IBANGS MADRID 2017

B Business Meeting C Coffee Break D Dinner E Executive Session K Keynote Talk L Lunch P Poster Session
M Pre-Meeting Social R Registration S Selected Talk Y Symposium T Travel Awards W Welcome

MAY 15 • MONDAY

5:30pm – 7:30pm **M Pre-Meeting Social at Mercado Moncloa** Mercado Moncloa (Arcipreste de Hita, 10, next to Hotel Exe Moncloa)
All Welcome

4 minutes walk from metro Moncloa

7:30pm – 10:00pm **D Dinner - Pay as you go - All Welcome** TBA
Pay As You Go - Stay with Group or Explore Madrid

MAY 16 • TUESDAY

8:00am – 8:15am **R Registration** Faculty of Medicine, Complutense University (Sala Duran Sacristan)

8:15am – 8:25am **W Welcome Address** Faculty of Medicine, Complutense University (Sala Duran Sacristan)

8:25am – 8:30am **W Welcome: Dr Elissa Chesler, President IBANGS** Faculty of Medicine, Complutense University (Sala Duran Sacristan)

8:30am – 9:30am **K Young Investigator Award Talk - Dr Amy Lasek, New Pathways in Drug Addiction: Discovery and Characterization of Novel Genes** Faculty of Medicine, Complutense University (Sala Duran Sacristan)

Speakers: Amy Lasek

New pathways in drug addiction: discovery and characterization of novel genes

Lasek, Amy W.1

The etiology of drug and alcohol addiction consists of environmental and genetic components. Whole-genome approaches have been used to identify genes in several organisms (human, mouse, fruit fly, worm) that are associated with phenotypes related to addiction. However, the challenge remains to validate and understand the molecular and cellular function of these genes in the mammalian brain and how aberrant expression of these genes alters behavior. My laboratory uses the mouse as a model organism to characterize novel genes that regulate behavioral responses to alcohol and cocaine. Three of these genes, *Lmo3*, *Lmo4*, and *Alk*, were originally identified in fruit flies as regulators of acute behavioral responses to ethanol and cocaine. Using gene knockout mice and viral delivery of short hairpin RNAs to specific neuroanatomical locations, we found that all three of these genes regulate behavioral responses to cocaine, and that *Lmo3* and *Alk* regulate behavioral responses to ethanol. Our focus is now on delineating the molecular mechanisms through which *Lmo3* and *Alk* act in the brain to regulate ethanol consumption and reward. For example, we found that *Alk*, which encodes a receptor tyrosine kinase, regulates the trafficking of the dopamine D2 receptor through a protein kinase C-dependent pathway in the ventral tegmental area. Regulation of D2 receptor trafficking impacts the firing of dopamine neurons, which might explain how ALK signaling regulates ethanol consumption and reward. Pharmacological inhibitors of ALK decrease ethanol consumption, suggesting that targeting the ALK pathway may represent a novel therapeutic strategy for treating alcohol use disorder.

1Department of Psychiatry and Center for Alcohol Research in Epigenetics, University of Illinois at Chicago, Chicago, IL USA; Supported by NIH P50 AA022538, U01 AA016654, U01 AA020912 and R01 DA033429.

9:30am – 11:30am **Y Symposium 1: Epigenetic of Brain Disorders in Animal Models** University of Madrid, Faculty of Medicine (XXX)

Moderators: Ian Maze, Igor Ponomarev

Speakers: Jerremy Day, Alfredo Ghezzi, Dr Iiris Hovatta

Symposia Title: Epigenetics of brain disorders
Chairs: Igor Ponomarev & Ian Maze

9.30 am -10.00 am Iiris Hovatta
10.00 am - 10.30 am Alfredo Ghezzi
10.30 am - 11.00 am Jeremy Day
11.00 am - 11.30 am Ian Maze

Epigenetic mechanisms play a key role in cellular differentiation and regulation of cell type specific transcriptional

programs, producing a remarkable heterogeneity of cellular transcriptomes that reflect the physiological properties and functional states of individual cells. There is an emerging appreciation for the role of epigenetic processes in neuropsychiatric disorders. The proposed symposium focuses on the roles of epigenetics in regulation of molecular and cellular functions as well as behavior in animal models of depression and drug addiction. Speakers will cover a broad range of epigenetic techniques and models examined across 3 commonly studied species: fly, mouse and rat. The session will begin with a brief presentation from Igor Ponomarev introducing the field of epigenetics/epigenomics and end with a brief summary discussion led by Nigel Atkinson.

1. Iiris Hovatta
Gene-environment interaction in microRNA expression of a mouse model for anxiety and depression. Iiris Hovatta (University of Helsinki) investigated the effect of genetic background on brain gene and miRNA expression profiles after psychosocial stress. She used chronic social defeat paradigm to induce anxiety and depression-like behavior in mice as well as genomic and bioinformatics approaches to identify miRNAs critical for genotype-specific gene expression and behavior.
https://ibangs.memberclicks.net/mcdatafiles/receiptattach/ibangs/11860209/8239561/IBANGS_2017_abstract_Hovatta.docx

2. Alfredo Ghezzi
Homeostatic regulation of alcohol tolerance gene networks in Drosophila. Alfredo Ghezzi (University of Puerto Rico) used a combination of genomic and genetic approaches to explore the involvement of the histone acetyl-transferase CBP in regulating a recently identified network of genes with a direct role in the development of alcohol tolerance. He proposed that CBP regulates gene expression by the targeted acetylation of specific gene promoters, including the BK channel gene slo, a central component of the homeostatic response to alcohol and other organic solvent anesthetics.
https://ibangs.memberclicks.net/mcdatafiles/receiptattach/ibangs/11807901/8239561/Ghezzi.docx

3. Jeremy Day
Epigenetic regulation in brain reward systems. Jeremy Day (University of Alabama) will present recent advances in the application of CRISPR-dCas9 technology to understand how epigenetic mechanisms regulate neuronal function in brain reward circuits, with a specific focus on epigenetic dysregulation following experience with drugs of abuse in rodent models.
Full Abstract shown below.
4. Ian Maze
Histone monoaminylation: novel mechanisms of epigenetic plasticity. Ian Maze (Icahn School of Medicine at Mount Sinai) will present a novel epigenetic phenomenon of histone monoaminylation in a broad context of neuronal development and plasticity. He utilized a unique combination of biochemical, genome-wide and functional neurobiological approaches to show that brain monoamines, such as dopamine and serotonin, contribute directly to neuronal gene expression via a neurotransmission-independent epigenetic mechanism, which will likely have broad implications within the field of neuroscience and beyond.
https://ibangs.memberclicks.net/mcdatafiles/receiptattach/ibangs/11808005/8239561/IBANGS_2017_Abstract_Ian_Maze.docx

3. Full abstract by Jeremy Day
Title: *Control-Alter-Delete: Epigenetic regulation in brain reward systems*
Authors: Jeremy J. Day
Affiliations: Department of Neurobiology and Evelyn F. McKnight Brain Institute, University of Alabama at Birmingham, Birmingham, AL
Text:
Introduction
Epigenetic mechanisms are central regulators of the function and information storage capacity of neuronal systems. Methylation of cytosine nucleobases in DNA is a multifunctional epigenetic regulatory modification capable of exerting powerful control gene. In the brain, activity-dependent changes in DNA methylation are critical for synaptic plasticity and memory formation, and have been implicated in a broad range of neuropsychiatric disease states, including drug addiction. However, although activity-related DNA demethylation requires the *Gadd45* (*Growth arrest and DNA-damage-inducible*) protein family, very little is known about how DNA demethylation regulates the function of brain reward circuits or the role that *Gadd45* family members play in

behavioral responses to drugs of abuse.

Methods

Here, we combined unbiased genome-wide transcriptional profiling, pharmacological tools, and CRISPR/dCas9 transcriptional activation with traditional knockout and behavioral approaches in rodent model systems (both *in vitro* and *in vivo*) to dissect the role of *Gadd45* family members in dopamine-dependent epigenetic regulation.

Results

We show that acute cocaine administration induced upregulation of *Gadd45b* mRNA in rat nucleus accumbens, but did not alter expression of other methylation-related transcripts. Similarly, acute dopamine treatment in striatal neuron cultures increased expression of *Gadd45b* and *Gadd45g* mRNA. This effect was mimicked by the Drd1 agonist SKF38393, suggesting upregulation in Drd1-containing neurons. *In vitro*, CRISPR-targeted transcriptional activation of either *Gadd45b* or *Gadd45g* with a dCas9-VP64 fusion construct was capable of unsilencing a methylated reporter gene, suggesting a mechanistic link between *Gadd45* induction and DNA demethylation. Finally, we show that both dopamine treatment (*in vitro*) and cocaine administration (*in vivo*) induce DNA demethylation, and that *Gadd45b*-/- mice exhibited impaired conditioned place preference for cocaine.

Conclusions

These results suggest that striatal *Gadd45b* functions as a dopamine-dependent immediate early gene to coordinate demethylation of DNA at downstream target genes, and that this action is important for cocaine-related behavioral plasticity.

11:30am – 12:00pm **C** **Coffee Break** University of Madrid, Faculty of Medicine (XXX)

12:00pm – 12:30pm **S** **Selected Talk Session 1: Genome-wide association of delay-discounting identifies a role of common variation, and demonstrates genetic overlap with human psychopathology**

Speakers: Sandra Sanchez-Roige Faculty of Medicine, Complutense University (Sala Duran Sacristan)

Genome-wide association of delay-discounting identifies a role of common variation, and demonstrates genetic overlap with human psychopathology

Sandra Sanchez-Roige1, Pierre Fontanillas2, Sarah Elson2, Gray J3, deWit H5, Lea Davis4, MacKillop J6, Abraham A. Palmer1

Delay-discounting has been proposed as a Research Domain Criteria (RdOC) element that cuts across multiple neuropsychiatric diseases, including drug and alcohol abuse. Although this trait is heritable, it remains unclear which genes/loci influence delay-discounting. In collaboration with the genetics company 23andMe, Inc., we performed a genome-wide association study (GWAS) of delay-discounting using the self-reported Monetary Choice Questionnaire. Our sample consisted of 23,217 male and female adult research participants of European ancestry. We estimated chip-heritability, and demonstrated that 12% of the variation of delay-discounting can be explained by single-nucleotide polymorphisms (SNPs). We detected one genome-wide significant hit on the X-chromosome (2.4 × 10−8; rs6528024), centered on the gene *GPM6B*, which is known to regulate internalization of the serotonin transporter; and a suggestive nominal loci (1.4 × 10−7; rs2665993), which is associated with the expression of several nearby genes. Next, to identify the top cortically associated genes mediating the role of common variants, we used MetaXcan, a gene-based association analysis that estimates the genetically determined component of gene expression, and correlates the predicted expression levels with the phenotype of interest. This analysis identified the gene *CDK3*, which showed higher predicted gene expression in the hippocampus (FDR 0.05). We used polygenic methods to examine co-heritability between delay-discounting and several personality and psychiatric traits. We identified strong genetic correlations between delay-discounting, smoking behavior, educational attainment, obesity and other neuropsychiatric conditions. This study is the first to demonstrate a role for common genetic contribution to individual differences in delay-discounting, and genetic overlap with human psychopathology.

1 Department of Psychiatry, University of California San Diego, La Jolla, CA, 92093, USA 2 23andMe, Inc., Mountain View, CA, USA 3 Department of Psychology, University of Georgia, USA 4 Vanderbilt Genetics Institute Division of Genetic Medicine, Department of Medicine, Vanderbilt University, Nashville, TN, USA 5 Department of Psychiatry and Behavioral Neuroscience, University of Chicago, Chicago, IL 60637, USA 6 Center for Alcohol and Addiction Studies, Brown University School of Public Health, Providence, RI 02903, USA; Peter Boris Centre for Addictions Research, McMaster University/St. Joseph's Healthcare Hamilton, Hamilton, ON L8N 3K7, Canada; Homewood Research Institute, Guelph, ON N1E 6K9, Canada

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12:00pm – 12:50pm **S** **Selected Talks Session 1: Characterising a developmental syndrome associated with KPTN mutations through mouse modelling.** Faculty of Medicine, Complutense University (Sala Duran Sacristan)

Speakers: Maria Levitin

Characterising a developmental syndrome associated with *KPTN* mutations through mouse modelling.

