

# KEYSTONE SYMPOSIA

on Molecular and Cellular Biology

## Neural Environment in Disease: Glial Responses and Neuroinflammation (Z1)

Scientific Organizers: Richard Daneman, Dorothy Schafer, Michael V. Sofroniew and Vanda A. Lennon

Sponsored by BioLegend, Inc.

## Neurodegenerative Diseases: New Insights and Therapeutic Opportunities (Z2)

Scientific Organizers: Valina L. Dawson, Joseph W. Lewcock and Fred H. Gage

June 16-20, 2019 • Keystone Resort • Keystone, CO, USA

Sponsored by BioLegend, Inc., Biogen, BlueRock Therapeutics, Genentech, Inc., Ionis Pharmaceuticals, Inc., Roche and Takeda Pharmaceutical Company Limited

Discounted Abstract & Scholarship Deadline: February 13, 2019 / Abstract Deadline: March 13, 2019 / Discounted Registration Deadline: April 16, 2019

### SUNDAY, JUNE 16

#### Arrival and Registration

### MONDAY, JUNE 17

#### Welcome and Keynote Address (Z1)

\***Richard Daneman**, University of California, San Diego, USA

\***Dorothy Schafer**, University of Massachusetts Medical School, USA

**Li-Huei Tsai**, Massachusetts Institute of Technology, USA  
*Neuron-Glia Interaction in Health and Disease*

#### Welcome and Keynote Address (Z2)

\***Fred H. Gage**, The Salk Institute for Biological Studies, USA

**Marc Tessier-Lavigne**, Stanford University, USA  
*Molecular Control of Axon Degeneration in Development, Disease and Adult Plasticity*

#### Neuronal Response to Injury (Z1)

\***David M. Holtzman**, Washington University, USA  
*TREM2 Function Regulates A $\beta$  linked Tau Seeding and Spreading in Neuritic Plaques*

**Eric J. Huang**, University of California, San Francisco, USA  
*Neuron-Glia Interaction in Human Germinal Matrix: Implications in Neurodevelopmental Disorders*

\***Marc R. Freeman**, Oregon Health & Science University, USA  
*Mechanisms of Axon Degeneration*

**Katie Ennis**, Biogen, USA  
*Short Talk: The Cytokine Receptor Fn14 is Required for Hippocampal Synaptic Plasticity Deficits that Occur Following Acute Ischemic Stroke*

**Lucas Cheadle**, Harvard Medical School, USA  
*Short Talk: Sensory Experience Engages Microglia-to-Neuron Cytokine Signaling to Remodel Developing Synapses*

#### Aggregation Mediated Toxicity (Z2)

\***Xiaobo Mao**, Johns Hopkins University, USA

**Rudolph E. Tanzi**, Massachusetts General Hospital, USA  
*Amyloid Beta Organoid Model*

**Valina L. Dawson**, Johns Hopkins University School of Medicine, USA  
*Alpha Synuclein Toxicity*

**Patrik Verstreken**, KU Leuven, Belgium  
*Tau Toxicity at the Synapse*

**Thomas Brannstrom**, Umea University Hospital, Sweden  
*Short Talk: Transmissibility of SOD1 Prion Strains Between Mice Expressing Different Mutant Human SOD1s*

#### Workshop 1: Modulating Microglia Inflammatory Signaling (Z1)

\***Kim N. Green**, University of California, Irvine, USA

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

**Ying Cao**, Peking University, China  
*Transcriptional Mechanism of IRF8 and PU.1 Governs Microglial Activation in Neurodegenerative Condition*

**Rouven Schulz**, Institute of Science and Technology Austria, Austria  
*Topological Classification of Microglia*

**Yajing Xu**, University College London, UK  
*Microglia Mediate Restructuring of Spinal Somatosensory Circuits During Normal Postnatal Development and After Injury*

**Youtong Huang**, University of California, San Diego / Salk Institute, USA  
*Investigating Microglial TAM Receptors as Modulators of Alzheimer's Pathology*

