Neuroscience

Retreat

2019

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Albert Einstein College of Medicine

Montefiore

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Letter from the Committee

Dear Colleagues,

It is our pleasure to welcome you to the 2019 Neuroscience Department Retreat. It was a privilege to serve as the first student and postdoc led department retreat committee, with the support of our department chair, Dr. Kamran Khodakhah. We are excited for this opportunity to celebrate the fantastic research conducted here at Einstein and to continue to grow as a community. We would like to express our most sincere gratitude to all of our speakers and presenters and we are especially honored to be joined this year by our dean, Dr. Gordon Tomaselli, and our invited external speaker, Dr. Nima Mesgarani.

Finally, this spring, we lost a dear colleague and our department namesake, Dr. Dominick P. Purpura. We are grateful to those that will help celebrate and remember his life during the retreat, and we look forward to honoring his legacy through discussion of our vision for the department.

Kind regards,

Kevin Fisher Heather Snell Noelie Cayla

Agustina Frechou Kelsey McDermott Claire Ward

Monday June 17th, 2019

8:00 AM - 9:00 AM **Check-In/Registration**

9:00 AM - 9:10 AM **Opening Remarks:** Kamran Khodakhah, Ph.D.; Chair, Dominick P. Purpura Department of Neuroscience

9:10 AM - 9:55 PM **Keynote Speaker:**
Research and a Vision for an Integrated Academic Medical Center
Gordon F. Tomaselli, M.D. Marilyn & Stanley M. Katz Dean, Albert Einstein College of Medicine; Executive Vice President and Chief Academic Officer, Montefiore Medicine

9:55 AM - 10:55 PM **Scientific Session I: Developmental Neuroscience**
Chairs: Rayna Birnbaum and Meera Trivedi

9:55 AM Maisha Rahman	The function of a glycosylation enzyme (aman-2) in somatosensory dendrite patterning
10:15 AM Hayden Hatch	Lysine Demethylase 5 (KDM5) as a key regulator of early neurodevelopment and cognitive function in a *Drosophila* model of Intellectual Disability
10:35 AM Peri Kurshan	Studying synaptic development and function using *C. elegans*

10:55 AM - 11:10 AM **Break**

11:10 AM - 12:10 PM **Scientific Session II: Human and Translational Research**
Chairs: Seyandur Tikir and Victoria Sedwick

11:10 AM Pierfilipo De Sanctis	Aging impacts stride-to-stride regulation of gait dynamics: A mobile brain/body imaging (MOBI) study
11:30 AM Frank Soldner	*In vitro* modeling of complex neurological diseases
11:50 AM Jonathan Vacher	Human Visual Segmentation: Experiment and Model

12:10 PM - 3:00 PM **Lunch** (Main building) followed by **Activities by the Lake**

3:00 PM - 3:45 PM **Poster Session I** (All posters up; Presenters at *odd*-numbered posters)

3:45 PM - 4:30 PM **Poster Session II** (All posters up; Presenters at *even*-numbered posters)

4:30 PM – 5:30 PM **External Keynote Speaker:**
Cortical mechanisms of speech perception in noise.
Nima Mesgarani, Ph.D.; Associate Professor, Electrical Engineering Department, Neurobiology and Behavior Program, Columbia University in the City of New York

6:00 PM - 7:30 PM **Wine Tasting** (Main building, outside patio)

7:30 PM - 9:30 PM **Dinner and Activities** (Main building)

9:30 PM – 11:30 PM **DJ, *Select Beer, Wine* & Soda** (Main building, dining room)

11:30 PM – 12:30 AM **DJ, *Cash Bar*** (Main building, dining room)

Tuesday June 18th, 2019

8:00 AM - 9:00 AM **Breakfast** (Main building)

9:00 AM - 10:00 AM **Ethics Session (Mandatory Participation): Considering and Correcting our Unconscious and Cognitive Biases**
Hosted by: Ruben Coen-Cagli and Claire Ward

10:00 AM - 11:00 AM **Scientific Session III: "Operation IDD Gene Team – A new initiative of the Rose F. Kennedy IDDRC"**

10:00 AM Steve Walkley, D.V.M., Ph.D, Director, Rose F. Kennedy Intellectual and Developmental Disabilities Research Center: A Children's Brain Initiative

10:20 AM Abigail Carbonell: Microdeletions in the ANKS1B gene encoding AIDA-1 leads to a novel neurodevelopmental syndrome

10:40 AM Melissa Wasserstein, M.D., Associate Professor, Department of Pediatrics (Pediatric Genetic Medicine) and Department of Genetics; Chief, Division of Pediatric Genetic Medicine, Department of Pediatrics: NYCKidSeq

11:00 AM – 11:15 AM **Break**

11:15 AM – 12:00 PM **In Memoriam: Dr. Dominick P. Purpura**

12:00 PM – 1:00 PM **Departmental Group Discussion** (Auditorium)

1:00 PM – 3:15 PM **Lunch** (Main Building) followed by **Activities by the Lake**

3:15 PM – 4:15 PM **Scientific Session IV: Neuronal Populations**
Chairs: Dylan Festa and Michelle Gulfo

3:15 PM Amir Aschner — Testing the Efficient Coding Hypothesis of Adaptation in Primary Visual Cortex

3:35 PM James Lederman — Neural encoding of reward and locomotion in the ventral pallidum

3:55 PM Luke Sjulson — Hippocampus-acumbens interactions in striatal value coding

4:15 PM – 4:30 PM **Break**

4:30 PM – 5:30 PM **Scientific Session V: Cellular and Molecular Mechanisms**
Chairs: Marta Gronska-Peski and Roland Ferger

4:30 PM Kyle Jensen — Presynaptic LTP and Endocannabinoid-Mediated Metaplasticity in the Hippocampus

4:50 PM Deep Sharma — Premature birth results in dysmaturation of dentate granule neurons and cognitive deficits

5:10 PM Jingqi Yan — Activation of autophagy rescued cognitive and social deficits in Fragile X mice

5:30 PM **Concluding Remarks:** Kamran Khodakhah, Ph.D.; Chair, Dominick P. Purpura Department of Neuroscience

Abstracts

Presenter: Ana Alves Francisco
Title: *Response inhibition in 22q11.2DS: Delayed differentiation between go and no-go stimuli and a marked reduction in the error-related positivity*
Contributing Author(s): Douwe Horsthuis, Julia Denison, John J. Foxe, Sophie Molholm
Poster 1

22q11.2DS is characterized by increased vulnerability for neuropsychiatric symptoms, with approximately 30% of these individuals developing schizophrenia. Behaviorally and clinically, deficits in executive function have been noted in this population, but the underlying neural processes are not well understood. Here, using high-density electrophysiology, we sought to investigate the neural dynamics of inhibition of a prepotent response (a critical component of executive function) in individuals with 22q11.2DS. Eighteen individuals diagnosed with 22q11.2DS (14-35 years old) and 18 neurotypical controls (14-38 years old) participated in a go/no-go task while EEG was recorded. Analyses were focused on the N2-P3 go/no-go response and error-related positivity (Pe), and their relation to psychotic symptoms and cognitive measures of executive function. Behaviorally, individuals with 22q11.2DS were not able to inhibit prepotent go responses as were age-matched controls, with significantly fewer hits and more false alarms. The corresponding N2/P3 responses suggested a delayed differentiation between go and no-go stimuli in the 22q11.2DS group. Moreover, the Pe was significantly reduced, suggesting impaired ability to register errors (i.e., false alarms) in 22q11.2DS. To our knowledge, this is the first study looking at electrophysiological measures of response inhibition in 22q11.2DS. The delayed differentiation between go and no-go stimuli in 22q11.2DS may reflect difficulties not only in inhibiting a motor response, but also in recognizing that no response is necessary. The Pe reduction here observed has also been shown in schizophrenia and suggests a diminished error awareness in 22q11.2DS and, possibly, a consequent difficulty in adjusting response strategies.

Presenter: Amir Aschner
Title: *Testing the Efficient Coding Hypothesis of Adaptation in Primary Visual Cortex*
Contributing Author(s): Adam Kohn
Speaker- Day 2, 3:15PM

The responses of sensory neurons are strongly influenced by fluctuations in environmental statistics and depend on recent experience, a process known as adaptation. Adaptation is a fundamental and ubiquitous feature of sensory encoding, yet how it affects sensory representations is unclear. One theory proposes that adaptation's purpose is to maximize representational efficiency – the amount of information available in the neural code. This longstanding theory has had limited experimental testing in cortex. We hypothesize that neuronal populations and adjust their responses to the statistical structure of recent inputs to maximize representational efficiency. We tested this hypothesis by performing extracellular recordings in primary visual cortex (V1) of awake and anesthetized macaques during the presentation of continuous sequences of oriented gratings in two environments – 1) the probability of any orientation being present was approximately equal; 2) one orientation was overrepresented. We will use several approaches to determine how adaptation affected sensory representations. First, we will measure how the tuning properties and shared variability of V1 neurons change, as these are a proxy for redundancy. We will use information theoretic approaches to quantify the amount of information available in the population responses. Lastly, we will apply decoding strategies to determine if adaptation effects orientation discrimination performance. This work will provide important insight in to how a canonical operation of cortex influences information processing and addresses a longstanding question in the systems neuroscience field about the function of adaptation.

Presenter: Shlomit Beker
Title: Foreseeing the next step: Temporal anticipation in individuals with autism
Contributing Author(s): John J. Foxe, Sophie Molholm
Poster 2

The neural processing of predictable stimuli is significantly facilitated compared to that of non-predictable stimuli. Temporally predictive information modulates neural processing and speeds up the execution of related actions. Autism spectrum disorder (ASD) is a neurodevelopmental condition characterized by impaired social communication and restricted or repetitive behaviors and interests. Clinical observations and behavioral tasks, as well as physiological data, suggests that people with ASD have deficits in applying predictive information to generate expectations. This inability to form expectation based on environmental cues has been interpreted as reduced weighting of prior expectation relative to sensory inputs. Thus, in individuals with ASD, perception of external events is not influenced by the statistics of those events, but instead, is inferred by the current event per

se. Using EEG, we recently found that while typically-developing (TD) children show strong entrainment and anticipation to isochronous sensory events, these are dramatically reduced for children with ASD (Beker et al., in preparation). To characterize the fundamental dynamics that underlie altered anticipation and entrainment in ASD, we presented variations of auditory and visual rhythmic patterns with different degrees of predictive values. Preliminary analysis of the EEG data from 20 participants indicates a reduction in neural entrainment and anticipatory processes in the ASD group (N=10). Impairment in temporal anticipation, a cognitive process built upon highly precise timing, might be due to disruption of white matter microarchitecture in the ASD population leading to impaired neuronal oscillations.

Presenter: Coralie Berthoux
Title: *Molecular mechanisms and functional relevance of activity-dependent plasticity of an associative hippocampal circuit*
Contributing Author(s): Kaoutsar Nasrallah, Pablo Castillo
Poster 3

The dentate gyrus (DG), the principal input region of the hippocampus, plays a key role in memory formation by transforming patterns of cortical inputs into new patterns of output to the CA3 area. Excitatory hilar mossy cells (MCs) send extensive projections (intralamellar, contralateral and along the longitudinal axis of the hippocampus) that synapse onto dentate granule cells (GCs) and establish an associative circuit. Our lab recently reported that physiologically-relevant patterns of MC activity induce a robust long-term potentiation (LTP) whose induction requires postsynaptic BDNF/TrkB signaling. However, whether BDNF is derived from pre- and/or postsynaptic neurons, and what are the downstream signaling pathways remain unknown. Using fluorescent BDNF sensor (BDNF-pHluorin) and cell-specific conditional knock-out, we found that BDNF is released from both MC axonal boutons and GC proximal dendrites following repetitive activation of MCs, suggesting that both anterograde and retrograde BDNF/TrkB signaling are involved in MC-GC LTP. Ongoing studies strongly suggest that protein synthesis is required for MC-GC LTP. Lastly, given the wide distribution of MC axons, it is expected that activity-dependent plasticity of MC-GC transmission significantly contributes to information processing and is essential to most experience-dependent adjustments of brain functions. We found that MC-GC LTP occurred in 2-week enriched environment (EE)-exposed mice, as indicated by LTP occlusion and increase in MC-GC synaptic efficacy in EE-exposed mice compared to SE-exposed mice. Altogether, these findings may represent a novel mechanism supporting learning and memory formation in the hippocampus.

Presenter: Rayna Birnbaum
Title: *Running with Scissors: The Regulation of the Microtubule Severing Enzyme, Fidgetin-Like 2*
Contributing Author(s): Jeetayu Biswas, Robert Singer, David Sharp
Poster 4

Fidgetin-Like 2 (FL2) is a microtubule severing enzyme that localizes to the leading edge of migratory cells and to the growth cone of outgrowing neurites, where it severs dynamic microtubules. Upon knockdown (KD) of FL2 via siRNA, cellular migration velocity increases more than 2 fold. In injury models, FL2 is rapidly upregulated including just 15 minutes after in vivo spinal cord compression and five minutes after an in vitro wound healing assay. We have utilized the increase in migration velocity and outgrowth upon FL2 KD to develop therapeutics for many injury scenarios; however, the regulation mechanisms of FL2 are still widely unknown. We hypothesize that FL2-mRNA is localized and transcriptionally repressed because of the local, cytoplasmic upregulation of FL2 and the presence of a bipartite zipcode in the FL2 mRNA sequence. To investigate if FL2 mRNA localizes, we have utilized single molecule fluorescence in situ hybridization (smFISH) and unbiased polarization analysis (Park et al., 2014). Compared to an mRNA with well characterized leading edge mRNA localization, beta actin, FL2 mRNA showed a more dispersed and less polarized pattern across cells. Since FL2 protein is highly localized to the leading edge and to growth cones -areas where cytoskeletal elements are highly dynamic- we investigated the role of cytoskeletal dynamics in the localized expression pattern of FL2. After treating an actin polymerization inhibitor, we observed a abnormal localization of FL2 protein. Taken together, these findings indicate that FL2 is regulated post translationally in an actin dependent manner.

