NATIONAL ACADEMIES Sciences Engineering Medicine

FORUM ON TRAUMATIC BRAIN INJURY

Biomarkers for Traumatic Brain Injury: A Workshop

National Academies' Keck Center, Room 100
500 Fifth Street, NW
Washington, DC

Access the livestream online.

Traumatic brain injury is a complex condition with differing mechanisms and severities of injury, affecting all ages and populations. This heterogeneity provides challenges to accurate assessment of injury, effective delivery of care, and optimization of outcomes for people and families that experience a TBI. To advance care and research, an ongoing goal for the field has been to identify and validate a toolkit of biomarkers able to more precisely and objectively diagnose and categorize a suspected TBI, better guide and monitor treatment after injury, and refine future research studies. This remains an active and important area of investigation and clinical implementation.

Neuroimaging has been one crucial tool to characterize the nature, location, and extent of injury after a suspected TBI. A variety of blood-based biomarkers have also been identified, with several now reaching clinical practice. The FDA recently approved detection of glial fibrillary acidic protein (GFAP), an indicator of glial injury, and ubiquitin carboxy-terminal hydrolase L1 (UCH-L1), an indicator of neuronal injury, for assessment after suspected injury. Additional molecules indicative of cellular damage or inflammation continue to actively be investigated. In addition to these technologies, physiological measures such as electroencephalogram (EEG), which measures electrical activity in the brain, and wearable biosensors are being explored for their utility in assessing brain injury and recovery. No single biomarker is likely to capture the full pathophysiology of TBI, particularly the dynamic and longer-term nature of recovery. Approaches that analyze and monitor information from multiple sources are likely to be needed. Continued discussions will also be needed on translation and effective incorporation of biomarkers into clinical practice, including validation across diverse patient populations and incorporation of approved biomarkers into clinical guidance in different care settings.

Now is thus a fruitful time for the new TBI Forum to review recent advances and open questions in this field. This workshop reflects an initial Forum activity in this area. The workshop will explore the landscape of biomarker types, the impact biomarkers may have on phases of TBI care and research, and key questions and potential opportunities to help advance the field.

Workshop Objectives

- Review the landscape of TBI biomarkers, including blood-based, imaging-based, and other types of relevant physiological markers;
- Explore clinical needs, challenges, and potential opportunities to advance implementation of FDA-approved biomarkers for TBI;
- Discuss open research questions, evidence needs, and potential opportunities to inform further biomarker design and validation for TBI.

Definition of a Biomarker for Purposes of the Workshop: A defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes or responses to an exposure or intervention (FDA-NIH Biomarker Working Group 2016).

(All times ET)

9:15–9:30 am **WELCOME: INTRODUCTION AND GOALS OF THE WORKSHOP**

Corinne Peek-Asa, University of California San Diego; Acting Chair, Forum on Traumatic Brain Injury

Stuart Hoffman, Department of Veterans Affairs, Workshop Planning Committee

9:30–10:40 am **SESSION 1: Orientation to TBI Biomarkers and Clinical Needs**

Moderator: Geoffrey Manley, University of California San Francisco

- What information can biomarkers provide the TBI community and how can a toolkit of sensitive, specific, and objective biomarkers inform the research and care pathway? What needs are not yet met with current biomarkers?
- What are the contexts of use where biomarkers will impact clinical research and care
- What can the TBI community learn from the cardiology community's experiences in clinical validation and use of biomarkers to inform cardiology assessment and care?

How Can Biomarkers for TBI Inform Clinical Care and Research

Ramon Diaz-Arrastia, University of Pennsylvania

Perspectives from the TBI Community on the Role of Biomarkers in Addressing Unmet Needs

Rachel Lazarus, AARP

Jeffrey Bazarian, University of Rochester

Lessons from Validation and Use of Biomarkers to Inform Cardiology Care and Research

Alan Wu, San Francisco General Hospital

Discussion

10:40–11:00 am **Break**

11:00–12:40 pm **SESSION 2: Major Classes of TBI Biomarkers**

Moderator: Luca Marinelli, GE Research

Syntheses of several classes of TBI biomarkers, including where on the continuum of care such biomarkers have demonstrated utility, barriers to their implementation in clinical practice, and open research gaps and

questions.

Neuroimaging Biomarkers
Elisabeth Wilde, University of Utah

Biomarkers Detectable in Blood
Jessica Gill, Johns Hopkins University

Electrophysiological Biomarkers
Paul Rapp, Uniformed Services University and University of California, Irvine

Other Physiological Markers
Christina Master, University of Pennsylvania

Discussion

12:40–1:30 pm **Lunch**

1:30–2:30 pm **SESSION 3: Development of Biomarkers in the Translational Pipeline**

Moderator: Stuart Hoffman, U.S. Department of Veterans Affairs

Pharmacodynamic Response Biomarkers
Patrick Kochanek, University of Pittsburgh

Combining Multimodal Information to improve Diagnosis, Prognostication and Understanding of Longer-Term Outcomes
David Okonkwo, University of Pittsburgh

Discussion

2:30–2:50 pm **Break**

2:50 – 3:50 pm **SESSION 4: Needs and Opportunities to Advance the Use of Biomarkers for TBI Care and Research**

Moderator: Frederick Korley, University of Michigan

- How can biomarkers be incorporated into a new classification scheme for TBI?
- What approaches are needed to validate and incorporate new biomarker tools into an improved approach?

Panelists:
Martin Schreiber, Oregon Health and Science University
Beth McQuiston, Abbott Laboratories

Allison Kumar, Arina Consulting

Carol Taylor-Burds, National Institute of Neurological Disorders and Stroke (NINDS), National Institutes of Health

Narayan Iyer, Biomedical Advanced Research and Development Authority (BARDA), Department of Health and Human Services

CAPT Travis Polk, Combat Casualty Care Research Program, Department of Defense

3:50 – 4:45 pm **SESSION 5: Looking Ahead: Workshop Themes and Key Messages**

Moderator: Leslie Prichep, BrainScope Company

- Taking stock: Where are we now and what have been the outcomes and lessons learned?
- Where does the TBI community want to go and how can this vision be achieved? What are opportunities, and concrete ideas for moving forward?

4:45 pm **WRAP UP REMARKS**

Corinne Peek-Asa, Acting Chair, Forum on Traumatic Brain Injury

4:50 pm **ADJOURN**

Forum reception to follow