

# KEYSTONE SYMPOSIA

on Molecular and Cellular Biology

## Drug Delivery to the Brain: Challenges and Progress (A1)

January 23-26, 2023 • Beaver Run Conference Center • Breckenridge, CO, USA

Scientific Organizers: Robert G. Thorne and Reina Bendayan

Sponsored by Biogen, BlueRock Therapeutics, Genmab A/S, Ionis Pharmaceuticals, Inc. and Ultragenyx Pharmaceutical Inc.

Scholarship Deadline: November 4, 2022 / Abstract Deadline: November 17, 2022 / Discounted Registration Deadline: November 22, 2022

### MONDAY, JANUARY 23

#### Arrival and Registration

### TUESDAY, JANUARY 24

#### Welcome and Keynote Address

**Georg Terstappen**, Cambrian Biopharma, USA  
*Drug Delivery to the Brain: History, Strategies, Needs, & Opportunities*

#### CNS Barriers: Categorization and Essential Physiological Considerations for Drug Delivery

**Britta Engelhardt**, Theodor Kocher Institute/Universitat Bern, Switzerland  
*The BBB and Beyond: Regulatory Barriers between the CNS and Blood*

**Maria Lehtinen**, Harvard Medical School, USA  
*Physiology and Dynamics of the Cerebrospinal Fluid and Adjacent Interfaces*

**Andrew Yang**, University of California, San Francisco, USA  
*A Molecular Map of the Human Brain Vasculature: Implications for CNS Drug Delivery*

**Nannan Lu**, Stanford University, USA  
*Short Talk: Specialized Microglia Accumulate Select Circulatory Proteins in an Age and Brain-region Specific Manner*

#### Workshop: Imaging, Big Data & Systems Pharmacology

**Meredith EK Calvert**, Denali Therapeutics, USA  
*State-of-the-Art Imaging and Analysis for Studies Focused on CNS Delivery*

**Patrick Ronaldson**, University of Arizona, USA  
*Predictive Network Analysis for Identification of Therapeutics Targeting SLC Transporters: Relevance to the Treatment of Neurological Diseases*

**Kapil Gadkar**, Denali Therapeutics, USA  
*Utilizing Quantitative Systems Pharmacology to deconvolute complex PK/PD relationships in CNS Delivery Studies*

**Elizabeth Kathleen Neumann**, UC-Davis, USA  
*Diversity Matters: Developing Multimodal Imaging Approaches for Assessing the Cellular and Molecular Architecture of Complex Biological Systems*

#### Delivery to the Brain: PK/PD, Imaging and Emerging Methods

**Tetsuya Terasaki**, University of Eastern Finland, Tohoku University, Japan  
*Transporter Proteomics of the CNS Barriers for the Understanding of Rational Drug Delivery to the Brain*

**Stina Syvänen**, Uppsala University, Sweden  
*PET Imaging Approaches for Assessing CNS Drug Delivery and Discovery*

**James Gorman**, Wyss Institute, USA  
*In Vitro-In Vivo Correlation of BBB Transport Assays*

**Rebecca L. Pinals**, MIT Picower Institute, USA  
*Short Talk: A Human iPSC-derived BBB-on-Chip to Model Nanoparticle-Based Delivery to the Brain*

**Zhengyuan Pang**, The Scripps Research Institute, USA  
*Short Talk: Brain-wide in situ Visualization of Cellular Drug Targets*

#### Poster Session 1

### WEDNESDAY, JANUARY 25

#### Crossing Barriers from the Bloodstream

**Reina Bendayan**, University of Toronto, Canada  
*Regulation of Folate Transport into the Brain*

**Allan Jensen**, Lundbeck, Denmark  
*Antibody Transport into the Brain from the Bloodstream: Insights from Imaging*

**Danica Stanimirovic**, National Research Council of Canada, Canada  
*Receptor-Mediated Transcytosis Systems at the BBB: Many Potential Targets for CNS Drug Delivery?*

**Dionna W. Williams**, Johns Hopkins University, USA  
*Learning from Virus and White Cell Transmigration Across the BBB: Therapeutic Insights*