**Guy C. Brown**, University of Cambridge, UK  
*Blocking the Microglial P2Y6 Receptor Prevents Microglial Phagocytosis of Neurons and Synapses, and Prevents Neurodegeneration Induced by Neuroinflammation, Beta Amyloid, TAU and Ageing in vivo*

**Monique S. Mendes**, University of Rochester, USA  
*In vivo Imaging of Microglial Self-Renewal and Maturation in the Adult Mouse Brain*

**Nicole Vo**, University of Washington, USA  
*CD33 and CD45 interaction in AD*

**Sanda Mimouna**, Hospital for Special Surgery, USA  
*The Role of Transcriptional Coregulator GRIP1 in Myeloid Cells in Neuroinflammation*

#### Workshop 1 (Z2)

\***David V. Hansen**, Brigham Young University, USA

**Michael Henderson**, University of Pennsylvania, USA  
*Using Quantitative Pathology Mapping and Network Modeling to Understand  $\alpha$ -Synuclein Spread*

**Sang Su Kwak**, Genetics and Aging Research Unit, Massachusetts General Hospital, USA  
*Amyloid- $\beta$  42/40 Ratio Drives Tau Pathology in 3D Human Neural Cell Culture Models of Alzheimer's Disease*

**Evan T. Lester**, University of Colorado, USA  
*Interactions between RNA and Tau in Models of Frontotemporal Dementia*

**Silvia Porta**, Center for Neurodegenerative Disease Research, USA  
*Patient-Derived Frontotemporal Lobar Degeneration Brain Extracts Induce Formation and Spreading of TDP-43 Pathology in vivo*

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**Stephanie K. See**, University of California, San Francisco, USA  
*Identification of Cellular Mechanisms that Control  $\alpha$ -Synuclein Aggregation Using a CRISPRi/a Functional Genomics Platform*

**Meghan Kerrisk Campbell**, Alkahest, USA  
*A Therapeutic Human Plasma Fraction Enhances Cognitive Function in Aging and Neurodegenerative Disease through Multiple Mechanisms of Action*

### Transmission and Spread of Disease Pathology (Z2)

\***Karen Hsiao Ashe**, University of Minnesota, USA

**Xiaobo Mao**, Johns Hopkins University, USA  
*The Mechanism of Pathological  $\alpha$ -synuclein Transmission*

**John Collinge**, University College London, UK  
*Prion Neurodegeneration: Towards an Effective Treatment and its Relevance for Alzheimer's Disease*

**Karina Fog**, H. Lundbeck A/S, Denmark  
*Alpha-Synuclein Antibodies as Therapeutics in Synucleinopathies – How Antibodies Affect Cellular Handling of Misfolded  $\alpha$ -synuclein*

**Amanda Engstrom**, Emory University, USA  
*Short Talk: Pathological Tau Induces Neurodegeneration Through the Sequestration and Inhibition of LSD1 Function*

**Xuyuan Kuang**, Rutgers University, USA  
*Short Talk: Association of Transmissible PolyQ Aggregates with Lipid Vesicles and Its Implications in Mutant Huntingtin Seeding*

### Astrocytes (Z1)

**Michael V. Sofroniew**, University of California, Los Angeles, USA  
*Astrocyte Roles in Repair and Regeneration*

\***Jin-Moo Lee**, Washington University, USA  
*Astrocytosis and Amyloid Plaque Pathogenesis*

\***Cagla Eroglu**, Duke University Medical Center, USA  
*How do Glia Sculpt Synaptic Circuits?*

**Blanca Diaz Castro**, University of Edinburgh, UK  
*Striatal Astrocytes: Identity, Form, Function and Roles in Huntington's Disease*

### Poster Session 1

### TUESDAY, JUNE 18

#### Microglia and Innate Immunity (Z1)

**Dorothy Schafer**, University of Massachusetts Medical School, USA  
*Targeting Microglia-Mediated Synapse Loss for Therapeutic Intervention in Multiple Sclerosis*

