represent a standard reference interval.

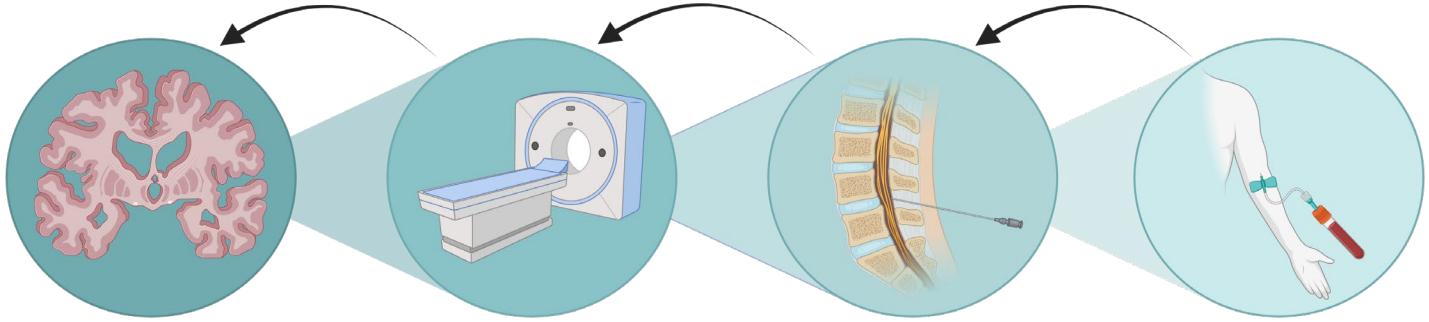
Aβ42/40 decreased by ~1% per year.

p-tau-181, NfL, and GFAP displayed U or J-shaped curves:

- High in the earliest ages with levels decreasing over time
- Level out in early adulthood
- Begin to increase by ~3-5% per year in older adulthood

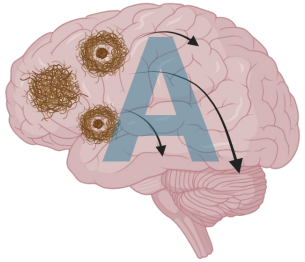
Biomarkers also increase in variability with aging.

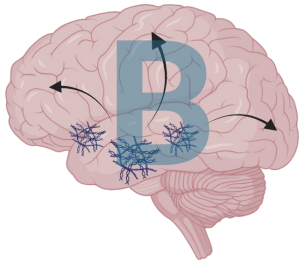
Validation of Plasma Biomarkers Against Neuropathology

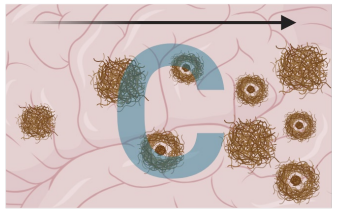


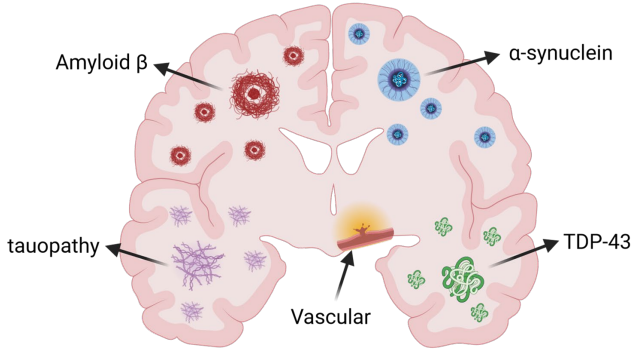
Validating against autopsy provides the true diagnostic accuracy of the test whereas validation against PET and CSF has a larger margin for error → The test can only be as good as what it's validated against

Allows for investigation of:









How strongly do various measures of AD pathology associate with plasma biomarkers?

