Quanterix

PUBLICATION BRIEF

Traumatic Brain Injury (TBI)

NEUROLOGY

Blood-Based Biomarker Detection for Sports-Related Head Injuries

Sports-related concussions (SRCs) are prevalent across a variety of sports and are challenging to diagnose clinically. Return-to-sport (RTS) timing decisions are critical for ensuring athlete health and safety, as repeated trauma prior to full recovery can lead to long-term negative neurological consequences. Development of ultrasensitive blood-based biomarker tests to identify neuronal damage and to monitor recovery progress can help support appropriate decision-making for injured athletes. Listed below are just a few of the potential biomarkers that have been studied in the setting of SRC and TBI and are often measured simultaneously in order to understand the full extent of potential damage and recovery.

Quanterix Potential Biomarkers of Interest

Neurofilament light (NfL) is a cytoskeletal intermediate filament protein that is expressed in neurons and can be highly released into the cerebrospinal fluid (CSF) and bloodstream after neuroaxonal injury. NfL has been shown to be associated with traumatic brain injury and neurodegeneration. Studies using Simoa® technology have identified elevated circulating NfL levels after repetitive concussive impacts in contact-sport athletes[3] and it may be an important marker to study in longitudinal athletic careers.

Glial fibrillary acidic protein (GFAP) is a class-III intermediate filament expressed in astrocytic glial cells in the central nervous system, and often serves as a marker of astroglial injury. It has been reported GFAP may be increased within the first 24 hours post-traumatic brain injury[4] and may be useful as a biomarker during the acute postinjury period.

Tau is a microtubule-stabilizing protein primarily localized in central nervous system neurons, but also expressed at low levels in astrocytes and oligodendrocytes. Tau elevation is observed in the CSF of patients with neurodegenerative disease and head injuries, suggesting its extracellular release during neuronal damage and its role as a biomarker with specificity for brain injury. Studies have shown higher concentrations of total tau are associated with a longer RTS time post-SRC in athletes[2]. Reports of plasma tau increasing not only with brain injury[5], but also during times of physical exertion not associated with concussion open the door for additional studies on the role this protein may play in traumatic brain injury.

Phosphorylated tau 181 (p-tau181), while commonly associated with neurodegenerative diseases such as Alzheimer's, may also be useful for identifying patients with brain abnormalities related to repeated concussion. Studies using ultrasensitive Simoa® detection have shown elevated plasma pTau-181 levels in retired athletes compared to healthy controls[1] and more research is currently being performed to determine the utility of p-tau181 in TBI cohorts.

Ubiquitin C-terminal hydrolase-L1 (UCH-L1) is one of the most abundant brain proteins, representing between 1 – 2% of total soluble brain protein. More recently, UCH-L1 has been proposed as a potential biomarker for brain injury, as it is released from injured neurons into the CSF and peripheral blood.

References

1. Investigating the use of plasma pTau181 in retired contact sports athletes. *J Neurology* 2022 https://doi.org/10.1007/s00415-022-11223-7
2. Plasma Biomarker Concentrations Associated with Return to Sport Following Sport-Related Concussion in Collegiate Athletes—A Concussion Assessment, Research, and Education (CARE) Consortium Study. *JAMA Netw Open* 2020 https://doi.org/10.1001/jamanetworkopen.2020.13191
3. Prolonged elevation of serum neurofilament light after concussion in male Australian football players. *Biomark Res.* 2021 https://doi.org/10.1186/s40364-020-00256-7
4. Association of Blood Biomarkers With Acute Sport-Related Concussion in Collegiate Athletes. J*AMA Netw Open* 2020 https://doi.org/10.1001/jamanetworkopen.2019.19771
5. Acute plasma tau relates to prolonged return to play after concussion. *Neurology* 2017 https://doi.org/10.1212/WNL.0000000000003587

Simoa® Technology Enables Best-in-Class Research to Advance Scientific Breakthroughs

Below represents a curated list of peer-reviewed publications where the Quanterix Simoa® assays were used as part of TBI/concussion studies.

Exposure to Repetitive Head Impacts Is Associated with Corpus Callosum Microstructure and Plasma Total Tau in Former Professional American Football Players
Journal of Magnetic Resonance Imaging 2021
doi.org/10.1002/jmri.27774

Serum neurofilament light in professional soccer players: goal on safety
Neurological Sciences 2022
doi.org/10.1007/s10072-022-06109-5

The effect of omega-3 fatty acids on a biomarker of head trauma in NCAA football athletes: a multi-site, non-randomized study
Journal of the International Society of Sports Nutrition 2021
doi.org/10.1186/s12970-021-00461-1

Serial Assessment of Gray Matter Abnormalities after Sport-Related Concussion
J Neurotrauma 2017
doi.org/10.1089/neu.2017.5002

Longitudinal assessment of white matter abnormalities following sports-related concussion
Human Brain Mapping 2016
doi.org/10.1002/hbm.23072

Effect of Player Position on Serum Biomarkers during Participation in a Season of Collegiate Football
Neurotrauma 2022
doi.org/10.1089/neu.2022.0083

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Blood Biomarkers for Return to Play after Concussion in Professional Rugby Players

J Neurotrauma 2023

doi.org/10.1089/neu.2022.0148

Complex Autoantibody Responses Occur Following Moderate to Severe Traumatic Brain Injury

J Immunol. 2021

doi.org/10.4049/jimmunol.2001309

Tau aggregation and increased neuroinflammation in athletes after sports-related concussions and in traumatic brain injury patients-a PET/MR study

NeuroImage: Clinical 2021

doi.org/10.1016/j.nicl.2021.102665

Association between Serum Neurofilament Light and Glial Fibrillary Acidic Protein Levels and Head Impact Burden in Women's Collegiate Water Polo

J Neurotrauma 2022

doi.org/10.1089/neu.2022.0300

Extracellular vesicle concentrations of glial fibrillary acidic protein and neurofilament light measured 1 year after traumatic brain injury

Sci Rep. 2021

doi.org/10.1038/s41598-021-82875-0

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