

KEYSTONE SYMPOSIA

on Molecular and Cellular Biology

Brain Therapeutics: Disruptive Technologies and Opportunities (Q3)

Scientific Organizers: Maria-Jesus Blanco, Kalpana M. Merchant and Mabel Loza

Supported by the Directors' Fund

Cerebral Fluid Flow and Function: Lymphatics, Glymphatics and the Choroid Plexus (Q4)

Scientific Organizers: Edwin S. Monuki, Maria Lehtinen and Maiken Nedergaard

February 16-19, 2020 • Eldorado Hotel & Spa • Santa Fe, NM, USA

Supported by the Directors' Fund

Discounted Abstract & Scholarship Deadline: October 29, 2019 / Abstract Deadline: November 19, 2019 / Discounted Registration Deadline: December 17, 2019

SUNDAY, FEBRUARY 16

Arrival and Registration

MONDAY, FEBRUARY 17

Welcome and Keynote Address (Q3)

***Maria-Jesus Blanco**, Sage Therapeutics, USA

***Kalpana M. Merchant**, Vincere Biosciences, Inc., USA

***Mabel Loza**, BioFarma Research Group, University of Santiago de Compostela, Spain

Darryle Schoepp, , USA
Talk Title to be Announced

Welcome and Keynote Address (Q4)

***Edwin S. Monuki**, University of California, Irvine, USA

***Maiken Nedergaard**, University of Copenhagen, Denmark

***Maria Lehtinen**, Harvard Medical School, USA

Kari K. Alitalo, University of Helsinki, Finland
Role of Lymphangiogenic Factors in Cerebral Fluid Flow and Neuropathological Processes in the CNS

Challenges and Opportunities for Brain Therapeutics: Preclinical to Clinical Translation (Q3)

***Maria-Jesus Blanco**, Sage Therapeutics, USA

Kalpana M. Merchant, Vincere Biosciences, Inc., USA
De-Risking Approaches for Disease-Modifying Therapies for Parkinson's Disease: Opportunities and Challenges Exemplified by the Parkin Activator Program

Chas Bountra, University of Oxford, UK
New Technologies, Collaborations and Processes, to Accelerate the De-Risking of Pioneer Drug Targets, for Neuro-Psychiatric Conditions

Shoichiro Ando, Niigata University, Japan
Short Talk: Gene Therapy for DRPLA Model Mice by AAV-Delivered CRISPR / Cas9

Trevor John Gonzalez, Duke University, USA
Short Talk: Engineering Synthetic Circular RNAs for AAV Mediated Expression in the Brain

Chao-Hsien Chen, University of Texas MD Anderson Cancer Center, USA

Short Talk: Reversal of Neurodegeneration through Clearance of pTau by Engineered Monocytes

Andrea Crotti, Astellas Pharma, USA
Short Talk: BIN1 Favors the Spreading of Tau via Extracellular Vesicles

Choroid Plexus and CSF Regulation of Stem Cells (Q4)

***Edwin S. Monuki**, University of California, Irvine, USA

Norman Ruthven Saunders, University of Melbourne, Australia
The Choroid Plexus: Mechanisms that Limit Drug Entry into the Developing Brain

Nanna MacAulay, University of Copenhagen, Denmark
Mechanism of CSF Secretion – Conventional Osmosis versus Active Water Transport

Maria Lehtinen, Harvard Medical School, USA
Illuminating the Choroid Plexus

Neil Dani, Boston Children's Hospital, USA
Short Talk: A Cellular and Spatial Map of the Choroid Plexus across Ventricles and Ages

Annarita Patrizi, German Cancer Research Center, Germany
Short Talk: Rescuing Cortical Features in Rett Syndrome through the Choroid Plexus

Roundtable: Collaboration & Knowledge Integration Models for Successful Brain Therapeutics (Q3)

***Mabel Loza**, BioFarma Research Group, University of Santiago de Compostela, Spain

James E. Audia, Chicago Biomedical Consortium, USA
Drug Discovery in the Academic and Not-For-Profit Community

Sohini Chowdhury, Michael J. Fox Foundation, USA

Suzana Petanceska, NIA, National Institutes of Health, USA

Workshop 1 (Q4)

***Julie Siegenthaler**, University of Colorado Denver, USA

Alexandra E. Hochstetler, Indiana University Purdue University Indianapolis, USA
Functional Studies of Ion Transport in Choroid Plexus Epithelial Cells

Engin Deniz, Yale University, USA
Building Xenopus as a Model System for Hydrocephaly and Ependymal Ciliogenesis