Maria O Levitin1, Gabriela Sánchez-Andrade1, Mark Sanderson1, Stephen J Sawiak2,3, Chris Lelliott1, Binnaz Yalcin4, Emma L Baple5, Andrew H Crosby5, Matthew E Hurles1, Sebastian S Gerety1, Darren W Logan1

Although individually rare, together developmental disorders affect 2-3 % of live births and are a major cause of infant mortality and morbidity. Many developmental disorders have a genetic cause, yet few affected children receive a genetic diagnosis. Windows of Hope (WOH) and the Deciphering Developmental Disorders project (DDD) are genomic studies, aimed at understanding the underlying mutations of uncharacterised developmental disorders. Mouse models of these disorders can provide evidence supporting a causal link between the candidate genes and the previously uncharacterised developmental disorders, shed light on their disease mechanisms, and potentially inform treatment.

WOH project identified nine patients with a distinct, previously uncharacterised, developmental delay syndrome carrying two founder loss of function recessive mutations in the *KPTN* gene. All the affected individuals display macrocephaly, cognitive disability, and behavioural abnormalities as their main phenotypes. Our study is the first one to date to model this syndrome in mice, using an engineered loss of function allele. We have performed a series of cognitive and behavioural tests, as well as morphometric brain analyses. Our findings in mouse recapitulate the main phenotypes observed in the patients, including macrocephaly and cognitive impairment. To further understand the molecular and cellular mechanisms underpinning this neurodevelopmental disorder, we are carrying out RNA-sequencing of several distinct brain regions, as well as hypothesis-driven developmental work. Moreover, we have employed the robust cognitive and molecular array of tests used in this study on several further mouse models, each with mutations in a gene identified by the DDD project.

1Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, UK; 2Behavioural and Clinical Neuroscience Institute, University of Cambridge, Cambridge, UK; 3Wolfson Brain Imaging Centre, Department of Clinical Neurosciences, University of Cambridge, Cambridge, UK; 4Center for Integrative Genomics, University of Lausanne, Lausanne, Switzerland; 5Medical Research, RILD Wellcome Wolfson Centre, Royal Devon & Exeter NHS Foundation Trust, Barrack Road, Exeter, UK.

12:50pm – 1:10pm **S** **Selected Talks Session 1: Effects of Cyfip1 haploinsufficiency on binge eating and compulsive behavior** Faculty of Medicine, Complutense University (Sala Duran Sacristan)

Speakers: Keith Babbs

Effects of Cyfip1 haploinsufficiency on binge eating and compulsive behavior

R. Keith Babbs1, Stacey L. Kirkpatrick1, Qiu T. Ruan1,2, Fred A. Rodriguez1, Johanne Pierre1, Fabiola A. Benitez1, Camron D. Bryant1

Binge eating (BE) is consumption of a large quantity of food in a relatively short period of time. BE is a highly heritable trait associated with eating disorders; however, genome-wide association studies (GWAS) have yet to identify genetic risk factors. We recently identified cytoplasmic FMR-interacting protein 2 (*Cyfip2*) as a genetic factor underlying binge eating and compulsive-like behaviors in mice. *CYFIP1* is a gene homolog of *CYFIP2* that is deleted in a subset of patients with Prader-Willi Syndrome (PWS). PWS is a neurodevelopmental genetic disorder caused by a paternal deletion of 15q11-q13 that is characterized by binge-like hyperphagia, obsessive-compulsive behavior, and cognitive disability. CYFIP proteins are important in regulating neuronal development and protein translation for synaptic plasticity. In this study, we investigated involvement of *Cyfip1* in BE by comparing binge intake and escalation in a heterozygous *Cyfip1* knockout to wild-type mice in a conditioned place preference (CPP) paradigm. We also measured expression levels of both *Cyfip1* and *Magel2*, an imprinted gene in the PWS locus implicated in hyperphagia. Additionally, we used naïve *Cyfip1* knockout and wild-type mice in a series of compulsive behavior tests. Finally, because maternal imprinting can underlie PWS, we investigated parent-of-origin (PO) effects in mice with one maternal copy versus one paternal copy of the *Cyfip1* knockout allele. These findings suggest for the first time that *CYFIP1* could represent an important component of the hedonic aspect of hyperphagia in a subset of PWS patients which could have implications for treating specific aspects of this debilitating phenotype.

1Laboratory of Addiction Genetics, Dept. of Pharmacology and Experimental Therapeutics, Boston University

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2NIGMS Ph.D. Program in Biomolecular Pharmacology, Dept. of Pharmacology and Experimental Therapeutics, Boston University School of Medicine

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1:10pm – 1:30pm **S** **Selected Talk Session 1: Using a zebrafish to investigate GABBR2 as a gene of unknown significance in clinical disease.** Faculty of Medicine, Complutense University (Sala Duran Sacristan)

Speakers: Karl Clark

Using a zebrafish to investigate GABBR2 as a gene of unknown significance in clinical disease.

AN Sigafoos, NJ Boczek, RH Gavrilova, EW Klee, and KJ Clark

Whole exome sequencing (WES) utilized in diagnostic odyssey cases identify the underlying genetic substrate responsible for the patient phenotypes in about 1 of 4 cases. The residual ~75% of cases remain genetically elusive until more information becomes available in the literature or applicable functional studies are pursued. In a diagnostic odyssey case, we have identified a candidate mutation in GABBR2 that may lead to observed developmental delay, hypotonia, cyanosis, and among other clinical diagnosis in our patient.

GABBR2, gamma-aminobutyric acid beta receptor 2, is known for its regulation of neurotransmitter release in the brain. The *de novo* variant, p.M702V, falls within a highly conserved 6th transmembrane spanning region of GABBR2 and is absent in the publicly available exome/genome databases. A recent manuscript examining epileptic encephalopathy identified *de novo* GABBR2 variants, p.S695I and p.I705N, in the 6th transmembrane spanning domain of GABBR2 in two cases with similar phenotypes to our proband.

We have made targeted mutations to the zebrafish *gabbr2* gene. Homozygous mutant zebrafish (gabbr2-/-) demonstrate a hypo-responsive locomotor response to a stressor, but a hyper-responsive locomotor response to nicotine exposure. Currently, we are assessing how well human GABBR2 mRNA can rescue knockout phenotypes and whether GABBR2 variants are capable of rescuing to the same degree. Additionally, we have produced transgenic fish that overexpress human GABBR2 and variants in a Cre-recombinase dependent manner. We are assessing the phenotypic consequences of overexpressing the various human GABBR2 proteins.

Center for Individualizing Medicine, Mayo Clinic, Rochester, MN USA

1:30pm – 3:00pm **L** **Mentoring Lunch - Special Welcome Lunch** Faculty of Medicine, Complutense University (Sala Duran Sacristan)

Speakers: Laura Anderson, Molly Bogue, Elissa Chesler, John Crabbe, Wim Crusio, Anna Delprato, Marissa Ehringer, Judy Grisel, Consuelo Guerri, Gordon Hagar, Helen Kamens, Amy Lasek, Jose Antonio Lopez Moreno, Antonia Noronha, Clarissa Parker, Mark Rutledge-Gorman, Leo Schalkwyk, Lisa Tarantino, Rob Williams

Amy Lasek, Phamacology Researcher, Industry

Wim Crusio, Science Writer

TBD, Private Sector Entrepreneur

Judy Grisel & Clarissa Parker, Liberal arts college/university professor with teaching and research

Marissa Ehringer & Helen Kamens, Large university with heavy teaching and research

John Crabbe & Lisa Tarrantino, Medical School/VA Medical Center with heavy research & teaching

Elissa Chesler, Biostatistician, Computational Sciences - Statistics & Analysis

Antonio Noronha, NIH Administrator, public information officer

Gordon Hager, NIH Intramural researcher

Molly Bogue & Consuelo Guerri, Researcher in independent research institute

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Consuelo Guerri

Jose Antonio Lopez Moreno & Leo Schalkwyk, European Union University professor

Rob Williams, Large scale project manager

Laura Anderson, Behaviour core manager

Anna Delprato & Mark Rutledge Gorman, Research administration, educational outreach, public info officer

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3:00pm – 4:20pm **T** **Outstanding Travel Award Talks** Faculty of Medicine, Complutense University (Sala Duran Sacristan)

Moderators: Mark Rutledge-Gorman

Speakers: Seung-Hee Lee, Nicholas Miner, Annie Park, Wei Wei

15.00 pm - 15.20 pm Annie Park
15.20 pm - 15.40 pm Nicholas Miner
15.40 pm - 16.00 pm Wei Wei
16.00 pm - 16.20 pm Seung-Hee Lee

1. Annie Park

Measuring Ethanol Preference Using BARCODE: Sexually Dimorphic Ethanol Behaviors Modulated by FruM In Distinct Brain Regions
A Park1,2, T Tran2, R Bohm3, N Atkinson1,2
1Waggoner Center for Alcohol Research, 2Institute for Neuroscience, University of Texas in Austin, Austin, TX 3Department of Biological and Health Sciences, Texas A&M University-Kingsville, Kingsville, TX.
NIH: T32 AA07471

Alcohol Use Disorder is a devastating and costly disease affecting millions of people in the United States. Flies are used to study this disorder because of their substantial genetic toolkit, sizable conservation of genes, and the similarity to human alcohol behaviors. Flies can acquire functional tolerance, exhibit withdrawal seizures, and will overcome aversive stimuli to obtain alcohol. One challenging behavior to measure in flies is ethanol drinking preference due to their small meal size. We have designed an assay called BARCODE, which measures alcohol drinking preference. Oligomers non-endogenous to the fly genome are added to ethanol- and ethanol-free fly food on a food tray. A cohort of flies are placed in the population chamber and their consumption of ethanol and ethanol-free food is measured by qPCR quantification of the oligomers. Using BARCODE, I observed that male flies are aversive to ethanol at 5% ABV (Alcohol By Volume) whereas females show robust preference for the ethanol food.
To examine the origins of this sexually dimorphic response to ethanol, I genetically feminized male fly neuropil by knocking down FruM (FruitlessM), a transcription factor only active in male flies. Feminization of Mushroom Body lobes (MB) αβ, α'β', and γ in male flies increased ethanol preference. Males with feminized MB lobes also showed diminished ability to acquire functional alcohol tolerance, and αβ feminized males lacked this ability completely. FruM mRNA was also seen to decrease following a single ethanol vapor treatment in male CS flies 24 hours and 6 hours after treatment.

2. Nicholas Miner
Trace Amine-Associated Receptor 1 (TAAR1) modulates thermal response to 3'4-methylenedioxymethamphetamine in selected line mouse model
NB Miner1,2, TJ Phillips1,2,3, A Janowsky1,2,3,4
Activation of the trace amine-associated receptor 1 (TAAR1) modulates core body temperature. 3'4-methylenedioxymethamphetamine (MDMA) is a methamphetamine (MA) analogue and non-selective TAAR1 agonist that elicits an initial hypothermic response (+30 min) followed by an increase in body temperature under normothermic conditions (22±1 °C). Here, a bidirectional selected breeding line mouse model was used to investigate thermal response to MDMA: mice selectively bred to voluntarily consume high amounts of MA (MAHDR) and possessing a *Taar1* allele that encodes a non-functional TAAR1 were compared to low consumers of MA (MALDR) expressing a functional TAAR1. Behavioral assays using these mice suggest that TAAR1 function conveys sensitivity to MA aversion. These data have clinical relevance because humans express TAAR1

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polymorphisms. A neurotoxic regimen of 4 i.p. injections, spaced 2-hr apart, of saline or MDMA (20 mg/kg), was administered. Temperature was non-invasively recorded every 15 min by telemetry. Thirty min after first injection, a hypothermic drop in body temperature occurred in MALDR (max. change: -1.9±0.4 °C) mice receiving MDMA, while this response was significantly diminished in MAHDR (-0.4 ±0.5 °C) mice. MAHDR/MALDR mice also received the same dosing regimen of methylone (4 injections of 25 mg/kg), a substituted methcathinone lacking affinity for TAAR1. Methylone elicited an initial hypothermic response with no significant difference between MALDR (-1.7±0.4 °C) and MAHDR (-1.9±0.2 °C) mice. MDMA-induced hyperthermia is correlated with neurotoxicity and hypothermia with neuroprotection. Therefore, a non-functional TAAR1 receptor mitigates the hypothermic response to the TAAR1 agonist MDMA, potentially increasing the risk of neurotoxicity.
1 Research Service, VA Portland Health Care System, Portland, OR, USA, 2 Department of Behavioral Neuroscience, Oregon Health & Science University, Portland, OR, USA, 3 The Methamphetamine Abuse Research Center, Oregon Health & Science University, Portland, OR, USA, 4 Department of Psychiatry, Oregon Health & Science University, Portland, OR, USA
Funding Support: NIDA training grant: T32DA007262 and The Methamphetamine Abuse Research Center: 1P50 DA018165.