Presenter: Kelin Brace
Title: *Human Auditory Memory Maintains Representations of Attended and Unattended Streams During Task-Switching*
Contributing Author: Elyse Sussman
Poster 5

In natural listening environments, there are multiple sound streams present. Human listeners are able to alternate attention between distinct sound streams. The goal of this study was to examine the neural mechanisms underlying auditory task switching. We did this by measuring the neural response during task switching and task repeating. We presented participants with ambiguous tone sequences that had multiple possible perceptual interpretations, which allowed participants to perform two different tasks using the same stimuli. Participants were trained to listen for each of the different interpretations of these sounds and perform a unique task with each perceptual interpretation. The task required participants to detect deviations in the duration or intensity of the tones. Electroencephalogram (EEG) was recorded while participants performed each task: half of the trials consisted of a repeated task and half a switching task. In another session, EEG was recorded on the same participants while they watched a movie and passively listened to the same sounds. We extracted time and phase locked event-related potentials (ERPs) from the EEG data, and measured entrainment of the brain to the rhythms present in the sound sequence using Fourier transform. ERP results show that during task switching, task repeating, and sound ignoring, participants detected the regularities and deviations in both possible interpretations of the sounds. This indicates that regardless of task demands, the brain is automatically processing both possible interpretations. This processing of both attended and unattended sound streams may underlie the behavioral ability to rapidly alternate attention between different auditory streams.

Presenter: Abigail Carbonell
Title: *Microdeletions in the ANKS1B gene encoding AIDA-1 leads to a novel neurodevelopmental syndrome*
Contributing Author(s): Changhoon Cho, Jaafar Tindi, Sophie Molholm, Bryen Jordan
Speaker – Day 2, 10:20AM

Neurodevelopmental disorders, including autism spectrum disorder (ASD) and comorbid conditions, have complex polygenic etiologies. Single-gene mutations identified in patients can help define the genetic risk factors and molecular mechanisms that underlie neurodevelopmental disorders. Here we describe individuals with monogenic heterozygous microdeletions in *ANKS1B*, a gene previously predicted to contribute to genetic risk for autism and neuropsychiatric diseases. Affected individuals present with a spectrum of neurodevelopmental phenotypes, including ASD, attention-deficit hyperactivity disorder (ADHD), and speech and motor deficits. Neurons generated from patient-derived induced pluripotent stem cells (iPSCs) show that observed microdeletions lead to loss of the *ANKS1B* encoded protein AIDA-1, a brain-specific protein highly enriched at neuronal synapses. A newly generated transgenic mouse model of *Anks1b* haploinsufficiency recapitulates a range of phenotypes observed in patients, including social behavior deficits, hyperactivity, and sensorimotor dysfunction. Identification of the AIDA-1 interactome using quantitative proteomics reveals protein networks involved in synaptic function and the etiology of neurodevelopmental disorders. Our findings formalize a link between the synaptic factor AIDA-1 and a rare, previously undefined genetic disorder we term *ANKS1B*Syndrome.

Presenter: Ilaria Carta
Title: *Inputs to urocortin3 positive cells in the mouse Perifornical Area and their involvement in infant aggression and parenting*
Contributing Author(s): Brenda Abdelmesih, Victoria Sedwick, Anita Autry
Poster 6

In mice, both mothers and fathers participate in the care of the offspring. However, male mice switch from being aggressive when they are virgin, to being parental after they have mated and expected their own pups. The pup-directed aggressive behavior shown by virgin males correlates with the activity of a subpopulation of hypothalamic cells which are located in the Perifornical Area of the Hypothalamus (PeFA) and express the marker urocortin3 (ucn3). $PeFA^{UCN3}$ cells receive abundant projections from the Paraventricular Hypothalamus (PVH), and the medial preoptic area (MPOA). Within these two areas, two prominent groups of input cells express common markers: AVP (arginin vasopressin) in the PVH, and GAL (galanin) in the MPOA. In order to understand how these two projections modulate the

activity of ucn3 cells to affect pup-directed aggression, we are currently conducting experiments to express GCamp in both genetically defined input populations and record their calcium dependent activity in freely behaving mice, during pup exposure. In parallel, we are investigating changes in peptide-related gene expression in virgin males and fathers with in situ hybridization.

Presenter: Antonio Cibelli
Title: *Role of cholesterol and cytokines on Pannexin1 cell plasma membrane mobility*
Contributing Author(s): E. Scemes, D.C. Spray
Poster 7

Pannexin1 (Panx1) forms large conductance channels permeable to ATP. In the nervous system Panx1 is expressed in both glia and neurons and plays a pivotal role in several pathological conditions such as epilepsy, migraine, inflammation and ischemia. In order to understand factors that regulate distribution of Panx1 in the cell membrane, we have used Fluorescence Recovery After Photobleaching (FRAP) to evaluate mobility of Green Fluorescent Protein (GFP)-tagged Panx1. Cells used for these studies were Neuro2a neuroblastoma cells in which Panx1 was CRISPR-deleted and astrocytes from Panx1 null mice. In initial studies we examined the effects of cholesterol, pro-inflammatory cytokines and cytoskeletal elements on Panx1 cell surface dynamics. Our experiments indicate lower lateral diffusion parameters of Panx1 in cholesterol-depleted cell plasma membrane caused by treatment with lovastatin, methyl-β-cyclodextrin (MβCD) and other cyclodextrins which was restored when cholesterol was added with the cyclodextrin. In addition, we found that the lateral diffusion was increased after Tumor Necrosis Factor-alpha (TNFα) stimulation, although effects were not seen with interleukin (IL)-5 or IL-1B. Panx1 mobiilty was independent of alteration of cytoskeleton as evidenced by insensitivity to Lantruculin B and Nocodozol, although microtubule polymerization by taxol decreased membrane mobility. We conclude from these studies that cholesterol and TNFα modulates Panx1 mobility through effects on membrane organization. Mobility is not greatly restrained by cytoskeletal actions.

Presenter: Charles Crouse
Title: *Reward Prediction Error in a Probabilistic 2-Lever Choice Task*
Contributing Author(s): Saleem Nicola
Poster 8

In order to survive and reproduce, animals must learn which outcomes are associated with cues in their environment, then act on them to obtain food and safety. This learning process is likely mediated by reward prediction error, in which animals compare the expected value from their actions to the actual value, then update their predictions accordingly. Dopamine neurons in the ventral tegmental area encode this prediction error signal in order to guide animals' choices. We developed a probabilistic 2-choice lever task to investigate this process, then used a reinforcement learning model to better understand animals' trial-by-trial decision making. In the future, we aim to record DAergic VTA neuronal activity via fiber photometry to investigate how value representations change over time and explore a possible role for cerebellar projections to the VTA in this process.

Presenter: Eliezyer Fermino de Oliveira
Title: *Nucleus accumbens neurons exhibit cell-type specific coupling to hippocampal inputs*
Contributing Author(s): Lucas Sjulson
Poster 9

The Nucleus Accumbens (NAc) is a key brain area involved in reward-guided behavior and drug addiction. Besides its many inputs from critical areas responsible for cognitive functions (including prefrontal cortex, amygdala, and thalamus), one of prime interest is hippocampus (HPC). The HPC plays a key role in memory formation and generation of sequences representing environmental variables. The HPC-NAc pathway has the potential to be involved in reinforcing representations developed in the HPC, as presented in previous work. However, little is known about how HPC representations are transformed in the NAc and how the NAc performs computations on HPC inputs. Here, we investigated how NAc units respond to network activity from HPC, such as theta oscillations and sharp-wave ripples (SWRs). We split the NAc units into putative cell types (medium spiny neurons (MSN) expressing D1 and D2, tonically active neurons (TAN) and fast spiking interneurons (FSI) and looked at their firing behavior with respect to HPC activity. Our preliminary results show that these cell types respond differentially to theta oscillations and SWRs. FSIs show selective modulation by HPC theta oscillations but not SWRs. TAN, MSN D1 and MSN D2 expressing neurons can be modulated by both theta and SWRs, but surprisingly, the same cells are not generally modulated by both. These

results suggest that cells in the NAc are performing different computations with HPC inputs, and these computations are brain state dependent.

Presenter: Pierfilippo De Sanctis
Title: *Aging impacts stride-to-stride regulation of gait dynamics: A mobile brain/body imaging (MOBI) study.*
Contributing Author(s): Johanna Wagner, Brenda R. Malcolm, Michael J. Crosse, Sophie Molholm, John J. Foxe
Speaker – Day 1, 11:10AM

Walking in the real world requires frequent gait adjustments, an ability that weakens with age. We investigated how young (n=16) and older (n=17) adults regulate strides in order to follow the speed imposed by the treadmill. A Mobile Brain/Body Imaging (MoBI) approach for synchronized recordings of gait kinematics and EEG activity was applied to gain insight into the cortical underpinnings of gait adjustments. We computed stride-to-stride (St-to-St) differences between consecutive strides and identify sudden large changes during steady state walking, classifying differences as deviant (below/above the 15/85 percentiles) and minimal (between 35/65 percentiles) fluctuations. Gait adjustment were defined as events for which St-to-St differences marked as deviant in one direction were followed by deviant differences in the opposite direction. Young and older adults executed on average 35% and 34% deviant strides, respectively. In about 43% of cases, deviant St-to-St fluctuations were immediately followed by deviants in the opposite direction. There was no difference between groups. Furthermore, young adults showed stronger right/left sensorimotor activation coinciding with the stance phase of the left/right foot during gait adjustments. In contrast, results in older adults seem to reveal alteration in hemispheric lateralization of sensorimotor activation and stronger reliance on medial-frontal regions during gait adjustments. The *stance phase* is linked to preparation and execution of forward propulsion and is therefore critical for gait adjustment. Alterations in the contralateral organization of sensorimotor processes and stronger reliance on frontal regions might be linked to the loss of efficient, stable and adaptable locomotion in aging.

Presenter: Fabio Echeverry
Title: *Molecular complexity of electrical synapses at zebrafish club endings*
Contributing Author(s): Sundas Ijaz, Adam Miller, John O'Brien, Alberto Pereda
Poster 10

Electrical synapses directly transfer electrical signals between neurons through gap junction (GJ) channels. Each channel results by the apposition of two hexamers of connexin (Cx) proteins, termed hemichannels. Hemichannels made of the same or different connexins form homotypic or heterotypic GJ channels, respectively. Recent studies at mixed synaptic contacts (club endings, CEs) on the goldfish Mauthner cell revealed that electrical synapses are formed by heterotypic channels, made of presynaptic Cx35- and postsynaptic Cx34.7-hemichannels. Genetic analysis in zebrafish identified two orthologue genes of gjd2 (cx35.1 and 35.5) and of gjd1 (cx34.1 and cx 34.7). To better understand the molecular composition of electrical synapses at CEs, we generated transgenic zebrafish in which these neuronal connexins were tagged with fluorescent proteins. We found that both Cx34.1 and Cx34.7 are expressed in CEs. Double-immunolabeling using anti-Cx34.1 and anti-GFP antibodies in Cx34.7-oxGFP transgenic zebrafish confirmed their co-localization. These findings contrast the suggestion that only Cx34.1 was expressed postsynaptically. Immunochemical analysis using anti-Cx35 antibodies (which recognize the presynaptic connexin) on wild type and Cx34.1-mutant zebrafish revealed no difference in number of CEs and GJs per ending. Electrophysiological recordings on zebrafish Cx34.1 mutants showed electrical and chemical transmission, suggesting that Cx34.7 might compensate for the lack of Cx34.1. This unexpected molecular complexity suggests the existence of distinct functional roles of subsets of GJ channels within an electrical synapse.

Presenter: Roland Ferger
Title: *Implementing a Virtual Reality approach to test Biases in Human Sound Localization*
Contributing Author(s): Miguel Vivar, Elyse S. Sussman, José L. Peña
Poster 11

We have recently started a project in which we want to leverage modern virtual reality (VR) technologies to advance research in human sound localization. This project will test hypotheses on prior biases and adaptive coding that the lab has proposed in birds and humans. The approach will combine uprising visual field VR technology with virtual acoustic stimuli generated from head-related transfer functions (HRTF). Here we present our progress towards implementing these experiments using the HTC Vive VR headset. Participants in these experiments will be asked to localize virtual sound sources in an audiovisual virtual space. Head position and direction can be readily read out from the VR headset throughout the experiment. This approach, which can be controlled via a Python interface, allows the easy implementation of stimulus paradigms that directly test our hypotheses. This approach can also be combined with EEG recordings later on. We expect it to provide a fast "prototyping" platform for testing experimental paradigms in humans that are later performed with birds.

Presenter: Dylan Festa
Title: *Fitting normative probabilistic models of visual coding to single-trial neuronal responses*
Contributing Author(s): Amir Aschner, Adam Kohn, Ruben Coen-Cagli
Poster 12

Recent theoretical advances have revealed that cortical activity can be viewed as the result of probabilistic inference about features of the environment. In primary visual cortex (V1), inference based on a class of models termed Gaussian scale mixtures (GSM) explains a wide range of nonlinear contextual effects. These models have been adapted successfully to obtain quantitative predictions of V1 neural responses; however, fitting the GSM parameters directly requires prohibitive amounts of experimental data. In contrast, purely descriptive models can fit data more easily, but they do not provide unified explanations for different aspects of neural responses (e.g. contextual effects or response variability). To bridge this gap, we propose a general method for fitting inference-based models, which captures the full statistics of single trial spike counts over stimuli and repetitions. We assume that counts are sampled from a mixture model with sparse coefficients. We use as mixture components GSMs with different parameters, pre-trained on natural images (not on neuronal data). We then fit these mixtures to data with a maximum-a-posteriori procedure. On synthetic data, when the ground-truth model is included among the mixture components, few datapoints are sufficient to identify it unambiguously. When the ground-truth is not included, the method approximates it with multiple coefficients. We also tested the method on awake macaque V1 data, and found that it captured well orientation selectivity and spatial contextual effects on firing rate. This work represents a first step towards a more quantitative approach to the understanding of neural coding.