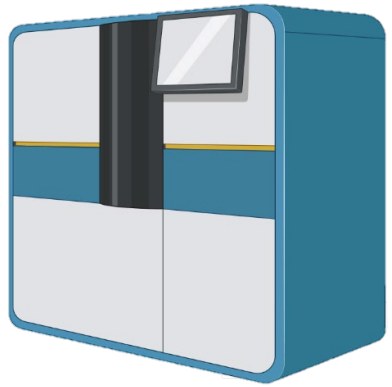
Are these associations impacted by the presence of common co-pathologies?

Validation Against Neuropathology

UBC Clinic for Alzheimer's and Related Disorders

N=94 Diagnosed with dementia at CARD
(N=60 AD, N=34 non-AD)

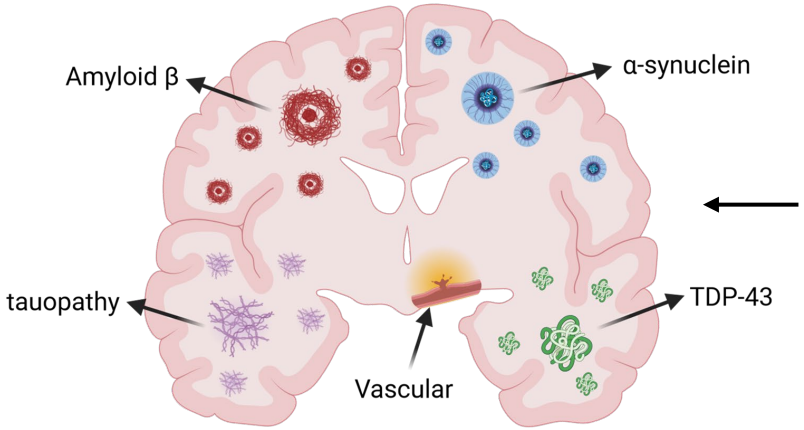
Plasma specimens collected during life



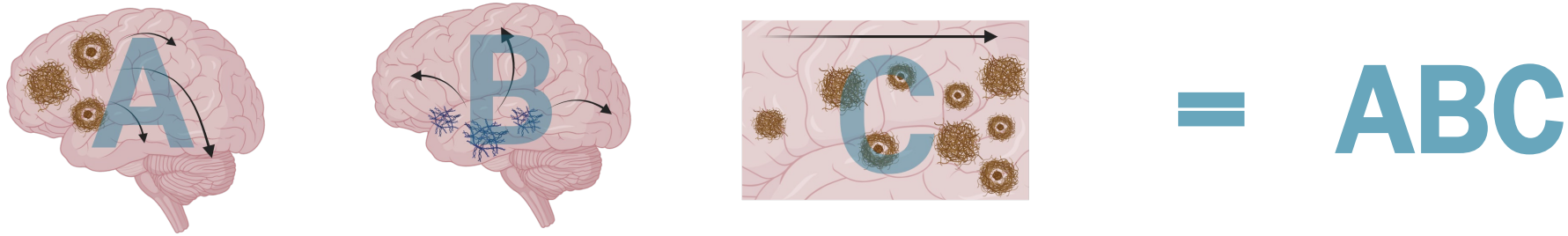
Neurology 4-plex E
(Aβ40, Aβ42, NfL, GFAP)
p-tau-181, p-tau-217