3. Wei Wei

Discovery of a new mechanism of ING1 regulating extinction memory in mice

Wei Wei1, Xiang Li2, Qiongyi Zhao1, Chuanyang Dai1, Laura Leighton1 and Timothy W. Bredy1,2
Our understanding of the effects of experience on brain function has advanced in recent years with the realization that a variety of epigenetic processes regulate gene expression underlying learning and memory. Inhibitor of growth family member 1 (ING1) is a key epigenetic regulator, which has been identified as a reader protein for the DNA modification, 5-formylcytosine (5fC). 5fC has recently been shown to be a stable epigenetic mark; however, it is not known whether the accumulation of 5fC is functionally relevant in the adult brain. The importance of ING1 in learning and memory also remains to be demonstrated. Here, using lentiviral-mediate gene transfer, we show that ING1 activity in the medial prefrontal cortex (mPFC) is critically involved in fear extinction memory in mice. To investigate the mechanism underlying, we have developed a novel fluorescence-activated cell sorting (FACS)-based method to enrich for neurons that have been selectively activated by learning. We applied this method to dissociate cells from the mPFC of mice immediately following extinction training, then performed ING1 ChIP-seq derived from those activated neurons. In this way, we targeted ING1 binding exclusively in neurons that are involved in the formation of the memory trace, and elucidate genes that are directly involved with extinction memory. Importantly, we have discovered that some ING1 binding sites are associated with the accumulation of 5fC, together with DNA structure change during extinction learning. These finding represent a potentially new mechanism of gene regulation by functional interaction between ING1 and 5fC in the adult brain.
1Queensland Brain Institute, The University of Queensland, Brisbane, Australia 4072
2 Department of Neurobiology and Behavior and Center for the Neurobiology of Learning and Memory, University of California Irvine, Irvine, CA, USA 92697

4. Seung-Hee Lee

A neural circuit for auditory dominance over visual perception

You-Hyang Song, Jae-Hyun Kim, Hye-Won Jeong, Ilsong Choi, Daun Jeong, Kwansoo Kim, Seung-Hee Lee
Department of Biological Sciences, Korea Advanced Institute of Science and Technology,
291 Daehak-ro, Yuseong-gu, Daejeon 305-701, Korea
When conflicts occur during integration of visual and auditory information, one modality often dominates the other, but the underlying neural circuit mechanism remains unclear. Using auditory-visual discrimination tasks for head-fixed mice, we found that audition dominates vision in a process mediated by interaction between inputs from the primary visual (VC) and auditory (AC) cortices in the posterior parietal cortex (PTLp). Co-activation of the VC and AC suppresses VC-induced PTLp responses, leaving AC-induced responses. Furthermore, parvalbumin-positive (PV+) interneurons in the PTLp mainly receive AC inputs, and muscimol inactivation of the PTLp or optogenetic inhibition of its PV+ neurons abolishes auditory dominance in the resolution of cross-modal sensory conflicts without affecting either sensory perception. Conversely, optogenetic activation of PV+ neurons in the PTLp enhances the auditory dominance. Thus, our results demonstrate that AC input-specific feedforward inhibition of VC inputs in the PTLp is responsible for the auditory dominance during cross- modal integration.
This work is supported by the CISS NRF-2016M3A6A6930773 and HI14C2437 funded by
MSIP and MHW, Korea

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4:30pm – 7:00pm **P Poster Session - With Snacks Provided** University of Madrid, Faculty of Medicine (XXX)

Speakers: Amanda Barkley-Levenson, Darya Bazovkina, Susan Bergeson, Mirela Bilc, Natalya Bondar, Camron Bryant, Andrea Burri, Corey Calhoun, Angela Caruso, Michael Caruso, Christa Christ, Erika Cuellar, M. Imad Damaj, Samara Damasceno, Anna Delprato, Silke Dietze, Marissa Ehringer, Maya Eid, Judit Garcia-Gonzalez, Kristin Hamre, Frank Hillary, Kim Hoke, James Ingersoll, Neri Kafkafi, Maryam Keshavarz, Louis El Khoury, Kristel Klaus, Sulev Koks, Natalia Kulesskaya, Vivek Kumar

1. *Glyoxalase 1* involvement in alcohol drinking and alcohol-motivated behaviors
A.M. Barkley-Levenson1, A. Der-Avakian1, A.A. Palmer1

2. Effect of acute emotional stress on behavior, level of plasma corticosterone and brain monoaminergic systems in tumour necrosis factor-α knockout mice
DV Bazovkina1, DV Fursenko2, YV Antonov3, AV Pershina1, EY Bazhenova2, EA Kulikova1, VS Naumenko1

3. Toward Understanding Tetracycline Analog Efficacy of Alcohol Use Disorder Treatment
DC Curtis1, JM Martinez1, PC Marquardt1, CL Allison1, JA Groot1, H Blanton1, JL Redondo1, PJ Syapin1, DS Edwards2, J Guindon1 and SE Bergeson1

4. Genetic and environmental contributions to individual differences in emotion regulation: Preliminary results from the Romanian Twin Registry
Mirela Bîlc, Mădălina Buciuman, & Andrei C. Miu

5. Long-lasting consequences of early life stress in mice: changes in gene expression and H3K4me3 profile.
Bondar N.P. 1, Reshetnikov V.V.*1, Studenikina A.A.1,3, Ryabushkina Yu.A.1.2, Lepeshko A.A.1.2, Ershov N.I.1, Merkulova T.I.1

6. Systems genetic analysis and fine mapping in a reduced complexity cross rapidly leads to the identification of compelling candidate genes underlying behavioral addiction traits
Lisa R. Goldberg, B.A.1,2, Stacey L. Kirkpatrick, B.S.1, Alexander M. Luong, Kimberly P. Luttik1, Jiayi Wu, M.S.1,3,4, Eric R. Reed, M.S.1,5, David F. Jenkins, B.S.5,6, Julia C. Kelliher, Neema Yazdani, M.S.1,2,3, W. Evan Johnson, Ph.D.6, Megan K. Mulligan, Ph.D.7, Camron D. Bryant, Ph.D.1*

7. Pain catastrophizing, neuroticism, fear of pain, and anxiety: defining the genetic and environmental factors
Andrea Burri PhD1,2, Soshiro Ogata PhD3,4,5, David Rice PhD1,2, Frances Williams PhD FRCP(E)6

8. 5-HT1A and 2 Adrenergic Receptors Modulate Anxiety-like Behavior and Impulsivity in Selectively Outbred Long-Evans rats
Corey Calhoun1, B.A., Tim Niedzielak2, B.S., Becky Ravenelle3, B.S., Marie Joseph1, B.S., S. Tiffany Donaldson1, Ph.D.

9. An altered neurodevelopmental profile in mice deficient for autism-associated *Neurexin1* gene: communicative and motor aspects at an early stage
A Caruso1,2, S Della Notte1, C Fernandes3, ML Scattoni4

10. ADOLESCENT SOCIAL STRESS DIFFERENTIALLY IMPACTS AFFECTIVE BEHAVIORS AND NICOTINE SENSITIVITY IN C57BL/6J AND BALB/cJ MICE
Caruso, M.J.1, Reiss, D.E.1, Thomas, J.L.1, Caulfield, J.I.1,2,3, Crowley, N.A.4, Baker, A.N.3, Cavigelli, S.A.1,2,3, & Kamens, H.M.1,2

11. The Contribution of a Polygenic Risk Score and Experiences of Childhood Maltreatment to the Use of Maladaptive Coping Strategies
CC Christ1,2, S Bowler1, J Savolainen3, SF Stoltenberg1,4

12. Genetically correlated reward and aversion traits across generations of selection for methamphetamine consumption
E Cuellar1, H Baba1, J Erk1, CS McKinnon1, C Reed1, TJ Phillips1,2,

13. A comparative phenotypic analysis of paclitaxel-induced neuropathy in C57BL/6J and C57BL/6N mouse strains

M. Imad Damaj1, Deniz Bagdas1, Wisam Toma1 and Camron D. Bryant2

14. Transcription profile of animal model of seizures Wistar Audiogenic Rat
Damasceno, S1; Menezes, NB1; Rocha, CS2 ; Lopes-Cendes, IT2; Godard, ALB1

15. A QTL on chromosome 1 modulates intermale aggression in mice
WE Crusio1,2, M-P Algéo1,2, B. Bonheur1,2, R Hagigal3, A Murillo3, L Lu4, RW Williams4, A Delprato1,2,3

16. Thermoregulation and Postsynaptic 5-HT1A receptors in mice.
Silke Dietze, Bettina Noto, Heidrun Fink and Malte Feja

17. Examining the interaction between *in utero* nicotine exposure and the D397N CHRNA5 nicotinic acetylcholine polymorphism (rs16969968) on alcohol intake in mice
MS Powers1, HC O'Neill1, JA Stitzel1 & MA Ehringer1

18. The Heritability of Cocaine-Conditioned Avoidance Behavior
Maya Eid, Dominika Pullman, & Thomas C. Jhou

19. *SLIT3* pathways regulate zebrafish nicotine preference and human smoking behavior
Alistair J. Brock1, Judit García-González1, Matthew O. Parker1, Valerie Kuan2, David Jolliffe2, Ari Sudwarts1, Muy-Teck Teh2, Elisabeth M. Busch-Nentwich3, Derek L. Stemple3, Adrian R. Martineau2, Robert T. Walton†2, Caroline H. Brennan†1

20. Prenatal exposure to delta-9-tetrahydrocannabinol (THC) alters adolescent behavior and neurochemistry.

A.J. Elberger1, K.M. Hamre1, M.K. Mulligan2, B.M. Moore, II3

21. The influence of APOE status on functional network dynamics after traumatic brain injury
1Bernier, RA, 1Gilbert, N., 1Richards, J., 1Roy, A., 2Grove, D., 1Einat Brenner, 1Emily Grossner, 3Rajtmajer, S.M., 1Hillary, F.G.