Presenter: M. Agustina Frechou
Title: *Effects of environmental enrichment on hippocampal circuitry and function*
Contributing Author(s): Kelsey McDermott, Elizabeth Wood, Roland Ferger, Tiago Goncalves
Poster 13

How does behavioral experience shape the function of the dentate gyrus (DG)? Exposure to enriched environments (EE) improves performance in behavioral tasks that depend on the DG, such as context discrimination. It also increases the number of newborn neurons added to the DG in the adult brain and can delay the onset of symptoms in mouse models of neurodegenerative diseases. Conversely, decreasing adult neurogenesis results in cognitive deficits. Changes in connectivity patterns have also been observed in the adult-born neurons of mice exposed to EE compared to mice housed in standard conditions. But overall, it is still unknown how the functional properties of the DG change in EE and the mechanisms underlying these changes. We hypothesize that exposure to behavioral experience during adult neuronal development results in changes in the functional patterns of the DG, resulting in altered spatial memory encoding and local network activity in the DG. To evaluate this, we use two-photon microscopy and calcium imaging in head-fixed mice on a self-propelled treadmill to record the activity and spatial tuning of granule cells, in mice exposed to EE compared to standard housing controls. Our preliminary data indicates that spatial tuning and activity are increased in the DG of animals exposed to EE. Furthermore, we also observed an increase in activity levels in CA1. Our short-term goal is to parse out the effects of EE-dependent changes on the hippocampus

and the contribution of ABNs to the observed effects. Understanding these changes and their underlying mechanisms will provide potential targets for therapies in neurodegenerative diseases.

Presenter: Basia Galinski
Title: *Determining how NF-kB signaling contributes mechanistically to selinexor and bortezomib synergy in high-risk neuroblastoma*
Contributing Author(s): Marcus Luxemburg, Jean Hebert, Daniel Weiser
Poster 14

Our proteomic analysis shows that Exportin-1 (XPO1), a nuclear export protein responsible for shuttling tumor suppressors and anti-apoptotic proteins, is overexpressed in neuroblastoma patients with poorer outcomes. XPO1 recognizes nuclear export signals (NES) of numerous (200+) tumor suppressor and growth regulatory proteins and shuttles them into the cytoplasm. Treatment with selinexor, an XPO1 inhibitor, results in nuclear accumulation of cell regulatory proteins like IkB (an NF-kB inhibitor), which leads to growth arrest and apoptosis of malignant cells. NF-kB activity has been associated with inflammation and uncontrolled cell proliferation. The proteasome inhibitor bortezomib has shown efficacy in neuroblastoma by stabilizing regulatory proteins such as IkB, leading to decreased NF-kB signaling. While the combination of these drugs has been studied, debate continues over whether p53 activity is required to produce synergistic effects. We hypothesize use of selinexor will potentiate the effects of bortezomib by increased nuclear retention of IkB that will recognize and halt excessive cellular proliferation and produce cell death independent of p53 status in relapsed and refractory neuroblastoma. We have used dose-response based strategies to determine that bortezomib followed by selinexor treatment is synergistic. We examine how synergy is disrupted through siRNA silencing of IkB that regulates the transcription factor activity of NF-kB. We assess cell lines with wild type p53, mutated p53, and siRNA knockdown of p53 and measure synergy of selinexor and bortezomib. Our work will provide insight into the mechanism of this novel treatment combination, thus informing our future in vivo work with xenograft neuroblastoma mouse models.

Presenter: Marta Gronska-Peski
Title: *Enriched environment acts through FGFRs to increase adult hippocampal neurogenesis*
Contributing Author(s): Jean Hebert
Poster 15

Understanding adult neurogenesis, or generation of new neurons, in the hippocampal dentate gyrus (DG) in mice has potential therapeutic value for age-related memory decline and cell replacement. Fibroblast Growth Factor Receptors (FGFRs)1-3 are differentially expressed throughout the rodent brain but the roles for FGFR-dependent intracellular signaling to guide the generation, maturation and integration of newly born neurons are poorly understood. We previously showed that loss of FGFR1-3 in DG adult-born stem cells and early progenitors leads to decreased stem cell maintenance and progenitor cell proliferation. To address this knowledge gap, we are examining stem/progenitor cell proliferation and dendritic elaboration in the DG of FGFR1-3 conditional mutant mice. We found that loss of FGFR1-3 in neurogenic cells generates defects in cell maintenance and dendritic growth. Stem/progenitor cells also display a defect in proliferation after placement in the enriched environment, suggesting a significant role of FGFR in this process. Using FGFR1 mutants that lack binding sites for the downstream mediators Phospholipase-C gamma (PLCɣ) or Fgf Receptor Substrate (FRS) proteins, we demonstrated that both FRS and PLC-ɣ are non-redundantly required to maintain stem/progenitor cell numbers in the DG. Unexpectedly, FGFR1-PLC-ɣ mutants had a dendritic overgrowth phenotype in immature neurons while FGFR1-FRS mutants displayed no dendritic phenotype, suggesting a novel role for FGFR1-PLCɣ signaling. We are currently conducting experiments to determine which intra- and extracellular pathways differentially affect adult stem cell expansion and the maturation of new neurons which may provide better potential therapeutic targets for reversing deficiencies that lead to age-related memory decline.

Presenter: Julian Guarque-Chabrera
Title: *PNN expression and activity changes around cerebellar Golgi cell in cocaine-induced preference memory*
Contributing Author(s): Isis Gil-Miravet, Marta Miquel
Poster 16

Human studies in drug addicts show that prefrontal impairment is accompanied by cerebellar hyperactivation. Hence, the cerebellum might acquire higher functional relevance when the prefrontal function is compromised by disease or chronic drug use. Perineuronal nets (PNNs) are cartilage-like structures of extracellular matrix molecules that enwrap in a net-like manner the cell-body and proximal dendrites of special subsets of neurons. PNNs stabilize their incoming connections and restrict plasticity. Consequently, they are considered to contribute to the maintenance of drug-induced conditioned memories. In the cerebellar cortex PNNs surround only inhibitory Golgi cells. Previous studies from the lab showed that a lesion in the dorsal cerebellum promote preference towards cocaine-associated cues and increased the expression of PNNs in the infralimbic (IL) cortex. The present research aimed to assess PNN expression and activity changes around Golgi cells in the dorsal cerebellum after an IL deactivation in animals trained to acquire cocaine-induced preference conditioning. Also, Golgi cells expressing PNNs were phenotyped in order to determine whether there is a special population of Golgi cells that express those structures. Finally, we used vGluT1, vGluT2, VGAT, and calretinin expression to estimate changes in neural activity around PNNs. Our results showed that the IL deactivation promoted the acquisition of preference memory. Also, PNNs intensity and vGlut2-mediated activity around cerebellar Golgi cells was increased. Moreover, the expression pattern of Golgi-related proteins in those neurons surrounded by PNNs was modified. These findings suggest that the IL has the capacity to regulate plasticity and activity in the dorsal cerebellar cortex.

Presenter: Michelle Gulfo
Title: *Assessing dopaminergic modulation of an associative circuit within the dentate gyrus*
Contributing Author(s): Pablo E. Castillo
Poster 17

The dentate gyrus (DG) plays a central role in hippocampal function by acting as a gate to the hippocampus, transforming similar cortical inputs into distinct outputs that constitute the main excitatory drive to the hippocampus proper. The DG is implicated in specific forms of learning as well as in temporal lobe epilepsy and anxiety. Hilar mossy cells (MCs) of the DG are uniquely positioned to shape DG information processing due to their relationship with dentate granule cells (GCs), which transmit DG output to the hippocampus proper. MCs mediate an associative circuit with GCs (GC-MC-GC circuit) and also provide feed-forward inhibition to GCs, thus enabling them to affect the excitatory/inhibitory (E/I) balance of inputs to GCs. MC-GC LTP, a novel form of plasticity recently discovered by the Castillo Lab, shifts the input E/I balance toward excitation and increases GC firing. The dynamic properties of the GC-MC-GC circuit, especially modulation of MC inputs and outputs, are not well understood. Evidence supports the presence of dopaminergic inputs and functional dopamine receptors in the GC-MC-GC circuit. In addition, dopaminergic signaling in GCs has been implicated in DG-dependent learning. We hypothesize that dopamine is a critical neuromodulator of the GC-MC-GC circuit and plays a central role in DG-dependent learning. We will investigate the role of optogenetic dopamine release on excitability and synaptic function within this circuit and assess the role of dopaminergic signaling in GCs and MCs in DG-dependent learning. This work can help elucidate mechanisms of DG function in normal physiology and disease states.

Presenter: Hayden Hatch
Title: *Lysine Demethylase 5 (KDM5) as a key regulator of early neurodevelopment and cognitive function in a Drosophila model of Intellectual Disability*
Contributing Author(s): Helen Belalcazar, Sumaira Zamurrad, and Julie Secombe
Speaker – Day 1, 10:15AM

Intellectual disability (ID) disorders affect 2% of the population and are characterized by an IQ score lower than 70 with deficits in adaptive functioning. Approximately 1000 primary ID genes have been identified to-date, with ID patients often presenting with additional syndromic features such as seizures, short stature, and aggressive tendencies. Our research focusses on the KDM5 family of transcriptional regulators, mutations in which account for 1-3% of inherited ID ranging from mild to severe. The molecular mechanisms by which KDM5 proteins impact neuronal function remain largely unknown, leaving patients without effective treatment strategies. Thus, the overarching goal is to understand how

KDM5 contributes to neuronal and transcriptional outputs that influence cognition, and how these are altered by mutations associated with ID. Here, we demonstrate that *Drosophila* serves as a genetically tractable model to investigate the molecular, cellular, and behavioral defects associated with ID. Specifically, we present a demethylase-independent role for KDM5 during early neurodevelopment in regulating neuronal morphology of the mushroom body (MB), a brain structure critical for cognition. We (1) demonstrate that KDM5 is required, independent of its canonical transcriptional regulatory-associated demethylase activity, within immature neurons for proper MB development, (2) show that a subset of *kdm5* ID mutants display similar MB morphological defects, and (3) propose to use Targeted DamID (TaDa), a cell-specific, *in vivo* method to identify differentially-expressed KDM5 target genes within immature neurons of *kdm5* knockdown and ID mutant strains, allowing us to elucidate KDM5 transcriptional regulatory networks critical for neuronal morphology and cognitive function.

Presenter: Daniel Herrera
Title: *Contextual modulation of naturalistic visual texture perception in peripheral vision*
Contributing Author(s): Leonel Gomez, Ruben Coen-Cagli
Poster 18

Central and peripheral vision fulfill different roles in the act of seeing, as clearly reflected by their different information processing capabilities, yet the properties and limitations of peripheral vision are poorly understood. An influential model of vision, the summary-statistics (SS) model, proposes that peripheral vision represents the visual input as a set of local statistics, or equivalently, as local texture. To test this model and advance understanding of peripheral vision, we studied naturalistic texture perception in peripheral vision in human subjects using Portilla-Simoncelli (PS) textures, which fully capture the summary statistics of natural textures. Specifically, we studied how processing of a region of the stimulus is affected by its surroundings. Such contextual modulation is known to be strong in peripheral vision, but prominently missing in the SS model. We found that, in agreement with studies of peripheral perception of objects, cues for segmentation or ungrouping of center and surround stimuli strongly affect contextual modulation. Furthermore, the contextual modulation we observed did not conform to the definition of visual crowding, a specific form of contextual modulation that strongly limits object perception in the periphery. Last, we studied how surround statistics affected contextual modulation. We found a strong effect for Fourier spectrum similarity, but not for similarity of higher-order SS, and also a strong effect of surround naturalness. Our results suggest that V1 plays a key role in peripheral texture perception, and that the SS model should be extended to include gated surround suppression as observed in V1 physiology studies.

Presenter: Kyle Jensen
Title: *Presynaptic LTP and Endocannabinoid-Mediated Metaplasticity in the Hippocampus*
Contributing Author(s): Pablo E. Castillo
Speaker – Day 2, 4:30PM

Within the dentate gyrus of the hippocampus, excitatory hilar mossy cells (MCs) synapse extensively onto granule cells (GCs), the principal cell type and main output of the dentate gyrus. Although information transfer from MCs to GCs is proposed to be important for multiple forms of hippocampal-dependent learning and memory, we know very little about the dynamic properties of MC-GC synapses. Using electrophysiology in acute rat hippocampal slices, our lab recently discovered a novel type of presynaptically-expressed long-term potentiation (LTP) of MC-GC transmission, which involves both PKA and BDNF-mediated signaling. Importantly, MC-LTP is induced by physiologically-relevant patterns of activity. It remains unknown however, if and how this easily-induced form of plasticity can be regulated. Here we show that endocannabinoid (eCB) release from GCs, either before or during MC-LTP induction, can powerfully regulate the magnitude of MC-LTP. This eCB-mediated regulation utilizes distinct branches of the type-1 cannabinoid receptor (CB1R)—such that brief eCB release *during* MC-LTP induction, engages the βγ-limb of the CB1R, to significantly decrease LTP magnitude, and more sustained eCB release, *prior* to induction, engages the α-limb of the CB1R, to also reduce MC-LTP magnitude. Furthermore, when eCBs are released prior-to *and* during MC-LTP induction, MC-LTP is abolished. We also found that MC-GC synapses are under tonic CB1R regulation, which is most likely due to constitutive CB1R semi-activation, in the *absence* of CB1R ligands. This study highlights multiple ways eCBs and CB1Rs can powerfully modulate MC-GC synapses. These phenomena likely play major roles in dentate-dependent forms of learning and memory.

