

# KEYSTONE SYMPOSIA

on Molecular and Cellular Biology

## Neurodegenerative Diseases: Genes, Mechanisms and Therapeutics (EK48)

Scientific Organizers: Eric J. Huang, Alison Goate and Richard M. Ransohoff

Sponsored by BlueRock Therapeutics, Cell Research, Genentech, Ionis Pharmaceuticals, Inc. and Ultragenyx Pharmaceutical Inc.

## NeuroImmune Interactions in Health and Disease (EK49)

Scientific Organizers: Beth Stevens, Jonathan Kipnis and Kate Monroe

June 7-9, 2021 • Virtual at your computer

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### MONDAY, JUNE 7

#### Welcoming Remarks and Keynote Session (Joint) (7am Denver/Mountain Time Start)

\***Eric J. Huang**, University of California, San Francisco, USA  
Session Chair

\***Beth Stevens**, Boston Children's Hospital, Harvard Medical School, USA  
Session Chair

**Akiko Iwasaki**, Yale University School of Medicine, USA  
*Manipulating Immune Trafficking In and Out of the CNS*

**Christopher K. Glass**, University of California, San Diego, USA  
*Exploiting Dynamic Enhancer Landscapes to Infer Pathogenic Mechanisms in Neurodegenerative Diseases*

#### Disease Mechanisms and Therapeutic Targets (Joint) (8:10am Denver/Mountain Time Start)

**Holly Kordasiewicz**, Ionis Pharmaceuticals, USA  
*Antisense Oligonucleotides for the Treatment of Neurological Diseases*

\***Joseph W. Lewcock**, Denali Therapeutics, USA  
*Therapeutic Strategies for the Treatment of Neurodegenerative Disease Based on Human Genetics*

\***Kate Monroe**, Denali Therapeutics, USA  
*Enhancing Microglia Function with ATV:TREM2*

**Johan Luthman**, Lundbeck, Denmark  
*Neuroimmunological Target Considerations - To Be or Not To Be in the Brain*

**Raz Dvir Szternfeld**, Weizmann Institute of Science, Israel  
*Short Talk: TREM2-Independent Neuroprotection Mediated by Monocyte-Derived Macrophages in a Mouse Model of Alzheimer's Disease*

**Christiane D. Wrann**, Massachusetts General Hospital / Harvard Medical School, USA  
*Short Talk: Myokine Irisin Is a Critical Regulator of Cognitive Function*

**Elise Marsan**, University of California, San Francisco, USA  
*Short Talk: Highly Conserved Glial Pathology and Human-Specific Neuronal Pathology Promote Neurodegeneration in FTL-GRN*

#### Mapping Immune Cell States in Health and Disease (11am Denver/Mountain Time Start) (EK49)

\***Francisco J. Quintana**, Harvard Medical School and the Broad Institute of MIT and Harvard, USA  
Session Chair

\***Beth Stevens**, Boston Children's Hospital, Harvard Medical School, USA  
*Mapping Microglia State to Function in Health and Disease*

**Burkhard Becher**, University of Zürich, Switzerland  
*The T Cell-Myeloid Axis in Neuroinflammation*

**Shane Antony Liddelow**, New York University Langone Medical Center, USA  
*Redefining Astrocytes States in Health and Disease*

**Kevin Guttenplan**, Oregon Health & Science University, USA  
*Short Talk: Identification of a Novel Astrocyte Toxic Factor*

**Frederick "Chris" Bennett**, University of Pennsylvania, USA  
*Short Talk: Brain Macrophage Transplantation for Research and Therapy Development*

#### From Therapeutic Targets to Clinic (11am Denver/Mountain Time Start) (EK48)

\***Joseph W. Lewcock**, Denali Therapeutics, USA  
Session Chair

\***Charlotte J. Sumner**, Johns Hopkins School of Medicine, USA  
*The Evolving Challenges of Gene Targeted Therapeutics for SMA*

**Lorenz Studer**, Memorial Sloan Kettering Cancer Center, USA  
*iPSC-Derived Dopaminergic Neurons and Parkinson's Disease Therapy*

**Priyanka Narayan**, National Institute of Health, USA  
*Short Talk: Discovering and Reversing the Metabolic Consequences of APOE4 in iPSC-Derived Glia*

#### Poster Session 1 (Joint) (1pm Denver/Mountain Time Start)

### TUESDAY, JUNE 8

#### Genetic Contributions to Neurodegeneration (7am Denver/Mountain Time Start) (EK48)

\***Valina L. Dawson**, Johns Hopkins University School of Medicine, USA  
Session Chair