Avg 3-8 y later

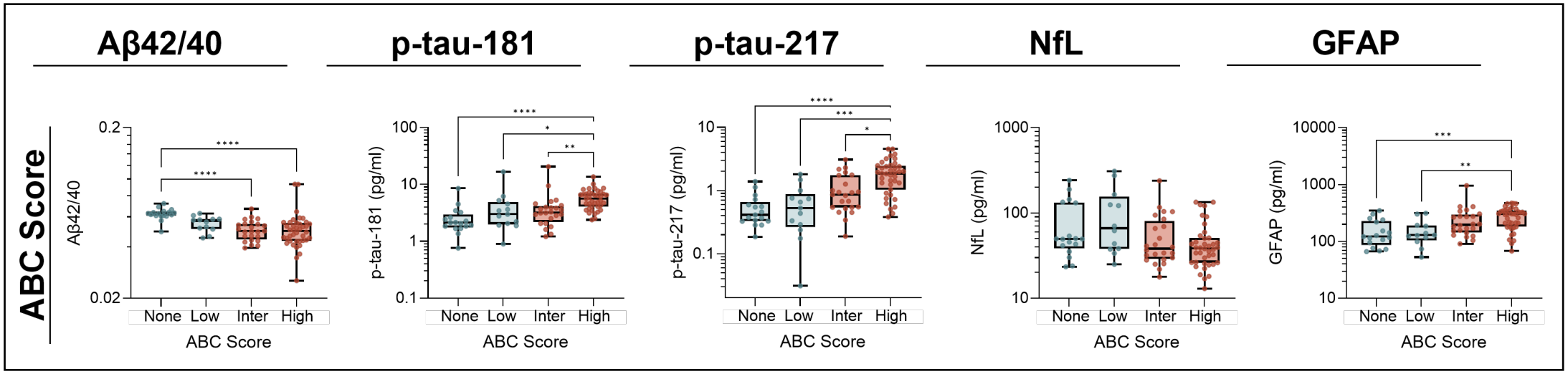
Autopsy neuropathology examination



AD Neuropathology Grading



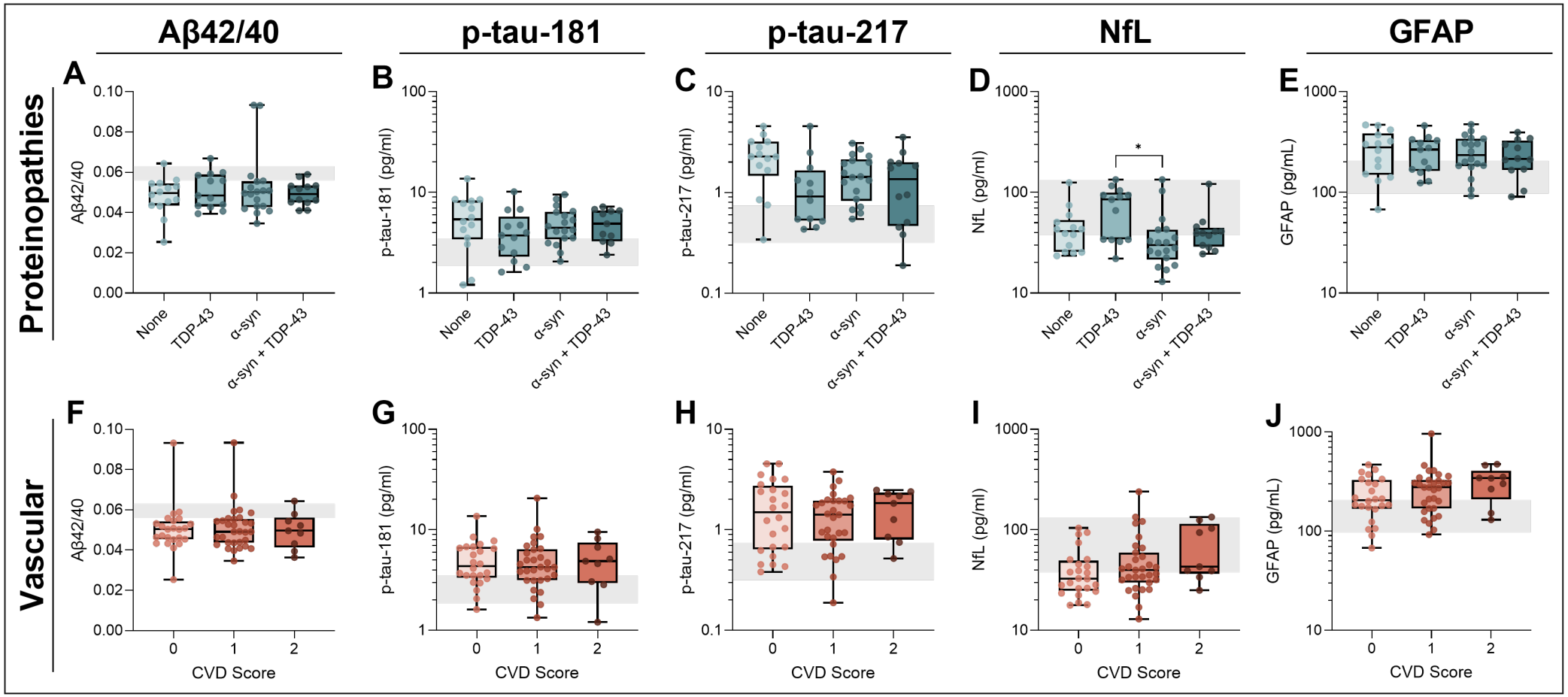
Thal Phase | Braak Stage | CERAD Score



Biomarkers changed gradually with pathology grading, with significant differences only seen between the lowest and highest grades of pathology

Effect of Co-Pathology Presence

In n=64 participants with significant ADNC, we investigated if common co-pathologies influence biomarker levels



Key AD biomarkers were robust to the presence of co-pathologies

Key Conclusions:

Plasma biomarkers of AD pathology are significantly associated with age, likely requiring age-specific reference intervals. Further these biomarkers were unaffected by the presence of co-pathologies.

Implication

These results support the use of these plasma biomarkers to indicate presence of significant ADNC regardless of other neuropathologies. However other biomarkers will be needed to indicate presence of other pathologies that may be contributing to cognitive decline or assess suitability for therapeutic intervention.