**Kim N. Green**, University of California, Irvine, USA  
*Microglia Facilitate Plaque Development and Mediate the Downregulation of Synaptic Genes in Alzheimer's Disease Mice*

\***Anne Schaefer**, Icahn School of Medicine at Mount Sinai, USA  
*Epigenetic and Signaling Controlled Brain Region-Specific Microglia Functions*

\***Francisco J. Quintana**, Harvard Medical School and the Broad Institute of MIT and Harvard, USA  
*Molecular Control of Astrocyte Pathogenic Activities in MS*

**Serena Becchi**, University of New South Wales, Australia  
*Short Talk: The Role of Microglia when Decision Making is Impaired by a High Fat and Sugar Diet in Rats*

**Manana Kutsia**, Okinawa Institute of Science and Technology Graduate University, Japan  
*Short Talk: Importance of Microglia for Neural Tissue Regeneration in Zebrafish Model of Traumatic Brain Injury*

**Sandra Siegert**, Institute of Science and Technology Austria, Austria  
*Short Talk: Sex Specific Microglia Response to Transient Reduction of Neuronal Activity*

#### New Therapeutic Opportunities (Z2)

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

**Frank Rigo**, Ionis Pharmaceuticals, USA  
*RNA Targeting Therapeutics for the Treatment of Neurodegenerative Diseases*

**Eric J. Huang**, University of California, San Francisco, USA  
*Microglia Toxicity and TDP-43 Proteinopathy in Neurodegeneration*

**Don W. Cleveland**, University of California, San Diego, USA  
*Gene Silencing Therapy for Neurodegenerative Disease*

**Li Gan**, Weill Cornell Medicine, USA  
*Sex-Dimorphic Effects of Microglial Dysfunction in Neurodegeneration*

**Dieter Willbold**, Forschungszentrum Jülich, Germany  
*Short Talk: First Clinical Data of the First Anti-Prionic PRI-002 that is Orally Available, Reverts Cognition Deficits, and Decelerates Neurodegeneration in Transgenic AD Mouse Models*

**Daniel Heinzer**, University of Zurich, Switzerland  
*Short Talk: Whole Genome RNAi Screen Identifies Novel Regulators of PrPC as Potential Therapeutic Targets in Prion Diseases*

**Alessandro Sette**, La Jolla Institute for Immunology, USA  
*Short Talk: T Cell Reactivity to Tau and Alpha-Synuclein in PD*

#### Blood Brain Barrier (Z1)

**Richard Daneman**, University of California, San Diego, USA  
*Regulation of the Blood-Brain Barrier in Health and Disease*

\***Alexandre Prat**, Université de Montréal, Canada  
*Influence of Cytokines on the Blood-Brain Barrier*

\***Eric V. Shusta**, University of Wisconsin-Madison, USA  
*Modeling the Neurovascular Unit Using Human iPSCs*

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**Sidar Aydin**, University of Bern, Switzerland

*Short Talk: Endothelial Antigen-Presentation Stops the Migration of CD8+ T Cells Across the Blood-Brain Barrier in Neuroinflammation*

**Matthew N. McCarroll**, University of California, San Francisco, USA

*Short Talk: An Inducible Zebrafish Model of Pineal Gland Ablation Reveals Dynamics of Neuronal Cell Death, Regeneration and Microgliosis in vivo*

### Developing Effective Preclinical Disease Models (Z2)

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

**Martin Kampmann**, University of California, San Francisco, USA

*Elucidating Cellular Mechanisms and Therapeutic Strategies for Neurodegenerative Diseases with Multimodal CRISPR-based Genetic Screens in iPSC-Derived Neurons and Glia*

