

The National Academies of
SCIENCES • ENGINEERING • MEDICINE



Forum on
NEUROSCIENCE and
NERVOUS SYSTEM DISORDERS

Biomarkers of Neuroinflammation: A Workshop

March 20 and 21, 2017
National Academy of Sciences Building
2101 Constitution Avenue, NW | Washington, DC

Background: Innate and adaptive immunity have become very important areas of investigation for psychiatric disorders, neurologic disorders, neurodevelopmental disorders, and neurodegeneration resulting from traumatic brain injury. For example, compelling genetic and other biologic data are demonstrating critical roles of innate and adaptive immunity in Alzheimer’s disease pathogenesis. Several conferences and meetings are being held in this hot area, but it is not clear how best to translate recent findings to therapeutics; developing biomarkers that can be validated and used in clinical development and regulatory decision making is a critical step in this process. Many efforts are already underway to identify biomarkers of neuroinflammation, including biomarkers in cerebrospinal fluid and blood, as well as PET imaging agents for targets such as translocator protein (TSPO). Given the intense activity in academic research and private sector settings and across many nervous system disorders, there is an opportunity to take stock of current knowledge, provide a venue for coordination, and identify potential opportunities to advance work in this domain. This public workshop will bring together key stakeholders from government, academia, industry, and disease-focused organizations to explore and advance efforts to identify biomarkers of neuroinflammation that can be validated and used in clinical development and regulatory decision making.

Workshop Objectives:

- Provide an overview of current knowledge on the role of neuroinflammation in nervous system disorders—including psychiatric and neurologic disorders, neurodevelopmental disorders, and neurodegeneration resulting from traumatic brain injury—discuss the various definitions of neuroinflammation in use across the field, and the contribution of the peripheral and CNS innate immune systems to normal brain function and disease pathophysiology.
- Explore the state-of-the-science of neuroinflammation biomarkers and research needed to enable the use of these biomarkers at the individual level. Do any biomarkers under development/validation implicate glia, neurons, immune cells, endothelial cells, should these be deployed singly or in combination, and where are the gaps in current approaches?
- Facilitate coordination among consortia and companies that are developing biomarkers of neuroinflammation. How might a study be designed to establish the disease relevance or drug-development utility of a neuroinflammation biomarker? Are such studies underway, and if not, why not? If not, what more do we need to facilitate these, and are there opportunities for “add-on” studies to current clinical trials?
- Highlight approaches, tools, and lessons learned that may apply across disorders and opportunities to advance the development of these biomarkers.

DAY 1: March 20, 2017, Room 120

- 1:00 p.m. **Welcome and Overview of Workshop**
 RITA BALICE-GORDON, SANOFI (CO-CHAIR)
 LINDA BRADY, NATIONAL INSTITUTES FOR MENTAL HEALTH (CO-CHAIR)

SESSION 1: OVERVIEW OF NEUROINFLAMMATION IN CNS DISORDERS

Session Objectives:

- Provide brief background information on inflammatory processes and the role of neuroinflammation in adaptive repair and protection as well as pathophysiology of the brain.
- Discuss the various definitions of neuroinflammation in use across the field.

- 1:15 p.m. **Introduction**
 RITA BALICE-GORDON, Sanofi
- 1:20 p.m. **Neuroinflammation: Peripheral Immunity and CNS Cell Types**
 THOMAS MÖLLER, Abbvie Foundational Neuroscience Center
- 1:50 p.m. **Discussion**
 LINDA BRADY, National Institutes for Mental Health
- 2:10 p.m. **Break**

SESSION 2: STATE-OF-THE-SCIENCE OF NEUROINFLAMMATION IN CNS DISORDERS

Session Objectives:

- Survey current knowledge on the role of neuroinflammation in nervous system disorders—including psychiatric and neurologic disorders, and neurodegeneration resulting from traumatic brain injury—and common pathways for neuroinflammation across different disorders.
- Discuss desirable biomarker characteristics for quantitatively tracking neuroinflammation in disease progression and therapeutic interventions in different CNS disorders.

- 2:25 p.m. **Session Overview**
 STEVIN ZORN, MindImmune Therapeutics and University of Rhode Island (Co-Moderator)
- 2:35 p.m. **The Acute to Chronic Neuroinflammation Continuum [20 minute talks]**
 FIONA CRAWFORD, Roskamp Institute
 AMIT BAR-OR, University of Pennsylvania
 GARY LANDRETH, Case Western Reserve University
 BETH STEVENS, Boston Children's Hospital
 ELLIOTT HONG, University of Maryland
 RICHARD DANEMAN, University of California, San Diego
- 5:00 p.m. **Discussion**
- 6:00 p.m. **Adjourn Day 1**

DAY 2: March 21, 2017, Lecture Room

- 8:30 a.m. **Welcome and Review of Day I**
 RITA BALICE-GORDON, Sanofi (Co-Chair)
 LINDA BRADY, National Institute of Mental Health (Co-Chair)
- 8:40 a.m. **Keynote Presentation**
 ED BULLMORE, University of Cambridge, GlaxoSmithKline
- 9:10 a.m. **Discussion**
 PATRICIO O'DONNELL, Pfizer Neuroscience Research Unit (Moderator)
- 9:30 a.m. **Break**

