

# KEYSTONE SYMPOSIA

on Molecular and Cellular Biology

## Neurodegenerative Diseases (Z3)

Scientific Organizers: Leonard Petrucelli, Stacie Weninger and Soyon Hong

Sponsored by Lilly USA, LLC

## Neuroimmune Interactions: Nervous System and Immune Cell Heterogeneity in Health and Disease (Z4)

Scientific Organizers: Nicola J. Allen, Anna Victoria Molofsky and Francisco J. Quintana

June 3-6, 2024 • Santa Fe Community Convention Center • Santa Fe, NM, USA

Supported by the Directors' Fund

Scholarship Deadline: February 28, 2024 / Abstract Deadline: February 28, 2024 / Discounted Registration Deadline: April 3, 2024

### MONDAY, JUNE 3

#### Arrival and Registration

### TUESDAY, JUNE 4

#### Welcome and Keynote Session (Joint) (Start 8:00AM)

**Tony Wyss-Coray**, Stanford University School of Medicine, USA  
*Aging, the Immune System and Neurodegeneration*

**Beth Stevens**, Boston Children's Hospital, Harvard Medical School, USA  
*Microglia and the Complement System in Neurodegeneration*

#### Immune-CNS Interactions in Neurodegeneration (Joint) (Start 9:50AM)

**Christopher K. Glass**, University of California, San Diego, USA  
*Transcriptional Regulation of Macrophage Development*

**S. Pablo Sardi**, Sanofi, USA  
*Therapeutic Development for Neurodegenerative Disorders*

**Anne Schaefer**, Icahn School of Medicine at Mount Sinai, MPI Ageing, USA  
*Epigenetic Regulation of Microglia*

#### Poster Session 1

#### Workshop 1: Immune-CNS Interactions in Neurodegeneration (Start 2:30PM) (Z3)

**Lynn van Olst**, Northwestern University, USA  
*Spatial Transcriptomics Reveals Neuroimmune Mechanisms of A $\beta$  Clearance in Immunized Alzheimer's Disease Patients*

**Ravi Jagasia**, Pharma Research and Early Development, Switzerland  
*Genome-wide CRISPR-Cas9 based screening for modifiers of lysosomal GCase activity uncovers candidate risk factors for Parkinson Disease*

**Georg Werner**, Ludwig-Maximilians-Universität München, Germany  
*Single Cell Analysis Reveals a Neurodegeneration Specific Microglia Population Resistant to CSF1R Inhibition in a Mouse Model with FTLD-like Pathology*

**Urs Langen**, F. Hoffmann-La Roche AG, Switzerland  
*Beyond the Shuttle: Advances in Brain Delivery of Biologics for the Treatment of Neurodegenerative Diseases*

**Kyle J. Travaglini**, Allen Institute for Brain Science, USA  
*An Integrated Multimodal Cell Atlas of Alzheimer's Disease*

**Maylin Fu**, Stanford University, USA  
*Controlling Endogenous mRNA Localization in the Peripheral and Central Nervous Systems in vivo*

**Philip L. De Jager**, Columbia University Medical Center, USA  
*Human Microglia Expressing High Levels of CD74 Expression are Associated with Activation and Cognitive Decline*

**Ian Peikon**, Cajal Neuroscience, USA

*Dire straits: loss of translational regulation of SNCA by iron unifies the genetics of PD and LBD at the SNCA locus*

#### Workshop 1: Communication Across Brain Barriers (Start 2:30PM) (Z4)

**Miguel Marin-Rodero**, Harvard Medical School, USA  
*The Meninges Host a Unique Compartment of Regulatory T Cells That Bulwarks Adult Hippocampal Neurogenesis*

**Nagela Ghabdan Zanluqui**, National Institutes of Health, USA  
*Venous Plexus-Associated Lymphoid Hubs Support Meningeal Humoral Immunity*

**Nannan Lu**, Stanford University, USA  
*Exploring the Interaction between Blood Plasma Proteins and Microglia: Insights into Brain-Peripheral Communication*

**Amy Joy Dashwood**, University of Cambridge, UK  
*Novel Genetic Systems Show Feedback from CD4 T Cell Infiltrate in Aged Mouse Brain Shapes and Selects Microglia Populations*

**Helena Barr**, Harvard University, USA  
*Diurnal Regulation of Brain Border Macrophage Phenotype and Function Across the Lifespan*

