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 MOLLER, Abbvie Foundational Neuroscience Center

1:50 p.m. **Discussion**  
LINDA BRADY, National Institutes for Mental Health

2:10 p.m. **Break**

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### 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 1
       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:
  o How well do neuroimaging methods differentiate between adaptive and pathological neuroinflammatory processes?
  o Are current imaging agents useful in identifying specific patient populations?
  o 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 AKASSOGLOU, 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**

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**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