

Symposium Proposals GBB 2022

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Symposium Chair

Chair Name:

Oksana Poleskaya

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Preferred

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Organization:

University of California - San Diego

Department:

Psychiatry

Position:

Research Scientist

Species:

Rat

Description

Title:

Genetic studies of drug addiction-related traits in outbred rats

Symposium:

A major impediment to the development of effective therapies to treat drug abuse and dependence is our extremely limited understanding of the biological basis of drug abuse. The NIDA Center for Genome-wide association studies (GWAS) in Outbred Rats is focused on genetic analysis of numerous behavioral traits that have well-established relevance to drug abuse using outbred rats. Dr. Abraham Palmer will present the overview of the research conducted by the Center and affiliated projects. At this symposium we will showcase four studies in HS rats that demonstrate that using HS rats enable the discovery of previously unidentified genetic variants influencing addiction-related traits. Dr. Paul Meyer will talk about addiction vulnerability that is associated with non-drug traits such as the tendency to attribute incentive salience to reward cues, using Pavlovian conditioned approach paradigm. GWAS identified multiple associated regions, which include genes *Dlg2*, *Tenm4*, *Mir708*, and *Taar1*. Some of these genes have been previously associated with addiction-related behaviors, others have not, presenting a potential to identify novel biological pathways involved in these traits. Dr. Hao Chen will present genetic analysis of open field behaviors (locomotion, novel object interaction, and social interaction) in 1,246 adolescent male and female outbred HS rats. This study identified 30 genome-wide significant quantitative trait loci (QTL). Co-localization with eQTLs helped to pinpoint 13 candidate genes. Although some of these genes

replicate findings from prior human GWAS, others likely represent novel findings that can be the catalyst for future molecular and genetic insights into human psychiatric diseases. Dr. Francesca Telesse will talk about identifying the molecular mechanisms that give rise to addiction liability, using extended access model of cocaine self-administration in HS rats. Gene expression and chromatin accessibility were profiled by conducting single-nuclei RNA-seq and ATAC-seq in individual cells of the amygdala collected from HS rats with high or low addiction index. The analysis has identified several signaling pathways associated with cocaine addiction, including glucose metabolism. The predictions were validated by perturbing this pathway, which led to rescuing of addictive behavior in relapse assay. Alexandria M. Szalanczy will discuss studies of body composition that have been performed to extend the impact of the center. Those studies took advantage of the fact that thousands of HS rats were genotyped for GWAS of behavioral traits, and collected multiple physiological traits, including measuring fat pad weight, body weight and body length. GWAS analysis of these traits identified several candidate genes. Alexandria M. Szalanczy will talk about one of the candidate genes, Krtcap3, which modifies adiposity traits via regulating the HPA axis and therefore impacts feeding behavior.

Speaker 1

Name:

Abraham Palmer

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Organization:

University of California - San Diego

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Psychiatry

Position:

Professor & Vice Chair for Basic Research, Department of Psychiatry

Species:

Rat

Speaker 2

Name:

Paul Meyer

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Organization:

University at Buffalo

Department:

Department of Psychology

Position:

Associate Professor, Behavioral Neuroscience Area Head

Species:

Rat

Speaker 3**Name:**

Hao Chen

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Organization:

University of Tennessee Health Science Center

Department:

Department of Pharmacology, Addiction Science, and Toxicology

Position:

Associate Professor

Species:

Rat

Speaker 4**Name:**

Francesca Telese

Email:**Preferred**

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Organization:

University of California - San Diego

Department:

Medicine

Position:

Assistant Professor

Species:

Rat

Speaker 5 (Optional)**Name:**

Alexandria Szalanczy

Email:**Preferred**

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Organization:

Wake Forest University

Department:

Molecular Medicine

Position:

Graduate Student

Species:

Rat

Symposium Proposals Genes, Brain and Behavior 2023

Abstract (500 word limit)

Symposium Chair**Chair Name:**

Kristin Hamre

Co-Chair Name (Optional):

Megan Mulligan

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Organization:

Univ. of Tennessee Health Science Center

Department:

Dept. of Anatomy & Neurobiology

Position:

Assoc. Prof.

Species:

mice, rats, worms

Description**Title:**

Impact of Environmental Exposures Across Species and Lifespan: Untangling complex regulation of genes and behavior

Abstract:

All four talks involve the study of complex traits and how they are influenced by various factors such as cis-regulatory variation, parent-of-origin effects, environmental conditions, and gene-by-environment interactions. Each speaker utilizes different species (mouse, rat, and worm) to study the effects of various exposures, such as diet, rearing environment, and prenatal alcohol and cannabis exposure, on gene expression and/or brain and behavioral development. Finally, all four talks highlight the importance of incorporating or controlling for environmental variables to accurately understand the effects of a particular context or exposure on complex trait variation. Chairs are Kristin Hamre and Megan Mulligan. Chairs will introduce the speakers and moderate the discussion. Speakers include Dan Goldowitz, Jennifer Thomas, Celine St. Pierre, and Catharine Rankin. Speakers represent diverse regions, professional levels, and gender identities. Dan uses inbred and reciprocal F1 mice and a multi-pronged molecular approach to identify regulatory mechanisms mediating the impact of prenatal alcohol exposure on the developing hindbrain. Using this approach, he: (1) captured gene x environment (GxE) interactions related to enhanced cell death in the hindbrain of susceptible strains; (2) showed that there are cis-acting factors mediating GxE interactions; (3) showed that there is a strong maternal strain effect on increasing susceptibility to ethanol exposure; and (4) showed that certain imprinted alleles, involved in fetal growth, are more sensitive to ethanol-induced expression changes than other alleles. Jennifer uses Sprague-Dawley rats to demonstrate that the essential nutrient choline can improve behavioral and developmental outcomes that occur as a result of prenatal alcohol or cannabis exposure, specifically by ameliorating cognitive deficits caused by these exposures. Further, she presents data demonstrating that choline may be working through epigenetic mechanisms and by reducing neuroinflammation. Celine uses advanced intercrosses from the LG/J and SM/J mouse strains combined with high- and low-fat dietary conditions to evaluate variation in metabolic and musculoskeletal traits and regulation of gene expression across contexts. Comparisons across brain and peripheral tissue uncover allele-specific gene regulation, parent-of-origin effects, gene-by-environment interactions, cis-regulatory variation, and provide insights into how all of these factors work in concert to influence complex traits. Catherine uses *c. elegans* to investigate the role of subtle changes in experimental protocols on growth and behavior. She demonstrates that variation in rearing parameters related to the preparation and age of the agar Petri

Plates used to grow worms results in significant changes in sensitization of locomotor responses and morphology. Her findings emphasize that complex traits are exquisitely sensitive to changes in the environment and also highlight the importance of controls.

Speaker 1

Name:

Daniel Goldowitz

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Organization:

Univ. of British Columbia

Department:

Centre for Molecular Medicine and Therapeutics,

Position:

Professor

Species:

Mouse

In Person or Remote:

In person

Speaker 2

Name:

Jennifer Thomas

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Organization:

San Diego State University

Department:

Dept. of Psychology

Position:

Professor

Species:

Rats

In Person or Remote:

In person

Speaker 3**Name:**

Celine St. Pierre

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Organization:

Washington University in St. Louis

Department:

Dept. of Genetics

Position:

Graduate Student

Species:

Mice

Speaker 4**Name:**

Catharine Rankin

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Organization:

University of British Columbia

Department:

Dept. of Psychology

Position:

Professor

Species:
c. elegans