Eri Iwasawa, Cincinnati Children's Hospital Medical Center, USA
Neuroinflammation and Impaired Neural Differentiation in a Novel Rat Model of Neonatal Hydrocephalus Lacking Motile Cilia-mediated CSF Flow

Huixin Xu, Boston Children's Hospital, USA
Developmental Control of Cerebral Fluid Distribution and CSF-K+ by Choroid Plexus

Jo Stratton, McGill University, Canada
Ependymal Cells: Their Transcriptional Landscape and Role in Brain Injury

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Jessie Newville, University of New Mexico School of Medicine, USA
Disruption and Rescue of Ependymal Motile Cilia Function in a Model of Posthemorrhagic Hydrocephalus of Prematurity

Haley Masters, University of California, Irvine, USA
Single Cell Transcriptomic and Cell Biological Analysis of Human Choroid Plexus Epithelial Cells Derived from Pluripotent Stem Cells

Michael Neel, University of California, Irvine, USA
Characterization of an Aging-Related Amyloid of the Human Choroid Plexus

Advances in Technologies to Garner Insights into Disease Biology (Q3)

***Chas Bountra**, University of Oxford, UK

Edoardo Marcora, Icahn School of Medicine at Mount Sinai, USA
From Human Genetics to Causal Biology in Alzheimer's Disease

Lena F. Burbulla, Northwestern University, Feinberg School of Medicine, USA
Modeling Pathogenesis of Parkinson's Disease Using iPSC

Damian G. Wheeler, Translucence Biosystems, Inc, USA
Short Talk: Brain-Wide Cellular Resolution Measurement of Neuronal Activity and Neuroinflammation

Xiaoqing Li, University of Texas at Dallas, USA
Short Talk: Optical Opening of the Blood-Brain Barrier by Laser Excitation of Vasculature-Targeting Plasmonic Nanoparticles

Daniela Lecca, National Institute on Aging, National Institutes of Health, USA
Short Talk: Neuroinflammation as a Therapeutic Target in Neurodegenerative Diseases

Glymphatics (Q4)

***Christopher Moore**, Brown University, USA

Maiken Nedergaard, University of Copenhagen, Denmark
Sleep Regulation and Disease Roles of the Glymphatic System

Jeffrey J. Iliff, Oregon Health and Science University, USA
Molecular and Cellular Regulation of the Glymphatic System

Helene Benveniste, Yale School of Medicine, USA
Glymphatic Flow, Regulation and Function

Iben Lundgaard, University of Lund, Sweden
Short Talk: Cerebral Blood Flow Drives Efflux of CSF from the Ventricular System

Judith de Vos, Amsterdam University Medical Center, Netherlands
The Imaging Cryomicrotome: A Setup for Large Volume 3D Mesoscopic Visualization

Poster Session 1

TUESDAY, FEBRUARY 18

Integrating Novel Medicinal Chemistry Approaches Targeting the Brain (Q3)

***James E. Audia**, Chicago Biomedical Consortium, USA

Anastasia Khvorova, University of Massachusetts Medical School, USA
RNAi-Based Modulation of Gene Expression in Central Nervous System

Jacob M. Hooker, Harvard Medical School, USA
Integrating PET Tracers into CNS Drug Discovery: Impact on the Discovery of Novel HDAC Ligands

Maria-Jesus Blanco, Sage Therapeutics, USA
Discovery of Novel Clinical Compounds for CNS Disorders

Speaker to be Announced

Paula Perez Pardo, Utrecht University, Netherlands

Short Talk: Positive Effects of Small Molecule Tryptophan-2,3-Dioxygenase Inhibitors on Motor and Non-Motor Symptoms in a Mouse Model of Parkinson's Disease

Xavier Barril, Gain Therapeutics, Spain
Short Talk: Correcting Protein Misfolding with Structurally Targeted Allosteric Regulators (STAR): Applications in Rare Diseases and Brain Therapeutics

Lymphatics and CSF Dynamics (Q4)

***Maiken Nedergaard**, University of Copenhagen, Denmark

Jonathan Kipnis, University of Virginia, USA
Lymphatic-Glymphatic Roles in Aging and Disease

Erik N.T.P. Bakker, University of Amsterdam, Netherlands
The Impact of High Blood Pressure on the Brain: Studies in Spontaneously Hypertensive Rats

Steffi Dreha-Kulaczewski, University Medical Center Göttingen, Germany
Breathe to Drive CSF Flow