**Elena Cattaneo**, University of Milano, Italy

*Organoid Models of Triple Repeat Diseases*

**Fred H. Gage**, The Salk Institute for Biological Studies, USA

*iPSC to Study Repair and Neurodegeneration*

**Zhuohao He**, University of Pennsylvania, USA

*Short Talk: Studying Tau Transmission in AD and FTLN Using Novel Mouse Models*

### Poster Session 2

#### WEDNESDAY, JUNE 19

#### Glymphatics and Lymphatics (Z1)

\***Kari K. Alitalo**, University of Helsinki, Finland

*CNS Lymphatics*

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

*Glymphatics*

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

*Orchestration of Embryonic Brain Development by the Choroid Plexus*

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

*Meningeal Fibroblast Identity and Function: New Insights from scRNA-Sequencing*

**Percy Griffin**, Washington University in St. Louis, USA

*Short Talk: Circadian Regulation of Neuroinflammation and Neurodegeneration by Rev-Erba*

**Celia McKee**, Washington University in St. Louis, USA

*Short Talk: The Astrocyte Circadian Clock Regulates Amyloid Beta Deposition and Degradation*

**Caio Mazucanti**, NIA, National Institutes of Health, USA

*Short Talk: Serotonergic Regulation of Insulin Expression & Release in Choroid Plexus*

#### Translating Therapeutics for Neurodegeneration to the Clinic (Z2)

\***Karina Fog**, H. Lundbeck A/S, Denmark

**Joseph W. Lewcock**, Denali Therapeutics, USA

*Therapeutic Strategies Based on Human Genetics*

**Matthew Kennedy**, Merck Research Labs, USA

*Discovery and Development of LRRK2 Inhibitors*

**David V. Hansen**, Brigham Young University, USA

*Microglial Activation States in Alzheimer's Disease: Are You a (Wo)man or a Mouse?*

**Jeffrey L. Cleland**, Orpheris, Inc., USA

*Short Talk: OP-101: Human Safety and Pharmacokinetics of a Microglia-targeted Systemic Therapy for Neuroinflammation*

**Anna Ettore**, 4D Pharma Research Ltd., UK

*Short Talk: From Screening to Pre-Clinical Efficacy of*

*Microbiome-Derived Bacterial Strains that Modulate*

*Neuroinflammatory and Neurodegenerative Processes in Parkinson's Disease*

**Garrett S. Gibbons**, University of Pennsylvania, USA

*Short Talk: Conformation-Selective Tau Monoclonal Antibodies as*

*Immunotherapy Candidates for Alzheimer's Disease (AD) and*

*Frontotemporal Lobar Degeneration-tau (FTLD-tau)*

#### Round Table Discussion from Industry, Government and Academia - Challenges and Opportunities (Z2)

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

**Gene W. Yeo**, University of California, San Diego, USA

**Matthew Kennedy**, Merck Research Labs, USA

**Frank Rigo**, Ionis Pharmaceuticals, USA

**Amir Tamiz**, NINDS, National Institutes of Health, USA

**Aaron D. Gitler**, Stanford University School of Medicine, USA

#### Adaptive Immune Responses (Z1)

**Vanda A. Lennon**, Mayo Clinic, USA

*Astrocytic and Oligodendroglial Autoimmunity*

\***Daniel S. Reich**, NINDS, National Institutes of Health, USA

*Imaging Lesion Repair in Multiple Sclerosis*

\***Jorge I. Alvarez**, University of Pennsylvania, USA

*CNS Intrinsic Mechanisms Suppressing T Cell Driven*

*Neuroinflammation*

**Keita Saeki**, National Institutes of Health, USA

*Short Talk: IRF8 Shapes Long-Term Endotoxin Memory in Microglia*

**Tiffany J. Petrisko**, West Virginia University, USA

*Short Talk: CXCL10-CXCR3 Axis Mediates Induction of Cerebral Hyperexcitability by Peripheral Viral Challenge*



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### Molecular Mechanisms of ALS/FTD (Z2)

\***Shanthini Sockanathan**, Johns Hopkins University School of Medicine, USA

**Aaron D. Gitler**, Stanford University School of Medicine, USA  
*Expanding Mechanisms and Therapeutic Targets for Neurodegenerative Disease*