22. Parent-of-origin effects and flexible covariance structure in guppy antipredator behaviors
LR Stein1, KA Hughes2, KL Hoke1

23. Effects of early postnatal ethanol exposure on medium spiny neuron morphology and synaptic protein expression
JD Ingersoll1, TH Reekes1, EBD Clabough1

24. Testing the Replicability of Mouse Phenotyping Experiments
N Kafkafi1, S Yaacoby1, I Jaljuli1, Y Benjamini1

25. The First Molecular Mechanism for Personality Trait
Maryam Keshavarz, Rebecca Krebs-Wheaton, Diethard Tautz

26. Forced Beach Test: A Novel Behavioral Despair Assay for the Zebrafish Model
LY El Khoury, H Lee, JL Slivinski, KJ Clark

27. The role of *DRD2 C957T* and *ANKK1 Taq1A* polymorphisms in working memory performance: a systematic review and meta-analysis
K. Klaus1, K. Butler1, C. Bridle2, K. Pennington1

28. ER stress markers in WFS1-deficient mice
Sulev Kõks1,2, Marilin Ivask1,2

29. Susceptibility to psychosocial stress associates with morphological differences in the prefrontal cortex mitochondria of DBA/2NCrl and C57BL/6NCrl mice.
N Kulesskaya1, Z Misiewicz1, M Laine1, L Salminen1, E Sokolowska1, V Voikar2, I Hovatta1

30. Deep learning for mouse behavior recognition.
Vivek Kumar, Brian Geuther, Kai Fox, Sean Deats

COMPLETE ABSTRACTS - SEE DOCUMENT BELOW

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4:31pm – 7:01pm **P Poster Session - With Snacks Provided** Faculty of Medicine, Complutense University (Sala Duran Sacristan)
Speakers: Wlater McCulley III, Eun Young Jang, Youngsoo Kim, Petrina Lau, Han Lee, Orna Levran, Anne Stephanie Mallien, Josephine McGowan, Marie Mennesson, John Mootz, Kristen Onos, Angela Ozburn, Isadora Paiva, Clarissa Parker, Susanna Pietropaolo, Inga Poletaeva, Igor Ponomarev, Cheryl Reed,

Chaoran Ren, Qiu Ruan, Su Yeon Seo, Min Seol, Burt Sharp, Jennifer Smith, Dai Stephens, Grace Sullivan, Lisa Tarantino, Anna Maria Tartaglione, Jayme Temple, Guilan Vodjdani, David P Wolfer, Kim Hee Young

31. Synaptic fusions in regulating sleep and wake activity in mice
Lau P Y P, Banks G T, Heise I, and Nolan P M

32. Stressor modality and recruitment of the hypothalamic-pituitary-adrenal (HPA) axis in rapid locomotor response to acute challenges in larval zebrafish
Han B. Lee1, Tanya L. Schwab2, Jennifer L. Gauerke2, Randall G. Krug II1, MaKayla R. Serres2, Ashley N. Sigafoos2, Dakota C. Jacobs2, Morgan O. Petersen2, Biswadeep Das2, Bethany C. Berry2, and Karl J. Clark1,2

33. Variant in stress-related genes may contribute to maintaining long-term abstinencein former addicted subjects who are not treated with opioid agonist
Orna Levran 1, Einat Peles2,3, Matthew Randesi1, Joel Correa da Rosa4, Miriam Adelson1,2,5 and Mary Jeanne Kreek1

34. Cognitive flexibility/stability using touchscreen technology and simultaneous severity assessment in mice
AS Mallien1,5, N Pfeiffer1,5, SH Richter1,5, G Koppe2,5, K Ueltzhoeffer4,5, D Armbruster-Genc4,5, C Fiebach4,5, R Palme6, MA Riva7, D Bartsch3,5, D Durstewitz2,5, B Vollmayr1,5, P Gass1,5

35. Alpha-Adrenergic Modulation of Ethanol Intake in C3H/HeJ mice.
Walter D. McCulley III1, Michael C. Fixaris1, and Alan M. Rosenwasser1, 2, 3

36. Prophylactic ketamine reduces fear expression but does not facilitate extinction
Josephine C. McGowan1,2, Christina T. LaGamma2.3, Sean C. Lim3, Melina Tsitsiklis1, Yuval Neria4,5, Rebecca A. Brachman4, and Christine A. Denny3,4*

37. A broad analysis of anxiety-like behavior in *Neto1* knock-out mice
Marie Mennesson 1, Ewa Sokolowska 1, Saija-Anita Callan 1, Vootele Voikar 2, Iiris Hovatta 1

38. Neuronal activation associated with genetically-determined methamphetamine consumption differences and drug-related thermal regulation disruptions
J Mootz1, Z Zhu1, TJ Phillips1,2

39. Connecting genes to behavior in Alzheimer's disease – utilizing mouse genetic diversity.
Kristen D. Onos1, Kelly J. Keezer1, Casey J. Acklin1, Harriet M. Jackson1, Travis L. Cossette1 and Gareth R. Howell1, 2

40. Putative involvement of Lrrk2 gene on the inflexible ethanol preference behavior in adult Zebrafish.
Paiva, IM1; Assis, IL2; Souza, JG2; Virote, BCR2; Murgas, LDS2; Silva e Silva, DA3; Godard, ALB1.

41. Genome-wide mapping of conditioned fear in the Diversity Outbred mouse population
CC Parker1, D Gatti2, T Wilcox2, E Busch3, S Kasparek1, D Kreuzman1, B Mansky1, S Masneuf3, E Sagalyn3, K Sharif1, D Taterra1, W Taylor1, M Thomas1, EJ Chesler2, A Holmes3

42. Environmental enrichment in the form of nesting material partially rescues the neurobehavioral abnormalities of a genetic mouse model of Fragile X syndrome.
I. Bouzón Arnáiz1,2,3, N. Mons2,3, V. Lemaire-Mayo2,3, N. Henkous2,3, W.E. Crusio2,3, S. Pietropaolo2,3

43. Multifaceted cognitive ability in selected mouse line

OV Perepelkina, AYu Tarassova, IG Lilp, Il Poletaeva

44. Audiogenic epilepsy – visibly simple, but complicated in the intrinsic mechanisms brain pathology.
IB Fedotova, N.M. Surina, Il Poletaeva

45. Transcriptome analysis reveals common networks of alcohol-related genes in mice and men: focus on neuronal plasticity in the extended amygdala
LB Ferguson1, L Zhang2, D Kircher1, S Wang2, RD Mayfield1, JC Crabbe3,4, RA Morrisett1, RA Harris1, I Ponomarev1

46. Evidence for an epistatic effect of *Oprm1* and *Taar1* on methamphetamine-induced hypothermia
C Reed1, H Baba1, Z Zhu1, J Erk1, A Janowsky1,2, TJ Phillips1,2

47. LED Green light treatment improves learning and memory in mice
Meijie Tan1, Chaoran Ren1

48. Candidate molecular mechanisms linking *Hnrnph1* polymorphisms with psychostimulant and opioid-induced behaviors
Qiu Ruan1,2, Neema Yazdani1,2, Kim Luttik1, Justin Cheung1, Eric R. Reed3, Kathryn Hixon1, Kristen Hokenson1, Lisa R. Goldberg1, Shelley J. Russek1, Benjamin Wolozin1, W. Evan Johnson4, Camron D. Bryant1,2,5

49. **Enhanced empathic fear with thalamocortical dysrhythmia in phospholipase-C beta4 deficient mice**
Sehoon Keum1, Charles Latchoumane1, Min Seol1, Gireesh Gangadharan1, Dongmyeong Lee1, Joonhyuk Lee1, Bomi Chang1, Arie Kim1, Boyoung Lee1, Ji Su Ma2, Yong Ryoul Yang3, Masahiro Yamamoto2, Pann-Ghill Suh3, and Hee-Sup Shin1#

50. GABA in basolateral amygdala mediates the effects of stress on enhanced reacquisition of nicotine self-administration
Burt M Sharp

51. PhenoMiner: A unique resource for mining and analyzing quantitative behavioral phenotype data in the rat
Jennifer R. Smith1, Matthew J Hoffman1, Stan Laulederkind1, G. Thomas Hayman1, Shur-Jen Wang1, Monika Tutaj1, Yiqing Zhao1, Omid Ghiasvand1, Jyothi Thota1, Marek A. Tutaj1, Jeff De Pons1, Melinda Dwinell1, Mary Shimoyama1

52. Are the effects of early-life stress on cocaine effects in adulthood due to long-term down regulation of GABRA2 expression?
DN Stephens1, CI Dixon1, SE Walker1, SL King1, JJ Lambert2, D Belelli2, J Swinny3

53. Predictors of women's eating problems: The moderating role of triallelic serotonin transporter and serotonin receptor 2A genotypes on the effect of objectification

GA Sullivan1, SJ Gervais1, RL Brock1, & SF Stoltenberg1

54. The critical role of micronutrients in neurodevelopment: short- and long-term behavioral outcome in a Selenium-deficient rat model

Tartaglione AM1,2, Scalfari A1, Attorri L3, Di Biase A3, Minghetti L4 and Calamandrei G1

55. Characterization of the ventral tegmental area in socially monogamous prairie voles.
J.A. Temple[1], K. Gordon[2], Z.R. Donaldson[1,2]

56. Unpredictable chronic mild stress: behavioral responses, neurotransmitter systems and effect of regional deficit in serotonin synthesis
F Saurini1, S Salam1, C Joubert1, M Hary-Lenglet1, A Lecomte1, D-Y Yefsah1, P Venault1, S Berrard1, M Nosten-Bertrand2, Y Clément3, G Vodjdani1

57. A continuous fully automated progressive ratio task for the IntelliCage

AK Fritz1,2, DP Wolfer1,2

58. Autosomal-dominant sensory ataxia linked to the loss of RNF170 function
Youngsoo Kim1, Seong Hun Kim2, Kook Hwan Kim3, Sujin Chae4, Myung-Shik Lee3,5, Daesoo Kim1

59. **Estradiol-independent BDNF-NPY cascade involves in antidepressant-like effect of mechanical acupuncture instrument in ovariectomized rats**
Su Yeon Seo, Ji Young Moon, Suk Yun Kang, O Sang Kwon, Sunoh Kwon, Se kyun Bang, Soo Phil Kim, Kwang-Ho Choi, Yeonhee Ryu*

60. **Spinal pathways involved in somatosensory inhibition of the psychomotor actions of cocaine**
Suchan Chang1,#, Yeon-Hee Ryu2,#, Young Seob Gwak1, Nam Jun Kim1, Jin Mook Kim1, Jun Yeon Lee1, Seol Ah Kim1, Bong Hyo Lee1, Scott C. Steffensen3, Eun Young Jang1, Chae Ha Yang1, Hee Young Kim1,*

61. Effect of acupuncture on brain temperature, dopamine release in the nucleus accumbens and 50–kHz ultrasonic vocalizations in methamphetamine-treated rats
Eun Young Jang, Nam Jun Kim, Bong Hyo Lee, Suchan Chang, Young Seob Gwak, Chae Ha Yang, Hee Young Kim

62. Genes and the environment: Measuring stress response in the Collaborative Cross
Schoenrock SA1,2, Farrington J2, Kumar P4, Manuel de Villena FP2 and Tarantino LM2,3,5.

63. A high-throughput behavioral screen of addiction related traits in Mice
Leona H. Gagnon1, Stacey J. Sukoff-Rizzo1, J. David Jentsch4, Lisa M. Tarantino2, Ryan W. Logan3, Colleen M. McClung3, Vivek M. Philip1, Laura G. Reinholdt1, Michael Leonardo1, Ashley Olsen1, Rainy Dodd1, Tyler Roy1, Troy Wilcox1, Price E. Dickson1, Jason A. Bubier1, C. Herbert Pratt1, Elissa J. Chesler1

64. **Investigation of the bidirectional relationship between alcohol and circadian gene expression**
T Batish, S Kanadibhotla, K LeBlanc, R Champaigne, A Tran, E Firsick, S Powell, W Hack, A Ozburn

COMPLETE ABSTRACTS - SEE DOCUMENT BELOW

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6:00pm – 7:30pm **E Closed Executive Committee Meeting, 2nd Floor, Sala de Profesores**
Faculty of Medicine, Complutense University (Sala Duran Sacristan)

7:30pm – 10:00pm **D Dinner - On Your Own** Madrid

MAY 17 • WEDNESDAY

8:00am – 8:15am **R Registration** Faculty of Medicine, Complutense University (Sala Duran Sacristan)

8:30am – 9:30am **K Presidential Address - Yoav Benjamini** Faculty of Medicine, Complutense University (Sala Duran Sacristan)

Speakers: Yoav Benjamini

Yoav Benjamini

Department of Statistics and Operations Research School of Mathematical Sciences

The Sagol School of Neuroscience, Tel Aviv University.

