

KEYSTONE SYMPOSIA

on Molecular and Cellular Biology

Neuro-Immune Interactions in the Central Nervous System (Z1)

Scientific Organizers: Marco Colonna, Shilpa Sambashivan and Michael T. Heneka

Sponsored by BioLegend, Inc., Cell Research and PhenoVista Biosciences

Neurodegeneration: The Biological Pathways Driving the Future of Therapeutic Development (Z2)

Scientific Organizers: Dimitri Krainc and Alfred Sandrock

June 5-9, 2022 • Keystone Resort • Keystone, CO, USA

Sponsored by Biogen, Ionis Pharmaceuticals, Inc., Lilly USA, LLC, Merck & Co., Inc. and PhenoVista Biosciences

Global Health Travel Award Deadline: May 26, 2022 / Scholarship Deadline: February 22, 2022 / Abstract Deadline: March 1, 2022 / Discounted Registration Deadline: April 5, 2022

SUNDAY, JUNE 5

Arrival and Registration

MONDAY, JUNE 6

Welcome and Keynote Session (Joint)

Thomas C. Südhof, Stanford School of Medicine, USA
Synapse Biology in Alzheimer's Disease

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

Genetics of Neuro-Immune Interactions (Joint)

David Gate, Northwestern University, USA
Cerebrospinal Fluid Immunity in Aging and Neurodegenerative Disease

Alison Goate, Icahn School of Medicine at Mount Sinai, USA
Alzheimer's Disease Susceptibility Alleles Implicate Efferocytosis in Microglia

Workshop 1: Neuro-Immune Interactions in Neurological Diseases (Z1)

Zahara M. Keulen, UC Irvine, USA
Neuronal Tau Pathology Alters Human Microglial Morphology, Transcriptome, and Function

Denise Jurczynszak, Icahn School of Medicine at Mount Sinai, USA
Investigation of Neuroinflammation in Down Syndrome

Gregory Williams, La Jolla Institute for Immunology, USA
PINK1 Identified as a Target of Autoantigenic T Cells Responses in Patients with PD

Esra Yalcin, Boston Children's Hospital, USA
Viral Expression of Anti hC4 Nanobody (hC4Nb8) Rescues Schizophrenia like Phenotypes in hC4A Mice

Sean Ryan, Sanofi, USA
Microglia Ferroptosis is Prevalent in Neurodegenerative Disease and Regulated by SEC24B

Xiaoying Chen, Washington University School of Medicine, USA
Microglia-mediated T cell Infiltration in Tauopathy

Maria Serena Paladini, University of California San Francisco, USA
Fate Mapping Of Peripherally Derived Macrophages After Traumatic Brain Injury

Gabrielle Childers, University of Alabama at Birmingham, USA
Exploring the Role of B Cells in a Mouse Model of Multiple System Atrophy

Understanding Immune Receptors in the CNS (Z1)

Greg E. Lemke, The Salk Institute for Biological Studies, USA
TAM Receptor Regulation of Neurodegenerative Disease

Marco Colonna, Washington University School of Medicine, USA
ITAM Signaling in Neurodegeneration

Hugo Peluffo, Institut Pasteur de Montevideo/UDELAR/Universitat de Barcelona, Uruguay

Short Talk: CD300f Immune Receptor Contributes To Healthy Aging By Regulating Inflammaging, Metabolism And Cognitive Decline

Jose Ledo, Rockefeller University / Boston Children's Hospital - Harvard Medical School, USA

Short Talk: Microglia Modulate Neuronal Activity and Learning and Memory via Presenilin 1-Trem2

Nelli Blank, University Bonn, LIMES Institute, Germany
Short Talk: Impact of Aging and Cxcr4-deficiency on the Immune Response of Microglia and Monocytes upon Experimental Stroke

James Hamilton, Eli Lilly and Company, USA
Short Talk: TREM2 Limits Age-related Neurodegeneration and Modifies β -amyloid Environment to Restrict Tau Seeding and Spreading