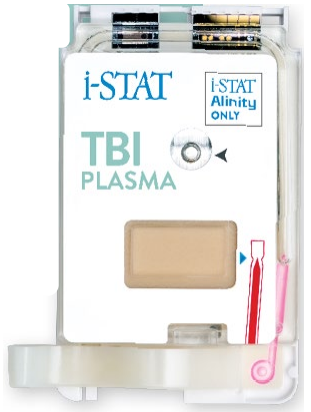
Point-of-Care Technology: Repurposing Available Tools

Point-of-Care Blood Biomarker Testing

Quanterix HD-X

- Large, expensive (500k), high maintenance piece of equipment likely only to be found in specialized labs
- Require highly trained personnel to not only operate the machine, but to interpret results
- Optimized to do testing in batches; minimizes cross lot variability & maximizes efficiency

Abbott iSTAT



- Clinically used point-of-care device, portable, robust, inexpensive (15k) and simple to use
- Duplex cartridge that simultaneously measures GFAP and UCH-L1 in 20uL of plasma in 15min
- Health Canada approval (2022 & 2025) to rule out need for head CT in adults with mild TBI

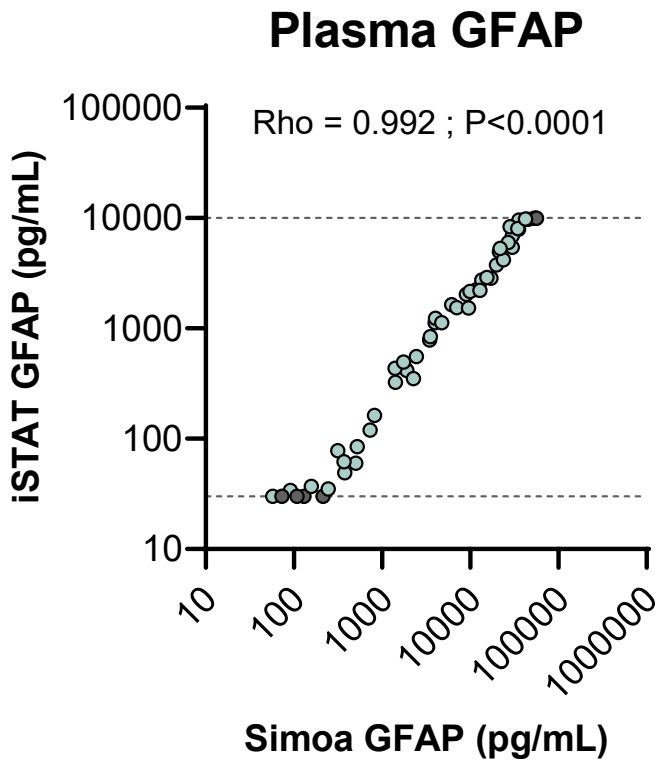
Can we repurpose tools designed for mild injuries for more critically ill patients?

