BioConnetiX

Overview

Blood-based biomarker tests measure proteins released from brain and neuronal tissue following injury. GFAP and UCH-L1 are well established for detecting or ruling out mild to moderate TBI. S100ß supports early severity assessment; p-tau217 and total tau aid in evaluating neurodegenerative changes, recovery trajectories, and secondary injury risk; and NfL/NfH provide sensitive markers of axonal damage, treatment response, and progression. Genetic markers ApoE and MTHFR guide individual susceptibility and prognostic risk profiles relevant to TBI recovery.

Daubert Reliability Reference | Blood-Based Biomarker Testing for Traumatic Brain Inury (TBI)

A concise reference for establishing the scientific reliability and admissibility of blood-based biomarker testing for traumatic brain injury (TBI) under Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993).

TBI Biomarker Testing

>90%	>95%
SENSITIVITY	SPECIFICITY

How Biomarkers Guide Earlier, More Precise Care

https://www.facs.org/media/vgfgjpfk/best-practices-guidelines-traumatic-brain-injury.pdf

Clinically Valid Testing Window: 30 Days to 5+ Years Post-Injury

- **Acute Phase (0–72 hours)** Biomarker levels help risk-stratify emergency-department patients and support early specialty follow-up, even when CT imaging is negative. Elevated results warrant timely neurology referral, targeted headache and sleep management, and a structured return-to-activity plan.
- **Sub-Acute Phase (4 days–12 weeks)** Biomarkers can differentiate recent injury from prior damage and indicate injury severity. For positive findings, prioritize cognitive rehabilitation, vestibular or oculomotor therapy, and mood/PTSD screening, while establishing a baseline for recovery tracking.
- **Chronic Phase (3–12 months)** Biomarkers remain clinically viable for confirming injury and for tracking treatment efficacy and disease progression. Patients benefit from multidisciplinary, guideline-based care pathways across acute and post-acute stages (e.g., ACS TQP Best Practices).
- **Long-Term Phase (12 months–5+ years)** Biomarker testing remains clinically valid for confirming TBI; continued biomarker testing supports longitudinal monitoring, correlating treatment history with persistent or evolving deficits.

Key Peer-Reviewed Publications

Edwards et al., Frontiers in Neurology (2024) — Serum GFAP, NfL, and tau Concentrations are Associated with Worse Neurobehavioral Functioning Following Mild, Moderate, and Severe TBI: A Cross-Sectional Multiple-Cohort Study.
https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2023.1223960/full

Brett et al., Neurology (2023) — TRACK-TBI LONG study linking biomarker trends to long-term outcomes.
https://pubmed.ncbi.nlm.nih.gov/37344231/

Reyes et al., Neurology (2023) — Utility in CT-negative mild TBI.
https://pubmed.ncbi.nlm.nih.gov/37788938/

Lewis et al., Frontiers in Neurology (2020) — Plasma biomarker accuracy: 90% sensitivity, 95% specificity.
https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2020.00685/full

Shahim et al., Neurology (2020) — Longitudinal validation of GFAP, UCH-L1, NfL, and tau.
https://pubmed.ncbi.nlm.nih.gov/32641529/

American Academy of Sciences
https://nap.nationalacademies.org/catalog/26932/biomarkers-for-traumatic-brain-injury-proceedings-of-a-workshop

Papa et al., JAMA Neurology (2016) — Diagnostic accuracy of GFAP and UCH-L1 in trauma cohorts.
https://pubmed.ncbi.nlm.nih.gov/27018834/

Daubert Factor	Supporting Evidence
Testability / Scientific Validity	The analytical validity and clinical utility of GFAP and UCH-L1 have been demonstrated across multiple large-scale, peer-reviewed studies, with reproducible biomarker kinetics that correlate with CT and MRI findings. Biomarkers and decision thresholds are supported by the National Academy of Sciences. These biomarkers are also widely used in the monitoring of Alzheimer's disease, multiple sclerosis (MS), ALS, Parkinson's disease, chronic traumatic encephalopathy (CTE), and frontotemporal dementia (FTD). For Alzheimer's disease and MS, they are incorporated directly into published clinical management guidelines.
Peer Review and Publication	There are more than 7,000 peer-reviewed publications supporting these biomarkers and the underlying testing methodologies. Ongoing research – such as Edwards et al., Frontiers in Neurology (2024), which demonstrates associations between serum GFAP, NfL, and tau levels and neurobehavioral functioning across TBI severities – continues to accelerate the incorporation of these biomarkers into longitudinal clinical standards.
Known or Potential Error Rate	Controlled studies demonstrate consistent diagnostic performance exceeding 90% sensitivity and 95% specificity. Analytical error rates are established and monitored under CLIA (42 CFR Part 493).
Standards and Controls	All testing is performed within federally regulated quality systems, including CLIA certification (42 CFR Part 493) and FDA oversight of Laboratory Developed Tests (21 CFR Part 820).
General Acceptance	p-tau217 is FDA-cleared, and several GFAP and UCH-L1 devices are FDA-cleared for acute CT-triage within 12 hours of injury, reflecting regulatory recognition of their reliability. The biomarkers employed use non-proprietary, non-algorithmic analytical methods that can be replicated across laboratories. They are also in ongoing clinical use by the U.S. Department of Defense and the Veterans Affairs health system, and are reimbursed by major commercial carriers – some with uniquely assigned codes, others currently progressing toward finalized coding and coverage determinations.