**Clotilde Lagier-Tourenne**, Massachusetts General Hospital, USA  
*Molecular Mechanisms of Disease in ALS and FTD*

**Gene W. Yeo**, University of California, San Diego, USA  
*Protein-RNA and Stress Granules Dysregulation in ALS*

**Hideyuki Takahashi**, Yale University, USA  
*Short Talk: Progranulin Deficiency Induces Expression of Microglial TYROBP Gene Network and Differentially affects Alzheimer's disease pathologies*

**Evangelos Kiskinis**, Northwestern University Feinberg School of Medicine, USA

*Short Talk: Nucleocytoplasmic Proteomic Analysis Highlights ETF1 and Nonsense Mediated Decay as Therapeutic Targets in C9ORF72-Related ALS/FTD*

### Poster Session 3

### THURSDAY, JUNE 20

#### Oligodendrocytes and Inflammation (Z1)

**David H. Rowitch**, University of Cambridge, UK  
*Neuronal Vulnerability and Multilineage Diversity in Multiple Sclerosis*

\***Kelly Monk**, Oregon Health & Science University, USA  
*Molecular and Genetic Mechanisms of Myelin Formation and Repair*

**Dimitry Ofengeim**, Sanofi, USA  
*Understanding the Nature of Microglial Phenotypes through the Interplay of Cell Death and Inflammation*

**Stefan Berghoff**, Max-Planck Institut for Experimental Medicine, Germany  
*Short Talk: Cell-Type Specific Cholesterol Synthesis Coordinates Inflammation and Remyelination in Demyelinated Lesions*

**Claudia Fuchs**, University of Bologna, Italy  
*Short Talk: Loss of CDKL5 Enhances Microglia Activation: Are Neuro-Inflammatory Mechanisms Implicated in the Pathophysiology of CDKL5 Deficiency Disorder?*

**TrangKimberly T. Nguyen**, Emory University, USA  
*Short Talk: Proteomic Analyses Reveal that Glia-Specific and Seizure-Protective Receptors GPR37L1 and GPR37 Regulate S100A Calcium-Binding Protein Expression and Secretion*

#### Drivers of Synaptic Loss in Disease (Z2)

\***Clotilde Lagier-Tourenne**, Massachusetts General Hospital, USA

**Paul F. Worley**, Johns Hopkins School of Medicine, USA  
*Immediate Early Genes and Alzheimer's Disease*

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

*Dynamic Microglia States and Functions in Health & Disease*

**Karen Hsiao Ashe**, University of Minnesota, USA  
*Synaptic and Cognitive Dysfunction from Non-fibrillar Tau*

**Shanthini Sockanathan**, Johns Hopkins University School of Medicine, USA  
*Control of ADAM10  $\alpha$ -Secretase Cleavage of Amyloid Precursor Protein by GDE2-RECK*

**Ryan Douglas Hallam**, University of Guelph, Canada  
*Short Talk: Synuclein Fibrils Inhibit Synaptic Function in Cortical Neurons through Induction of Nitrosative Stress*

**Claire E. Le Pichon**, NICHD, National Institutes of Health, USA  
*Short Talk: Enhancing the Benefits of DLK Inhibition in a Mouse Model of ALS by Restoring an Adaptive Neuronal Response*

#### Workshop 2: Astrocyte-Microglia Crosstalk during Inflammation (Z1)

\***Blanca Diaz Castro**, University of Edinburgh, UK

**Lilianne Barbar**, New York Stem Cell Foundation Research Institute, USA

*Developing in vitro Models of Neurodegeneration Based on Human iPSC-Derived Astrocytes*

**Cristina Gutierrez-Vazquez**, Harvard Medical School, USA  
*EphrinB3 Signaling Promotes Pathogenic Activities in Astrocytes during Central Nervous System Inflammation*

**Weikang Cai**, Joslin Diabetes Center, USA  
*Insulin Signaling-Dependent ATP Release from Astrocytes is Important for Dopamine Release and Depressive-Like Behavior*

