# “THREATS TO THE NEURONAL GENOME”

## APRIL 9, 2024

University of Pennsylvania

A joint symposium hosted by the Institute on Aging (IOA)
in partnership with the Penn Center for Genome Integrity (PCGI)

# "Threats to the Neuronal Genome"

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The IOA and PCGI share missions to bring basic, translational, and clinical researchers together. In recognition of this mission, and the role of genome maintenance in neurogenerative disease, we have joined to host this symposium “Threats to the Neuronal Genome” to cover topics such as neuronal DNA damage and neuronal somatic variants.

This full-day symposium will feature keynotes by Drs. Michael B. Miller, Li-Huei Tsai, and Andre Nussenzweig, with faculty and trainee talks from experts here at Penn, as well as a poster session to round out the day.

Institute on Aging
University of Pennsylvania

PCGI Penn Center for Genome Integrity

ABOUT THE SYMPOSIUM

**9:30am** **Registration & light breakfast buffet**

**10:00am** **Welcome & Introduction from PCGI and IOA leaders**

**10:05am** **Keynote Address: Michael B. Miller, MD, PhD**
Assistant Professor of Pathology
Brigham and Women's Hospital
Harvard Medical School

***Talk title: "Single-Neuron Genomes: Lenses into the Pathogenesis of Neurodegeneration"***

**10:45am** **Trainee Talk: Elizabeth Burton**
CAMB Graduate Student, Laboratories of Stuan Grant & Casey Brown

***Talk title: "Variant-to-function mapping of a late-onset Alzheimer's disease GWAS locus in microglial models implicates RTFDC1, a DNA damage gene, at the CASS4 locus"***

**11:05am** **Trainee Talk: Naemeh Pourshafie, PhD**
Postdoctoral Researcher, Laboratories of Shelley Berger & Nancy Bonini

***Talk title: "ACSS2 upregulation enhances neuronal resilience to aging and neurodegeneration"***

**11:25am** **Faculty Talk: Yuanquan Song, PhD**
Assistant Professor, Department of Pathology and Laboratory Medicine

***Talk title: "Neuronal reprogramming to promote neural repair"***

**11:50am** **Lunch Break & Poster Viewing**

**1:00pm** **Keynote Address: Li-Hui Tsai, PhD**
Director, Picower Institute for Learning and Memory
Picower Professor of Neuroscience
Massachusetts Institute of Technology

***Talk title: "Transcriptional and epigenomic changes caused by DNA damage in neurons in Alzheimer's disease"***

**1:40pm** **Trainee Talk: Michael Guo**
Instructor, Department of Neurology
Jennifer Philips-Cremins Laboratory

***Talk title: "Short tandem repeats as a novel genetic driver of Alzheimer's disease"***

# AGENDA

**2:00pm** **Trainee Talk: Vidhya Krishnamoorthy, PhD**
Postdoctoral Researcher, Greenberg Lab

***Talk title: "A new macromolecular machine in DNA replication protein quality control"***

**2:20pm** **Faculty Talk: Eric Joyce**
Assistant Professor, Department of Genetics

***Talk title: "Discovering novel factors important for 3D Genome Organization"***

**2:45pm** **Coffee Break**

**3:00pm** **Faculty Talk: Fange (Kathy) Liu, PhD**
Assistant Professor of Biochemistry and Biophysics

***Talk title: "Building the nucleolus: how ribosome biogenesis shapes nucleolar architecture"***

**3:25pm** **Faculty Talk: Guilherme Nader, PhD**
Assistant Professor of Pathology and Laboratory Medicine
The Children's Hospital of Philadelphia

***Talk title: "Compromised nuclear integrity drives tumor cell invasion"***

**3:50pm** **Short Break**

**3:55pm** **Faculty Talk: Jonathan Miner, MD, PhD**
Associate Professor of Medicine
Director, RVCL Research Center

***Talk title: "TREX1 mislocalization causes age-related DNA damage phenotypes and multi-organ small vessel disease"***

**4:20pm** **Keynote Address: Andre Nussenzweig, PhD**
NIH Distinguished Investigator, Laboratory of Genome Integrity
National Cancer Institute, CCR, NIH