**Tarek Elmazzahi**, German Center for Neurodegenerative Diseases, Germany  
*Identification of a Tissue-Specific Molecular Program Governing the Formation and Function of Brain-Resident CD8+ T Cells*

**Brittany M. Hemmer**, Icahn School of Medicine at Mount Sinai, USA  
*Youth-Associated Plasma Protein TIMP2 Regulates Microglial State in the Context of Aging and Alzheimer's Pathology*

#### Neuroimmune Interactions Relevant to NDD (Start 5:00PM) (Z3)

**Kate Monroe**, Denali Therapeutics, USA  
*Leveraging Human Genetics for Novel Therapeutic Approaches for Alzheimer's Disease*

**Christian Haass**, Ludwig-Maximilians University Munich, Germany  
*PGRN/ApoE*

**David M. Holtzman**, Washington University, USA  
*Role of APOE in Modulating the Innate and Adaptive Immune Response in Neurodegeneration*

**August Yue Huang**, Boston Children's Hospital, USA  
*Short Talk: Alzheimer's Disease Microglia Exhibit Enriched Proliferation-related Clonal Somatic Mutations Associated with Inflammatory States*

**John D. Fryer**, Mayo Clinic, USA  
*Short Talk: Anti-amyloid Immunotherapy Induces Sustained Microglial and Immune Alterations*

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### Sterile and Pathogen-Mediated Brain Injury (Start 5:00PM) (Z4)

**Robyn S. Klein**, Washington University School of Medicine, USA  
*Impact of Viral Infection on CNS Function*

**William H. Robinson**, Stanford University School of Medicine, USA  
*The Role of EBV in Multiple Sclerosis*

**Anna-Maria Globig**, The Salk Institute for Biological Studies, USA  
*Short Talk: Sympathetic Nerves Instruct T Cell Exhaustion in Viral Infection and Cancer via the Noradrenaline Receptor ADRB1*

**Christopher A. Baker**, Yale School of Medicine, USA  
*Short Talk: Novel Infectious and Autoimmune Animal Models of Post-Acute COVID Syndrome Exhibit Central and Peripheral Neuropathology and Behavioral Changes*

**Elizabeth Balint**, McMaster University, Canada  
*Short Talk: Bystander Activated CD8+ T Cells Mediate Neuropathology During Viral Infection via Antigen-Independent Cytotoxicity*

**Zeynep Ilgin Kolabas**, Helmholtz Center Munich, Germany  
*Short Talk: Decoding the Neuroimmune Interface: Unique Molecular Insights from Skull Bone Marrow in Health and Disease*

### WEDNESDAY, JUNE 5

#### Molecular Mechanisms in NDD (Start 8:00AM) (Z3)

**Soyon Hong**, University College London, UK  
*Neuroimmune signaling across gut-brain axis modulates brain synucleinopathy*

**Speaker to be Announced**

**Leonard Petrucelli**, Mayo Clinic Jacksonville, USA  
*Tmem/PGRN*

**Bakhos Tadros**, Baylor College of Medicine, USA  
*Short Talk: LMO7 Modulates Tau Levels by Regulating CHIP-BAG5 Interplay: Novel Insights into Tauopathy Mechanisms*

**Alexi Nott**, Imperial College London, UK  
*Short Talk: Vascular-immune Epigenetic Mechanisms Underlying Age-related Brain Disorders*

**Dalya Rosner**, Alector, USA  
*Short Talk: The Alzheimer's Risk Genes MS4A4A and MS4A6A Cooperate to Regulate Key Microglial Functions*

**Roy R. Parker**, HHMI/University of Colorado, USA  
*Short Talk: Polyserine Domain RNA-binding Proteins as Cellular Factors Enhancing Tau Aggregation*

#### Glial-Immune Interactions (Start 8:00AM) (Z4)

**Anna Victoria Molofsky**, University of California, San Francisco, USA  
*Cytokines in CNS Development*

**Francisco J. Quintana**, Harvard Medical School and the Broad Institute of MIT and Harvard, USA  
*Astrocytes and Inflammatory Signaling*

**Nicola J. Allen**, The Salk Institute for Biological Studies, USA  
*Astrocyte-Neuron Interactions in Aging and Neurodegeneration*

**Naomi Habib**, Hebrew University of Jerusalem, Israel  
*Reconstruction of Multi-Cellular Dynamics Underlying Aging and Alzheimer's Disease: One Cell at a Time*