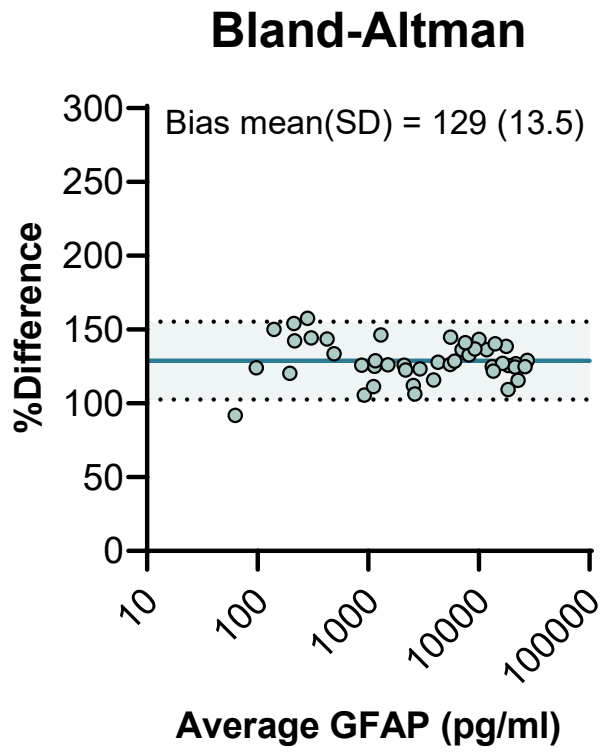
GFAP Testing in Spinal Cord Injury

Traumatic spinal cord injury (SCI) in a life-changing event for the patient and their family.

Work lead by Dr. Brian Kwon (surgeon-scientist at UBC & VGH) has demonstrated that GFAP levels in the blood measured using Simoa are associated with initial SCI injury and are predictive of motor function at 6-months.

To asses feasibility, we measured plasma GFAP in 53 samples across the dynamic range using both Simoa and iSTAT technology.





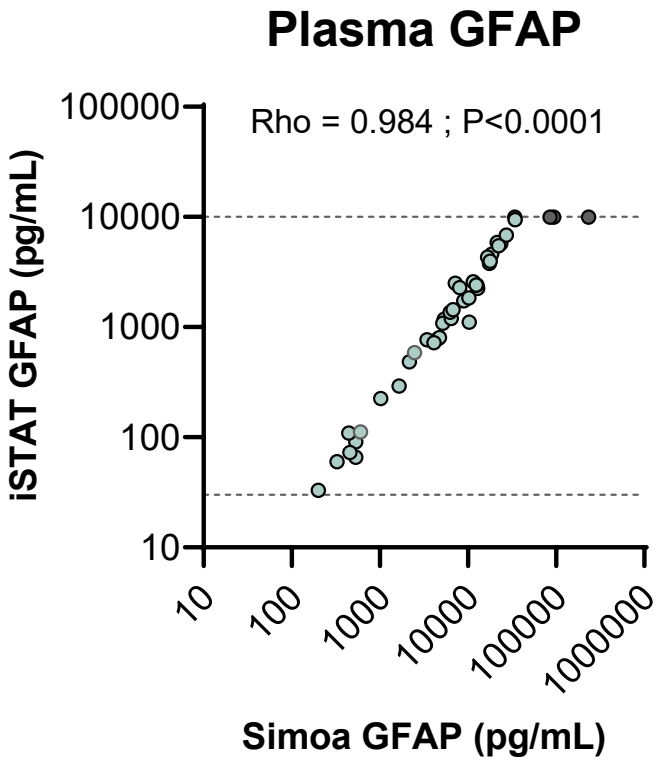
Plasma GFAP was **quantifiable in >90% of samples tested** and very strong agreement was observed between methods.