Presenter: Nachiket Kamatkar
Title: *Development of a monomeric inhibitory RNA aptamer specific for FGFR3 that acts as an activator when dimerized*
Contributing Author(s): Matthew Levy, Jean Hebert
Poster 19

Manipulating FGF signaling prior to or during pathogenesis may help curb symptoms associated with FGF signaling related diseases. Currently, however, there are limited therapeutic options available that target the receptors of the FGF signaling pathway. FGFR3 in particular has been implicated in a number of different pathological states including multiple myeloma and developmental disorders. To this end, we developed RNA-based aptamers to target FGFR3. We identified a number of nuclease-stabilized ligands to FGFR3 after in vitro selection. One aptamer specifically, iR3 (*i*nhibitor of FGF*R3*), demonstrated high affinity for FGFR3 and inhibited FGF2 from binding FGFR3. Moreover, upon dimerizing iR3 this new FGF-like aptamer, aR3 (*a*ctivator of FGF*R3*) reversed its role and behaved as an agonist, mimicking FGF2 in its function. I have characterized these molecules on FGFR3 protein, engineered BaF3 cell lines, and in a primary culture model. These studies confirm (1) the specificity of the molecules towards FGFR3 (2) function of the molecules (their agonist/antagonist properties) and (3) efficacy of the molecules to effect downstream signaling of FGFR3.

Presenter: Marcin Kazmierczak
Title: *Handling-induced arousal abolishes the effects of D1, but not D2 dopamine receptor antagonism on cued sucrose seeking in rats.*
Contributing Author(s): Saleem Nicola
Poster 20

While the importance of mesolimbic dopamine for reward seeking has been ascribed to its involvement in reinforcement and motivation, dopamine is also critical for arousal. Cued reward seeking can be particularly susceptible to changes in arousal, since long intervals between cues can promote drowsiness. To investigate this possibility, we trained rats to enter a receptacle in response to an auditory cue to obtain sucrose. Systemic or intra-accumbens administration of the D1 blocker SCH23390 immediately or 1 h before the 2 h operant session did not affect high initial rates of sucrose seeking but caused a gradual extinction-like decline in performance. Handling animals in the middle of the session restored high rates of cue responding. We hypothesized that the vigorous initial performance was caused by arousal elicited by transferring animals to the operant chambers. Consistently, high initial performance was abolished when animals were placed in the operant box after drug administration and allowed to wait for 1 h before the session commenced. In contrast, administration of a D2 blocker haloperidol 1 h before the session caused an immediate decrease in sucrose seeking that was not affected by handling. Unlike handling, caffeine alleviated the effects of either drug and was more efficacious when co-administered with haloperidol. While both drugs increased immobility, only SCH23390-treated animals assumed curled-up and ball positions characteristic of sleep. We conclude that a gradual decrease in arousal, rather than an extinction-like phenomenon, causes the within-session decline in cued reward seeking after administration of D1, but not D2 receptor antagonists.

Presenter: Joanna Krzyspiak
Title: *Neovascularization for Optimal Survival of Neural Transplants*
Contributing Author(s): Jingqi Yang, Basia Galinski, Pablo Lituma, Daniel Weiser, Suzanne Zukin, Pablo Castillo, Kamran Khodakhah, Jean Hebert
Poster 21

The transplantation of neural stem cells holds great promise for improving function in the injured and aging brain. There is growing evidence in the field that supporting cell types may be required to facilitate the success of a transplant in contrast to transplanting pure populations of cells. Specifically, there is evidence that neovascularization may be critical for transplant cell survival. Our preliminary studies with transplants of embryonic forebrain cells into the young adult neocortex of unaffected and stroke-affected mice suggest that vascular endothelial precursors may be required in the transplant cell population for efficient survival of the neural precursors and the neurons they generate. We observe that within transplants on the stroke affected side, blood vessels primarily develop from donor-derived cells, in contrast to the control side, and appear to fuse with the host vasculature. We are currently determining the importance of including vascular cells with neural cells when transplanting to young,

middle-aged, and old mice. To determine the requirement of vascular precursor cells for enhanced cell survival, we are currently experimenting with two mixes of cell types for transplantation: one that contains the complete heterogeneous population of cells harvested from mouse embryonic cortices and one that lacks specifically the vascular precursor cells. We are also experimenting with larger stroke models to determine the effect of lesion and transplant size on the requirement of donor-derived vascular progenitor cells. These studies are directly relevant to the effective use of neural cell transplants in future clinical trials.

Presenter: Peri Kurshan
Title: *Studying synaptic development and function using C. elegans*
Speaker – Day 1, 10:35AM

Defects in the proper development and function of synapses lead to neurodevelopmental disorders such as Autism and Intellectual Disability, however the molecular mechanisms underlying these processes are still largely unknown. We use the nematode *C. elegans*, which has a simple and stereotyped nervous system and whose connectome has already been fully mapped out, to investigate the conserved molecular mechanisms of synapse development. In particular, we study how presynaptic components including cell adhesion molecules, active zone scaffold proteins, calcium channels and synaptic vesicles arrive at the synapse and form a mature and fully functional presynaptic compartment. We combine the power of worm genetics with high resolution imaging and optical physiology readouts to elucidate the role of key molecules. These approaches have led to discoveries suggesting that the role of synaptic cell adhesion molecules such as Neurexin may be different than initially hypothesized, since its role in presynaptic development is independent of extracellular activation and downstream of other initiating factors.

Presenter: James Lederman
Title: *Neural encoding of reward and locomotion in the ventral pallidum*
Contributing Author(s): S. Lardeaux, S.M. Nicola
Speaker – Day 2, 3:35PM

The ventral pallidum (VP) receives a major inhibitory input from the nucleus accumbens (NAc), and both structures are components of the basal ganglia essential for translating limbic sensory, value and motivation signals into motor output. How they do so is unknown. In this study we ask how neuronal firing in the VP relates to both spontaneous and reward-directed locomotor movements. Rats were food-restricted and trained on a discriminative stimulus (DS) task. The DS was an auditory cue, which directed the rat to approach and press a lever to obtain 10% sucrose reward. Trained animals were implanted with microelectrode arrays in the VP, allowing multi-unit recording of neuronal activity, while video tracking of head-mounted LEDs enabled detection and measurement of locomotion. Approximately half the recorded neurons were excited by DS presentation. Moreover, DS-related firing was positively correlated with the mean speed of the subsequent movement towards the lever, and negatively correlated with the initial starting distance from the lever. During inter-trial intervals, a population of neurons showed changes in activity tightly aligned with initiation and cessation of spontaneous locomotor movements. These results demonstrate a previously unknown role for the ventral pallidum in locomotor control, and provide a starting point for further interrogation of the NAc-VP projection.

Presenter: Garrett Lee
Title: *Understanding the development, plasticity, and function of synaptic asymmetry in C. elegans*
Contributing Author(s): Leo Tang, Steven Cook, Scott Emmons, Hannes Buelow
Poster 22

The human brain asymmetrically processes faculties across the left and right hemispheres, and impaired functional lateralization has been implicated in depression, schizophrenia, and autism spectrum disorders. However, whether asymmetric connectivity exists in anatomically symmetric structures and what its function may be remains largely unknown. Serial electron micrograph (EM) reconstruction of the *C. elegans* connectome revealed that the chemosensory ASE neurons exhibit left-right asymmetry in their connection to the odorsensory AWC neurons. While morphologically symmetric, ASEL and ASER exhibit differential gene expression and function, sensing Na^+ and Cl^-, respectively. To confirm the EM data as well as study the connection's development, maintenance, plasticity, and function, we created a fluorescent reporter of this connection using *in vivo* Biotin Labeling

of Intercellular Contacts (iBLINC). iBLINC analysis confirmed that ASEL tends to form more synaptic contacts onto AWC than ASER. Genetic conversion of both ASE neurons to an ASEL fate reversed the asymmetry. In contrast, neither changing both ASE neurons to the ASER fate nor symmetrizing the postsynaptic AWC neurons displayed altered synaptic lateralization. Interestingly, the left-right lateralization is changed when *C. elegans* are exposed to different salt environments, suggesting that the lateral connectivity is plastic. Finally, we identified genes in the insulin signaling pathway required to establish or maintain the ASE/AWC synaptic asymmetry. Further experiments will assess the functional relevance of this connectivity on olfaction by quantifying synapses after analyzing worms' behavior in chemotaxis assays. In analyzing this connection, we aim to understand fundamental aspects of the formation and function of asymmetric connectivity.

Presenter: Pablo Lituma
Title: *Presynaptic NMDA receptors contribute to short-term plasticity at hippocampal mossy fiber-CA3 synapses*
Contributing Author(s): Hyung-Bae Kwon, Rafael Lujan, Pablo E. Castillo
Poster 23

Neurotransmitter release is a highly regulated process that controls the strength of neuronal communication. Presynaptic Ca^{2+} rise is a key component of this process not only for triggering action-potential driven transmitter release, but also for facilitating transmitter release during repetitive activity. Hippocampal mossy fiber (MF) synapses, which carry the main excitatory input to the hippocampus proper, express uniquely robust activity-dependent facilitation. Although the molecular mechanisms underlying this form of short-term plasticity remain poorly understood, there is evidence that glutamate autoreceptors may participate. Here, we test the hypothesis that preNMDARs likely due to their high Ca^{2+} permeability contribute to robust short-term plasticity at MF synapses. To identify and assess the functional role of preNMDARs we used immune-gold labeling electron microscopy, electrophysiology, selective pharmacology, molecular knockdown, optogenetics, and calcium imaging in acute rodent hippocampal slices. Together, our findings reveal that during repetitive activity preNMDARs facilitate glutamate release from MF boutons and thus, may contribute to dentate gyrus-CA3 information transfer.

Presenter: Stefano Lutzu
Title: *Bidirectional plasticity of NMDA receptor-mediated transmission is associated with different postsynaptic calcium dynamics*
Contributing Author(s): Karina Alvina, Pablo Castillo
Poster 24

NMDA-type glutamate receptors (NMDARs) are crucial for excitatory transmission, synaptic plasticity and cognitive processes such as learning and memory. While thought to be a static entity, NMDARs have been shown to undergo bidirectional activity-dependent long-term plasticity (NMDAR-LTP/LTD) at several key brain areas. However, the molecular basis of NMDAR-plasticity remains largely unexplored. In the hippocampus, a key structure for learning and memory, the mossy fiber-to-CA3 pyramidal cell (MF-CA3) synapse, expresses robust, bidirectional NMDAR-plasticity which is elicited with physiologically-relevant burst-activity. Both NMDAR-LTP and LTD depend on postsynaptic calcium rise but the calcium requirements differ –e.g. NMDAR-LTP, but not NMDAR-LTD, requires calcium release from internal stores. We therefore hypothesize that different calcium dynamics determines the bidirectionality of NMDAR-plasticity. To test this hypothesis, we combined electrophysiology with 2-photon microscopy in acute rat hippocampal slices and measured postsynaptic calcium transients (CaTs) in CA3 pyramidal neurons. At thorny excrescences (TEs), the postsynaptic target of MFs, CaTs were significantly larger during the induction of NMDAR-LTP than NMDAR-LTD. Furthermore, depletion of calcium released by the internal stores, or blockade of metabotropic glutamate receptor type 5 (mGluR5), which are required for the induction of NMDAR-LTP, significantly reduced the difference in CaTs associated with NMDAR-LTP and LTD. In contrast, blockade of mGluR1 receptors, required for NMDAR-LTD did not affect the difference between CaTs associated to NMDAR-LTP and LTD, suggesting a different mechanism of action of mGluR1 and mGluR5. Consistent with a two-threshold hypothesis, our findings indicate that distinct postsynaptic calcium levels likely determines the bidirectionality of NMDAR-plasticity at MF-CA3 synapses.

Presenter: Sean McCutcheon
Title: *Connexin 43-mediated miRNA Changes in Astrocytes Promote Glioblastoma Invasion*
Contributing Author: David C. Spray
Poster 25

Glioblastoma multiforme (GBM) is the most aggressive and deadly CNS cancer. Its dismal prognosis is attributed to difficulty of resection, resistance to traditional chemotherapeutics, and invasion along the brain vasculature. Finding mechanisms by which GBM invades is critical for development of more effective surgical protocols and adjuvant therapies. Invasion of GBM involves alteration of non-cancerous cells, such as endothelial cells and astrocytes, in the tumor microenvironment toward a cancer-friendly phenotype. Evidence suggests post-transcriptional regulation by miRNAs may be the culprit. Astrocytes express gap junction proteins Connexin 30 and Connexin 43. Here we present evidence that functional Cx43 homotypic gap junctions form between GBM and astrocytes *in vitro*, and presence or absence of Cx43 causes a shift in miRNA profile for cells cocultured with the GBM cell line U87-MG. Further, presence/absence and functionality of astrocyte-GBM Cx43 channels alter the invasion potential of GBM in vitro and ex vivo. Our data indicate that GBM-GBM Cx43 junctions limit invasion, while astrocyte-GBM junctions promote invasion, consistent with literature. Previous studies have highlighted the potential transfer of miRNAs from GBM to astrocytes by means of gap junction channels, however it is widely accepted that gap junctions have a size exclusion of approximately 1 kDa, and miRNAs are on the order of 14 kDa. From here we seek to address the question of how gap junctions are implicated in the expression or transfer of miRNAs whether by direct passage through Cx43 junctions, exosomal release and uptake, or cell-cell endocytosis of Cx43 itself.

Presenter: Kelsey McDermott
Title: *Microglia and Complement Signaling in Dendritic Morphogenesis and Behavioral Output of Adult-born Neurons*
Contributing Author(s): Tiago Goncalves
Poster 26

The dentate gyrus (DG) of the hippocampus, one of the few locations of adult neurogenesis, allows us to study new cells integrating into an existing circuit. The dendrites of dentate granule cells (DGCs) develop through trial and error, but the underlying mechanisms and functional implications of this growth process are not known. Microglia, the resident immune cells in the brain, prune synapses and eliminate apoptotic newborn neurons through phagocytosis. While microglia are known to affect adult neurogenesis, studies have focused on their role in cell survival rather than the development of adult-born neurons. Their contribution to the dendritic development of these neurons is not well understood. We hypothesize that microglia are necessary for the proper morphological and functional maturation of adult-born neurons in the dentate gyrus. We are investigating the role of microglia in adult-born DGC development through a combination of cell labeling, ablation, and in vivo imaging. First, we are studying the effects of microglia ablation on the dendritic complexity of adult-born DGCs. We are also exploring the molecular mechanisms that underlie pruning in the DG through the complement pathway, which has been implicated in synaptic pruning. Finally, we will study how remodeling of dendrites and synapses by microglia translates into functional and behavioral outputs. Overall, we expect this work to elucidate the role of microglia in the development of adult-born neurons. We also anticipate that a better understanding of the mechanisms enabling adult-born neurons to properly integrate into the adult circuit will enhance future strategies for neuronal repair.