**Kristine Zengeler**, University of Virginia, USA  
*Short Talk: Astrocyte Inflammasome Signaling Modulates Synaptic Plasticity*

**Stefan Bittner**, University Medical Center Mainz, Germany, Germany  
*Short Talk: TRPA1 Channels Control Central Nervous System Inflammation via MHC Class II Modulation on Astrocytes*

#### Career Roundtable (Joint) (Start 2:30PM)

#### Susceptibility vs. Resilience: Understanding Region Vulnerability in NDD (Start 5:00PM) (Z3)

**Cagla Eroglu**, Duke University Medical Center, USA  
*In vivo Proteomic Tools TurboID*

**Henne Holstege**, Amsterdam UMC, Netherlands  
*Cognitively Healthy Centenarians are Genetically Protected Against Alzheimer's Disease*

**Speaker to be Announced**

**Guoyan Zhao**, Washington University, USA  
*Short Talk: Transcriptomic Changes in Lewy Body Disease and Alzheimer's Disease Linked to Selective Regional and Neuronal Vulnerability*

**Mohammad Abbasi**, Arizona State University, USA  
*Short Talk: Unveiling Microglial Heterogeneity in Spatial Context*

#### Immune Regulation of Behavior (Start 5:00PM) (Z4)

**Jessica Osterhout**, University of Utah School of Medicine, USA  
*Immune Regulation of Sickness Behavior*

**Helen Vuong**, University of Minnesota, Twin Cities, USA  
*Talk Title to be Announced*

**Marco Prinz**, University of Freiburg, Germany  
*Innate Immune Cells at Human CNS Borders Mapped across Space, Time and Perturbation*

**Anna C. Geraghty**, Stanford University, USA  
*Short Talk: Immunotherapy-Related Cognitive Impairment After CAR T Cell Therapy in Mice*

#### Poster Session 2

### THURSDAY, JUNE 6

#### Modelling Human NDD in a Dish (Start 8:00AM) (Z3)

**Tarja Malm**, University of Eastern Finland, Finland  
*Modeling Early Alzheimer's Disease in Human Context*

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**Paola Arlotta**, Harvard University, USA

*Human Brain Organoids as Models for Inter-Individual Variation in Disease Susceptibility*

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

*Elucidating Mechanisms and Therapeutic Targets for Neurodegenerative Diseases by CRISPR-Based Functional Genomics*

**Nilesh Sharma**, University of Calgary, Canada

*Short Talk: Metabolic Perturbation in Ependymal Cells Leads to Progressive Peri-ventricular Pathology and Recapitulates Alzheimer's Disease Pathogenesis*

**Jean Paul Chadarevian**, UC Irvine, USA

*Short Talk: Therapeutic Potential of Human Microglial Transplantation in a Chimeric Model of CSF1R-related Leukoencephalopathy*

**Lulu Jiang**, University of Virginia, USA

*Short Talk: The Innovative Neuron-Glial Brain Assembloid Model of Alzheimer's Disease Reveals the Differential Role of ApoE Isoforms in Pathological Tau Propagation*

**Mireia Gomez-Budia**, University of Eastern Finland, Finland

*Short Talk: Unravelling LTP-like Synaptic Plasticity in Human Cortical Biopsies on Microelectrode Arrays*

### Peripheral Immune Signaling and Impact on Neural Circuits (Start 8:00AM) (Z4)

**Francesca Odoardi**, University Medical Center Göttingen, Germany

*Lung Microbiome Regulation of Brain Autoimmunity*

**Michael D. Burton**, University of Texas at Dallas, USA

*Neuroimmune Regulation of Pain and Depression*

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

*Gut Immunity Impacts on Brain Function*

**Scott J. Russo**, Icahn School of Medicine at Mount Sinai, USA

*Immune-brain Interactions in Stress and Depression*

**Yangyang Zhu**, Harvard Medical School, USA

*Short Talk: A Chemogenetic Screen for Neuroimmune Interplay Reveals Trpv1+ Neuron Control of Tregs in the Gut*

**Timothy Cox**, University of Pennsylvania, USA

*Short Talk: Microbiome Regulation of Age-Associated Cognitive Decline*

### Workshop 2: Steps Toward Precision Medicine for NDD (Start 2:30PM) (Z3)

**Jordan D. Marks**, Mayo Clinic, USA

*TMEM106B Risk SNP Alters Disease Duration and Fibril Deposition in FTLD-TDP*

**Zhe Zhang**, Johns Hopkins University, USA

*PTP $\alpha$ -Mediated PI3P Regulation as a Therapeutic Strategy for C9ORF72-ALS/FTD*