***Talk title: "Neuronal genome integrity"***

**5:00pm** **Poster Session and Reception**
BRB II/III Lobby

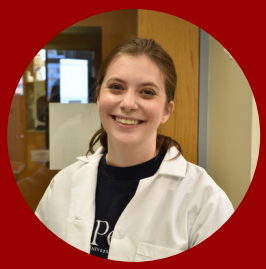
# AGENDA

## Michael B. Miller, MD, PhD

Brigham and Women’s Hospital
Harvard Medical School

Michael B. Miller is a physician-scientist interested in the mechanisms of neurodegenerative diseases, serving as Principal Investigator and Associate Pathologist at Brigham and Women's Hospital and Assistant Professor at Harvard Medical School. Dr. Miller obtained his Bachelor's degree from Grinnell College in Spanish and Biological Chemistry, where he studied in the inquiry-based biology curriculum, inspiring his passion for basic research and genetics. He then did a postbaccalaureate IRTA fellowship on genetic imprinting at NIH and completed his combined MD/PhD training at the Dartmouth Geisel School of Medicine. Dr. Miller completed residency in Anatomic Pathology and fellowship in Neuropathology at Brigham and Women's Hospital and Boston Children's Hospital and then performed postdoctoral research with Christopher Walsh in neuronal somatic genomics at Boston Children's Hospital and the Howard Hughes Medical Institute.

Dr. Miller opened his independent laboratory at Brigham and Women's Hospital in 2022, focusing on the mechanisms of neurodegenerative diseases, with a major focus on the role of somatic mutations in pathogenesis. The Miller laboratory synergizes approaches from multiple disciplines, including genomics, neuropathology, computational biology, and protein biochemistry. Dr. Miller’s research has been recognized nationally, including by the Doris Duke Clinical Scientist Development Award and the NIH Director’s New Innovator Award.



## Elizabeth Burton

University of Pennsylvania

Elizabeth Burton received her Bachelor of Science degree in Biochemistry/Molecular Biology from Gettysburg College in 2018. She is currently completing her doctoral studies in microglial Alzheimer's disease genetics in the labs of Dr. Struan Grant, and formerly Dr. Casey Brown, at The University of Pennsylvania in the Cell and Molecular Biology Program. She also holds a Bachelor of Arts in Music (piano) from The Sunderman Conservatory of Music.

# ABOUT OUR SPEAKERS

## Naemeh Pourshafie, PhD

University of Pennsylvania

Dr. Naemeh Pourshafie received her B.S. in neuroscience from the University of Maryland College Park, and her PhD in Molecular Medicine from George Washington University-National Institutes of Health (NIH) Partnership Program in 2020. Her doctoral research was conducted under the mentorship of Dr. Kurt Fischbeck at the National Institute of Neurological Disorders and Stroke (NINDS/NIH). During her PhD, she studied the molecular mechanism underlying motor neuron degeneration in Spinal and bulbar muscular atrophy.

Currently, she is a post-doctoral fellow at UPenn Epigenetics Institute, co-mentored by Dr. Shelley Berger and Dr. Nancy Bonini, studying the epigenetics of AD and age-related dementia. She is actively working towards the development of therapies that can improve cognitive decline in patients affected with AD and dementia. She is the recipient of the Brody Family Medical Trust Foundation, the American Parkinson's Disease Association, and the National Research Service Award fellowship from the National Institute of Aging (NIA).

## Yuanquan Song, PhD

University of Pennsylvania

Dr. Yuanquan Song received his Bachelor's degree in Biotechnology from Shanghai Jiao Tong University in China and his PhD in Neuroscience from Penn. He did his postdoctoral training in the Jan lab at UCSF, where he started the journey in neuroregeneration. In 2016, Dr. Song established his own lab at Penn and CHOP. His lab aims to understand the cellular and molecular basis governing the formation, maintenance and function of neural circuits under physiological and pathological conditions.