Presenter: Hannah Monday
Title: *Protein synthesis supports presynaptic structural plasticity at excitatory hippocampal mossy fiber presynapses*
Contributing Author(s): Young Yoon, Robert Singer, Pablo E Castillo
Poster 27

Activity dependent changes at synapses critically underlie information storage in the brain. Protein synthesis is required for long-lasting plastic changes of the postsynaptic compartment, but whether and how local protein synthesis contributes to presynaptic structure and function remains unclear. We examined the excitatory hippocampal mossy fiber (MF)-CA3 synapse which expresses robust presynaptic plasticity and has notably large and complex boutons. Using electrophysiology, we first confirmed that long-term potentiation (MF-LTP) requires protein synthesis and show that transected MF axons are capable of MF-LTP, suggesting that protein synthesis in the soma is not required for

plasticity. Using high-resolution microscopy, we found that MF-LTP is associated with an enhancement of bouton volume that was also protein synthesis-dependent. Importantly, we demonstrate that MF boutons are capable of synthesizing actin protein using a cell-specific Halotag labeling strategy. By selectively genetically labeling ribosomes in the presynaptic neuron, we also show that MF boutons and axons contain ribosomes. Lastly, given that the Fragile X mental retardation protein (FMRP), a critical regulator of translation, is highly expressed in mossy fiber boutons, we tested whether conditional presynaptic KO of FMRP results in changes in bouton structure. Presynaptic KO resulted in a loss of the activity-dependent increase in bouton volume. Together, these results point to an important role of presynaptic protein synthesis in the regulation of boutonal structure and function at diverse synapse types in the mature brain. This ability could support input-specificity of presynaptic plasticity and may represent a novel mechanism supporting memory formation in the hippocampus.

Presenter: Kaoutsar Nasrallah
Title: *Activity-dependent LTP at mossy cell-dentate granule cell synapse is mediated by the non-conventional adenosine/A2AR retrograde signaling*
Contributing Author(s): Yuki Hashimotodani, Andres Chavez, Michelle Gulfo and Pablo E. Castillo
Poster 28

The dentate gyrus, a major input area of the hippocampus, contains two types of excitatory neurons: dentate granule cells (GCs) and hilar mossy cells (MCs). MCs receive inputs from GCs and project back to GCs locally (intralamellar), contralaterally, and along the dorsoventral axis of the hippocampus, thereby establishing an associative positive-feedback loop (GC-MC-GC). However, how MCs contribute to dentate gyrus function remains poorly understood. We recently reported that MC-GC synapses express a robust presynaptic form of long-term potentiation (MC-GC LTP), which is NMDA receptor-independent and requires postsynaptic BDNF/TrkB and presynaptic cAMP/PKA signaling. MC-GC LTP requires retrograde signaling but the identity of the retrograde signal remains unknown. While investigating the synaptic learning rules of MC-GC LTP in rodent hippocampal slices, we discovered that theta-burst firing (TBF) of a single GC by direct depolarization is sufficient to induce plasticity in an input-selective manner (MC but not perforant path inputs undergo LTP). Using this single cell manipulation, we found that conventional retrograde messengers such as endocannabinoids and nitric oxide play no role in MC-GC LTP. However, we discovered that adenosine/A2A receptor signaling is necessary and sufficient for MC-GC LTP, while A1 receptor activity dampens LTP induction. Interfering with adenosine release from GCs completely abolished the plasticity. Altogether, these results strongly suggest that adenosine may act as a retrograde messenger to mediate MC-GC LTP through A2A receptor activation. By increasing the strength of MC inputs onto GCs, TBF-LTP could facilitate information transfer between dorsal and ventral hippocampus, and contribute to memory formation and epilepsy. Supported by R01 grants DA017392, MH081935 to PEC and the Fondation pour la Recherche Médicale (Postdoctoral Fellowship for a research abroad) and the Fondation Bettencourt Schueller (Prix pour les Jeunes Chercheurs 2016) to KN.

Presenter: Maritza Onate
Title: *Neuroanatomical characterization of cerebellar monosynaptic projections to the ventral midbrain*
Contributing Author(s): Victoria Lovallo, Navida Wazeed, Kamran Khodakhah
Poster 29

Increasing evidence show that the cerebellum, in addition to its role in planning and execution of movement, also contributes to cognitive functions. However, the detail circuitry behind these functions is still not well understood. Our laboratory has showed that the cerebellum sends monosynaptic excitatory projections to different areas in the ventral midbrain. The deep cerebellar nuclei (DCN) targets the substantia nigra (both *pars compacta* (SNc) and *pars reticulata* (SNr)), particularly dopaminergic and non-dopaminergic neurons, driving its activity on a fast time scale, and the ventral tegmental area (VTA), where cerebellar inputs are rewarding and required for a social behavior task. However, a number of questions regarding the neuroarchitecture of these circuits remain unresolved. Using a combination of anterograde and retrograde transynaptic viral tracing in mice we studied these cerebellar projections. We injected AAV.Cre virus in the DCN of *RCE:loxP* mice, to identify all the postsynaptic targets of the cerebellum through EGFP expression. With this approach, we studied the spatial distribution of targeted cells along the ventral midbrain. To study where in the DCN these projections originated from, we performed retrograde tracing using G-deleted rabies virus in DAT-Cre

and GAD-Cre mice to identify the cellular identity of Cb-targeted neurons, and to establish the spatial organization of DCN-projecting neurons. We found that neurons from different regions of the DCN projected to dopaminergic and GABAergic neurons in the different regions. Further delineation of the neuroarchitecture of these circuits would contribute to our understanding of the mechanisms that underlie different cerebellar functions.

Presenter: Kristin Palarz
Title: *Cerebellar Dysfunction in Spinocerebellar Ataxia Type 3*
Contributing Author(s): Andreia Carvalho, Patricia Maciel, Kamran Khodakhah
Poster 30

Ataxia (uncoordinated movement) is a debilitating disorder that interferes with a patients' ability to perform activities of daily living. Ataxia is often caused by dysfunction of the cerebellum, a brain area involved in motor coordination and maintenance of balance. Our laboratory has shown that regularity of the cerebellar output nuclei can predict disability in several mouse models of ataxia. Spinocerebellar ataxia type 3 (SCA3) is the most common dominantly inherited ataxia, caused by a trinucleotide repeat expansion of the Ataxin 3 gene. To better understand the role of the cerebellum in SCA3, we performed behavioral, electrophysiological, and proteomic analysis of the cerebellum in a SCA3 mouse model. To assess motor performance, mice were assessed on the disability scale and parallel rod floor test, demonstrating that SCA3 mice have a progressive ataxic motor phenotype. Using *in vivo* and *in vitro*recordings, we show irregular firing of the cerebellar output nuclei and the Purkinje cells (the principle neuron of the cerebellar cortex). To further elucidate how this cerebellar dysfunction arises, we performed a quantitative proteomic analysis on cerebellar lysates from SCA3 mice and littermates. Using a stringent filter, the proteins identified are part of a network that involved the serotonin 1A receptor, which is currently being investigated as a therapeutic target. Using less stringent filters, the altered proteins are identified to be involved in several pathways, including Protein Kinase A and Nitric Oxide signaling, amongst others. Future analysis will explore the dataset to gain insights into the pathogenesis of SCA3.

Presenter: Morgan Porch
Title: *The S1166A KI mouse exhibits impaired synaptic plasticity and cognition*
Contributing Author(s): JY Hwang, AE Chavez, RS Zukin
Poster 31

NMDA receptors (NMDARs) are glutamate-gated ion channels that are enriched at excitatory synapses, where they are strategically positioned to play a crucial role in regulation of synaptic function. A unique feature of NMDARs is their high permeability to Ca^{2+}, which is essential for synaptogenesis, plasticity of neural circuitry, and learning and memory. We recently identified serine 1166 (Ser1166) in GluN2B to be the molecular target of PKA phosphorylation relevant to PKA-dependent NMDAR Ca^{2+} permeability. The impact of loss of Ser1166 on NMDAR-dependent synaptic plasticity and cognition is, as yet, unclear. To address this issue, we generated a S1166A KI mouse by means of CRISPR/cas technology. We found that whereas synaptic plasticity in the form of HFS-LTP was normal in the KI mice, TBS-LTP at the CA1 synapse was nearly abolished in slices from KI mice. A hypothesis under consideration is that KI mice lack the PKA-dependent, NMDAR-mediated Ca^{2+} influx required to insert Ca^{2+}-permeable AMPARs. We found that, upon induction of TBS-LTP, AMPARs EPSPs are inwardly rectifying and that the LTP is blocked by inhibition of Ca^{2+}-permeable AMPARs. TBS-LTP in KI mice was rescued by activation of PKA which leads to the insertion of Ca^{2+}-permeable AMPARs. We also found that visual cognition was markedly impaired in KI mice. Thus, loss of a single site within the GluN2B subunit not only eliminates PKA-induced Ca^{2+} signaling in spines, but greatly diminishes synaptic plasticity in the form of TBS-LTP and visual cognition.

Presenter: Maisha Rahman
Title: *The function of a glycosylation enzyme (aman-2) in somatosensory dendrite patterning*
Contributing Author(s): Carlos A. Diaz-Balzac, Hannes E. Bülow
Speaker – Day 1, 9:55AM

Dendrite development is essential for the transmission and processing of sensory stimuli. Abnormalities in dendrite morphology have been found in several neurological disorders. We use the *C. elegans* PVD neurons, which have complex menorah-like dendritic arbors, as a model to study the genes involved in dendritogenesis. Studies have shown that a conserved cell-adhesion complex, comprised of MNR-1/Menorin and SAX-7/L1CAM, acts from the skin to regulate PVD dendrite branching through the transmembrane receptor, DMA-1/LRR-TM. Recently, we determined that *Leukocyte Cell-Derived Chemotaxin 2*, or *lect-2/Chondromodulin II*, also functions to pattern PVD dendrites. In order to identify genetically interacting factors of LECT-2/ChM-II, we performed a forward genetic screen to isolate modifiers of a *lect-2/ChM-II* hypomorphic allele. We determined that mutations in *aman-2/Golgi alpha-mannosidase II*, an enzyme that is required for the formation of complex N-glycans, enhances the severity of the *lect-2/ChM-II* and *mnr-1/Menorin*hypomorphic phenotypes, but looks wildtype on its own. AMAN-2 acts cell-autonomously to rescue defects in PVD, suggesting that N-glycosylation of a 'menorin' complex component in PVD itself, such as DMA-1/LRR-TM, may be essential. To test this hypothesis, we first performed Western blot analysis after treating proteins with a reagent that cleaves all N-glycans. We established that DMA-1/LRR-TM is glycosylated *in vivo*. We aim to test our candidate by selectively mutating its N-glycosylation sites. We will further characterize the role of *aman-2/GM-II* in the binding of the 'menorin' complex in future pull down assays to gain a fuller understanding of this novel factor and its *in vivo* role in dendrite development.

Presenter: Cindy M. Reyes
Title: *The role of nucleus accumbens proximity encoding in target selection*
Contributing Author(s): Saleem M. Nicola
Poster 32

The preference for rewarding options that are nearby rather than distant, known as "proximate reward bias," is well established in humans and animals, but the neural basis is unknown. Proximity to an approach target is strongly encoded by neurons in the nucleus accumbens (NAc) in animals performing cued approach tasks and this NAc proximity signal drives proximate reward bias by promoting impulsive approach to the nearest rewarding option even when it resulted in greater effort expenditure and delay to reward. However, due to proximity of levers in previous studies, target location could not be fully disentangled. In order to further understand the role of NAc neuronal activity in proximate reward bias I will use a same reward, different target discriminative stimulus task. We will determine whether cue-evoked neuronal firing is related to the specific cue (left vs right lever) or to the animal’s proximity to the cue. Consistent with previous work, analysis of neuronal data does not show any distinguishable difference in the cue evoked excitations when animals respond on the active or inactive lever, although magnitude of cue evoked excitations is smaller when animals do not respond to a cue. Additionally, cue evoked excitations are similar in magnitude when animals are near the active or inactive lever at cue onset while the magnitude is lower when animals are far from both. Video tracking data will be further used to determine the relationship between cue evoked neuronal firing in the NAc and other factors known to influence cue evoked excitations.

Presenter: Stacy Roudabush
Title: *Genetic Reduction of Rictor Corrects Aberrant Cofilin Signaling in Fragile X mice*
Contributing Author(s): Yan JY, Vasquez BC, Zukin RS
Poster 33

Fragile X syndrome (FXS) is one of the most common heritable forms of intellectual disability and the leading genetic cause of autism. The neuroanatomical hallmark of Fragile X is an increased density of immature spines, a factor thought to underlie synaptic dysfunction and impaired cognition in Fragile X mice. Our laboratory previously identified cofilin, an actin depolymerizing agent that regulates spine structure, and its upstream effector Rac1, a Rho GTPase, to be dysregulated in Fragile X mice and casually related to dendritic spine abnormalities. Because mTORC2 is thought to be upstream of Rac/cofilin signaling and actin polymerization, we hypothesized that genetic reduction of Rictor, a defining component of mTORC2 and binding partner critical to mTOR function and stability, might rescue synaptic defects in Fragile X mice. Since Rictor-null mice are embryonically-lethal, we generated Fmr1 KO mice in which Rictor could be conditionally knocked out, Fmr1 KO Rictor conditional knockout

(cKO). In preliminary experiments, we showed that delivery of lentivirus synapsin-Cre into the somatosensory cortex of neonatal Rictor cKO mice successfully knocked out Rictor protein and is sufficient to return phosphorylated (overactive) cofilin and components of the Rac/PAK pathway to wildtype levels. Ongoing studies will determine if cKO of Rictor in layer V of the somatosensory cortex of neonatal Fmr1 KO mice is sufficient to rescue aberrant dendritic spine morphology and density. Future studies will determine whether cKO of Rictor can rescue aberrant synaptic plasticity and somatosensory-mediated behavioral phenotypes in FXS mice.