Synaptic Mechanisms and Molecular Events (Z2)

Pietro V. De Camilli, Yale University School of Medicine, USA
Synaptic Membrane Endocytosis

Morgan H. Sheng, Broad Institute of MIT and Harvard, USA
Mechanisms of Synapse Loss in Neurodegenerative Disease

Maria Grazia Spillantini, University of Cambridge, UK
Synaptic Dysfunction in Parkinson's Disease

Volker Haucke, Leibniz Forschungsinstitut für Molekulare Pharmakologie, Germany
The Alzheimer's Disease Risk Factor CALM Controls Synaptic Plasticity by a GluA1-specific Endocytic Mechanism

Emma L. Clayton, King's College London, UK
Short Talk: A Novel Synaptopathy- Defective Synaptic Vesicle Protein Trafficking in the Mutant CHMP2B Mouse Model of Frontotemporal dementia

Poster Session 1

TUESDAY, JUNE 7

Microglia, Other Glial Cells and Macrophages in Neurodegenerative Diseases (Z1)

Michael T. Heneka, University of Luxembourg, Luxembourg
Microglia Support Neurons through Tunneling Nanotubes

Rosa C. Paolicelli, University of Lausanne, Switzerland
Metabolic Control of Microglial Function

Marco Prinz, University of Freiburg, Germany
Origin and Fate of Brain Macrophages

Dorothy Schafer, University of Massachusetts Chan Medical School, USA
Microglial-Astrocyte Wnt Signaling: A Key Regulator of Neural Circuit Remodeling

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Mickaël Audrain, AC Immune, Switzerland

Short Talk: Microglia and the NLRP3 Inflammasome Pathway Contribute to Tau-mediated Pathology in vivo

Lindsay De Biase, UCLA, USA

Short Talk: Microglia Drive Pockets of Neuroinflammation in Middle Age

Autophagy and Disease (Z2)

Ivan Dikic, Goethe University Medical School, Germany

ER-phagy: From Molecular Principles to Pathogenesis of Neuropathies

Xinnan Wang, Stanford University School of Medicine, USA

Converging Cellular Pathways in Parkinson's Disease

Dana Clausen†, Rutgers University, USA

ECE-1 Protects Neurons from β -amyloid Accumulation in Endosomal/Lysosomal Vesicles

Rebecca Wallings, University of Florida, USA

Short Talk: Bi-phasic, Age-dependent Alterations in Lysosomal Function and Immune Responses in R1441C-Lrrk2 Macrophages

Kang-Chieh Huang, Indiana University Purdue University Indianapolis, USA

Short Talk: Autophagy Impairment Contributes to Neurodegeneration via Repression of mTORC1 Signaling in a Human Pluripotent Stem Cell Model of Glaucoma-Associated Neurodegeneration

Dan Dou, University of Pennsylvania, USA

Short Talk: LRRK2 Hyperactivity Induced by Parkinson's Disease-associated Mutations Disrupts Autophagic Vesicle Transport along the Axon

Celia McKee, Washington University in St. Louis, USA

Short Talk: The Astrocyte Circadian Clock Regulates Autophagy and Endolysosome Function

Poster Session 2

Workshop 2: iPSC and Organoids for the Study of Neurodegeneration (Z1)

Alice Buonfiglioli, Icahn School of Medicine at Mount Sinai, USA

A New Cerebral Organoid Culture Model to Study the Effects of Novel Drugs Targeting Microglia

Jean Paul Chadarevian, UC Irvine, USA

Harnessing iPSC-derived Microglia to Delivery Therapeutics in the Brain

Olivia Teter, UCSF, USA

Uncovering Regulators of Synaptic Pruning by CRISPRi in an iPSC-derived Microglia-neuron Co-culture System

Marvin Reich, German Center for Neurodegenerative Diseases, Germany

Neuron-microglia Crosstalk in a Human iPSC-based FTD Model

Amanda McQuade, Institute for Neurodegenerative Diseases, UCSF, USA

Dampening Purinergic Signaling in TREM2-knockout iPSC-microglia Rescues Chemotactic Deficit

Caleb C. Stokes, University of Washington, USA

Single Cell RNA Sequencing of Zika Infection in Human Neural Tissues Reveals an Astrocyte-Driven Innate Immune Response Governed by Interferon Beta.

