Quanterix®
The Science of Precision Health

ABOUT QUANTERIX™

Quanterix is a company that is digitizing biomarker analysis with the goal of advancing the science of precision health. The company's ultra-sensitive detection solution, Simoa®, has the potential to transform the way in which healthcare is provided today by giving researchers the ability to closely examine the role of biomarkers in the continuum of health to disease.

The Simoa platform offers the ability to detect neurological biomarkers at ultra-low levels, providing the potential to radically change the way brain injuries and diseases are diagnosed. Simoa's ultra-sensitive technology paired with Quanterix' comprehensive range of assays can detect biomarkers associated with brain injury and disease at much earlier stages to understand the long-term effects and disease pathology. Most notably, thanks to Simoa's unparalleled sensitivity, researchers are able to measure biomarkers such as Tau, NfL, and amyloid beta in plasma or serum, obviating the need to obtain cerebrospinal fluid. Quanterix has a strategic focus in neurodegeneration, neuroinflammation, traumatic brain injuries (TBI) and multiple sclerosis (MS) and is working with a rapidly growing network of academic researchers and pharmaceutical and biotech partners to drive advancements in head health research.

Missed Connections:

The **Structural** and **Biochemical Markers** of **Neurodegeneration**

Highly specialized, neurons receive, propagate, and transmit electrical and chemical signals to control motor actions, regulate body functions, and interpret and respond to external stimuli. The ability to perceive and interact with the world hinges on neuronal function – and, naturally, physical damage to neurons is a core cause of many neurological pathologies. Understanding the extent of this damage is the first step to repairing the destruction that has been wrought, and scientists use the presence of **biomarker molecules**, released when cellular or tissue integrity has been compromised, to detect and gauge neurological injury.

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Biomarker Abbreviations

$A\beta_{1-42}$: Amyloid beta peptide fragment containing amino acids 1-42
CCL11: C-C motif chemokine 11
GFAP: Glial fibrillary acidic protein
JC Virus: John Cunningham Virus
MBP: Myelin basic protein
NF-H: Neurofilament heavy chain
NF-L: Neurofilament light chain
UCH-L1: Ubiquitin C-terminal hydrolase-L1

The Blood-Brain Barrier (BBB)

The BBB separates the cardiovascular circulation from the brain and cerebrospinal fluid. Comprised primarily of endothelial cells sealed by tight junctions, pericytes, and astrocyte end-feet, the BBB is highly selective, allowing only water, lipid-soluble molecules, and select gases to cross unassisted via passive diffusion. Other molecules, including glucose and amino acids required for neuronal function, need active transporters to enter the brain. There is a concentration gradient from brain to CSF and blood and as a consequence brain-enriched molecules are of low abundance in blood.

BBB disruption leads to excessive permeability and loss of homeostasis, resulting in neuronal cytotoxicity via mechanisms including inflammation, oxidative stress, and the accumulation of proteins linked to neurodegenerative disorders such as $A\beta_{1-42}$.[18,19]

BBB dysfunction itself can be detected by investigating biomarkers associated with endothelial permeability, including **junction proteins**, **adhesion proteins**, and **matrix metalloproteinases**. It can also be examined by probing **inflammatory biomarkers (e.g., cytokines)**. Finally, BBB dysfunction allows **CSF molecules** to enter the circulation in greater abundance, allowing them to be measurable using blood-serum-targeted assays.[20]

Traumatic Brain Injury (TBI)

- TBI occurs due to physical trauma to the brain resulting in axon damage; mechanical force can cause axonal tearing, swelling, disconnection, and changes in excitation/inhibition capability and metabolism[14]
  - TBI biomarkers include **NF-H** (elevated in CSF and blood), **NF-L** (elevated in CSF and blood), **GFAP** (elevated in blood), **UCH-L1** (elevated in blood), and **tau** (elevated in blood and CSF in the cleaved form c-tau)[15]
    - Repeated TBI has been linked to chronic traumatic encephalopathy (CTE), a progressive neurodegenerative disease characterized by frontal and temporal lobe atrophy[16]
      - CTE cases present postmortem with abnormal deposits of phosphorylated tau protein, with more severe cases also showcasing **NFT** formation and **Aβ** deposition[16]
        - Currently, CTE is diagnosed using postmortem analysis, clinical criteria, and PET imaging in living subjects; **CCL11** may be a potential biomarker, as elevated levels are found in the brain and cerebrospinal fluid (CSF) of CTE patients[17]

Alzheimer's Disease (AD)

- Structurally characterized by neuronal death and brain atrophy, particularly in the hippocampus and posterior cortex; histologically characterized by amyloid beta (Aβ) plaques and neurofibrillary tangles (NFTs)[1]
- Aβ plaque formation can be detected via decreased levels of CSF **$A\beta_{1-42}$ peptide species**[4]
- NFTs arise due to abnormal tau protein hyperphosphorylation, resulting in the disintegration of axonal microtubules;[3] elevated **total tau** levels in the CSF present a potential diagnostic biomarker for AD[4]
- Using the **$A\beta_{1-42}$/total tau** ratio increases diagnostic accuracy versus either marker alone[4]
- Plasma protein panels are being used to detect blood-borne biomarkers for AD onset and progression[5,6]

Multiple Sclerosis (MS)

- A chronic autoimmune disease where immune cells attack, damage, and destroy axonal myelin sheaths;[11] acute axonal injury (e.g., transection) may also occur[12]
  - While the exact mechanism is unclear, elevated **Th1** and **Th17** T-cell counts can be observed[13]
    - Treatment largely centers around inhibiting/blunting immune system activation/function[11,13]
      - Immunosuppressive agents used to treat MS can lead to **JC virus** activation, resulting in encephalopathy; JC viral titers are therefore screened for prior to treatment[13]
        - Other biomarker candidates include **NF-L** (released by axon injury) and **GFAP** (released upon astrocyte injury)[13]
          - All are readily detectable in the CSF using techniques such as ELISA, with elevated levels indicative of MS[13]

Parkinson's Disease (PD)

- Characterized by the loss of dopaminergic neurons of the substantia nigra;[7] both axon and soma degeneration is observed – likely via independent mechanisms[8]
- Pathological morphology varies, with Lewy bodies, NFTs, plaques, vascular disorders, and argyrophilic inclusions all potentially present[9]
- Biomarkers for PD include **α-synuclein**[10]
- **α-synuclein** is the main protein contained by Lewy bodies found in PD patients and can be detected in the blood[10]

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