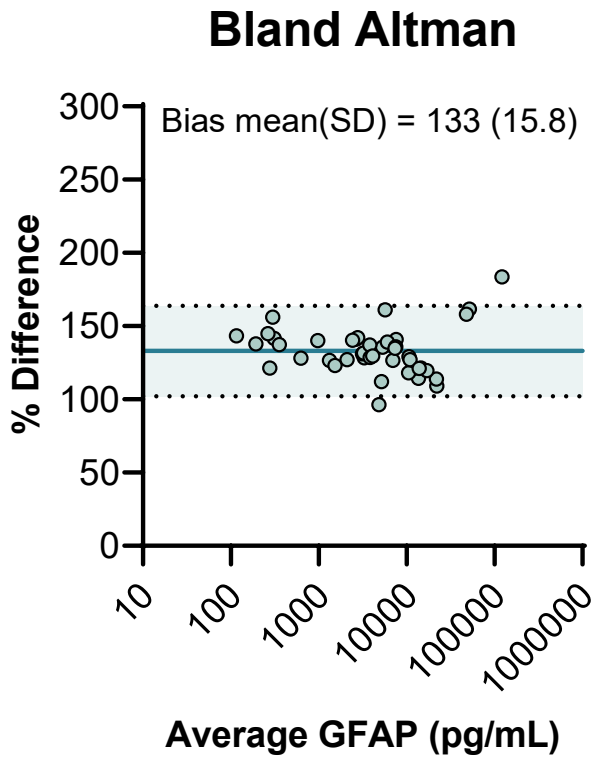
GFAP Testing in Subarachnoid Hemorrhage

Aneurysmal subarachnoid hemorrhage (aSAH) in a life-threatening emergency, caused when a blood vessel on the surface of the brain ruptures, causing bleeding into the subarachnoid space.

Work lead by Dr. Mypinder Sekhon and Dr. Dorothee Goulet is investigating whether plasma GFAP is predictive of neurological outcome.

Plasma samples from 43 patients with aSAH (Fisher Grade 3-4) taken within 72h of the bleed were measured for GFAP.





Once again, plasma GFAP was **detectable in >90% of samples**; Association between platforms was repeated using a separate lot of iSTAT TBI plasma cartridges

Key Conclusion:

There is a strong, linear association between plasma GFAP quantified using the Simoa HD-X and iSTAT platform, with iSTAT GFAP values being ~10-fold lower. GFAP was quantifiable in >90% of acute samples collected.

Implications:

While designed for use in mild brain injury, commercially available iSTAT cartridges demonstrated the range required to quantify GFAP in critically ill patients. The ability to use PoC testing across broad contexts of use has important considerations for patient transport, level/type of care, military applications, and testing equity and access.

Biomarker Pipeline From Research to Clinic

Team Approach to Science

Lab Medicine Researchers

Early integration and synergy across multidisciplinary teams is essential to building mutual understanding and common goals, while balancing feasibility and innovation

Critical Factors to Consider

What is required to make that translation from fundamental research science into clinical care?

Ideally, we want to develop a fundamental pipeline that can be repurposed for new biomarkers or additional contexts of use so that we aren't going back to square one

We need to build capacity – both people & infrastructure

How do we ensure equity and access?

Knowledge translation and societal impacts – inform patients about what tests are available and what they do and don't mean;

Factors unique to Canada – while we can learn much from what is being done around the world, in the end we need a solution that is built for Canadians

Acknowledgments

Wellington Lab:

Clinical
- Dr. Sophie Stukas
- Mohammad Ghodsi
- Kidus Achalu
- Isabella DiBerardino
- Dana Go
- Andrew Agbay
- Tessa Morelli
- Dr. Andrii Vislovukh
- Simren Ahuja

Pre-Clinical
- Dr. Jianjia Fan
- Dr. Tom Cheng
- Dr. Mehwish Anwer
- Tetiana Poliakova
- Anna Wilkinson
- Carlos Barron

Thank you to the patients, participants, and clinical staff

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