Sandra Siegart, Institute of Science and Technology Austria, Austria

How MorphOMICs Challenges Current Morphological Analysis Strategies and Links Shape to Function.

Juan J. Ramirez, Duke University, USA

An Astrocyte to Microglia Signaling Pathway that Controls the Balance Between Synapse Formation and Synapse Elimination

Workshop: Cellular Pathways Driving Disease (Z2)

Kelsey Babcock, Brown University, USA

Linking Defects in the Quiescent Neural Stem Cell Pool to Impaired Adult Hippocampal Neurogenesis in Alzheimer's Disease

Tianmin Fu, Ohio State University, USA

Roles of TMEM175 in Lysosomal pH Homeostasis and Parkinson's Diseases

Kelsey Krus, Washington University in St. Louis, USA

Loss of Stathmin-2, a Hallmark of TDP-43-Associated ALS, Causes Motor Neuropathy

Anthony Flamier, Whitehead Institute, USA

Impact Of DNA Methylation Changes on Alzheimer's Disease

Brian Hafler, Yale University, USA

Topological Analysis of Single-cell Hierarchy Reveals Inflammatory Glial Landscape of Macular Degeneration

Drew A. Gillett, University of Florida, USA

BMP Modification in a Progranulin (PGRN) Deficient Cell Line

Patrick W. Sheehan, Washington University in St. Louis, USA

Glial Reprogram Circadian Gene Transcription During Aging and Disease

Andy P. Tsai, Indiana University School of Medicine, USA

Impact of PLCG2 Variants on Microglial Biology and Disease Pathogenesis in Alzheimer's Disease

The Role of Brain Immune System in Shaping the CNS Connectivity (Z1)

Jun R. Huh, Harvard Medical School, USA

Impact of Gut Bacteria in Neurodevelopmental Abnormalities

Katerina Akassoglou, University of California, San Francisco, USA

Microglia Regulation of Brain Network Hyperexcitability

Anne Schaefer, Icahn School of Medicine at Mount Sinai, MPI Ageing, USA

Control of Neuronal Activity by Microglia

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Jerika J. Barron, University of California, San Francisco, USA
Short Talk: Type 2 Innate Lymphocytes Promote Inhibitory Synapse Development and Social Memory

Mario R. Capecchi, University of Utah, USA
Short Talk: Defective Hoxb8 Microglia are Causative for both Chronic Anxiety and OCS-like Behavior in Mice

Endolysosomal Dysfunction in Neurodegeneration (Z2)

Dimitri Krainc, Northwestern University, USA
Convergence of Mitochondrial and Lysosomal Dysfunction

Ralph A. Nixon, New York University, Langone Medical Center, USA
Endosomal-lysosomal dysfunction as a primary catalyst in Alzheimer's Disease

Roberto Zoncu, University of California, Berkeley, USA
mTOR and Lysosomes in Nutrient Sensing and Growth Control

Hankum Park, Seoul National University, South Korea
Short Talk: Spatial Snapshots of Amyloid Precursor Protein Intramembrane Processing via Early Endosome Proteomics

Sofia Massaro Tienze, Yale University, USA
Short Talk: Molecular Characterization of Lipofuscin Pathology in Neuronal Ceroid Lipofuscinosis

WEDNESDAY, JUNE 8

Application of Next Generation Technologies to Profile Neuro Immune Interactions (Z1)

Frederic Geissmann, Memorial Sloan Kettering Cancer Center, USA
Mosaicism in the Central Nervous System and Neurodegeneration