SESSION 3: NEUROIMAGING BIOMARKERS—CURRENT INITIATIVES AND OPPORTUNITIES

Session Objectives:

- Discuss current consortia, academic, and private sector efforts to identify and validate imaging biomarkers of neuroinflammation and share methodological approaches and lessons learned.
- Describe the use of neuroimaging biomarkers to identify changes in structure or tissue properties with respect to inflammation.
- Address key issues relevant across CNS disorders, such as:
 - How well do neuroimaging methods differentiate between adaptive and pathological neuroinflammatory processes?
 - Are current imaging agents useful in identifying specific patient populations?
 - What is the potential clinical utility of imaging agents and can they detect immediate and longer-term changes following therapeutic interventions?
- Describe the limitations of current imaging biomarkers of neuroinflammation and identify research and other potential next steps that would move the field forward.

- 9:45 a.m. **Session Overview**
 HARTMUTH KOLB, Johnson and Johnson (Moderator)
- 9:55 a.m. **Presentations**
 HARTMUTH KOLB, Johnson and Johnson
 ROBERT INNIS, National Institute of Mental Health
 MARTINA ABSINTA, National Institute of Neurological Disorders and Stroke
 KATERINA AKASSOGLU, Gladstone Institute of Neurological Disease
- 11:10 a.m. **Discussion**
- 11:35 a.m. **Lunch**

SESSION 4: CSF AND OTHER FLUID BIOMARKERS—CURRENT INITIATIVES AND OPPORTUNITIES

Session Objectives:

- Discuss current consortia, academic, and private sector efforts to identify and validate CSF and other fluid biomarkers of neuroinflammation and share methodological approaches and lessons learned.
- Address key issues relevant across CNS disorders, such as:
 - How well can CSF and other fluid biomarker detection methods differentiate between adaptive and pathological neuroinflammatory processes?
 - Are fluid biomarkers useful in identifying specific patient populations?
 - What is the potential clinical utility of fluid biomarkers and can they detect immediate and longer-term changes following therapeutic interventions?
 - How reliable are peripheral biomarkers as indicators of neuroinflammation?
- Describe the limitations of current fluid biomarkers of neuroinflammation and identify research and other potential next steps that would move the field forward.
- Explore the relationship between fluid and imaging biomarkers.

12:35 p.m.

Session Overview

BRIAN CAMPBELL, MindImmune Therapeutics and University of Rhode Island (Co-Moderator)

ELIEZER MASLIAH, National Institute on Aging (Co-Moderator)

12:45 p.m.

Presentations

BRIAN CAMPBELL, MindImmune Therapeutics and University of Rhode Island

RICHARD PERRIN, Washington University in St. Louis

STEVE MACCARROLL, Harvard Medical School

1:45 p.m.

Discussion

2:10 p.m.

Break

SESSION 5: MOVING FORWARD

Session Objectives:

- Highlight key themes from the workshop.
- Discuss approaches, tools, and lessons learned that may apply across disorders and opportunities to advance the development of these biomarkers.
- Identify specific barriers and opportunities for increased coordinating among ongoing efforts in academia, the private sector, and consortia.
- Brainstorm potential collaborative projects that could be submitted through the Biomarkers Consortium or other current or planned mechanisms.
- Consider potential regulatory issues for biomarkers of neuroinflammation as research, development, and validation move forward.

2:25 p.m.

Session Overview

LINDA BRADY, National Institute of Mental Health

RITA BALICE-GORDON, Sanofi

2:35 p.m.

Panel Remarks

THOMAS MÖLLER, Abbvie Foundational Neuroscience Center
 ED BULLMORE, University of Cambridge, GlaxoSmithKline
 GARY LANDRETH, Case Western Reserve University
 RICHARD PERRIN, Washington University in St. Louis
 AMIT BAR-OR, University of Pennsylvania
 HARTMUTH KOLB, Johnson and Johnson
 STEVIN ZORN, MindImmune Therapeutics and University of Rhode Island
 ANDREW MILLER, Emory University
 TAREK SAMAD, Pfizer

3:45 p.m.

Discussion

4:30 p.m.

Adjourn Workshop

Workshop Planning Committee

RITA BALICE-GORDON, Sanofi (co-chair)
LINDA BRADY, National Institute of Mental Health (co-chair)
BRIAN CAMPBELL, MindImmune Therapeutics and the University of Rhode Island
ROSA CANET-AVILES, Foundation for the NIH
TIM COETZEE, National Multiple Sclerosis Society
RICHARD HODES, National Institute on Aging
STUART HOFFMAN, Department of Veterans Affairs
ELIEZER MASLIAH, National Institute on Aging
PATRICIO O'DONNELL, Pfizer
WILLIAM POTTER, National Institute of Mental Health
RICHARD RANSOHOFF, Biogen
BETH STEVENS, Harvard Medical School
STEVIN ZORN, MindImmune Therapeutics and the University of Rhode Island