**Tina Schwabe**, Nine Square Therapeutics, USA

*Developing Parkin Activators to Enhance Mitochondrial Function for the Treatment of Parkinson's Disease*

**Francesca Cignarella**, FNIH, USA

*Enabling a Precision Medicine Approach to Target and Biomarker Discovery in Alzheimer's Disease: Accelerating Medicines Partnership® Alzheimer's Disease (AMP AD)*

**Tong Wu**, Washington University in St. Louis, USA

*Targeting SARM1 Inhibition Provides a Promising Therapeutic Strategy for DNA Damage-Induced Neurodegenerative Diseases, Including Amyotrophic Lateral Sclerosis (ALS)*

**Laura E. Koenig**, Harvard Medical School, USA

*TYK2 Kinase as a Novel Therapeutic Target in Alzheimer's Disease*

**Karthik Raju**, Denali Therapeutics, USA

*GPR34 Loss-of-function Rescues TREM2 Metabolic Dysfunction and Promotes Responsive Microglial States*

**Jing L. Guo**, NICO Therapeutics, USA

*Decreased Lipidated ApoE-receptor Interactions Confer Protection against Pathogenicity of ApoE and its Lipid Cargoes*

### Workshop 2: Neuroinflammation in Aging and Disease (Start 2:30PM) (Z4)

**Genevieve Curtin**, UCSD, USA

*Microglia, Macroproblems: Cellular Dysfunction in Microglia Derived from Down Syndrome Patients*

**Yingying Zhang**, Boston Children's Hospital, USA

*Spatial and Temporal Profiling of the Complement System Uncovered Novel Functions of the Alternative Complement Pathway in Brain Development*

**Sean Ryan**, Sanofi, USA

*Ferroptosis Activation in Multiple Sclerosis*

**Gerard Crowley**, University College London, UK

*Innate-Adaptive Immune Crosstalk Regulates Activity-Dependent Synapse Loss*

**Qihui Zhou**, DZNE Munich, Germany

*Microglia Mediated Cerebral Th17/Treg Imbalance Facilitate Neurodegeneration in C9orf72 ALS Mice*

**Christina Mayer**, Institute of Neuroimmunology and Multiple Sclerosis, Germany

*Complement Factor H Protects Against Neuronal Ferroptosis in Multiple Sclerosis*

**Anna Flury**, Advanced Science Research Center, CUNY Graduate Center, USA

*A Conserved Stress Response Associated with Dark Microglia Drives Neurodegeneration in Alzheimer's Disease*

**Lara Labarta-Bajo**, The Salk Institute, USA

*Investigating a Role for Astrocyte Stat1 in the Aged Brain*

### Designing Better: Steps Toward Precision Medicine for NDD (Start 5:00PM) (Z3)

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**Fiona C. Elwood**, Janssen R&D, USA

*Precision Medicine in Neurodegeneration*

**Jeremy S. Duffield**, Prime Medicine, Inc., USA

*Prime Editing as a Curative Therapeutic Approach for Neurodegenerative Diseases*

**Aimee Jackson**, Atlanta Therapeutics, USA

*Addressing CNS Indications using a Novel Di-siRNA Modality for Improved Potency, Distribution, and Duration*

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

*Defining ALS Mechanisms at Single Cell Resolution*

### Microglia Function (Start 5:00PM) (Z4)

**Takahiro Masuda**, Kyushu University, Japan

*Targeting Microglia for Genetic Manipulation*

**Borislav Dejanovic**, Vigil Neuroscience, USA

*Microglia Therapeutics for Neurodegeneration*

**Long-Jun Wu**, University of Texas Health Science Center, USA

*Short Talk: Microglia promote neuronal activity via shielding inhibitory synapses*

**Wangchao Xu**, Washington University in St. Louis, USA

*Short Talk: A Microbe-Neuroendocrine- Immune Axis in Health, Aging, and Infection*

**Hayley J. Strasburger**, Icahn School of Medicine at Mount Sinai, USA

*Short Talk: Dopamine-Mediated Control of Microglia-Neuron Interaction and Function*

### Meeting Wrap-Up: Outcomes and Future Directions (Organizers) (Z3)

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### Poster Session 3

**FRIDAY, JUNE 7**

Departure