\***Alison Goate**, Icahn School of Medicine at Mount Sinai, USA  
*Human Genetics Implicates Microglial Function in Alzheimer's Disease Risk*

**Jennifer Yokoyama**, University of California, San Francisco, USA  
*Immune Contributions to Early-Onset Neurodegenerative Disease*

**Martine Therrien**, Broad Institute, USA  
*Short Talk: Modeling the Impact of AD Genetic Risk on Microglia States and Function*

**Andy P. Tsai**, Indiana University School of Medicine, USA  
*Short Talk: Impact of PLCG2 Alzheimer's Disease Risk Variants on Microglia Biology and Disease Pathogenesis*

#### Neuroimmune Regulation of Sleep and Brain States (7am Denver/Mountain Time Start) (EK49)

\***Jonathan Kipnis**, Washington University School of Medicine, USA  
Session Chair

\***Maria Lehtinen**, Harvard Medical School, USA  
Session Chair

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**Maiken Nedergaard**, University of Rochester, USA  
*Sleep Regulation and Disease Roles of the Glymphatic System*

**David M. Holtzman**, Washington University, USA  
*APOE, Innate Immunity, and Neurodegeneration*

**Marco Colonna**, Washington University School of Medicine, USA  
*ILCs and Sleep*

**Constanze Martha Depp**, Max Planck Institute for Experimental Medicine, Germany  
*[NOT AVAILABLE ON DEMAND] Short Talk: Aging-Associated Myelin Dysfunction Drives Amyloid Deposition in Alzheimer's Disease*

### Cellular Pathways Targeted by Neurodegeneration (8:20am Denver/Mountain Time Start) (EK48)

\***Alison Goate**, Icahn School of Medicine at Mount Sinai, USA  
*Session Chair*

\***Valina L. Dawson**, Johns Hopkins University School of Medicine, USA  
*Mechanism of A-Synuclein-Mediated Neurodegeneration*

**Christian Hoffmann**, German Center for Neurodegenerative Diseases - DZNE, Germany  
*Short Talk: Synapsin and Synaptic Vesicle Condensates Recruit alpha-Synuclein*

**Kathryn M. Hixson**, UNC Chapel Hill, USA  
*Short Talk: Cerebellar Degeneration in ARSACS Disease Linked to Tau Hyperphosphorylation and Membrane-Protein Disruption*

**Noah Johnson**, University of Colorado Anschutz Medical Campus, USA  
*Short Talk: Identification of Small Molecule Drugs that Target Apolipoprotein E4-Catalyzed Amyloid- $\beta$  Fibrillization: A New Therapeutic Approach to Alzheimer's Disease*

### NeuroImmune Crosstalk at Brain Borders (8:30am Denver/Mountain Time Start) (EK49)

\***Jonathan Kipnis**, Washington University School of Medicine, USA  
*Lymphatic System Function and Dysfunction*

**Michal Schwartz**, Weizmann Institute of Science, Israel  
*Boosting Immunity to Combat Alzheimer's Disease*

\***Maria Lehtinen**, Harvard Medical School, USA  
*Imaging and Probing Choroid Plexus Influence on Brain Development and Function*

**Richard Daneman**, University of California, San Diego, USA  
*Control of Blood Brain Barrier Development, Function and Dysfunction*

**Alec Walker**, Boston Children's Hospital, USA  
*Short Talk: The Meninges Function as a Niche for B Lymphopoiesis in Early Life*

**Justin Rustenhoven**, Washington University in St Louis, USA  
*Short Talk: Skull and Vertebral Bone Marrow Are Myeloid Cell Reservoirs for the Meninges and CNS Parenchyma*

### Glial Contributions to Neurodegeneration (10:05am Denver/Mountain Time Start) (EK48)

\***Mathew M. Blurton-Jones**, University of California, Irvine, USA  
*Session Chair*

**Marco Prinz**, University of Freiburg, Germany  
*Novel Genetic Tools for Studying Myeloid Cells in the CNS*

**Ádám Dénes**, Hungarian Academy of Sciences, Hungary  
*Microglia Shape Neuronal and Vascular Responses via Compartment-Specific Purinergic Mechanisms*

**Anne Schaefer**, Icahn School of Medicine at Mount Sinai, MPI Ageing, USA  
*Control of Neuron Activity by Microglia*

\***Michael T. Heneka**, University of Luxembourg, Luxembourg  
*Inflammasome Activation in Alzheimer's Disease*

