



## Sex Differences in Brain Disorders: Emerging Transcriptomic Evidence and Implications for Therapeutic Development—A Virtual Workshop

September 23, 2020  
*Virtual via Zoom*

**Background:** The NIH instituted a new requirement for inclusion of sex as a biological variable in animal research in 2015. This policy change, along with earlier directives for inclusion of women in clinical studies, has resulted in a dramatic increase in our appreciation of sex differences across many disease states. Neurological and psychiatric disorders are among those most impacted. While there have been many studies over the years reporting subtle differences between men and women with respect to clinical features and treatment responses of several neuropsychiatric syndromes, our understanding of the biological underpinnings of such differences has advanced only recently with the advent of unbiased genome-wide data. Increasing evidence is now suggesting fundamental differences in transcriptomic abnormalities that occur in the brains of men versus women with a variety of brain disorders. There are also evolving data showing that genome-sequence variations influence disease risk in a sex-specific manner.

In 2010, the National Academies' Forum on Neuroscience and Nervous System Disorders hosted a workshop titled [Sex Differences and Implications for Translational Neuroscience Research](#). Over the past decade, the field has progressed significantly. Therefore, it is timely to revisit this topic, take stock of progress and new challenges, and identify future opportunities and potential directions.

### Workshop Objectives:

This public workshop will bring together experts and key stakeholders from academia, government, industry, and non-profit organizations to explore emerging evidence regarding differences in transcriptomic abnormalities that occur in the brains of men versus women with a variety of brain disorders including depression, post-traumatic stress disorder, drug addiction, neurodegenerative conditions, and other brain disorders.

Invited presentations and discussions will be designed to:

- Review the landscape of emerging evidence regarding sex differences in transcriptomic abnormalities in a variety of brain disorders, and discuss how this can be used to advance understanding of brain disorder pathophysiology.
- Explore ramifications for therapeutic development for these disorders, including identification of new targets, implications for preclinical and clinical study design, regulatory considerations, and potential sex-specific treatments.
- Discuss open research questions and opportunities to move the field forward.

### Workshop Planning Committee

**Eric Nestler, M.D., Ph.D. (Chair)**, Icahn School of Medicine at Mount Sinai  
**Li Gan, Ph.D.**, Weill Cornell Medical College  
**John Krystal, M.D.**, Yale University  
**Heather Snyder, Ph.D.**, Alzheimer's Association  
**Rita Valentino, Ph.D.**, National Institute on Drug Abuse  
**Donna Werling, Ph.D.**, University of Wisconsin-Madison  
**Stevin Zorn, Ph.D.**, MindImmune Therapeutics, Inc.

**September 23, 2020**

10:00am Welcome and Overview of Workshop

ERIC NESTLER, Icahn School of Medicine at Mount Sinai, *Workshop Chair*

<p><b>Session I: Current Landscape of Emerging Transcriptomic Evidence for Sex Differences in Brain Disorders</b></p>
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Objectives:

- Provide an overview of the current landscape of emerging evidence regarding sex differences in transcriptomic abnormalities in a variety of brain disorders.
- Consider how this evidence can be used to advance understanding of brain disorder pathophysiology.

10:15am Session overview

RITA VALENTINO, National Institute on Drug Abuse, *Session co-moderator*

**Part A: Stress- and Reward-Related Disorders**

10:20am Depression

MARIANNE SENEY, University of Pittsburgh

10:35am Posttraumatic Stress Disorder (PTSD)

MATTHEW GIRGENTI, Yale School of Medicine

10:50am Addiction

DEENA WALKER, Oregon Health & Science University

11:05am Pain

THEODORE PRICE, The University of Texas at Dallas

11:20am Panel discussion:

*The speakers above will be joined by panelists:*

FARAH LUBIN, The University of Alabama at Birmingham

ORNA ISSLER, Icahn School of Medicine at Mount Sinai

ROHAN PALMER, Emory University

11:40am General discussion

12:00pm Lunch Break

*Attendees will reconvene at 12:40pm for the following lunchtime talk and discussion.*

BRAIN Initiative Cell Census Network – Applications to understanding sex differences

JOHN NGAI, National Institutes of Health

## **Part B: Neurodevelopmental and Neurodegenerative Disorders**

1:00pm	Panel overview LI GAN, Weill Cornell Medical College, <i>Session co-moderator</i>
1:05pm	Autism DONNA WERLING, University of Wisconsin
1:20pm	Schizophrenia PANOS ROUSSOS, Icahn School of Medicine at Mount Sinai
1:35pm	Alzheimer's disease TIMOTHY HOHMAN, Vanderbilt University
1:50pm	Tauopathies LI GAN, Weill Cornell Medical College
2:05pm	Panel discussion: <i>The speakers above will be joined by panelists:</i> BARBARA STRANGER, Northwestern Feinberg School of Medicine BETH STEVENS, Harvard University NILÜFER ERTEKIN-TANER, Mayo Clinic
2:25pm	General discussion
2:45pm	BREAK

## **Session II: Moving Forward – Therapeutic Development and Policy Implications**

### Objectives:

- Explore ramifications for therapeutic development for brain disorders, including identification of new targets, implications for preclinical and clinical study design, regulatory considerations, and potential sex-specific treatments.
- Discuss open research questions and opportunities to move the field forward.

3:00pm	Session overview STEVIN ZORN, MindImmune Therapeutics, Inc., <i>Session moderator</i>
3:05pm	Speakers JANINE CLAYTON, National Institutes of Health KAVEETA VASISHT, Food and Drug Administration DAVID MICHELSON, Regenacy Pharmaceuticals MELISSA LAITNER, Society for Women's Health Research
3:55pm	Panel discussion

- 4:15pm General discussion
- 4:35pm Synthesis of key workshop themes and future directions  
ERIC NESTLER, Icahn School of Medicine at Mount Sinai, *Workshop Chair*
- 5:00pm ADJOURN WORKSHOP