There has been a growing concern that preclinical research is failing to replicate experimental results, a problem that is relevant to phenotyping genetically engineered mouse lines. We introduce a statistical method to estimate whether a single-laboratory discovery is likely to replicate in other laboratories, based on previously-estimated variability of genotype × laboratory interaction in large phenotyping databases. Future single-lab experiments can be used to further update the estimation, making the proposed method a true community effort. We validate the method by combining several datasets into the most inclusive analysis conducted to date of across laboratory replication in mouse phenotyping.

9:30am – 11:30am **Y Symposium 2: Advances in bioinformatics resources for brain and behavior**

Moderators: Elissa Chesler Faculty of Medicine, Complutense University (Sala Duran Sacristan)

Speakers: Molly Bogue, Gilbert Terri, Robert Williams

Symposia Title: Advances in bioinformatics resources for brain and behavior

Chair: Elissa Chesler

09.30 am - 10.00 am Terri Gilbert

10.00 am - 10.30 am Molly Bogue

10.30 am - 11.00 am Robert Williams

11.30 am - 12.00 pm Elissa Chesler

Genomic, neuroanatomical and behavioral data resources provide a valuable means of assessing the role of genes and gene products in brain function and behavior. Publicly available databases and analysis tools have been facilitating behavioral genetics research over the past 15 years, enabling researchers to rapidly and cost-effectively expand their inquiry to related genes, pathways, structures, behaviors and mechanisms. Advances in data availability, integration and analysis methods have enhanced the utility of neurobehavioral informatics resources, and there have been a growing number of successful applications of these tools and resources to the discovery of previously unknown mechanisms of behavioral variation. Cross-species, cross-population and cross-experiment analyses enable comparative research into the neurogenomic basis of behavioral traits. In this symposium, each presentation focuses on data resources and applications of a collection of tools that may be used to characterize and extrapolate findings on the roles of genes in brain and behavioral processes.

1. Dr. Terri Gilbert will describe data resources from multiple species (currently including mouse, non-human primate, human) in the Allan Brain Atlas which includes gene expression and reference atlases across development, connectomics, and new efforts to present standardized in vivo studies of electrophysiological activity and morphology towards developing a cellular taxonomy as well as the first step in our multi-modal characterization of functional activity in the awake behaving mouse brain.
https://ibangs.memberclicks.net/mcdatafiles/receiptattach/ibangs/11851286/8239561/IBANGSAbstractTG.docx

2. Dr. Molly Bogue will present advances in the Mouse Phenome Database, which includes curated and annotated mouse genetic studies in inbred mouse strains, Collaborative Cross, Diversity Outbred and a wealth of other populations, including the multiple species QTL Archive. The mouse phenome data have been used in the study of sex differences in behavior, laboratory environmental effects, and integrative studies aimed at understanding the relations among genome and phenome in behavior.

Mouse Phenome Database: An integrative database and analysis suite for curated primary mouse phenotypic data

MA Bogue

The Mouse Phenome Database (MPD; phenome.jax.org) is a widely used online resource providing access to primary experimental data, protocols and analysis tools for mouse phenotyping studies. Data are contributed by

investigators around the world and represent a broad scope of behavioral endpoints and disease-related characteristics in naïve mice and those exposed to drugs, environmental agents or other treatments. MPD houses individual animal data with detailed, searchable data acquisition protocols, and provides these data to other resources for further analysis. MPD provides rigorous curation of experimental data and supporting documentation. Most data in MPD are from inbred strains and other reproducible strains such that the data are cumulative over time and across laboratories. The resource now also includes the QTL Archive, and other primary phenotype data from mapping crosses, advanced high-diversity mouse populations including the Collaborative Cross and Diversity Outbred mice. MPD provides an important venue for compliance with data sharing policies and facilitates data reuse and data integration to provide a means of assessing replicability and reproducibility across experimental conditions and protocols, benchmarking assays in users' own laboratories, identifying sensitized backgrounds for making new mouse models with genome editing technologies, analyzing trait co-inheritance, finding the common genetic basis for multiple traits, and assessing sex differences and sex by genotype interactions.
There is an ongoing re-implementation of the MPD system. In this session, we will demonstrate several advances and future features, and highlight the applications of MPD data and analysis tools.
1The Jackson Laboratory, Bar Harbor Maine, USA

3. Dr. Robert Williams will present advances and discoveries in GeneNetwork, a resource for systems genetic analysis, featuring gene expression genetic studies, behavioral, physiological and morphological traits, and genetic variation across multiple populations and a range of species including drosophila, mouse, rat, macaque and human.

4. Dr. Chesler will present GeneWeaver, a service for the integration of heterogeneous functional genomics studies across species and experiment. She will describe the use of this system to identify common and specific roles of genes in behavioral and biological processes. Each will focus on recent discoveries and applications of their resources to demonstrate the types of results that can be obtained from their application in behavioral and neural genetic analysis.

GeneWeaver is a web service for the integration of heterogeneous functional genomics data from a variety of species, curated data resources and experiments. The system enables the detection of convergent evidence for the role of genes, gene products and gene modifiers in behavior and other biological functions. It also enables the comparison and classification of behaviors and other biological phenomena based on their biological substrates. Users of this system have been able to identify multiple novel relations among genes, gene regulation and behavior. A new fully executed application programming interface enables reproducible and traceable analyses, and a browser based version enables facile interactions. The system has been updated with a suite of new graph based tools and enhancements to visualization, data annotation and user managed curation.
Supported by NIH NIAAA 18776

11:30am – 12:00pm **C** **Coffee Break** University of Madrid, Faculty of Medicine (XXX)

12:00pm – 12:30pm **S** **Selected Talk Session 2: High Drinking in the Dark (HDID) mice are a selective animal model for screening novel compounds targeting alcohol binge-like drinking**

Speakers: Angela Ozburn Faculty of Medicine, Complutense University (Sala Duran Sacristan)

High Drinking in the Dark (HDID) mice are a selective animal model for screening novel compounds targeting alcohol binge-like drinking

Angela R Ozburn (1), Amanda M Barkley-Levenson (2), Pamela Metten (1), John C Crabbe (1)
(1) Portland Alcohol Research Center, Department of Behavioral Neuroscience, Oregon Health & Science University, and VA Portland Health Care System, Portland, OR 97239 USA
(2) Department of Psychiatry, University of California San Diego, 92093 USA

One characteristic of nearly all abusive alcohol drinking is the tendency to drink in binges, defined by the NIAAA as a pattern leading to blood alcohol levels (BALs) > 0.08% during a period of approximately 2 hr. We bred two mouse lines that drink to intoxication and reach high BALs (> 0.14%) after 2-4 hr access to alcohol early during their circadian dark period. In a series of studies, we have attempted to modulate ethanol drinking in HDID mice

using several drugs. Here we show that HDID mice fail to reduce drinking or BALs after drugs that reduce intake in other drinking models (e.g., naltrexone and several other experimental drugs). Three anti-inflammatory compounds, the peroxisome proliferator-activated receptor (PPAR)- alpha activators tesaglitizar and fenofibrate, and caffeic acid phenylester (CAPE), failed to reduce drinking in HDID mice, although all three had been found to reduce intake in C57BL/6J mice. In fact, fenofibrate increased alcohol intake, without affecting BAL. The drug gabapentin also had no effect in HDID mice. These studies varied in design and duration, but all data were negative. However, HDID mice are sensitive to the effects of some other compounds (e.g., baclofen, acamprosate, and several experimental drugs). Rolipram, a phosphodiesterase 4 (PDE4) inhibitor, reduced drinking and BALs in HDID mice. PDE4 inhibitors reduce drinking in C57BL/6J mice, as well as in multiple rat genotypes. Apremilast, another PDE4 inhibitor, also reduced ethanol drinking. Thus, HDID mice may represent a selective model for screening novel compounds and avoiding false positive findings.

Supported by the NIAAA [Integrative Neuroscience Initiative on Alcoholism (INIA-Neuroimmune) grant AA13519; NIAAA Center grant AA10760; NIAAA R24 AA020245; NIAAA F32 AA025515; NIAAA F31 AA22009; the US Department of Veterans Affairs Grants BX000313 and CDA2 BX002488; and the John R. Andrews Family.

12:30pm – 12:50pm **S Selected Talk Session 2: The Quality of the Living Environment Affects the Fluoxetine Treatment Outcome**

Faculty of Medicine, Complutense University (Sala Duran Sacristan)

Speakers: Silvia Poggini

The Quality of the Living Environment Affects the Fluoxetine Treatment Outcome

S. Poggini1, A.Viglione1, S. Alboni2, S. Garofalo3, L. Maggi3, I. Branchi1,4
1Istituto Superiore di Sanità, Center for Behavioral Sciences and Mental Health, Rome, Italy.
2University of Modena and Reggio Emilia, Department of Life Sciences, Modena, Italy.
3Sapienza University of Rome, Department of Physiology and Pharmacology, Rome, Italy.
4University of Zurich, Istitute of Anatomy, Zurich, Switzerland.

Selective serotonin reuptake inhibitors (SSRIs) affect mood also through changes in immune function. However, findings concerning their effects on inflammation are contradictory showing that these drugs act either as pro- or anti-inflammatory compounds. Since previous studies showed that SSRI effects are moderated by the quality of the living environment, we investigated whether the environment determines the effects of SSRI treatment. We treated adult male mice, showing a depression-like phenotype, with either fluoxetine or vehicle while exposing them to either an enriched or a stressful condition. We measured the most commonly investigated behavioral endophenotypes of depression and SSRI outcome, including anhedonia, cognitive bias, BDNF and corticosterone levels. In addition, in the whole hippocampus, we assessed expression levels of pro- and anti-inflammatory cytokines, and, in isolated microglia, we measured the expression levels of a number of pro- and anti-inflammatory-related genes. The treatment affected the investigated neurobehavioral endpoints according to the quality of the environment. In particular, mice treated with fluoxetine in an enriched condition improved their depression-like phenotype compared with controls, whereas those treated in a stressful condition showed a worsening. In addition, fluoxetine treated mice exposed to enrichment showed increased expression of pro-inflammatory cytokines and decreased expression of anti-inflammatory-related genes. Whereas, mice treated while exposed to stress showed the opposite profile: a decrease in pro- and an increase in anti-inflammatory cytokine expression. Our results indicate that the effects of SSRI treatment depend on the quality of the environment, providing a possible explanation for the inter-individual differences in SSRI action and effects.

The Effect of Varenicline on Ethanol Consumption and Striatal Gene Expression Using Classical Analytical Tools and High-Dimensional Mediation Analysis

Helen M. Kamens1,2, John Dziak2, Arielle R. Deutsch2, and Runze Li2,3
1 Department of Biobehavioral Health, Pennsylvania State University, University Park, PA 16802.
2 The Methodology Center, Pennsylvania State University, University Park, PA 16802.
3 Department of Statistics, Pennsylvania State University, University Park, PA 16802.

In recent years, varenicline has been shown to decrease ethanol consumption in adult rodents without effecting consumption of other sweet, rewarding solutions. Varenicline is a partial agonist at a4b2 nicotinic acetylcholine receptors, but has been shown to interact with other receptors at high concentrations. Importantly, removal of

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the a4 or b2 nicotinic subunits does not completely reverse varenicline's effect on ethanol consumption. Thus, in order to gain a greater understanding of the mechanisms by which vareincline decreases ethanol consumption, we performed RNA sequencing on striatal tissue from animals treated with varenicline or saline prior to an ethanol binge session. Using classical tools to analyze RNA sequencing, data we found 810 differentially expressed genes using Cuffdiff and 1 significant co-expression network using WGCNA. However, these analyses are not able to account for both treatment and expression differences to explain behavioral outcomes in the same model. As a novel strategy, we employed a high-dimensional mediation analysis. In this analysis, we selected top genes that were related to both the treatment group and the behavioral outcome (alcohol consumption). This analysis yielded a number of candidate genes that were not identified with the classic tools, some of which have previously shown relationships with drug abuse measures. These results identify novel candidate genes that may underlie the effects of varenicline on ethanol consumption.

Acknowledgements: P50 DA039838 (RL), K01 AA019447 (HMK)

Understanding the effects of chronic exposure to trace metals on neurocognitive functions from molecular and cellular perspectives.

