



FORUM ON NEUROSCIENCE AND NERVOUS SYSTEMS DISORDERS

**Enabling Novel Treatments for Nervous
System Disorders by Improving Methods for
Traversing the Blood-Brain Barrier:
A Workshop**

September 8, 2017

Washington, DC

Workshop Background

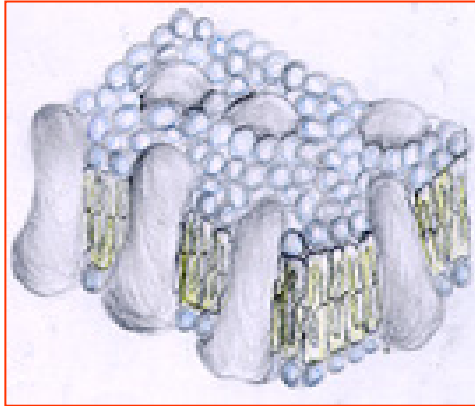
The blood-brain barrier (BBB) presents challenges for the development and delivery of effective therapeutic interventions for many CNS disorders.

- passive and active transport mechanisms, and adaptive function to control the exchange of substances between the blood and the CNS.
- Few therapeutics readily traverse the BBB to reach the brain or spinal cord, including most small molecule drugs and vast majority of large molecules (e.g., proteins)
- Several research groups are exploring innovative approaches and technologies to test delivery of therapeutics to the CNS (e.g., molecular Trojan horses, chemical modifications and physical disruption).
- Such strategies may greatly increase the armamentarium of potential treatments for psychiatric and neurological disorders.



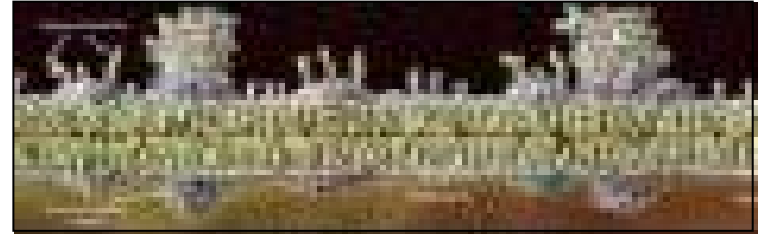
The Blood-Brain Barrier – Evolving Concept

Fluid, specialized membrane



Brain endothelial cells

'Intelligent' drug delivery



Shuttles
Pumps



Channels
Pores

Brick wall



Blood-Brain Barrier

Sledge and hammer approach



BBB Disruption

The Opportunity: Expanding CNS Therapeutic Pipeline

BBB Delivery Technologies

- Molecular Trojan Horses
 - Peptides
 - Antibodies
- Carrier-mediated
- Nanocarriers
- Virus-based
- Focused ultrasound

+ **Therapeutic:** =

- Peptide
- Bi-specific antibody
- Protein/cytokine
- Growth factor
- Enzyme
- Synthetic drug
- Traps and decoy receptors
- Gene therapy

New pipeline:

- Alzheimer's
- Parkinson's
- Brain tumors
- Multiple sclerosis
- ALS
- Lysosomal diseases
- Huntington's
- Neurodegeneration



The Challenge

Knowledge:

- BBB targets
- BBB in disease
- Distribution and disposition of therapeutics in the brain



Development:

- Complexity of molecules;
- Peripheral vs central exposure
- Translation
- Scales...

Regulatory:

- Complexity
- Toxicity
- CMC

Funding :

- Transformative technologies, but high risk
- Funding innovation

Workshop Objectives

To bring together key experts and interested stakeholders to explore current development of novel methods for traversing the BBB to deliver therapeutics for nervous system disorders and identify potential opportunities for moving the field forward.

- Provide an overview of current knowledge on the role of the blood-brain barrier biology and delivery mechanisms examining gaps in our current knowledge that future research may address.
- Discuss brain-blood barrier passive and active mechanisms that challenge development and delivery of effective therapeutic interventions to central nervous system targets.
- Highlight current data and innovative approaches for delivery of therapeutics across the brain-blood barrier harnessing methods including chemical modifications, Trojan horse approaches, physical targeting and disruption, nanoparticles, ultrasound, and other technologies.
- Explore potential opportunities for catalyzing development of novel treatments that cross the blood-brain barrier--from the preclinical to clinical phase--with an emphasis on risks, levers, and potential collaborative efforts among sectors.



Agenda

- **Opening Talks**
- **Session 1:** Traversing the BBB—Modalities and Technologies for Brain Delivery
- **Session 2:** Traversing the BBB—Pre-Clinical to Clinical Translation
- **Panel 1:** Regulatory Considerations in Development of Methods for Traversing the BBB
- **Panel 2:** Accelerating Research and Clinical Translation—Consortia and Public Private Partnerships



Acknowledgments

Workshop Planning Committee

HUSSEINI MANJI, Janssen Research & Development, LLC (co-chair)
DANICA STANIMIROVIC, National Research Council of Canada (co-chair)
FRANCESCA BOSETTI, National Institute of Neurological Disorders and Stroke
E.ANTONIO CHIOCCA, Harvard Medical School
VIVIANA GRADINARU, California Institute of Technology
CHENGHUA GU, Harvard Medical School
JIM KOENIG, National Institute on Neurological Disorders and Stroke
SARAH H. LISANBY, National Institute of Mental Health
ROGER LITTLE, National Institute on Drug Abuse
WILLIAM PARDRIDGE, University of California, Los Angeles
STEVEN PAUL, Voyager Therapeutics, Inc.
ERIC SCHAEFFER, Janssen Research & Development, LLC
AJAY VERMA, United Neuroscience

