

## Modernizing Neurotoxicology at NIEHS: Technologies to Applications in Environmental Health Sciences

Virtual Workshop  
April 19-20, 2022

Meeting participants are encouraged to use “#NIEHS\_Neurotox” for social media posts (Twitter, Instagram, Facebook, etc.).

### Day One – April 19, 2022

- 10:00 a.m. Brief Introduction to Workshop  
[Jonathan Hollander](#), NIEHS
- 10:10 a.m. Welcome  
[Richard Woychik](#), NIEHS

### Session 1: Advances in Neuroimaging (Chairs: [Robert Sills](#), [Kimberly Gray](#))

The goal of this session is to explore the application of recent neuroimaging advances to improve human health. Presentations will be focused on transformative technologies such as longitudinal MRI, lipid-exchanged, anatomically rigid, imaging/immunostaining compatible, tissue hydrogel (CLARITY), De-scattering with Excitation Patterning (DEEP) and two-photon fluorescence imaging. Discussions will be focused on how these technologies are aiding in further linking function, structure and molecular endpoints for understanding the pathogenesis of neurological diseases.

#### Speakers

- 10:20 a.m. Longitudinal Neuroimaging to Study Brain Development of Infants with Neurodevelopmental Disorders  
[Mark Shen](#), University of North Carolina at Chapel Hill
- 10:40 a.m. Combined Magnetic Resonance and Light Sheet Microscopy  
[G. Allan Johnson](#), Duke University
- 11:00 a.m. Two-photon Fluorescence Imaging of Neurovascular Dynamics and Neural Activity  
[Na Ji](#), University of California, Berkeley
- 11:20 a.m. Computational Neuroimaging using Wide-field Two-photon Microscopy  
[Dushan Wadduwage](#), Harvard University
- 11:40 a.m. Break (5 minutes)



- 11:45 p.m. Integrating Whole-brain Scanning Microscopy with Artificial Intelligence and Neural Network Analysis for High-throughput Quantitative Assessment of Neurotoxicity and Neurodegeneration  
[Ronald Tjalkens](#), Colorado State University
- 12:05 p.m. Panel Discussion (45 minutes)
- 12:50 p.m. Break (30 minutes)

## Session 2: In Vitro Approaches in Developmental Neurotoxicology Research (Chairs: [Christopher McPherson](#), [Shannah Witchey](#))

Understanding developmental neurotoxicology (DNT) is complicated by the inability to identify the underlying mechanisms responsible for adverse neurotoxic effects. This is especially difficult due to the complexity of the developing nervous system and the developmental window at the time of exposure of the organism. Examination of DNT potential of environmental compounds has historically used in vivo rodent models. Use of rodent models in DNT testing can result in scientific uncertainties extrapolating findings from rodents to humans related to temporal differences in brain development, toxicokinetics, and non-homologous behavioral tests. In the last two decades, scientific advances have been made which rely on human cell-based in vitro models for evaluating chemical interactions with the developing nervous system, with the aim to reduce extrapolation of in vitro DNT data to humans. DNT modeling is a new high priority area of focus globally and for the DNTP. This session focuses on advances in DNT modeling beginning with species-specific in vitro neuro stem cell development and building to a review of the complexity of the central nervous system and cell interactions in the 3-D brain organoid. Finally, the importance of including modeling of vascularization, blood brain barrier and cerebrospinal fluid to closer resemble in vivo (human) responses is discussed.

### Speakers

- 1:20 p.m. Status and Gaps of the Current DNT in vitro Battery  
[Ellen Fritsche](#), Heinrich Heine University Düsseldorf, Leibniz Research Institute for Environmental Medicine
- 1:40 p.m. A Human iPSC-derived 3D Brain Sphere Model to Assess Developmental Neurotoxicity  
[Helena Hogberg](#), NTP Interagency Center for the Evaluation of Alternative Toxicological Methods at NIEHS, and Johns Hopkins University Bloomberg School of Public Health
- 2:00 p.m. Break (5 minutes)
- 2:05 p.m. Engineering Organoid Models for Understanding the Impact of Environmental Factors on Human Neurodevelopment  
[Guo-Li Ming](#), University of Pennsylvania, Perelman School of Medicine
- 2:25 p.m. Modeling the Blood-Brain Barrier in a Microphysiological System Platform  
[Chris Hughes](#), University of California Irvine