Y Ben-Shahar1,2

Trace metals such as manganese are essential for diverse cellular and molecular processes in all cells. However, chronic environmental exposure to excess amounts of these essential elements can lead to debilitating neurocognitive deficits, especially in young children. In spite of the overwhelming evidence that decay of urban infrastructure leads to higher risks of chronic exposure to metals, the genetic, molecular, and cellular processes that drive metal-induced pathologies are still mostly unknown. To address this important gap, the Ben-Shahar lab is taking advantage of a genetically tractable model system, the fruit fly Drosophila melanogaster, to investigate the mechanisms that underlie the neurotoxic effects of environmental chronic exposure to manganese on behavior at the neuronal, molecular, and genetic levels. Specifically, our data indicate that chronic exposure of flies to manganese leads to neurocognitive abnormalities associated with innate decision-making processes such as food- and mate-choice. Furthermore, we find that genetic and pharmacological disruptions of brain manganese homeostasis lead to dramatic changes in dopaminergic axonal morphology, which may explain some of the observed abnormal neurodevelopmental behavioral phenotypes associated with such exposures in children.

1Department of Biology, Washington University in St. Louis, Missouri, USA, 2Department of Medicine, Washington University School of Medicine, St. Louis, Missouri, USA.

Funding Support: NINDS R21 NS089834, NIEHS R01 ES025991-02S1.

12:50pm – 1:10pm **S** **Selected Talk Session 2: The Effect of Varenicline on Ethanol Consumption and Striatal Gene Expression Using Classical Analytical Tools and High-Dimensional Mediation Analysis**

Speakers: Helen Kamens Faculty of Medicine, Complutense University (Sala Duran Sacristan)

The Effect of Varenicline on Ethanol Consumption and Striatal Gene Expression Using Classical Analytical Tools and High-Dimensional Mediation Analysis

Helen M. Kamens1,2, John Dziak2, Arielle R. Deutsch2, and Runze Li2,3

1 Department of Biobehavioral Health, Pennsylvania State University, University Park, PA 16802.

2 The Methodology Center, Pennsylvania State University, University Park, PA 16802.

3 Department of Statistics, Pennsylvania State University, University Park, PA 16802.

In recent years, varenicline has been shown to decrease ethanol consumption in adult rodents without effecting consumption of other sweet, rewarding solutions. Varenicline is a partial agonist at a4b2 nicotinic acetylcholine receptors, but has been shown to interact with other receptors at high concentrations. Importantly, removal of the a4 or b2 nicotinic subunits does not completely reverse varenicline's effect on ethanol consumption. Thus, in order to gain a greater understanding of the mechanisms by which vareincline decreases ethanol consumption, we performed RNA sequencing on striatal tissue from animals treated with varenicline or saline prior to an ethanol binge session. Using classical tools to analyze RNA sequencing, data we found 810 differentially expressed genes using Cuffdiff and 1 significant co-expression network using WGCNA. However, these analyses are not able to account for both treatment and expression differences to explain behavioral outcomes in the same model. As a novel strategy, we employed a high-dimensional mediation analysis. In this analysis, we selected top genes that were related to both the treatment group and the behavioral outcome (alcohol consumption). This analysis yielded a number of candidate genes that were not identified with the classic tools, some of which have previously shown relationships with drug abuse measures. These results identify novel

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candidate genes that may underlie the effects of varenicline on ethanol consumption.
Acknowledgements: P50 DA039838 (RL), K01 AA019447 (HMK)

1:10pm – 1:30pm **S Selected Talks Session 2: Understanding the effects of chronic exposure to trace metals on neurocognitive functions from molecular and cellular perspectives.**

Speakers: Yehuda Ben-Shahar Faculty of Medicine, Complutense University (Sala Duran Sacristan)

Understanding the effects of chronic exposure to trace metals on neurocognitive functions from molecular and cellular perspectives.

Y Ben-Shahar1,2

Trace metals such as manganese are essential for diverse cellular and molecular processes in all cells. However, chronic environmental exposure to excess amounts of these essential elements can lead to debilitating neurocognitive deficits, especially in young children. In spite of the overwhelming evidence that decay of urban infrastructure leads to higher risks of chronic exposure to metals, the genetic, molecular, and cellular processes that drive metal-induced pathologies are still mostly unknown. To address this important gap, the Ben-Shahar lab is taking advantage of a genetically tractable model system, the fruit fly Drosophila melanogaster, to investigate the mechanisms that underlie the neurotoxic effects of environmental chronic exposure to manganese on behavior at the neuronal, molecular, and genetic levels. Specifically, our data indicate that chronic exposure of flies to manganese leads to neurocognitive abnormalities associated with innate decision-making processes such as food- and mate-choice. Furthermore, we find that genetic and pharmacological disruptions of brain manganese homeostasis lead to dramatic changes in dopaminergic axonal morphology, which may explain some of the observed abnormal neurodevelopmental behavioral phenotypes associated with such exposures in children.

1Department of Biology, Washington University in St. Louis, Missouri, USA, 2Department of Medicine, Washington University School of Medicine, St. Louis, Missouri, USA.

Funding Support: NINDS R21 NS089834, NIEHS R01 ES025991-02S1.

1:30pm – 3:00pm **L Lunch** University of Madrid, Faculty of Medicine (XXX)

3:00pm – 5:00pm **Y Symposium 3: Neuroepigenetics of Stress-induced Affective and Cognitive Disorders**

Moderators: Gang Chen Faculty of Medicine, Complutense University (Sala Duran Sacristan)

Speakers: Xiang Li, A Mateus-Pinheiro, Eva Naninck, Dipak Sarkar, Wei Wei

Symposia Title: Neuroepigenetics of Stress-induced Affective and Cognitive Disorders
Chair: Gang Chen

15.00 - 15.25 Wei Wei on behalf of Xiang Li
15.25 - 15.45 Gang Chen
15.45 - 16.10 Eva Naninck
16.10 - 16.35 A Mateus-Pinheiro
16.35 - 17.00 Dipak Sarkar

Accumulating evidence supports that epigenetic mechanisms are integral for dynamic regulation of negative impacts of stress. Still, much information remains to be gleaned regarding the stress induced epigenetic process that influences the defined cellular pathways or networks and ultimately alters neuro-glia function and behavior. The speakers will present the latest findings on the novel epigenetic modification form, and epigenetic modification along distinct cell signaling or gene networks induced by postpartum stress, chronic stress, or early-life stress.

Dr. Li “A novel nucleobase modification associated with bdnf gene expression in extinction learning and memory formation”. This talk brings the first demonstration on a novel DNA methylation mark N6-methyl-2’-deoxyadenosine (m6dA) drives activity-induced gene expression in the adult brain and is associated with the formation of fear extinction memory in C57/Bl6 mice. In the infralimbic prefrontal cortex, increase in the deposition of m6dA is associated with an active chromatin state, the recruitment of the activating transcription factor Yin-Yang 1 and RNA polymerase II, and promotion of bdnf exon IV mRNA expression, which is reversed by a viral-mediated knockdown of m6dA-specific methyltransferase, resulting in impairment in extinction memory.
https://ibangs.memberclicks.net/mcdatafiles/receiptattach/ibangs/11794312/8239561/Xiang_Li_2017_IBANGS.docx

Dr. Chen “Epigenetic contribution to transgenerational impairment of hippocampal Akt-mTOR signaling and behavioral deficits in the offspring of mice that experience postpartum depression-like illness” Dr. Chen’s lab recently demonstrated deficient Akt-mTOR signaling in the hippocampus is responsible for persistent depression-like behavior across two generations of postpartum depression dams of Balb/c mice. By dissecting the epigenetic underpinnings of these transgenerational effects, their new data discovered abnormal methylation in the promoter regions of genes implicated in Akt signaling, including GHSR, and two subunits of PI3k, the activator of Akt and downstream to GHSR. This study revealed a epigenetically modified cell signaling pathway for depression, insightful for therapeutics of the disorder.
https://ibangs.memberclicks.net/mcdatafiles/receiptattach/ibangs/11799758/8239561/2017_ibangs_symposium_talk_abstract_GangChen.doc

Dr. Naninck “Early micronutrient supplementation ameliorates early-life stress induced cognitive impairments” Early-life stress (ES) is associated with lasting cognitive impairments later in life. Dr. Naninck investigated the role of nutrition in programming later cognition in an ES animal model. They found that ES reduced methionine levels in offspring plasma and brain, whereas supplementation of micronutrient 1-CMAM, important for epigenetic modifications, reversed the brain DNA methylation, prevented ES-induced stress axis hyperactivity, ameliorated ES-induced spatial learning and memory impairments in adulthood, with contribution of epigenetic re-modification.
https://ibangs.memberclicks.net/mcdatafiles/receiptattach/ibangs/11795026/8239561/Abstract_Naninck_IBANGS2017.docx

Dr. Mateus-Pinheiro “Epigenetic control of post-natal neuroplasticity in the healthy and stressed brain: exploring transcriptomic and methylomic landscapes” Dr. Mateus-Pinheiro systematically studied “stress-triggered" genetic and epigenetic factors that modulate neuro- and glio-plasticity and impact on brain networks so as to elicit susceptibility and resilience to depression. In chronically exposed Wistar-Han rats, they examined a batery of affective and cognitive behavior, hippocampal neurogenesis, dendritic morphological rearrangements, and performed microarray analysis, genome-wide DNA methylation and hydroxymethylation analysis. The findings revealed specific transcriptomic and methylomic patterns underlying depressive behavior.
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Dr Dipak Sarkar
Alcohol induced epigenetic modifications of stress regulatory genes transmit via germline
DK Sarkar, D. Govorko, C. Zhang, R. Bekdash, S. Jabbar, O. Gangisetty, L.G. Chastain, M.A. Cabrera, K. Sochacki K,
We tested whether alcohol-induced epigenetic modifications of proopiomelanocortin (POMC) gene, that control stress axis, transmit via germline to affect body stress regulation and health of the offspring. We employed two different animal models of alcohol feedings for the germline transmission studies. One model involves preconception alcohol exposure and another involves prenatal alcohol exposure and then studying DNA methylation and histone modifications of POMC genes and impairments related to coping with stress including stress hormone hyperresponse, anxiety behaviors, immune function and cancer growth in offspring. In both animal models we found maternal alcohol feeding significantly affects POMC gene methylation, gene expression and POMC endophenotypes. Genome-wide analysis identified changes in some key molecular substrates responsible for DNA methylation in the offspring. These data indicate that alcohol induced changes in some of the epigenetic machinery is transmitted across generations via germline. This work is supported by National Institute of Health grants R01 AA11591 and R37AA08757).
The Endocrine Program, Department of Animal Sciences, Rutgers, The State University of New Jersey, New Brunswick, NJ 08901, USA

5:00pm – 5:30pm	B	**IBANGS Society Business Meeting - All Encouraged to Attend**	TBA
7:30pm – 10:00pm	D	**Dinner - On Your Own**	TBA

MAY 18 • THURSDAY

8:00am – 8:15am	R	**Registration**	Faculty of Medicine, Complutense University (Sala Duran Sacristan)

8:30am – 9:30am **K Distinguished Investigator Award Talk - Dr. Kristin Scott**

Speakers: Kristin Scott Faculty of Medicine, Complutense University (Sala Duran Sacristan)

9:30am – 11:30am **Y Symposium 4: Neuro-epigenomic regulation by glucocorticoid receptors and consequences on behavior** Faculty of Medicine, Complutense University (Sala Duran Sacristan)

Moderators: Onno Meijer, Karen Mifsud

Speakers: Gordon Hagar, Tobias Wiechmann

Symposia Title: Neuro-epigenomic regulation by glucocorticoid receptors and consequences on behavior

Chairs: Karen Mifsud and Onno Meijer

09.30 am - 10.00 am Gordon Hager
10.00 am - 10.30 am Onno Meijer
10.30 am - 11.00 am Karen Mifsud
11.30 am - 12.00 pm Tobias Wiechmann

This symposium will bring together leaders working at the cross-roads of molecular neuroendocrinology and neuro-epigenomics to discuss recent advances in the understanding of how glucocorticoid hormones act at the genomic level in the brain and how disruption of these mechanisms can be detrimental to health. This session will be chaired by Karen Mifsud and Onno Meijer and will focus on Glucocortidoic Receptors in the brain. Given the ubiquitous nature of glucocorticoid receptors throughout the brain, and the involvement of these receptors in a diverse range of processes such as neurogenesis, synaptic plasticity, neurotransmission, learning and memory, this symposium will have broad audience appeal across the spectrum of neural disciplines.