Presenter: Todd Rubin
Title: *White matter microstructural changes in the corpus callosum and external capsule following highly repetitive subconcussive injury in the awake adolescent rat*
Contributing Author(s): Wouter Hoogenboom, Peter Davies, Craig Branch, Michael Lipton
Poster 34

In contact sports players can accumulate thousands of subconcussive hits to the head over the course of a single season, accumulating over a lifetime. Recent evidence has shown that these hits are associated with cognitive deficits and CNS symptoms independent of concussion and may lead to long term behavioral and cognitive changes associated with chronic traumatic encephalopathy (CTE). While various animal models have been developed to reproduce the biomechanical, neurological, and pathological aspects observed in human concussive injury, subconcussive injury has been largely unexplored. Here we developed a new model of highly repetitive subconcussive injury ¬to explore and characterize the changes in white matter and underlying mechanisms of injury. Young adult (~p35) rats underwent subconcussive TBI induction without scalp incision or anesthesia using a Leica Impact One^{TM} Impactor. Animals received either 10 hits/day (1 minute apart) or 20 hits/day (30s apart), to the left parietal bone, midway between the ear and bregma, every day for 7 days, totaling 70 or 140 hits. Sham animals underwent the same procedures but received no impacts. All animals underwent diffusion tensor imaging (DTI) prior to injury and 24 hours after the final injury. Animals receiving 140 total hits were followed longitudinally with follow-up imaging over the course of 1 month following injury. Animals were then sacrificed and sectioned for immunohistochemistry. The corpus callosum, and bilateral external capsule were manually traced and quantified for average fractional anisotropy (FA). Trauma animals had reduced longitudinal increases in FA, and prolonged microglial activation compared to controls.

Presenter: Chaitali Saqcena
Title: *Autophagy modulation as therapy for Niemann-Pick C1 disease*
Contributing Author(s): Xin Huang, Bin Cui, Kostantin Dobrenis, Steven U. Walkley
Poster 35

Niemann-Pick disease type C1 (NPC1) is a lysosomal storage disease. Lack of NPC1 function leads to widespread endolysosomal accumulation of unesterified cholesterol as well as GM2 and GM3 gangliosides in brain. Studies from several labs, including our own, have demonstrated increases in LC3-II/LC3-I in the brains of Npc1 mice suggesting abnormal regulation of autophagy. Conflicting views on manipulating the autophagy process (stimulation vs. inhibition) to reduce lysosomal cholesterol accumulation led to our initial studies on possible treatment strategies using 3 small molecule autophagy inducers (AKT inhibitor, trehalose; AMPK activator, metformin; and mTORC1 inhibitor, afinitor) and comparing the impact of these drugs on disease correction to the documented therapeutic agent, 2-hydroxypropyl-β-cyclodextrin (HPBCD). BALB/cNctr-Npc1^{m1N}/J, (NPC1) mice were administered 3% trehalose, 200 mg/kg metformin and 2 mg/kg afinitor independently. Biochemical analysis of cerebral cortex in treated Npc1 mice demonstrated no effect on normalizing increased LC3-II levels or Phospho-S6 ribosomal protein levels (mTORC1 activity) in all three studies, however trehalose caused a modest decrease in disease-elevated levels of p-AKT. None of the 3 autophagy inducers improved body weight loss or delayed/reduced neurological disease, nor did they decrease cholesterol and ganglioside storage in brain and liver in NPC1 mice. In comparison, 4000 mg/kg HPBCD improved weight gain, delayed neurological features, reduced cholesterol and ganglioside storage in brain and liver and essentially normalized LC3-II levels. Our studies suggest that stimulating autophagy in NPC1 disease does not reduce cholesterol or ganglioside storage in brain and liver or attenuate development of neurological symptoms. Additional studies are in progress.

Presenter: Victoria Sedwick
Title: *CRFR2 expressing neurons of the amygdalohippocampal area regulate infant-directed aggression*
Contributing Author(s): Ilaria Carta, Anita Autry
Poster 36

In many species, particularly mammals, parenting behavior is highly conserved. Virgin males, however, attack conspecific infants with no provocation and only become parental after mating. This robust, mating-induced behavioral switch in virgin male mice provides a tractable model to investigate the neurobiological mechanisms and circuitry underlying the positive and negative regulation of infant care and interaction. Urocortin 3 neurons of the peri-fornical area ($PeFA^{ucn3}$) have recently been found necessary for infant-directed aggression. In addition, the highest density of $PeFA^{ucn3}$ fibers project to the amygdalohippocampal area (AHi), a brain area with little known functional relevance for behavior. Optogenetic stimulation of $PeFA^{ucn3}$ terminals in the AHi facilitates infant-directed aggression in virgin females that are naturally maternal whereas inhibition of $PeFA^{ucn3}$ neurons abolishes the behavior in males. This suggests the AHi is a functionally relevant region in the parenting and infanticide behavioral circuits. The target population of $PeFA^{ucn3}\rightarrow$AHi projection is unknown, but it is likely that they express corticotropin releasing factor receptor 2 (CRFR2), ucn3's primary receptor. In situ hybridization (ISH) experiments have confirmed CRFR2 expression in AHi. CRFR2 and its corresponding ligands ucn3 and corticotropin releasing factor (CRF), have previously been shown be associated with physiological and behavioral stress responses. Stress is thought to contribute in some circumstances to infant-directed aggressive behavior. Therefore, I hypothesize the AHi is the primary functional locus for infant-directed aggression and that AHi neurons expressing CRFR2 are key regulators of this behavioral response. I aim to identify AHi^{CRFR2}behavioral contributions via loss and gain of function studies.

Presenter: Keanu Shadron
Title: *Evidence Supporting a Population Vector Readout in the Owl's Auditory Space Map*
Contributing Author(s): Roland Ferger, Michael V. Beckert, Brian Fischer, José L. Peña
Poster 37

Ensemble activity and network architecture coordinate natural and learned behavior. Owls provide easy access to a complete population representing auditory space in both normal and learned conditions and the correlated synaptic and network microanatomy can be determined. Here we present evidence supporting a population vector (PV) based model for the readout from the owl's auditory space map which approximates Bayesian statistical inference. We performed multi-electrode array (MEA) recordings of responses in the owl's optic tectum to binaurally presented auditory stimuli – conveying sound localization cues such as interaural time difference (ITD). We show that population response profiles match the conditions for a PV readout. A decoder that is based on the PV readout model can be used to estimate the ITD used for stimulation even from single trial responses of recorded sub-populations of five to seven units. When a stimulus becomes less reliable (e.g. by decorrelation of the binaural signal) an animal's performance becomes less accurate. The Bayesian model predicts that this should manifest in a broadening of the population response in the map and a bias towards frontal space. We show this broadening and that the PV decoder mimics the expected bias. Furthermore, we can show that the same PV decoder also works when competing auditory stimuli are presented. When two stimuli with different ITDs (i.e. from different directions) were presented, the population vector pointed towards the louder or more salient stimulus. Thus, our decoder was capable to estimate the ITD of the louder sound in a competing stimulus condition. This shaping of the population response is consistent with a global inhibition network recently discovered. These results show that the PV model can perform in complex auditory scenes.

Presenter: Deep Sharma
Title: *Premature birth results in dysmaturation of dentate granule neurons and cognitive deficits*
Contributing Author(s): Bokun Cheng, Divya Singh, Nirzar Parikh, Sahil Mamtani, Sunita Yadav, Manoj Jaiswal, Praveen Ballabh
Speaker – Day 2, 4:50PM

Preterm-born children suffer memory-learning disabilities, suggesting disrupted hippocampal development. As dentate gyrus develops perinatally, premature-birth can impact its maturation. Preterm infants are deprived of safe intrauterine environment and reared in the stressful environment of Neonatal Units. However, the effect of premature-birth on dentate gyrus development is obscure. We hypothesized that premature-birth and non-maternal care would disrupt the structure and function

of dentate gyrus and induce cognitive deficits. To test our hypotheses, we compared preterm (E28.5) and term (E32) rabbit kits at an equivalent post-conceptional age (P28). Object placement test revealed that preterm kits spent less time exploring the moved object compared to term kits. Modified Barnes maze showed that preterm kits had longer-latency and made more errors in finding food relative to term kits. This suggests reduced spatial memory and learning in preterm kits. Stereological Quantification showed that both $NeuN^+$ granule cells and interneurons--$GABA^+$, $Parvalbumin^+$ and somatostatin+ cells--were higher in number in the dentate gyrus of preterm kits compared to term controls. However, $calbindin^+$ neurons were reduced in preterm relative to term kits. Accordingly, Golgi stained sections showed more abundant granule cells in preterm compared to term kits. Despite granule cells were larger in number in preterm kits, $VGlut2\text{-}PSD95^+$ synaptic puncta in the molecular layer of dentate gyrus were reduced in preterm compared to term kits. Moreover, phospho-glucocorticoid-receptor expression was higher in preterm relative to term kits. Hence, dysmaturation of dentate granule neurons in premature kits results in reduced synaptic connectivity, and contributes to poor memory and learning.
Support: NIH grant # 1R01NS110760-01

Presenter: Heather Snell
Title: *Disruption of Purkinje Cell Pacemaking Underlies Attacks in Episodic Ataxia Type 2*
Contributing Author(s): Esra Tara, Ariel Vitenzon
Poster 38

Purkinje cells, the sole output neuron of the cerebellum, are intrinsically active, and disruption of this activity can result in movement disorders such as ataxias and dystonias. Episodic Ataxia type 2 (EA2) arises from loss of function mutations in the *CACNA1A* gene encoding the α1 pore forming subunit of P/Q-type voltage-gated calcium channels. In this disorder, a mild baseline ataxia is interrupted by attacks of severe motor dysfunction that are triggered by physical or emotional stress, or consumption of caffeine or alcohol. Previous work in our lab found the baseline ataxia is caused by reduced calcium influx through the P/Q type calcium channel, which decreases activity of SK channels. The mechanism behind the attacks remains unknown. *In vivo* single unit recordings in PCs of the *tottering* mouse showed that PC firing becomes markedly more erratic during attacks triggered by the stressors. We hypothesized that increased irregularity of PCs is caused by the activation of casein kinase 2 (CK2), which further decreases the activity of SK channels. *In vitro*experiments show that all three stressors increase irregular firing of PCs in the presence or absence of blockers of fast synaptic transmission. Norepinephrine, induced PC irregularity was also blocked by α1 adrenergic receptor antagonists. Caffeine blocks adenosine receptors. We found that perfusion of adenosine 1 receptor antagonists also caused erratic firing in PCs. To investigate the involvement of CK2 in the attacks, ShRNAs against CK2 were injected into the cerebellum of the *tottering*mice. All stressor induced irregularity was blocked in PCs containing the CK2 knockdown. Thus, CK2 could be a target for therapeutics to prevent attacks in EA2 patients.

Presenter: Sacha Sokoloski
Title: *Modelling Noise Correlations in Neural Populations*
Contributing Author(s): Ruben Coen-Cagli
Poster 39

Neurons in a given population do not generate spikes independently from one another. Rather, spike counts are correlated across neurons in complex ways. Some of these correlations are induced by neural tuning, as similarly tuned neurons will spike with a similar pattern. However, some correlations (known as noise correlations) persist even when controlling for tuning similarity. Noise correlations are known to impact information processing in neural circuits and often limit the accuracy of perception. Nevertheless, modelling noise correlations has proven challenging. In particular, modelling all pair-wise correlations amongst 'k' neurons requires 'k'-squared parameters, and fitting such models for large 'k' requires infeasible amounts of data. Furthermore, noise correlations can still depend on the stimulus, but existing models have a limited ability to account for such stimulus-dependence. To address these issues, we propose a novel model of neuronal population activity, in which stimulus-dependent noise correlations reflect fluctuations of a small number of underlying factors (latent variables). The complexity of the model may be flexibly scaled; in the simplest case neural responses are modelled as independent, and parameters may be continually added to model ever more complex correlations. Moreover, we have developed an algorithm to effectively train the model on populations of hundreds of neurons with realistic amounts of data. We demonstrate that the model successfully captures noise correlations in the responses of macaque V1 neurons to oriented gratings. In future work we plan to

apply this model to definitively answering questions about the effect of noise correlations on neural computation.

Presenter: Randy Stout
Title: *The Gap Junction Nexus Modifies Synaptic Transmission*
Contributing Author(s): Daniel Tanis, Sean McCutcheon, Viraj Modi, David C. Spray
Poster 40

We recently found that the mobility of gap junction channels within the supramolecular gap junction nexus organelle is controlled by cysteine residues within the carboxyl-terminus of the connexin proteins that form gap junction intercellular channels. We also found that channel mobility is acutely modifiable. Here we present data showing that gap junctions modify location and mobility of other proteins in diverse manners through multiple underlying mechanisms. In parallel with our demonstration of such a dynamic gap junction nexus supramolecular structure, a separate concept has emerged from the work of groups using phospho-specific connexin antibodies and studies indicating anchored kinase regulation of gap junction channel activity. This concept leads to a widely held hypothesis in the field of gap junction research which can be summarized as: The small percentage (<10%) of active gap junction channels within the larger gap junction are spatially ordered via step-wise and spatially-regulated phosphorylation of the connexin carboxyl-termini. However, such restriction of active and inactive gap junction channels to sub-regions of the gap junction plaque structure is impossible in an unstably arranged gap junction nexus. Therefore, we hypothesize that intercellular communication established by connexins that form stably arranged gap junctions can be controlled by a form of metaregulation via the stability of the supramolecular structure itself. We used ensemble techniques such as FRAP to study mobility of gap junction channels and a suite of interacting proteins. We will present results of spatially realistic cell modelling simulations and describe how we integrate experimental results from our microscopy experiments with published biophysical studies to generate model parameters for the mesoscale computational model of the tripartite synapse.