**Pilar Cejudo-Martin**, Janssen Research and Development, USA  
*Short Talk: Talk Title to be Announced*

**Shradha S. Sadekar**, Genentech, USA  
*Short Talk: Leveraging FcRn to Enhance Antibody Transport Across the Blood Brain Barrier*

#### Career Roundtable

#### Bypassing the Barriers: Central Approaches for CNS Delivery

**Holly Kordasiewicz**, Ionis Pharmaceuticals, USA  
*Delivering Antisense Oligonucleotide Therapeutics to the CNS for the Treatment of Neurodegenerative Diseases*

**Michelle M. Boyd**, Cerebral Therapeutics, USA  
*Short Talk: Comparison of Biodistribution of Malat1 ASO Administered via the ICV or IT-L Route of Administration in Beagle Dogs*

**Jeff Kurz**, Alnylam Pharmaceuticals, USA  
*Short Talk: Intrathecal Delivery of siRNA-Conjugates to the CNS: ADME Characterization and PKPD Relationships*

**Krzysztof Bankiewicz**, Ohio State University, USA  
*Neurological Approaches for CNS Drug Delivery: The Intraparenchymal and Intraventricular Routes*

**Augustine Vinson**, University of Florida, USA  
*Short Talk: Cerebrospinal Fluid Flow Extends from the CNS to the Peripheral Nerves*

**Matthew D. Cain**, Washington University School of Medicine, USA  
*Short Talk: Intranasal Administration of IFN $\alpha$  Suppresses Early Replication and Neuroinvasion in Lethal Model of Venezuelan Equine encephalitis virus infection*

#### Poster Session 2

### THURSDAY, JANUARY 26

#### CNS Gene Therapy, Orphan Disorders & Neuro-Oncology

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**Kullervo Hynynen**, Sunnybrook Health Sciences Centre, Canada

*Application of Focused Ultrasound in the Clinical Treatment and Detection of Brain Disorders*

**Robert Bell**, Ascidian Therapeutics, USA

*Delivering Novel RNA Exon Editing Therapies for Rare Diseases of the Eye and CNS*

**Sadhana Jackson**, NINDS, National Institutes of Health, USA

*The Blood-Tumor Barrier: New Perspectives on Drug Delivery and Clinical Relevance*

**Benjamin E. Deverman**, Broad Institute of MIT and Harvard, USA

*Learning How to Engineer Capsids for CNS-wide Gene Delivery in Humans*

**Natalie Artzi**, Harvard Medical School, USA

*Short Talk: Engineering Therapeutic Immunity to Glioblastoma through the Intracranial Delivery of Chemoimmunotherapy using Adhesive Hydrogels*

**Maria Praggastis**, Regeneron Pharmaceuticals, USA

*Short Talk: Delivering Therapeutic Lysosomal Enzyme to the CNS: A Rapid, Large-scale in vivo Screen Identifies Optimal Characteristics of BBB-crossing TFRC Antibodies*

### Roundtable: Challenges and Opportunities in CNS Drug Delivery and Development: Academic, Biotech, Foundation, Pharma and Venture Capital Perspectives

**Praveen Raju**, Icahn School of Medicine at Mount Sinai, USA

**Inca Dieterich**, ARCH Venture Partners, USA

**Norman Matthew Ellinwood**, National MPS Society, USA

**Roberto Villaseñor**, Roche Innovation Center Basel, Switzerland

**Robert G. Thorne**, Denali Therapeutics / University of Minnesota, USA

### From CNS Drug Delivery to CNS Drug Development: Methodologies & Perspectives for the Future

**Ryan J. Watts**, Denali Therapeutics Inc, USA

*Engineering Brain Delivery to Treat Neurodegenerative Diseases*

**Martin Lauritzen**, University of Copenhagen, Denmark

*Real-Time in vivo Imaging of Transport Across the BBB using Multiphoton Microscopy*

**Peter Tessier**, University of Michigan, USA

*Short Talk: Extended Brain Delivery of Off-the-shelf IgGs using CD98hc Bispecific Antibodies*

### Closing Keynote Address

**Viviana Gradinaru**, California Institute of Technology, USA

*Imaging Targeted Expression with CNS Gene Therapy: Cutting Edge Approaches and Future Directions*

### Meeting Wrap-Up: Outcomes and Future Directions (Organizers)

## FRIDAY, JANUARY 27

### Departure