1. Professor Gordon Hager is a world-leading expert in steroid receptor dynamics based at the National Cancer Institute, Bethesda, Maryland, USA. Pioneering work from Professor Hager's laboratory has resulted in a paradigm shift in understanding how these receptors interact with the genome to facilitate chromatin remodelling in vitro. This talk will summarise these major advances in understanding and address some of the outstanding questions that remain such as what mechanisms are responsible for this behaviour and how this rapid exchange ('hit-and-run', time scale of seconds) is related to the development of altered activity promoter states on the time scale of minutes and hours.

2. Professor Onno Meijer has a longstanding interest and prolific publication record on the effects of glucocorticoid hormones under different conditions related to health and disease. His talk will cover genome-wide co-expression of steroid receptors in the mouse brain and the effect of these interactions on downstream signalling pathways and behaviour in mice in vivo.
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3. The third talk will be given by Dr Karen Mifsud describing the recent advances we have made into understanding the effects of stress on glucocorticoid-dependent gene transcription in vivo using state-of-the-art chromatin immunoprecipitation (ChIP) technologies. This work challenges existing assumptions about the relationships between plasma glucocorticoid levels, ligand binding to nuclear receptors and receptor/DNA interactions in rats in vivo. Furthermore, this work provides the first strong evidence for heterodimerization between distinct nuclear receptors in vivo.
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4. Finally, Mr Tobias Wiechmann will be representing Professor Elizabeth Binder to talk about GR activation, 3D DNA conformational changes and specific effects on DNA methylation in particular enhancer sites and the relationship between these changes and risk of developing psychiatric disease in humans.
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11:30am – 12:00pm **C Coffee Break** Faculty of Medicine, Complutense University (Sala Duran Sacristan)

12:00pm – 12:30pm **S Selected Talk Session 3: Genes involved in Alcohol's effects on habituation in Caenorhabditis elegans** Faculty of Medicine, Complutense University (Sala Duran Sacristan)

Speakers: Catharine H. Rankin

Genes involved in Alcohol's effects on habituation in *Caenorhabditis elegans*

Rankin, C.H., Lin, C.H., Mirhadi, S., Soo, S.

1. DM Centre for Brain Health, 2. Department of Psychology, UBC, Vancouver, BC, Canada. Funding: CIHR Operating and NSERC Discovery Grants to CHR

Alcohol intoxication impairs learning, however the underlying mechanisms are not well understood. Habituation is a form of non-associative learning measured as a gradual decrease in response to repeated stimuli. Using *Caenorhabditis elegans*, we investigated the roles of 27 candidate genes in the effects of alcohol on habituation. Animals were exposed to 400mM ethanol for 30mins (~0.3% BAC) and responses to 30 mechanical stimuli (taps) delivered at 10s inter-stimulus interval were collected and scored using the Multi-Worm Tracker. Wildtype animals respond to tap by locomoting backwards (reversals), and the probability and magnitude of this reversal response gradually decrease with repeated taps. On alcohol, wildtype worms habituate to tap faster and more deeply than unexposed animals. Interestingly, wildtype on alcohol also shifted their primary response to taps from reversal to fast forward. Our initial genetic analysis showed that some genes previously implicated in alcohol's other behavioral effects were also involved in alcohol-dependent habituation phenotypes (BK channel, Neuropeptide Y receptor), but some other implicated genes were not (D1 receptor), suggesting alcohol affects different components of habituation via one or more specific pools of genes. In addition, we discovered a novel, conserved gene, previously not implicated in ethanol's effects on behavior. This study identified novel mechanisms underlying learning impairment under alcohol intoxication.

12:30pm – 12:50pm **S Selected Talks Session 3: Evidence for an epistatic effect of Oprm1 and Taar1 on methamphetamine intake** Faculty of Medicine, Complutense University (Sala Duran Sacristan)

Speakers: Tamara Phillips

Evidence for an epistatic effect of *Oprm1* and *Taar1* on methamphetamine intake

TJ Phillips1,2, H Baba2, J Mootz2, J Erk2, A Janowsky1,2, C Reed2

The current studies further establish a role for the trace amine-associated receptor 1 (*Taar1)*gene in MA intake and examine the combined effects of mu-opioid receptor 1 (*Oprm1*) and *Taar1* allele types on MA intake. DBA/2 mice originating from a common ancestral population, but distributed by different vendors, were tested for MA intake and genotyped for a single nucleotide *Taar1* polymorphism that defines whether the translated receptor (TAAR1) is functional or non-functional. C57BL/6J (B6) x DBA/2J (D2) recombinant inbred strains (BXD RI) were genotyped for strain-specific *Oprm1* and *Taar1* alleles, and tested for MA intake. Only D2/J mice from The Jackson Laboratory (D2/J) possess the *Taar1* allele that negates TAAR1 function and D2/J consumed significantly more MA than D2 mice from 3 other vendors. BXD RI strains with the B6-*Taar1* consumed <1 mg/kg/d MA, whereas those with the D2/J-*Taar1* allele consumed 2.7-6.7 mg/kg/d. There was a significant *Oprm1* allele x *Taar1* allele interaction for MA consumption ($F[1,169]=8.9$, $p=.01$), with mice that were D2/J for both genes consuming more MA than all other *Oprm1/Taar1* genotypes. The correlation between *Taar1* genotype and MA intake for all animals ($N=221$) was $r=0.85$ ($p<1x10-5$); thus, *Taar1* genotype accounted for 72% of the phenotypic variance in MA intake. These data lend additional support for *Taar1* as a quantitative trait gene that impacts risk for MA intake. Furthermore, its impact may interact with *Oprm1* genotype. Data are needed in humans to determine the roles of these genes, alone and in combination, on risk for MA use disorders.

1Veterans Affairs Health Care System, 2Oregon Health & Science University, Portland, OR, USA. Funding Support: Department of Veterans Affairs I01BX002106, NIH NIDA P50DA018165, NIH NIDA U01DA041579

TBA **S Selected Talks Session 3: Genetic variation in initial sensitivity and rapid desensitization to THC**

Speakers: Megan Mulligan Faculty of Medicine, Complutense University (Sala Duran Sacristan)

Genetic variation in initial sensitivity and rapid desensitization to THC

B. Moore1, C.E. Watkins2, T. Abreo2, M. Dickerson2, S. Parker2, A. Kimes2, M.T. Houseal2, T. Shapaker2, B.C. Jones2, M.K. Mulligan2

Cannabis is used by millions worldwide. Approximately 30% of users develop cannabis use disorder (CD) characterized by dependence and an inability to regulate drug intake. CD heritability has been estimated at

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~40%, suggesting a substantial genetic component. However, the genetic factors involved in CD susceptibility are unknown. Cannabinoid receptor 1 (CB1) activation by the major psychoactive component in cannabis, Δ9–tetrahydrocannabinol (THC), produces hypolocomotion, hypothermia, and analgesia in rodent models. To determine the genetic contribution to initial sensitivity and tolerance to cannabis we profiled these responses in C57BL/6J (B6) and DBA/2J (D2)—and a subset (15 strains) of their recombinant inbred progeny (the BXDs) following 5 days of exposure to 10 mg/kg THC. For the parental strains, there was a significant ($p < 0.001$) effect of treatment and strain on locomotion and analgesia on THC day 1. Heritability ($h2$) estimates calculated for the BXD THC group after the first exposure, were 0.38 (locomotion), 0.28 (hypothermia), and 0.25 (analgesia) indicating that segregating variants in the BXDs modulate THC response. We also observed significant correlations between THC response and legacy phenotypes extant in GeneNetwork. For example, day 1 locomotion following THC treatment was strongly correlated ($r > |0.9|$ and $p < 0.0001$) with intravenous cocaine self-administration. This analysis demonstrates the feasibility of genetic mapping of THC traits in the BXDs to identify genes and networks that underlie susceptibility to CD, and that this population can be leveraged to discover novel endophenotypes that predict response to cannabis and other drugs of abuse.
1 Department of Pharmaceutical Sciences, 2 Department of Genetics, Genomics and Informatics, The University of Tennessee Health Science Center, Memphis, TN, USA. Funding Support: UTHSC Cornet Award.

1:10pm – 1:30pm **S** **Selected Talks Session 3: Cross-Species Comparison of Human and Non-Human Primate Brain Tissue for Alcohol Abuse** Faculty of Medicine, Complutense University (Sala Duran Sacristan)

Speakers: Sean Farris

Title: Cross-Species Comparison of Human and Non-Human Primate Brain Tissue for Alcohol Abuse

Authors: Sean P. Farris1, Ovidiu Iancu2, Nicole Walter2, Erich J. Baker3, Kathy Grant2, Robert Hitzemann2, R. Adron Harris1, R. Dayne Mayfield1

1 Waggoner Center for Alcohol and Addiction Research, The University of Texas at Austin, Austin, Texas 78759; 2 Oregon Health & Science University, Portland, Oregon 97239; 3 Baylor University, Waco, Texas 76798

Preference: oral presentation (preferred) or poster presentation

Abstract: Addiction to alcohol and other substances of abuse represent serious mental health conditions that adversely affect millions of individuals worldwide. Chronic substance abuse impairs normal brain functions governing positive and negative affectivity. The frontal cortex (CTX) and central amygdala (CEA) are brain regions with known involvement in addiction and stress; however, the molecular pathways impacted within these brain regions remains to be fully elucidated. To better understand the underlying changes that occur within the CTX and CEA we have conducted an unbiased RNA-Seq study for chronic alcohol consumption within human postmortem, and non-human primate rhesus macaque, brain tissue (N=28/brain/species). Leveraging individual variation, our analysis has discerned coordinately regulated gene expression networks related to chronic alcohol consumption that denotes potential conserved systems between the two species. Based on patterns of single-cell gene expression these gene expression networks are indicative of specialized CNS cell subtypes, which may represent specific inter- and intra-brain neural circuits. Integration of additional measures in the macaques demonstrates those gene networks related to alcohol consumption that are also associated with circulating neuroactive steroid precursors. Collectively, our parallel analysis of human and non-human primate CTX and CEA RNA-Seq data shows the system-wide perturbations that occur in relation to chronic and excessive alcohol abuse. The identified systems may assist in the rationale design of pharmacotherapies and biomarkers for the treatment of alcohol use disorder. *Supported by funding to the Integrative Neuroscience Initiative on Alcoholism (INIA) Stress & Neuroimmune consortia from the National Institute of Alcohol Abuse and Alcoholism (NIAAA)*.