Julie Siegenthaler, University of Colorado Denver, USA
Short Talk: Origins, Development and Function of the Arachnoid Barrier Layer, a Key Component of the Blood-CSF Barrier

Ji Hoon Ahn, Korea Advanced Institute of Science and Technology, South Korea
Short Talk: Meningeal Lymphatic Vessels at the Skull Base Drain Cerebrospinal Fluid

Fengfei Ding, Huazhong University of Science and Technology, China
Short Talk: Chronic Sleep Fragmentation Alters the Brain Glymphatic Function

Humberto Mestre, University of Rochester Medical Center, USA
Short Talk: Cerebrospinal Fluid Influx Drives Acute Ischemic Tissue Swelling

John R. Cirrito, Washington University, School of Medicine, USA
Short Talk: Using Micro-Immuno-electrodes to Study Rapid Mechanisms of A β Clearance from the Brain Interstitial Fluid of Mice

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Diagnostic and/or Disease-State Biomarkers (Q3)

***Kalpana M. Merchant**, Vincere Biosciences, Inc., USA

Gwenn A. Garden, University of Washington, USA
Emerging Glial Biomarkers of CNS Disease

Steffany A.L. Bennett, University of Ottawa, Canada
Lipidomic-Based Insights into Disease Mechanisms: A Targeted Lipidomics Discovery Pipeline for Network and Flux Analysis

David Nguyen, Sage Therapeutics, USA
Novel Digital Technologies towards CNS Translational Insights

Jagan A. Pillai, Cleveland Clinic, USA
Short Talk: Pathway Based Analysis to Evaluate Inflammatory Analytes of Significance for Therapeutic Targeting in Alzheimer's Disease

Sang Bin Hong, Seoul National University Hospital, South Korea
Short Talk: Initial Oligoclonal Band Positivity as a Disease-State Biomarker in Anti-NMDA Receptor Encephalitis

Integrating Brain-Body Signaling (Q4)

***Maria Lehtinen**, Harvard Medical School, USA

Fiona Doetsch, University of Basel, Switzerland
Choroid Plexus Regulation of Adult Neural Stem Cells

Claire Wyart, Institut du Cerveau et de la Moelle Epinière, France
Origin and Role of the Cerebrospinal Fluid Bidirectional Flow in the Central Canal

Craig Ferris, Northeastern University, USA
Imaging the Effect of the Circadian Light-Dark Cycle on the Glymphatic System in Awake Rats

Laura Lewis, Boston University, USA
Coordinated Neural, Vascular, and Cerebrospinal Fluid Dynamics in Human Sleep

Poster Session 2

WEDNESDAY, FEBRUARY 19

Ensuring Target Engagement: Innovative Approaches Towards Neuroimaging and Brain Delivery (Q3)

***Jacob M. Hooker**, Harvard Medical School, USA

Tetsuya Suhara, National Institutes for Quantum and Radiological Science and Technology, Japan
Strategies for Utilizing Neuroimaging Biomarkers in CNS Drug Discovery and Development

Mickael Tanter, Physics for Medicine, France
Functional Ultrasound Imaging of the Brain Activity: A Fast Growing Neuroimaging Modality with Unique Features for Preclinical and Clinical Studies

Maria José Alonso, University of Santiago de Compostela, Spain
Nanotechnology-Based Strategies for the Delivery of Biological Drugs to the Brain

Lisa L. Shafer, Cerebral Therapeutics, Inc., USA

Emerging Strategies for Brain Drug Delivery: Case Study Applications

Robert G. Thorne, Denali Therapeutics, USA
Characterizing Fusion Protein Transport Across CNS Barriers: Leveraging Imaging and Other Novel Methods to Assess Brain Delivery

Frances G. Ghinger†, University of Maryland, Baltimore County, USA
Short Talk: Optical Imaging of Ventromedial Prefrontal Cortex Activity Following Chronic Stress

Choroid Plexus and CSF Regulation of Neuroimmune Responses (Q4)

***Fiona Doetsch**, University of Basel, Switzerland

Adam Chodobski, Alpert Medical School of Brown University, USA
Choroid Plexus in Brain Injury and Neuroinflammation

Jean-François Gherzi-Egea, Lyon Neurosciences Research Center, France
Antioxidant Defence at the Choroid Plexus Influences CSF Inflammation during Systemic Perinatal Injuries

Michal Schwartz, Weizmann Institute of Science, Israel
Choroid Plexus Regulation of the Neuroimmune Response