**Swati Mishra**, University of Washington, USA  
*Short Talk: Depletion of AD Risk Gene Sortilin-Related Receptor (SORL1) Causes Cell-Type Specific Dysfunction of the Endo-Lysosomal Pathway in Human Neurons and Microglia – Implications in Alzheimer's Disease*

**Patrick W. Sheehan**, Washington University in St. Louis, USA  
*Short Talk: Astrocytic BMAL1 Regulates Protein Aggregation in Mouse Models of Alpha-Synuclein and Tau Pathology*

**Sabina Tahirovic**, Deutsches Zentrum für Neurodegenerative Erkrankungen e. V. - DZNE, Germany  
*Short Talk: Loss of NPC1 Enhances Phagocytic Uptake and Impairs Lipid Trafficking in Microglia*

### Immune Mechanisms of Synapse Function and Dysfunction (11:10am Denver/Mountain Time Start) (EK49)

\***Beth Stevens**, Boston Children's Hospital, Harvard Medical School, USA  
*Session Chair*

\***Jonathan Kipnis**, Washington University School of Medicine, USA  
*Session Chair*

**Dorothy Schafer**, University of Massachusetts Chan Medical School, USA  
*Neural-Immune Crosstalk at the Synapse*

**Betty Diamond**, Feinstein Institute for Medical Research, USA  
*Autoimmune Mechanisms of Cognitive Dysfunction*

**Borislav Dejanovic**, Vigil Neuroscience, USA  
*Short Talk: Synaptic Proteomics in an AD Mouse Model Reveals Complement-Dependent Synapse Elimination by Astrocytes*

**Susanna Rosi**, University of California, San Francisco, USA  
*Short Talk: Novel Microglia-Mediated Mechanisms Underlying Synaptic Loss and Cognitive Impairment after Traumatic Brain Injury*

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### Meet the Editors (Joint) (1:30pm Denver/Mountain Time Start)

**Swapnika Ramu**, Cell Press, USA

**Gabriel A. Gasque**, PLOS Biology, USA

**Sophie Morgan**, Nature Communications, UK

**Tim Spencer**, Journal of Cell Biology, USA

### Networking Lounge (Joint) (2:30pm Denver/Mountain Time Start)

### WEDNESDAY, JUNE 9

#### Phase Separation, Protein Aggregation and Transmission (7am Denver/Mountain Time Start) (EK48)

\***Eric J. Huang**, University of California, San Francisco, USA  
Session Chair

**J. Paul Taylor**, St. Jude Children's Research Hospital, USA  
Phase Separation of RNA Binding Proteins in Neurodegeneration

**Sjors Scheres**, MRC Laboratory of Molecular Biology, UK  
Cryo-EM Structures of Amyloid Filaments from Human Brain

\***Virginia M. Y. Lee**, University of Pennsylvania School of Medicine, USA  
Tau and A-Synuclein Aggregation and Spreading

**Alyssa Coyne**, Johns Hopkins University School of Medicine, USA  
Short Talk: Nuclear Accumulation of CHMP7 Initiates Nuclear Pore Complex Injury and Subsequent TDP-43 Dysfunction in Sporadic and Familial ALS

**Roberta Romano**, University of Salento, Italy  
Short Talk: Role of RAB7A Mutations in Charcot-Marie-Tooth Type 2B Disease

#### Epigenetics and Transcriptomics of the Aging Brain (8:45am Denver/Mountain Time Start) (EK48)

\***Richard M. Ransohoff**, Third Rock Ventures, USA  
Session Chair

\***Li-Huei Tsai**, Massachusetts Institute of Technology, USA  
Transcriptomic Dissection of Alzheimer's Disease at the Single Cell Resolution

**Philip L. De Jager**, Columbia University Medical Center, USA  
Epigenetics and Systems Biology of Alzheimer's Disease

**Anne Brunet**, Stanford University, USA  
Neuro-Immune Interactions in the Aging Neurogenic Niche

**Carlos Cruchaga**, Washington University School of Medicine, USA  
Short Talk: Multi-Tissue High-Throughput Proteomics Profiling for Neurodegenerative Disease

**Hyo Won Ahn**, National Institute of Child Health and Human Development, USA  
Short Talk: Transposable Element Insertions Associated with Risk of Neurologic and Psychiatric Diseases

#### Immune Regulation of Brain Development and Behavior (7am Denver/Mountain Time Start) (EK49)

\***Dorothy Schafer**, University of Massachusetts Chan Medical School, USA  
Session Chair

\***Burkhard Becher**, University of Zürich, Switzerland  
Session Chair

**Jonathan P. Godbout**, Ohio State University, USA  
The Impact of Social Stress on Immune Cell Trafficking and Neurobehavior