1:30pm – 3:00pm **L** **Lunch** Faculty of Medicine, Complutense University (Sala Duran Sacristan)

3:00pm – 3:20pm **S** **Selected Talk Session 4: Adolescent alcohol exposure decreases KDM6B and Arc in the adult amygdala to drive increased anxiety-like behaviors**

Speakers: Evan Kyzar Faculty of Medicine, Complutense University (Sala Duran Sacristan)

Adolescent alcohol exposure decreases KDM6B and Arc in the adult amygdala to drive increased anxiety-like behaviors

Evan J. Kyzar1,3, Huaibo Zhang1,3, Ritabrata Banerjee 1,3, Dadasaheb Kokare1,3, Tara Teppen1,3, Subhash C. Pandey1,2,3

Epigenetic changes in the amygdala are implicated in the effects of adolescent alcohol exposure, inducing lasting changes in chromatin conformation that confer risk for alcohol abuse and anxiety disorders in adulthood. Exposure to adolescent intermittent ethanol (AIE; 2g/kg) between postnatal day (PND; 28-41) increases anxiety-like behavior in adulthood (PND 92) and decreases lysine demethylase 6b (*Kdm6b*) mRNA in the amygdala compared to saline-exposed (AIS) controls. As KDM6B demethylates H3K27me3, AIE rats show increased H3K27me3 levels at the activity-regulated cytoskeleton-associated protein (*Arc*) synaptic activity response element (SARE), which contains a cyclic AMP response element binding protein (CREB) binding site. KDM6B complexes with members of the CREB pathway, and AIE adults show decreased amygdala expression of CREB binding protein (CBP) and phosphorylated CREB (pCREB). Acute alcohol challenge (2g/kg) in adulthood rescues the increased anxiety-like behaviors and decreased Arc and KDM6B protein levels seen in the amygdala of AIE rats. AIE causes increased H3K27me3 and decreased KDM6B, CBP, and H3K27 acetylation (H3K27ac) occupancy at the *Arc* SARE site in the amygdala, and adult alcohol exposure rescues these alterations. *Kdm6b* siRNA infusion into the central nucleus of the amygdala (CeA) in alcohol-naive rats is sufficient to evoke anxiety-like behavior and decreased *Arc* mRNA expression, along with increased H3K27me3 and decreased KDM6B, CBP, and H3K27ac occupancy at *Arc*. In conclusion, adolescent alcohol exposure impacts the dynamic interaction of KDM6B and CREB causing an increase in repressive H3K27me3 marks that inhibit *Arc* gene expression, and the aberrant regulation of this complex is operative in adult anxiety.

1Center for Alcohol Research in Epigenetics, Department of Psychiatry, 2Department of Anatomy and Cell Biology, University of Illinois at Chicago, Chicago and 3Jesse Brown Veterans Affairs Medical Center, Chicago, Illinois, 60612 USA

Funding support: National Institute on Alcohol Abuse and Alcoholism fellowship grant F30AA-024948 grant to EJK and UO1AA-019971 & U24AA-024605 (Neurobiology of Adolescent Drinking in Adulthood project) to SCP.

3:20pm – 3:40pm **S Selected Talks Session 4: Object-brain interface for learning-free steering of behavior in mice**

Speakers: Daesoo Kim Faculty of Medicine, Complutense University (Sala Duran Sacristan)

Object-brain interface for learning-free steering of behavior in mice

Sae-Geun Park1, Yong-Cheol Jeong1, Dae-GunKim2, Min-Hyung Lee1, Anna Shin1, Geunhong Park1, Cheol-Hu Kim2, Phill-Seung Lee2 and Daesoo Kim1

Animals continuously search extant objects to find resources. Here, we report a technique for learning-free steering of behaviors by exploiting a neural circuit that motivates interaction with objects. Photostimulation of medial preoptic area (MPA) neurons that send excitatory signals to the ventral periaqueductal gray (vPAG) induces a strong craving for an object located at the front of the visual field. Inspired by this finding, we devised an MPA-induced drive-assisted steering (MIDAS) technology, in which a head-mounted object and circuit photostimulation can be controlled wirelessly. MIDAS-equipped mice navigate along the programmed path to chase the head-mounted object in novel and fearful situations, but consciously obtain information en route. Thus, the MIDAS system provides a tool for learning-free behavioral control and for studying the neural mechanisms of object exploration and related disorders.

1Department of Biological Sciences, Korea Advanced Institute of Science and Technology, Daejeon, Korea, 305-701; 2Department of Mechanical Engineering, Korea Advanced Institute of Science and Technology, Daejeon, Korea, 305-701. Supported by Samsung Science & Technology Foundation

Measuring short- and long-term sensitization and habituation in Drosophila

Ana Filosevic1, Sabina Al Samarai1, Josipa Kolobaric1 and Rozi Andretic Waldowski1

Drosophila melanogaster due to its many genetic advantages and vast repertoire of complex behaviors is considered the best laboratory animal for identifying genes using forward genetics approach. It seems surprising that simple forms of learning, sensitization and habituation, have not been dissected in Drosophila using behavioral screens. The obstacle has been in the inadequacy of behavioral tests: they are often population based, use between group comparisons and are time consuming.

We have developed two tests that are high-throughput and quantify change in locomotor activity following repeated stimuli that lead either to short- (minutes) or long-term (hours) sensitization or habituation. We measure long-term sensitization or habituation (tolerance) to psychostimulants cocaine and methamphetamine and short-term sensitization and habituation to mechanical disturbance (air puffs). We quantify the response as change in

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locomotor activity using TriKinetics Drosophila monitoring system. The advantage of this system is that it allows the comparison of the amount of locomotion of an individual fly before and after the stimulus. The analysis of individual fly's based responses shows that the direction (habituation versus sensitization) and strength of locomotor response (before versus after) depends on the duration and intensity of a stimulus.
Our results agree with the Dual process theory of response plasticity, indicating that Drosophila can be used as a tool to advance the understanding of the genetic regulation of neural plasticity in mammals.
1Department of Biotechnology, University of Rijeka, Rijeka, Croatia, Founding support: Croatian Science Foundation Research Grant (HRZZ #4920), University of Rijeka Departmental Research Support.

3:40pm – 4:00pm **S Selected Talks Session 4: Measuring short- and long-term sensitization and habituation in Drosophila** Faculty of Medicine, Complutense University (Sala Duran Sacristan)

Speakers: Rozi Andretic Waldowski

Measuring short- and long-term sensitization and habituation in Drosophila

Ana Filosevic1, Sabina Al Samarai1, Josipa Kolobaric1 and Rozi Andretic Waldowski1

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We have developed two tests that are high-throughput and quantify change in locomotor activity following repeated stimuli that lead either to short- (minutes) or long-term (hours) sensitization or habituation. We measure long-term sensitization or habituation (tolerance) to psychostimulants cocaine and methamphetamine and short-term sensitization and habituation to mechanical disturbance (air puffs). We quantify the response as change in locomotor activity using TriKinetics Drosophila monitoring system. The advantage of this system is that it allows the comparison of the amount of locomotion of an individual fly before and after the stimulus. The analysis of individual fly's based responses shows that the direction (habituation versus sensitization) and strength of locomotor response (before versus after) depends on the duration and intensity of a stimulus.
Our results agree with the Dual process theory of response plasticity, indicating that Drosophila can be used as a tool to advance the understanding of the genetic regulation of neural plasticity in mammals.
1Department of Biotechnology, University of Rijeka, Rijeka, Croatia, Founding support: Croatian Science Foundation Research Grant (HRZZ #4920), University of Rijeka Departmental Research Support.

4:00pm – 4:30pm **C Coffee Break** Faculty of Medicine, Complutense University (Sala Duran Sacristan)

4:30pm – 6:30pm **Y Symposium 5: Neuroimmune Genes and Behavioral Response to Drugs of Abuse**

Moderators: Gonzalo Herradon, Amy Lasek Faculty of Medicine, Complutense University (Sala Duran Sacristan)

Speakers: Nigel Atkinson, F Rodriguez De Fonseca, Consuelo Guerri

Symposia Title: Neuroimmune Genes and Behavioral Responses to Drugs of Abuse
Chairs: Amy Lasek & Gonzalo Herradon
16.30 - 17.00 Consuelo Guerri
17.00 - 17.30 Nigel Atkinson
17.30 - 18.00 Gonzalo Herradon
18.00 - 18.30 F Rodriguez De Fonseca

Alterations in the neuronal immune response are associated with several psychiatric disorders, including alcohol and drug addiction. Repeated, chronic exposure to alcohol and illicit drugs such as cocaine and amphetamine induces an immune response in the brain. Converging evidence has demonstrated that manipulation of genes encoding neuroimmune factors can change behaviors related to excessive alcohol and drug use. These data suggest that targeting the innate immune system may be a novel approach in treating addiction and other psychiatric disorders. In this symposium, speakers will present data from multiple species showing that innate immune genes regulate behavioral responses to alcohol and drugs of abuse. This symposium will bring together researchers whose data demonstrate the behavioral relevance of the innate immune system in species ranging from invertebrates to humans, and will highlight the evolutionary importance of this signaling pathway in nervous system functioning.

1. Dr. Consuelo Guerri will show that adolescent binge alcohol exposure in mice induces cognitive deficits,

anxiety-like behavior, and increased alcohol preference in adulthood, effects that are ameliorated by knockout of the Toll-like receptor gene, Tlr4.
Elimination of the TLR4 response prevents ethanol-induced long- term behavioral effects in mice with intermittent ethanol treatment during adolescence Consuelo Guerri, Ph.D., Molecular and Cellular Pathology of Alcohol Laboratory, Research Center Prince Felipe, Valencia, Spain.
Elimination of the TLR4 response prevents ethanol-induced long- term behavioral effects in mice with intermittent ethanol treatment during adolescence
M Pascua M1, J Montesinos 1, M Rodriguez-Arias 2 , J Miñarro2 and C Guerri2
Adolescence binge drinking has been linked to a greater risk-taking and novelty-seeking behavior as well as higher prevalence of drug abuse and risk of relapse. Human studies also revealed that the onset of alcohol use is a reliable predictor of a later problematic use and dependence on alcohol and other drugs. Neuroimmune signaling has been recently involved in alcohol abuse, and our previous results indicate the critical role of the of the immune receptor TLR4 response, in some of the actions of ethanol on the adolescent brain. Using wild-type (WT) and TLR4-deficient (TLR4-KO) adolescent mice treated intermittently with ethanol (3 g/kg) for 2 weeks, we show that binge-like ethanol treatment in adolescent mice promotes long-term cognitive, rewarding and anxiogenic-related behavioral effects along with an increase in alcohol preference . These behavioral effects were associated with short- and long-term alterations in synaptic plasticity along with epigenetic changes in the promoter region of bdnf and fosb and increasing their expression in the mPFC of young adult animals. These results support the participation of the neuroimmune system activation and TLR4 signaling response, since deficient mice in TLR4 (TLR4-KO) are protected against molecular and behavioral alterations of ethanol on the adolescents brain. The findings open new avenues to the development of pharmacological treatments that could normalize the immune signaling responsible for the long-term effects during adolescence., including alcohol abuse and related disorders.
1Molecular and Cellular Pathology of Alcohol Laboratory,Centro de Investigacion Princie Felipe, Valencia, 2 Department of Psychobiology, Facultad de Psicología, Universitat de Valencia, Spain

2. Dr. Nigel Atkinson will show that alcohol activates the Toll innate immune signaling pathway and miRNAs in the fruit fly, Drosophila melanogaster, and that genetic manipulation of this pathway affects ethanol sedation sensitivity and preference in flies.
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/Abstract_Madrid_2017_2.doc

3. Dr. Gonzalo Herradon will introduce two novel cytokines, pleiotrophin (PTN) and midkine (MDK). Using Ptn and Mdk knockout mice, and transgenic mice overexpressing Ptn in specific brain areas, Dr. Herradon will demonstrate that these genes differentially regulate the activation of astrocytes and microglia in response to amphetamine and behavioral responses to several drugs of abuse and alcohol.
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/Herradon_Abstract_IBANGS.docx

4. Dr. Fernando Rodriguez will present data from humans showing that peripheral cytokine levels are associated with the severity of cocaine addiction and that the chemokine fracktalkine is involved in cocaine-associated memories in rats. In addition, he will show associations between plasma levels of chemokines in patients with alcohol use disorder and evidence that chemokines are induced in rats exposed to chronic ethanol.
Chemokines and addiction: from plasma biomarkers to modulators of drug-associated responses Fernando Rodrguez de Fonseca, Ph.D., Unidad Gestin Clnica de Salud Mental, Instituto de Investigacin Biomdica de Mlaga (IBIMA), Hospital Regional Universitario de Mlaga, Mlaga, Spain

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7:30pm – 11:00pm **D Banquet** Colonial Norte (Centro de Ocio Principe Pio - Paseo de la Floirda s/n, 28008 Madrid)
www. http://colonialnorte.net/contacto/

Colonial Norte
Centro d Ocio Principe Pio - Paseo de la Florida s/n, 28008 Madrid

Metro Principe Pio (4 stops from venue)