Li-Huei Tsai, Massachusetts Institute of Technology, USA
The Use of Induced Pluripotent Stem Cells to Model Alzheimer's Disease

Ido Amit, Weizmann Institute, Israel
The Power of ONE: Immunology in the Age of Single Cell Genomics

Christopher K. Glass, University of California, San Diego, USA
Decoding Microglia Enhancers in Health and Disease

Félix Distéfano-Gagné, Laval University, Canada
Short Talk: Dynamic Regulation of the Microglial Transcriptional Landscape During Neuroinflammatory Response

Inbal Benhar, Weizmann Institute of Science, Israel
Short Talk: Single-Cell Profiling of Non-Neuronal Retinal Cells Reveals Dynamic Multicellular Responses to Central Nervous System Injury

Mitochondrial Defects in Neurodegeneration (Z2)

Dalton James Surmeier, Northwestern University, USA
Bioenergetic Determinants of Selective Neuronal Vulnerability in Parkinson's Disease

Richard J. Youle, NINDS, National Institutes of Health, USA
Neuroinflammation Stemming from Mitochondrial DAMPs Linked to Parkinson's Disease Genes and Mitophagy Defects

Yvette C. Wong, Northwestern University, USA
Mitochondria-Lysosome Contact Sites: Roles and Regulation in Homeostasis and Neurodegenerative Diseases

Anna Barron, Nanyang Technological University, Singapore
Short Talk: Regulation of Microglial Immunometabolic Programming in Alzheimer's Disease

Isaac Pieter Heremans, UCLouvain, Belgium
Short Talk: Parkinson's Disease Protein PARK7 Prevents Metabolite and Protein Damage Caused by a Glycolytic Metabolite

Career Roundtable (Joint)

Anabella Villalobos, Biogen, USA

Yvette C. Wong, Northwestern University, USA

Brain Immune System in Neuroinflammation (Z1)

Menna Clatworthy, University of Cambridge, UK
Plasma Cells in the Meninges

Malu G. Tansey, University of Florida, USA
Immune Function and Inflammation in Parkinson's Disease

Francisco J. Quintana, Harvard Medical School and the Broad Institute of MIT and Harvard, USA
Impact of Aryl Hydrocarbon Receptor in Multiple Sclerosis

Stephanie Ann Michalski, Saint Louis University School of Medicine, USA
Short Talk: T-lymphocyte and Microglial Paracrine Signaling Promotes Epilepsy-Associated Neuroinflammation

Michelle Xiao Le Zuo, University of Toronto, Canada
Short Talk: Ageing Promotes Grey Matter Demyelination and Neurodegeneration that is Associated with Meningeal Neutrophil Accumulation in an Animal Model of Multiple Sclerosis

Neuronal Pathways in Disease (Z2)

Virginia M. Y. Lee, University of Pennsylvania School of Medicine, USA
Alpha-Synuclein from Patient Lewy Bodies Exhibits Distinct Pathological Activity that can be Propagated in vitro

Martin Kampmann, University of California, San Francisco, USA
CRISPR-based Functional Genomics for Neurological Disease

Juliana Laverde Paz†, University of Miami, USA
Evaluation of Neuronal DNA Damage in Primary Lateral Sclerosis

Rui Chang, Yale University, USA
Short Talk: From Gut to Brain: Understanding the Propagation of Parkinson's Disease

Jennifer Rauch, University of Massachusetts Amherst, USA
Short Talk: Deciphering the Molecular Features Underlying LRP1-Mediated Tau Spread

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Poster Session 3

THURSDAY, JUNE 9

Blood Brain Barrier (BBB), Glymphatics and Lymphatics (Z1)

Jonathan Kipnis, Washington University School of Medicine, USA
Meningeal Sinuses and Lymphatics in the Epicenter of CNS Immune Surveillance

Zsuzsanna Fabry, University of Wisconsin, USA
How does the Meningeal Lymphatics Respond to Neuroinflammation in Autoimmunity, Infection, and Trauma?