**Sonia Garel**, INSERM, France  
Microglia and the Crossroads of Cortical Wiring and Environmental Signals

**Gloria Choi**, Massachusetts Institute of Technology, USA  
Neuroimmune Interactions Shaping Social Behavior

**Jeffrey Stogsdill**, Harvard University, USA  
Short Talk: Pyramidal Neuron Subtype Diversity Governs Microglia States in the Neocortex

**Jiawei Chen**, University of California, San Francisco, USA  
Short Talk: Role of Microglia-Vasculature Interaction in Angiogenesis and Germinal Matrix hemorrhage in the Prenatal Brain

**Jason Shepherd**, University of Utah, USA  
Short Talk: The Role of Virus-Like Intercellular Communication in Neuroinflammation

#### Modeling Neuro-Immune Interactions in Neurodegeneration (11am Denver/Mountain Time Start) (EK48)

\***Li-Huei Tsai**, Massachusetts Institute of Technology, USA  
Session Chair

**Fred H. Gage**, The Salk Institute for Biological Studies, USA  
Cerebral Organoids and Neurodegeneration

**Hui-Hsin Tsai**, Biogen, USA  
Multiple Sclerosis Neurorepair – A Drug Discovery Perspective

\***Mathew M. Blurton-Jones**, University of California, Irvine, USA  
Neuro-Immune Interactions in AD Models

**Emmy Li**, University of California, San Francisco, USA  
Short Talk: CRISPRi-based Genetic Screens in iPSC-Derived 3D Neuron-Astrocyte-Microglia iAssembloids

#### T Cell Brain Communication (9:20am Denver/Mountain Time Start) (EK49)

\***Dorothy Schafer**, University of Massachusetts Chan Medical School, USA  
Session Chair

\***Burkhard Becher**, University of Zürich, Switzerland  
Session Chair

**Anthony J. Filiano**, Duke University, USA  
T Cell-Neural Interactions in Health and Disease

**Frauke Zipp**, Johannes-Gutenberg-Universität Mainz, Germany  
Immune Regulatory Processes within the Central Nervous System

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**Celia E. Shiao**, University of North Carolina at Chapel Hill, USA

*Short Talk: Neutrophil Trafficking to Brain Driven by Peripheral Inflammatory Macrophages Modulates CNS Control of Behavior*

**Stefan Bittner**, University Medical Center Mainz, Germany, Germany

*Short Talk: Direct Modulation of Neuronal Firing Patterns and Local Networks by Invading Lymphocytes*

**Ethan G. Hughes**, University of Colorado Anschutz Medical Campus, USA

*Short Talk: Microglia Engulf Myelin during Immune-Mediated Cortical Demyelination*

### Impact of Peripheral Signals and the Gut Brain Axis (10:55am Denver/Mountain Time Start) (EK49)

\***Burkhard Becher**, University of Zürich, Switzerland

*Session Chair*

**Daniel Mucida**, Rockefeller University, USA

*Neuronal Regulation of Innate Immune Cells*

\***Elaine Y. Hsiao**, University of California, Los Angeles, USA

*The Microbiome as a Modifier of Environmental Risk for Cognitive Impairment*

**Henrique Veiga-Fernandes**, Champalimaud Research, Portugal

*Neuronal Regulation of Innate Lymphoid Cells*

**Brian Kim**, Mount Sinai, USA

*Neuroimmune Regulation of Itch*

**Francisco J. Quintana**, Harvard Medical School and the Broad

Institute of MIT and Harvard, USA

*Microbial Regulation of Astrocyte Responses*

**Charlotte R. Wayne**, Columbia University Irving Medical Center, USA

*Short Talk: Mechanisms of Th17 Cell-Mediated Microglial Activation and BBB Dysfunction in Post-Infectious Basal Ganglia Encephalitis*

**Malu G. Tansey**, University of Florida, USA

*Short Talk: Colitis Disrupts Inflammatory Gene Networks and Nigrostriatal Integrity in the Brain and LRRK2 G2019S Mutant Mice Display Enhanced Vulnerability*

### Poster Session 2 (Joint) (1:30pm Denver/Mountain Time Start)

### Career Roundtable (Joint) (2:30pm Denver/Mountain Time Start)

**Holly Kordasiewicz**, Ionis Pharmaceuticals, USA

**Philip L. De Jager**, Columbia University Medical Center, USA

**Lorenz Studer**, Memorial Sloan Kettering Cancer Center, USA