**Elena Blanco-Suarez**, The Salk Institute for Biological Studies, USA  
*Astrocyte-Secreted Chrdl1 Promotes Synapse Maturation and Limits Synaptic Plasticity through GluA2-AMPA Increase*

**Martín M. Riccomagno**, University of California, Riverside, USA  
*Novel Combinatorial Approaches to Selectively Target Reactive Astrocytes*

**Kun Leng**, University of California, San Francisco, USA  
*Mapping Pathways Controlling the Reactive State of Astrocytes through CRISPRi Loss-of-Function Screening and Single-Cell RNA-Seq*

**Deepa Jonnalagadda**, Sanford Burnham Prebys Medical Discovery Institute, USA

*Sphingosine 1-Phosphate Signaling Effects in Immediate-Early Astrocytes (ieAstrocytes)*

#### Workshop 2 (Z2)

\***Katerina Akassoglou**, University of California, San Francisco, USA

**Irina Alexandra Leaf**, Biogen, USA

*Reverse Translational Multimodal Approach to Identify CSF Signatures Associated with Disease Progression in MS*

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**Chelsey J. LeBlang**, Boston University School of Medicine, USA  
*Modulation of the Inflammatory Response by the RNA-binding Protein TIA1 in the P301S Mouse Model of Tauopathy*

**Yihang Li**, Dana-Farber Cancer Institute, USA  
*SARM1 Interacts with the Bclw/IP3R Pathway in Paclitaxel-Induced Axon Degeneration*

**Michael A. Lodato**, Boston Children's Hospital, USA  
*Single-Cell, Whole-Genome Sequencing Reveals Mechanisms of DNA Damage and Somatic Mutation in the Human Brain during Aging and in Neurodegeneration*

**Michaela O. Lunn**, Carleton University, Canada  
*Contribution of Lrrk2 to the Modulation of Host Immunity during Infection*

**Jing Yang**, Peking University, China  
*Local Degeneration of Catecholaminergic Axons Acts as the Protective Mechanism in Colitis*

**Samara Reck-Peterson**, University of California, San Diego, USA  
*A Structural and Mechanistic Model for the Regulation of LRRK2's Interaction with Microtubules*

### Hot Topics (Z1)

**Erik M. Ullian**, University of California, San Francisco, USA  
*Novel Three-Dimensional Astrocyte-Containing Organoids Recapitulate Key Aspects of Human Neurodegenerative Disease*

\***Long-Jun Wu**, Mayo Clinic, USA  
*Neuronal Network Activity Controls Microglial Process Surveillance in Awake Mice via Norepinephrine Signaling*

\***Yi Ren**, Florida State University, USA  
*The Inflammatory Mechanisms Involved in Myelin-Debris-Induced Pathological Changes in Neural Injury*

**Julia A. Kuhn**, Genentech, Inc., USA  
*Short Talk: Sex Differences in Microglial Contributions to Pain*

### Glial Contributors to Neurodegeneration (Z2)

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

**Mathew M. Blurton-Jones**, University of California, Irvine, USA  
*Development of a Chimeric Model to Study and Manipulate Human Microglia in vivo*

**Katerina Akassoglou**, University of California, San Francisco, USA  
*Neurovascular Interactions: Mechanisms, Imaging, Therapeutics*

**Sandeep Robert Datta**, Harvard Medical School, USA  
*The MS4A Gene Family in Alzheimer's Disease*

**Anastasia Efthymiou**, Icahn School of Medicine at Mount Sinai, USA  
*Short Talk: Investigating the Effect of the MS4A locus on Alzheimer's Disease Risk*

### Meeting Wrap-Up: Outcomes and Future Directions (Z1)

**Vanda A. Lennon**, Mayo Clinic, USA

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

**Joseph W. Lewcock**, Denali Therapeutics, USA

**Fred H. Gage**, The Salk Institute for Biological Studies, USA

### FRIDAY, JUNE 21

### Departure