Presenter: Olga Sysoeva
Title: *Auditory processing atypicalities for pure tones and complex speech sounds in Rett Syndrome – towards neuromarkers of disease progression.*
Contributing Author(s): Sophie Molholm, Aleksandra Djukic, Hans-Peter Frey, John J. Foxe
Poster 41

Rett Syndrome is a neurological disease that affects predominantly females and in most cases is caused by the mutations in *MECP2* gene located on the X chromosome. The degree of language comprehension is hard to assess in this population due to profound motor impairments. We implemented high-density auditory evoked potential technique to examine early neurophysiological processing of tones and syllables in females with Rett Syndrome (RTT) and to objectively evaluate the severity of potential auditory processing deficits in this population. The comparison of 12 females with RTT with their 21 typically developing (TD) peers aged 4-21 years old revealed AEP abnormalities starting from 60-90 ms after stimuli presentation. P1 components peaking at these latencies was larger for speech than for tone stimuli in TD but not RTT group. Interestingly, this effect did not simply cascade up the auditory system. Rather, the subsequent N1 did not differ between groups, whereas the P2, the following major deflection, was hugely diminished in RTT as a group, regardless of stimulus type. The N2 was similarly smaller in RTT than in TD, and did not differ as a function of stimulus type. The P2 effect was remarkably robust in differentiating between groups, much more so than the N2, almost fully correctly classifying into group despite the wide age range of our samples. Moreover, it indexes the Rett Syndrome severity assessed with Rett Syndrome Severity Scale (RSSS). Given this robustness, the P2 has the potential to serve as an important biomarker of treatment efficacy.

Presenter: Seydanur Tikir
Title: *How flexible are you in updating your predictions? Evoked potentials suggest inflexible predictive processing in autism spectrum disorders*
Contributing Author(s): Michael J. Crosse, Sophie Molholm
Poster 42

Autism Spectrum Disorder (ASD) is a complex neurodevelopmental condition defined by difficulties in social interactions, insistence on sameness, and repetitive behaviors. Recent theories propose that impaired predictive processing plays a central role in the autism phenotype, drawing a link between insistence on sameness and abnormalities in making predictions (Van de Cruys et al., 2014; Lawson

et al., 2015; Sinha et al., 2014). We hypothesize that individuals with ASD are impaired in the ability to flexibly adjust the strength (precision) of their predictions according to statistics of environmental changes (volatility). To test this, we designed a task with four conditions where cue validity is manipulated at four levels (100%, 86%, 66%, 33%). Throughout an experiment, we introduce 12 volatility switches, while recording electrophysiology (EEG), response time, and pupil size of adult subjects with and without autism. Preliminary EEG analyses show that the amplitudes of the evoked potentials that are related to predictions are gradually modulated by changes in volatility (e.g. cue validity) in controls, while this is far less evident in the ASD group. More specifically, a lack of modulation in P3 amplitude implies that individuals with ASD do not effectively update their internal model of the environmental statistics, whereas reduced modulation in anticipatory activity suggests inflexibility in the updating of expectations about upcoming targets. Inefficient predictions about upcoming events in everyday life could be stressful, and it could lead to resistance to even trivial changes in life, which is a major feature in ASD.

Presenter: Jaafar Tindi
Title: *Elucidating the Role of Cerebellar AIDA-1 in Motor and Social Behavior in Mice*
Contributing Author(s): Abigail Carbonell, Bryen A. Jordan, Kamran Khodakhah
Poster 43

The cerebellum has canonically been considered a motor structure. However, recent work provides compelling evidence for the role of the cerebellum in non-motor tasks, including cognitive and emotional behaviors. Cerebellar injury is one of the most common risk factors for autism spectrum disorders in humans and mouse models of autism have been generated by targeted deletions of genes only in Purkinje neurons, which provide the sole output of the cerebellar cortex. We have recently shown that patients with AIDA-1 haploinsufficiency present with motor dysfunction, autism, and ADHD and these abnomalities can be faithfully reproduced in a heterozygous AIDA-1 mouse model whereby the gene encoding AIDA-1 is conditionally deleted in the entire nervous system. However, a forebrain-specific conditional knockout of AIDA-1, which does not target the cerebellum, failed to recapitulate the motor dysfunction and sociability deficits. Given the importance of the cerebellum in both motor function and autism, we hypothesized that AIDA-1 in the cerebellum might be critical for both motor function and sociability. Here we show by immunohistochemistry that in deed AIDA-1 is predominantly expressed in Purkinje neurons of the cerebellar cortex and is enriched in zebrinII positive bands. We then generate Purkinje neuron-specific AIDA-1 conditional knockout mice and conduct both behavioral and in vivo electrophysiological characterization experiments in an effort to understand the role of AIDA-1 in motor and social behavior and how a deficiency in AIDA-1 might contribute to both motor dysfunction and autism in human patients.

Presenter: Meera Trivedi
Title: *Characterizing Novel Pathways of Dendritic Tiling in C. elegans*
Contributing Author(s): Lourdes A. Martin Hernandez, Hannes Buelow
Poster 44

Neurons rely on dendrites for the acquisition of sensory and synaptic input from their particular receptive fields. Findings of aberrant dendritic morphology in disorders such as autism spectrum disorder (ASD) and schizophrenia highlight the importance of understanding how complex dendritic arbors are developed and maintained. During development, one of the goals of dendritic outgrowth is non-redundant coverage of a receptive field, which requires the avoidance of other dendrites both from the same neuron (self-avoidance) and from others (tiling). While tiling is a conserved property of many nervous systems, the molecular mechanisms by which it is established remain unclear. The goal of this project is to characterize the mechanisms of dendritic tiling using the multi-dendritic FLP and PVD mechanosensory neurons of *C. elegans* as a model. The dendritic arbor of FLP covers the head of the worm while the arbor of PVD covers the body. The mechanism by which these neurons establish distinct non-overlapping receptive fields remains unknown. Using an unbiased forward genetic approach, we isolated a mutant allele in *unc-33*, which displays altered FLP and PVD receptive field sizes. *Unc-33* encodes a member of the Collapsin Response Mediator Protein (CRMP) family, which regulate axon outgrowth and morphology by binding and organizing tubulin heterodimers. I hypothesize that *unc-33/CRMP* acts to define the border between FLP and PVD by organizing microtubules in outgrowing dendrites. Furthermore, I hypothesize that unbiased forward genetic approaches will uncover additional regulators of FLP and PVD tiling.

Presenter: Jonathan Vacher
Title: *Human Visual Segmentation: Experiment and Model*
Contributing Author(s): Pascal Mamassian, Ruben Coen-Cagli
Speaker – Day 1, 11:50AM

Visual segmentation is a key perceptual function that partitions visual space and allows for detection, recognition and discrimination of objects in complex environments. The processes underlying human segmentation of natural images are still poorly understood. Existing datasets rely on manual labeling that conflate perceptual, motor, and cognitive factors. In part, this is because we lack an ideal observer model of segmentation to guide constrained experiments. Our goal is two-fold (i) develop a model to probe human visual segmentation mechanisms and (ii) develop an efficient method to measure human visual segmentation. To this aim, first we propose a novel probabilistic generative model of visual segmentation that - combines knowledge about the sensitivity of neurons in the visual cortex to statistical regularities in natural images, and - local grouping priors over pixels (i.e. favoring contiguous partition of visual space). Second, we propose a new protocol to measure the capacity of humans to discriminate whether or not two cued locations belong to the same segment and show how, from the collected data, we can recover probabilistic segmentation maps that are compatible with our model. We test our segmentation model on natural images and we present preliminary data collected on 3 subjects on both artificial and natural images.

Presenter: Mercedes Vega Villar
Title: *Experience-dependent changes in the nucleus accumbens underlie acquisition of cued reward-seeking behavior.*
Contributing Author(s): Jon C. Horvitz, Saleem M. Nicola
Poster 45

Animals learn associations between contextual cues and the natural rewards they predict. As a result, reward-predictive cues come to trigger approach to locations where rewards are available. The nucleus accumbens (NAc) in the ventral striatum is implicated in the expression of such cued reward-seeking behaviors. Accordingly, many neurons in the NAc become excited upon presentation of an already-learned reward-predictive cue. Cue-evoked excitations encode the motivational value of the stimulus and are required for expression of the subsequent approach). However, whether and how cue-evoked excitations emerge during learning has not yet been established. In Experiment 1, we recorded the unit firing activity of NAc core neurons as rats learned to approach a reward receptacle upon presentation of a cue. Our results indicate that cue-evoked excitations begin to increase a few trials before cued approach behavior is detected and they continue to escalate as cued reward-seeking responses become more vigorous. Because infusion of NMDA receptor antagonists into the NAc during training impairs acquisition of similar reward-oriented behaviors, we hypothesized that the emergence of cue-evoked excitations during cued approach learning is due to NMDA receptor-dependent plasticity within the NAc. In Experiment 2, we performed colocalized simultaneous unit recordings and NMDA antagonist microinfusions in the NAc. We found that the potentiation of learning-related cue-evoked signals in the NAc depends on NMDA receptor-dependent plasticity within this structure. Our results link accumbens plasticity, changes in striatal activity and the emergence of conditioned behavior, revealing a neural mechanism via which the NAc participates in associative learning.

Presenter: Jorge Vera
Title: *Disynaptic, VTA-mediated, cerebellar modulation of the prefrontal cortex*
Contributing Author(s): Maritza Oñate, Chris Chen, Victoria Lovallo, Kamran Khodakhah
Poster 46

The cerebellum (Cb) has been associated with cognitive disorders that potentially affect the medial prefrontal cortex (mPFC), such as schizophrenia and autism. However, the causal link is unknown. The mPFC is thought to be involved in decision-making processes that guide behavior based on predicted outcomes. The ventral tegmental area (VTA) is a key region of the brain reward system that provides reward-related signals to the mPFC via dopaminergic and glutamatergic projections. We have recently shown that the Cb sends direct excitatory projections to the VTA, raising the possibility that there might be a disynaptic pathway from the Cb to the mPFC via the VTA. Here we describe experiments aimed at delineating the anatomical and functional properties of the Cb->VTA->mPFC circuit in the mouse brain. We found that a number of mPFC-projecting VTA neurons also received direct cerebellar inputs, thereby anatomically confirming the presence of this disynaptic circuit. In vivo Optogenetic stimulation

of Cb axons the VTA effectively drove the activity of half of mPFC cells recorded (latency 28 ± 10 ms, mean ± SD). The evoked response was composed of a transient fast (10-20 ms) increase in the firing rate of the recorded neurons that was often followed by a sustained (100-400 ms) increase, or reduction in firing, consistent with the involvement of both glutamatergic and dopaminergic VTA projections. Moreover, fiber photometry experiments support the functional connectivity of the proposed circuit. Collectively, our results show the presence of an effective, VTA-mediated, disynaptic projection from the cerebellum to the PFC.

Presenter: Ariel Vitenzon
Title: *Mechanisms Underlying Stress-induced Attacks in an Episodic Ataxia Type 2 Mouse Model*
Contributing Author(s): Esra Tara, Heather Snell
Poster 47

Episodic channelopathies are characterized by the expression of symptoms during discrete attacks superimposed on an unremarkable baseline phenotype. A common feature of these disorders is that attacks are induced by the same set of physical or psychological stressors. Understanding the mechanism by which the stressors trigger neurologic dysfunction, therefore, may identify potential intervention opportunities and therapeutic targets. Episodic ataxia type 2 (EA2) is one such disorder that arises from mutations in the *CACNA1A* gene encoding for the α1 pore forming subunit of P/Q-type voltage-gated calcium channels. In this disorder a mild baseline ataxia is interrupted by attacks of severe motor dysfunction triggered by physical or emotional stress or caffeine or alcohol consumption. The mechanism by which the stressors trigger the motor attacks is not known. We used the *tottering* mouse, a faithful model of EA2, to scrutinize the role of adrenergic transmission in triggering attacks of motor dysfunction. Using a combination of approaches, here we show that local noradrenergic transmission in the cerebellum of *tottering* mice is both sufficient and necessary to induce attacks. We further show that, at least at the receptor level, stress and caffeine do not seem to initiate attacks via the same mechanism.

Presenter: Qu Xing
Title: *Activation of Pannexin1 facilitates ATP-Mediated neuroblastoma process outgrowth during cell differentiation*
Contributing Author(s): Preeti Dohare, Qinghua Li, Antonio Cibelli, Fangxia Guan, David C. Spray
Poster 48

Pannexin1 (Panx1) is a channel-forming protein found in vertebrates that is related to invertebrate gap junction proteins. Functions of Panx1 channels include release of ATP, providing signaling through purinergic receptors, and playing major roles in such processes as neuronal migration and maturation. In our previous studies on a neuroblastoma cell line N2a where panx1 was deleted through CRISPR/Cas9, we found Panx1 deletion decreased cell proliferation, cell migration and neurite extension. To investigate further the relationships between panx1, axonal growth and neuronal differentiation, we expressed human and mouse Panx1 in the Panx1 null N2a cells. Our findings in Panx1-expressing N2a cells treated up to 5 days with retinoic acid [RA (40μM)] indicated that Panx1 enhanced neurite lengths and numbers of branch points at D3, D4, D5 ($P<0.05$). Studies by others have suggested that Collapsin response mediator protein-2 (CRMP2) is crucial for axonal regeneration. Our qRT-PCR results indicated CRMP2 was significantly increased ($P<0.05$) after mPanx1 transfection and GSK-3β was upregulated ($P<0.05$) during RA treatment. In order to evaluate maturation of the neuronal excitability, we recorded the voltage dependent inward currents during cell differentiation revealing larger currents ($P<0.05$) in N2a cells expressing Panx1. Furthermore, Panx1 blockers (Probenecid, Carbenoxolone) inhibited the development of cell excitability as did the ATPase Apyrase, implicating involvement of ATP release through Panx1 channels. Since increased intracellular calcium is required for neurite outgrowth, we performed fura-2 calcium imaging on Panx1-expressing cells finding that basal and ATP-evoked Ca^{2+} responses were augmented. In brief, we conclude that Panx1 plays a major role in controlling neuronal differentiation through signaling pathways including GSK-3β and intracellular Ca^{2+}.