- 2:45 p.m. Panel Discussion (45 minutes)
- 3:30 p.m. Day One Summary and Closing Comments  
[Brian Berridge](#), NIEHS
- 3:45 p.m. **Adjourn for the day**

## Day Two – April 20, 2022

- 10:00 a.m. Welcome and Goals for Day Two  
[Jonathan Hollander](#), NIEHS

### **Session 3: Chemogenetic, Optogenetic and Fiber Photometry for Advancing Neurotoxicology (Chairs: [Jonathan Hollander](#), [Jesse Cushman](#))**

The goal of this session is to provide an overview of modern neuroscience techniques for monitoring and manipulating neural activity in vivo in the context of neurotoxicology. Discussions will focus on circuit interrogation techniques like chemogenetics, such as DREADDS, and optogenetic approaches designed to probe the neural circuit changes induced by toxicant exposures and potentially provide insight into potential therapeutics. Optical imaging approaches such as fiber photometry and miniature endoscopes will also be discussed as powerful new tools that allow for unprecedented observations of neural activity in awake-behaving animals.

#### **Speakers**

- 10:05 a.m. Viral-based Circuit-specific Tools for Understanding Neurotoxic Outcomes in the Rodent Brain, and the Great Therapeutic Potential in Targeting Disrupted Circuits  
[Timothy Allen](#), Florida International University
- 10:25 a.m. Zebrafish as Model for Understanding the Cellular Targets of PFAS-induced Neurotoxicity  
[Jessica Plavicki](#), Brown University
- 10:45 a.m. Break (10 minutes)
- 10:55 a.m. Chemogenetic Approach to Rescue Parvalbumin Interneuron-related Deficits in the Reward Circuit Caused by Early-life Exposure to Deltamethrin  
[Fernanda Laezza](#), University of Texas
- 11:15 a.m. Multi-color Fiber Photometry for Assessing Neural Circuit Functions in vivo  
[Guohong Cui](#), NIEHS
- 11:35 a.m. Panel Discussion
- 12:20 p.m. Break (30 minutes)



## Session 4: Emerging Spatial Technologies (Chairs: [Jian-Liang \(Jason\) Li](#), [Benedict Anchang](#))

The goal of this session is to provide an overview of current advances, challenges and future opportunities within the spatial technologies as well as the utilization of spatial technologies and research in neurotoxicology and neuroscience. Discussions will focus on various single cell and spatially resolved transcriptomics methods, as well as technical challenges that need to be overcome to obtain their full potentials. The spatial transcriptomic data analysis, understanding spatial omics dataset using visualization, machine learning and spatial statistics as well as spatial computational approaches will also be covered.

### Speakers

- 12:50 p.m. Spatial Multi-Omics Mapping at Tissue Scale and Cellular Level  
[Rong Fan](#), Yale University
- 1:10 p.m. Methods, Tools, and Roadblocks in Spatial Transcriptomic Data Analysis  
[Ruben Dries](#), Boston University
- 1:30 p.m. Break (10 minutes)
- 1:40 p.m. Mapping Genetic Risk for Complex Brain Disorders Across the Spatial Topography of the Human Dorsolateral Prefrontal Cortex  
[Keri Martinowich](#), John Hopkins University
- 2:00 p.m. Single Cell Genomics in Cancer Immunotherapy and Neurotoxicity  
[Ansuman Satpathy](#), Stanford University
- 2:20 p.m. Panel Discussion

### Conclusion

- 3:05 p.m. Closing Remarks  
[Cindy Lawler](#), NIEHS
- 3:15 p.m. **Adjourn**

### American Disabilities Act Accommodations Requests

Individuals with disabilities who need accommodation to participate in this event should contact [Olivia Post](#) at 703-765-0060. TTY users should contact [NIH Interpreting Services](#). Requests should be made 5 days in advance of the event.