# ABOUT OUR SPEAKERS

## Li-Huei Tsai, PhD

Massachusetts Institute of Technology

Professor Li-Huei Tsai is the Director of the Picower Institute for Learning and Memory and a Picower Professor of Neuroscience, both at MIT, and an Associate Member of the Broad Institute. She obtained her PhD from the University of Texas Southwestern Medical Center in Dallas and completed her postdoctoral training at Cold Spring Harbor Laboratories and Massachusetts General Hospital. Dr. Tsai became an Assistant Professor of Pathology at Harvard Medical School and was promoted to tenured Professor in 2002. She relocated to MIT in 2006. She was an Investigator at the Howard Hughes Medical Institute from 1997 to 2013. Dr. Tsai is also a Fellow of the American Association for the Advancement of Science, a Fellow of the National Academy of Inventors, a Member of the National Academy of Medicine, an Academician of the Academia Sinica in Taiwan, and a Member of the American Academy of Arts and Sciences. Dr. Tsai is interested in elucidating the pathogenic mechanisms underlying neurological disorders that impact learning and memory. She is a recipient of the Mika Salpeter Lifetime Achievement Award, and the 2018 Hans Wigzell Research Foundation Science Prize. In 2022, she was named a Visiting Professor of the Vallee Foundation.

## Michael Guo

University of Pennsylvania

Michael Guo is an Instructor and physician-scientist in the Neurology Department at the University of Pennsylvania. He completed his PhD in Genetics and Genomics at Harvard, where he studied the genetic basis of human anthropometric traits including height, body mass index, and the timing of puberty. Following his MD and PhD, he pursued neurology residency and cognitive neurology training here at Penn. His clinical focus is on caring for patients and families with Alzheimer's disease and related dementias. During and after residency, he has been working with Drs. Jennifer Philips-Cremins and Edward Lee to uncover the role of short tandem repeats in Alzheimer's disease.

# ABOUT OUR SPEAKERS

## Vidhya Krishnamoorthy, PhD

University of Pennsylvania

Dr. Vidhya Krishnamoorthy graduated from the University of Mumbai in India with a Bachelor's and Master's degree in Biotechnology. She then went on to obtain her PhD in Cell Biology at CSIR-Centre for Cellular and Molecular Biology, India. Her PhD work focused on the role of ubiquitin proteolytic pathways in the etiology of muscular dystrophies and neuromuscular disorders caused by mutations in nuclear lamina proteins.

Dr. Krishnamoorthy joined the Greenberg lab as a postdoctoral researcher in 2019, where she has been studying novel replication stress response proteins and characterizing fundamental pathways of replisome proteostasis. Her research investigates the intersection of structural biology, biochemistry, and cell and molecular biology to identify a new AAA ATPase complex involved in DNA replication and protein quality control. Dr. Krishnamoorthy is also passionate about making science accessible and open to all.

## Eric Joyce, PhD

University of Pennsylvania

Eric Joyce, PhD, is an Associate Professor of Genetics and core member of the Epigenetics Institute at the Perelman School of Medicine. Dr. Joyce conducted his postdoctoral training with Dr. Ting Wu at Harvard Medical School, where he co-developed a novel type of FISH probe called Oligopaints. Dr. Joyce's lab continues to develop and utilize new technologies to interrogate chromosome structure at single-cell resolution. His lab aims to understand how the structure of chromosomes within the nucleus is established and inherited across cell divisions, and how dysfunctional organization contributes to genome instability and disease.

## Fange (Kathy) Liu, PhD

University of Pennsylvania

Kathy Fange Liu, PhD, is an Assistant Professor of Biochemistry and Biophysics, a Core Investigator in the Penn Center for Genome Integrity (PCGI), and a Member of the Penn Institute for RNA Innovation. Dr. Liu pursued her postdoctoral training with Dr. Chuan He at the University of Chicago, where she discovered the first tRNA demethylation and showed reversible tRNA methylation as a rapid way to impact protein translation. Dr. Liu's research laboratory at Penn employs a multidisciplinary approach, integrating enzymology, biochemistry, spectroscopy, structural biology, and RNA biology techniques to investigate key scientific inquiries, including: (1) the coordinated regulation of modifications across mRNA, tRNA, and rRNA; (2) the exploration of sex chromosome-encoded protein homologs; and (3) the elucidation of how dysregulation in these processes contributes to various human diseases.