Jan Remsik, Memorial Sloan Kettering Cancer Center, USA
Short Talk: Immunological Determinants of Leptomeningeal Metastasis

Frederick B. Shipley, Harvard University, USA
Short Talk: Tracking Calcium Dynamics and Immune Surveillance at the Choroid Plexus

Marcus Stoodley, Macquarie University, Australia
Short Talk: Physiological Drivers of Fluid Flow in the Spinal Subarachnoid Space and Spinal Cord

Gabriel Jensen, University of Maine, USA
Short Talk: The Meninges and Choroid Plexus are Prominent Telomerase Reverse Transcriptase-Expressing Adult Stem Cell Niches in the Mouse Brain

June Goto, Cincinnati Children's Hospital, USA
Short Talk: Impaired Glymphatic Flow and The Delayed Neural Differentiation in CCDC39-Deficient Rat Model of Neonatal Hydrocephalus

Workshop 2 (Q4)

***Iben Lundgaard**, University of Lund, Sweden

Jin Cui, Boston Children's Hospital, USA
Choroid Plexus as a Site of Immune Activation in a Model of Autism Spectrum Disorders

Marco Fanous, Duke University, USA
Aquaporin 4 Regulates Adeno-Associated Viral (AAV) Transport across the Blood Brain Barrier

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Juchen Li, Fudan University, China

Investigation of the Glymphatic System using Awake and Anesthetized Mouse MRI

Darshan Sapkota, Washington University School of Medicine, USA
Stop Codon Readthrough of Aqp4 Generates a Novel AQP4 Isoform with Pathophysiological Significance

Hannah Elizabeth Jones, University of Colorado Anschutz Medical Campus, USA

Developmental Timing and Origins of Perivascular Brain Fibroblasts

Daphne M.P. Naessens, Amsterdam UMC, Netherlands
Elucidating Brain Water Management in Spontaneously Hypertensive Rats

Dakota E R DeFreitas[†], Washington University in St. Louis, USA
Evaluation of CSF Distribution in Post-Hemorrhagic Hydrocephalus Rat Brain using Gold Nanoparticle Enhanced X-ray Nanotomography

Cameron Sadegh, Harvard University, USA
Choroid Plexus Epithelia Respond Rapidly to Hemorrhage to Minimize Ventriculomegaly Prior to Global Compensatory Increases in CSF Reabsorption

Jordan C. Xu, UC Irvine, USA
Dural Lymphatic Changes in Normal Pressure Hydrocephalus

Andrew T. Hale, Vanderbilt University School of Medicine, USA
Integration of Human Genetics and Multi-Omics Data Implicates Novel Pathways in Hydrocephalus

Innovative Therapeutic Approaches Targeting the Brain (Q3)

Aletta D. Kraneveld, University of Utrecht, Netherlands
Parkinson's Disease: No Guts No Glory

Giorgia Quadrato, University of Southern California - USC Stem Cell, USA
Modeling Human Brain Development and Disease at Single Cell Resolution with Organoids

Shun Mitsui, Tokai University School of Medicine, Japan
Short Talk: Neural Cell-Specific SQSTM1 Deficiency Accelerates the Onset of Disease in an ALS Mouse Model

Nicholas T. Hertz, Mitokin Inc., USA
Short Talk: Small Molecule Activators of PINK1 Activity Rescue Sporadic PD Associated alpha-Synuclein Pathology

Taotao Lao, Massachusetts General Hospital/ Harvard Medical School, USA
Short Talk: TREML2 Regulates Microglia Functions in an Alzheimer's Disease Model

Diagnostics and Therapies (Q4)

***Jeffrey J. Iliff**, Oregon Health and Science University, USA

Edwin S. Monuki, University of California, Irvine, USA
Towards a Choroid Plexus-Based Regenerative Medicine

Kristopher T. Kahle, Yale School of Medicine, USA
A Role for Inflammation: TLR-4-mediated Cerebrospinal Fluid Hypersecretion in Post-hemorrhagic and Post-infectious Hydrocephalus

Christopher Moore, Brown University, USA
A Systems Approach to the Choroid Plexus

Patricia I. Dickson, Washington University, USA
CSF Delivery of Therapeutics

Meeting Wrap-Up: Outcomes and Future Directions (Organizers) (Q3)

Meeting Wrap-Up: Outcomes and Future Directions (Q4)

Edwin S. Monuki, University of California, Irvine, USA
Maria Lehtinen, Harvard Medical School, USA

THURSDAY, FEBRUARY 20

Departure