Speakers to be Announced

Jorge I. Alvarez, University of Pennsylvania, USA
Short Talk: Heterogeneity in the CNS Endothelium Identifies the Blood Meningeal Barrier as an Orchestrator of Neuroinflammation

Matthew N. Poy, Johns Hopkins All Children's Hospital, USA
Short Talk: Glutamatergic Argonaute2 Regulates Formation of the Neurovascular Unit

Translational Considerations in Neurodegenerative Research (Z2)

Alfred Sandrock, Voyager Therapeutics, USA
Introduction "Challenges of going from Bench to Bedside in Neurology"

Sophie Eckel†, University of New Mexico, USA
A Downregulated Circular RNA in Alzheimer's Disease can Inhibit the Expression of Disease-associated Long APP and MAPT mRNA Isoforms in the Frontal Cortex

Carole Ho, Denali Therapeutics Inc., USA
Early Clinical Development: Achieving Proof of Biology and Dose Selection Prior to Registration Enabling Clinical Studies

Yemima Riani Butler, University of Michigan, USA
Short Talk: Fibril-specific Nanobody Prevents Prion-like α -Synuclein Spreading

Vivian Ko, UCSD, USA
Short Talk: CK1 ϵ -dependent TDP-43 Phosphorylation in ALS

Workshop 3: Immunotherapy of Neurodegeneration (Z1)

Gerard E. Crowley, University College London, UK
Chemogenetic Activation of Perforant Pathway Induces Microglial Complement Signalling and Synapse Loss

John F. Tuddenham, Columbia University, USA
Towards Manipulation of Microglial Subsets in Humans: A Toolkit for Modulating Microglia in a Targeted Fashion

Stephanie Bissel, Indiana University, USA
Reduced PLCG2 Expression Alters Microglial Responses and Exacerbates Disease Pathology in a Murine Model of Alzheimer's Disease

Zena K. Chatila, Columbia University, USA
Interaction of Alzheimer's Disease Risk Variants and Amyloid on Innate Immune Function

Hyuncheol Jung, Korea Advanced Institute of Science and Technology, South Korea
Anti-inflammatory Clearance of Amyloid Beta by a Chimeric Gas6 Fusion Protein

Lindsay N. Hayes, Johns Hopkins University, USA
Prenatal Immune Stress Induces Blunting of Microglia Reactivity that Impairs Striatal Connectivity

Afsana Sabrin, Columbia University, USA
Microglial and Astrocyte Signatures in CSF Proteome: Developing Markers for Glial Cell Subtypes in CSF

Christina Seitz, Karolinska Institutet, Sweden
T Cell Responses at Diagnosis of Amyotrophic Lateral Sclerosis Predict Disease Progression

Aging, Metabolism and Neurodegeneration (Z1)

Tony Wyss-Coray, Stanford University School of Medicine, USA
Remote Presentation: Systemic Regulation of Brain Aging

Katrin Andreasson, Stanford University, USA
Myeloid Cell Metabolism in Aging

Douglas R. Green, St. Jude Children's Research Hospital, USA
Autophagy in Alzheimer's Disease

Tal Iram, Stanford University, USA
Talk Title to be Announced

Future Directions for Therapeutics (Z2)

Anabella Villalobos, Biogen, USA
Therapeutic Modalities for Neuroscience Diseases

C. Frank Bennett, Ionis Pharmaceuticals, Inc., USA
Oligonucleotide-based Therapeutic Approaches

Jana Mitchell, Insitro, USA
Machine Learning for Unraveling the Complex Biology of CNS Disease

Juan A. Varela, University of St Andrews, UK
Short Talk: Clearance of Extracellular Amyloid-beta Aggregates from the Brain at the Nano-scale

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

Meeting Wrap-Up: Outcomes and Future Directions (Organizers) (Z2)

FRIDAY, JUNE 10

Departure