## Guilherme Nader, PhD

The Children's Hospital of Philadelphia

Dr. Nader is an Assistant Professor of Pathology and Laboratory Medicine at the Children's Hospital of Philadelphia Leonard and Madlyn Abramson Pediatric Research Center. A cell biologist by training, he has been studying the mechanisms modulating different migratory cell behaviors for the past 15 years. It is commonly appreciated that cells lack space when navigating complex 3D anatomical landscapes. These microenvironments constantly impose physical stresses that impact cell behavior, function, and fate. The Nader lab research focuses on nuclear mechano-sensing by cells that grow and move within dense microenvironments in both homeostasis and disease. Using a wide range of microscopy techniques and novel microfabricated and organ-on-a chip devices to mimic crowded spaces such as the tumor microenvironment, the Nader lab aims to better understand how cell and nuclear confinement influence transcriptional programs and cell function in cells experiencing mechanical stress. The Nader lab seeks to understand the molecular mechanisms underlying cell motility and invasion following repeated nuclear rupture and chronic DNA damage. Ultimately, the Nader lab would like to establish a link between nuclear mechano-sensing pathways and different cellular behaviors, from orchestrated signaling cascades to cellular perturbations and damage.

## Jonathan Miner, MD, PhD

University of Pennsylvania

Jonathan Miner, MD, PhD is an Associate Professor of Medicine at the University of Pennsylvania Perelman School of Medicine. He is a rheumatologist and expert on inherited rheumatic diseases caused by mutations in genes that regulate inflammatory responses triggered by DNA and RNA. He is also an expert in virology and antiviral immunity. Dr. Miner takes care of rare disease patients from around the world, and his team has generated numerous animal models with human disease-causing mutations. The Miner laboratory uses these models to define underlying mechanisms of disease and to facilitate the development of personalized therapies for patients.

## Andre Nussenzweig, PhD

National Institutes of Health

Dr. Andre Nussenzweig is the Distinguished NIH investigator and Branch Chief of the Laboratory of Genome Integrity at the Center for Cancer Research at the National Cancer Institute.
Dr. Nussenzweig is a world-renowned contributor to the study of mechanisms that maintain genomic stability and prevent cancer. His laboratory has elucidated many fundamental features of DNA damage and repair proteins and revealed the critical role they play in both normal and pathogenic states. His group has performed groundbreaking mechanistic studies on cancer predisposition in the context BRCA-deficiencies, ATM-deficiency, and microsatellite instability, which have opened up therapeutic windows for new chemotherapies. He has also devised several genomic technologies for studying DNA damage and repair. Most recently, he discovered a new paradigm for programmed DNA damage in the brain, which could be a pathogenic source of lesions contributing to neuronal dysfunction and disease.
Dr. Nussenzweig is the recipient of numerous awards including the Basser Global Prize for BRCA research (2021) and the Environmental Mutagenesis and Genomics Society Award (2024). He is a member of EMBO, the National Academy of Medicine, American Academy of Arts and Science, and the National Academies of Science.

# ABOUT OUR SPEAKERS

# ABOUT THE INSTITUTE ON AGING

The mission of the Institute on Aging (IOA) at the University of Pennsylvania is to improve the health of older adults by increasing the quality and quantity of clinical and basic research as well as educational programs focusing on normal aging and aging-related diseases across the entire Penn campus.

To learn more about the IOA, visit: www.med.upenn.edu/aging

or

SCAN ME

# ABOUT THE PENN CENTER FOR GENOME INTEGRITY

The overarching mission of the Penn Center for Genome Integrity (PCGI) is to integrate cutting-edge research in basic and clinical sciences from several key disciplines in order to advance our fundamental understanding of genome integrity and its contributions to human biology. Central to our vision is a mechanism to nucleate outstanding investigators with diverse areas of scientific and clinical expertise across the Penn campus.

To learn more about the PCGI, visit: www.med.upenn.edu/pcgi/

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NOTES

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