Presenter: Jingqi Yan
Title: *Activation of autophagy rescued cognitive and social deficits in Fragile X mice*
Contributing Author(s): Morgan W Porch, Brenda Court-Vazquez, Michael V.L. Bennett, and R. Suzanne Zukin
Speaker – Day 2, 5:10PM

Fragile X syndrome (FXS) is the most common form of heritable intellectual disabilities and a leading genetic cause of autism. Fragile X (*Fmr1* KO) mice exhibit aberrant dendritic spine structure and synaptic plasticity, hypersensitivity, cognitive and social deficits. Autophagy is a catabolic process of programmed degradation and recycling of proteins and cellular components via the lysosomal pathway. However, a role for autophagy in the pathophysiology of Fragile X syndrome is, as yet, unclear. Here we show that autophagic flux, a functional readout of autophagy, and biochemical markers of autophagy are impaired in hippocampal neurons of Fragile X mice. Activation of autophagy by delivery of shRNA to Raptor directly into the CA1 of living mice via the lentivirus expression system corrects aberrant spine structure, synaptic plasticity and cognition in Fragile X mice. Activation of autophagy corrects overabundant PSD-95 and Arc, synaptic proteins implicated in spine structure and synaptic plasticity, identifying a potential mechanism by which impaired autophagy is causally related to the Fragile X phenotype. In addition to cognitive deficits, Fragile X patients are associated with hypersensitivity to sensory stimuli and social deficits. Hypersensitivity to sensory stimuli is thought to underlie delayed maturation of the somatosensory cortex, occurrence of seizure, and deficits in social behaviors. Our findings indicated that autophagy is impaired in neurons of somatosensory cortex of Fragile X mice. Activation of autophagy rescued the downregulated autophagy in neurons of somatosensory cortex, hypersensitivity to sensory stimuli, and social deficits in Fragile X mice.

Presenter: Junichi Yoshida
Title: *Reward-related neural activity in substantia nigra pars compacta projecting deep cerebellar nuclei under Pavlovian learning*
Contributing Author: Kamran Khodakhah
Poster 49

A lot of research is reporting evidence for a cerebellar contribution to prediction error and reward value. However, how the cerebellar information is conveyed to other brain regions (e.g., basal-ganglia) remains unclear. The deep cerebellar nuclei (DCN), the primary cerebellar output, project to the substantia nigra pars compacta (SNc). SNc is thought to be critical for encoding reward value. We performed fiber photometry in Pavlovian conditioned mouse, and monitored neural activity in SNc projecting DCN axons, and dopaminergic SNc (DA-SNc) neurons. We examined the calcium signals associated with prediction timing, and reward evaluation. We found that the activity of the SNc projecting DCN axons increased at reward delivery, but not when the reward prediction cue was presented. The DA-SNc neurons, however, showed activity at both times. Interestingly, the activity of SNc projecting DCN axons reflected the quality and quantity of the reward. Similarly, the activity of DA-SNc neurons represented reward features. Together, the SNc projecting DCN axons seem to represent reward value, and are in a position to convey this information to the basal-ganglia via the DA-SNc neurons.

Ethics Vignettes Discussion Groups

(Vignette Assignments in Parentheses, Discussion Group Chairs in Bold)

Group 1 (#2, #6)
B. Abdelmesih
M. Akabas
A. Alves Francisco
T. Bassett
S. Beker
R. Birnbaum
N. Cayla
E. de Oliveira
D. Faber
B. Galinski
H. Hatch
B. Jordan
A. Martin
M. Mehler
A. Vitenzon
Y. Yang
J. Yoshida

Group 2 (#2, #6)
J. Alpert
R. Batista Brito
C. Berthoux
K. Fisher
K. Khodakhah
A. Krishna
S. Lutzu
H. Monday
S. Poser
J. Reynolds
C. Saqcena
V. Sedwick
F. Soldner
S. Solomon
M. Trivedi
J. Yan

Group 3 (#3, #7)
P. Ballabh
K. Brace
H. Byun
A. Francesconi
A. Frechou
J. Freund
K. Jensen
N. Killian
V. Lovallo
K. Nasrallah
S. Nicola
A. Pavuluri
M. Rahman
D. Sharma
S. Walkley
Q. Xing

Group 4 (#3, #7)
R. Anderson
M. Bennett
C. Cho
P. De Sanctis
D. Festa
T. Goncalves
J. Krzyspiak
I. Maroto
K. Palarz
C. Ramos
F. Rivera
K. Shadron
D. Spray
O. Sysoeva
J. Tindi
C. Ward

Group 5 (#4, #8)
A. Ashner
A. Carbonell
K. Clemenza
R. Coen-Cagli
I. Deyneko
R. Ferger
M. Gulfo
D. Herrera
P. Kurshan
G. Lee
S. McCutcheon
S. Molholm
V. Mudragel
M. Onate
B. Poulos
Y. Tai

Group 6 (#4, #8)
A. Autry
H. Buelow
B. Court Vazquez
F. Echeverry
J. Hebert
K. Hiciano
J. Jordan
K. McDermott
J. Ratliff
T. Rubin
J. Secombe
H. Snell
R. Stout
Ş. Tikir
N. Wazeed
A. Xu

Group 7 (#1, #5)
I. Carta
P. Castillo
A. Cibelli
A. Davila
M. Gronska
D. Hall
C. Hodelin
M. Kazmierczak
S. Kharod
R. Lo Bu
S. Roudabush
L. Sjulson
J. Vacher
J. Vera
V. Verselis
D. Wilson

Group 8 (#1, #5)
N. Cuevas
C. De Sanctis
K. Dobrenis
Ş. Gokhan
J. Guarque-Chabrera
A. Kohn
P. Lituma
D. Perez Vazquez
A. Quezada
C. Reyes
B. Tricomi
M. Vega Villar
S. Washburn
E. Wood
H. Yang
S. Zukin

Ethics Session: Considering and Correcting our Unconscious and Cognitive Biases

An introduction to the ethics session will be held in the main auditorium, followed by small group discussions. You can find your group assignment on the preceeding page. The room number assignment for each discussion group will be announced during the introduction.

The focus of this year's ethics session is how unconscious bias can both affect our interactions with colleagues (Vignettes #1-4) and can influence how we carry out and communicate our research (Vignettes #5-8).

There are many implicit or unconscious biases (gender, race, age, etc.) that shape both our interpersonal interactions and institutional policies. Unconscious biases are the information, beliefs and stereotypes that effect our information processing subconsciously. As researchers in a highly collaborative environment, often serving on committees both within our institution and the scientific community at large, we have the great responsibility of reflecting on this topic. For additional information on how to recognize and manage unconscious bias after our ethics session, you are encouraged to check out an excellent series of videos produced as a part of the Einstein Diversity and Inclusion Plan (1-3) and read the recent perspective piece on gender bias from Dr. Kay Tye (4).

While there are some concerning and extreme examples of research misconduct that hopefully none of us could even imagine doing, many issues of research reproducibility arise from bad habits that we may not even be aware of. We will reflect on how to identify and avoid "cognitive fallacies" outlined in a recent Nature news feature (5): *Hypothesis Myopia*—Collecting evidence to support a hypothesis, not looking for evidence against it, and ignoring explanations; *Texas Sharpshooter*—Seizing on random patterns in the data and mistaking them for interesting findings; *Asymmetric Attention*—Rigorously checking unexpected results, but giving unexpected ones a free pass; and "*Just So" Story Telling*—Finding stories after the fact to rationalize whatever the results turn out to be.

Resources

1. Understanding Unconscious Bias Module 1:
http://www.einstein.yu.edu/gadgets/video/hr/?video=site-wide/diversity/Diversity-Training-unconscious-bias-module-1

2. Understanding Unconscious Bias Module 2:
http://www.einstein.yu.edu/gadgets/video/hr/?video=site-wide/diversity/Diversity-Training-unconscious-bias-module-2

3. Crucial Diversity conversations:
http://streaming.einstein.yu.edu/videos/departments/hr/icims-portal/diversity-conversations.mp4

4. Tye, Kaye. Gender bias from a woman in science. *https://www.hellobio.com/blog/gender-bias-from-a-woman-in-science.html* (2019).

5. Nuzzo, Regina. How scientists fool themselves—and how they can stop. *Nature* **526,** 182–185 (2015).

Vignette #1

Part One: The Neuroscience Department at the Alfred Eldridge College of Medicine is conducting a faculty search to fill a tenure-track Assistant Professor position (with a special emphasis on recruiting research involving "exotic" model organisms). They are particularly interested in inviting candidates with superb publication records and excellent letters of recommendation to give a departmental presentation. Based on these criteria, the department invites the following two candidates to campus:

1) **Dr. Elizabeth Carter** is currently a postdoc in the lab of Dr. Roger Edwards, a renowned HHMI Investigator studying neural injury and repair in the Mexican walking fish (Axolotl). Dr. Carter recently published a high-impact, first author paper in *Neuron*, making this the 5th paper she has co-authored during her four-year postdoc. In a letter of recommendation to the department, her mentor describes her as "…hard-working and charismatic, with excellent organizational skills, especially when it came to organizing the lab's primer database."
2) **Dr. John Wick** is currently a postdoc in the lab of Dr. Ron Cooper, an investigator recently elected to the National Academy of Sciences for his work studying spinal ganglia in the slow loris. Dr. Wick was a co-first author on a recent paper published in the *Journal of Neuroscie*nce and has co-authored one other paper during the last four-years. He is described by his mentor as "…smart, with a natural talent for science."

Questions:

1) What scientific and/or personal criteria should be considered when deciding which candidates should be invited for an interview/recruitment seminar?
2) How might unconscious biases have entered and influenced the strength of Dr. Carter's and/or Dr. Wick's applications?

Part Two: Both candidates give departmental seminars. While presenting, Dr. Carter is interrupted and asked several questions including whether she has considered an alternative hypothesis, performed her analysis in a different brain area, or if the model organism is appropriate for this type of analysis. Although she plans to address these points later in her presentation, she answers all questions as they are asked, but unfortunately goes over her allowed presentation time by 15 minutes, forcing her to skip her future directions slide. After her seminar, she overhears one faculty member comment to another on how "the speaker could have been a bit more confident in her defense of her model organism and not have rushed at the end."

Dr. Wick, too, receives a couple of questions during his presentation, including one asking him to describe his patch-clamp recording method, and another asking how the lab obtained their slow lorises. He finishes on time and is able to field additional questions.

A survey is sent out to students, postdocs, and faculty asking them to assess the performance of both candidates in the following categories: quality of the applicant's research, the applicant's potential for carrying out future plans, and the applicant's potential for forming collaborations within the department.

Questions:

1) How might unconscious biases have influenced the strength of Dr. Carter's and Dr. Wick's presentations?
2) How is institutional bias different from interpersonal bias, and how could both have impacted Dr. Carter's and/or Dr. Wick's application, presentation or evaluation?
3) What could have been done differently to recognize and prevent implicit bias on the interpersonal and institutional levels? Whose responsibility is it to address such issues?
4) Is there anything Dr. Carter could/should have done differently?

Vignette #2

Part 1: You are a member of the planning/executive committee for SfN's 2021 conference. The committee is composed of mostly senior professors from the United States. The demographics of the committee are homogeneous. The conference allows for 10 keynote seminars that need to be filled from a large pool of pre-screened abstracts. The chair of the committee believes all abstracts should be reviewed blind and the top 10 by score should be offered the keynotes. Another committee member believes this process may disadvantage underrepresented groups. He/She suggests the abstracts should be separated into groups by factors like, gender, ethnicity, geography, and age/seniority. Then the top submission(s) from each group should be offered the keynotes, so as to maintain balance. Another member points out that there are large numbers of non-keynote seminars that will be filled by a diverse pool of applicants. These seminars can reflect the diversity of the science community and, thus, the keynotes do not need to be distributed with diversity in mind.

Questions:

1) Is it the responsibility of selection committees to consider underrepresented groups in science when selecting keynote speakers?
2) Are there merits to each committee member's proposal?
3) Which selection process is the most 'fair'?
4) Is there another method for evaluating abstracts you think should be considered?

Part 2: The chair's position won the argument and the committee reviews the abstracts blind. The top 10 rated abstracts are offered the keynotes. This process unintentionally led to the selection of a predominantly white, male, cis, North American-based group of speakers. However, 2 women and several countries are included in the group. All ten keynotes are excellent speakers and their science is exciting and cutting-edge.

Questions:

1) How should selection slots be allocated to promote representation when you cannot give to every deserving group (e.g. You can split your speakers by gender and geography, but not age)?
2) Should considerations of representation apply to other selection processes (i.e. grants reviews, department speaker invites)? Please explain.
3) Should there be an explicitly stated diversity requirement for the selection committee itself?
4) Are there other actions the committee can/should do to ensure high quality science and diverse representation?

Vignette #3

Part 1: Grad student Jon was super excited to start working in the lab of Dr. Targaryan, a well-known PI in her field. During his rotation after discussing with his PI potential projects in the lab that were available, they decided on trying to establish a 3D in vitro model of the gut that would include endothelial stem cells, as well as neural stem cells to try to simulate the enteric nervous system. The project was multifaceted and required several disciplines, a challenge that Jon thought would be fun. He had experience in engineering to generate the scaffolds required for the device but was having a hard time getting the stem cells to differentiate into the proper cell types, to survive, and to get the right signaling pathways activated in the culture to simulate the environment enough to be used as a model for drug delivery. Jon did his best to be a self-sufficient grad student, but stem cell biology was too far outside his expertise to make progress at an acceptable pace without some guidance. Unfortunately, Dr. Targaryan did not have expertise in stem cell biology, so she could only be useful as a sounding board to Jon for this high risk, high reward project. Jon tried to reach out to other PIs on campus to get advice, but his project was too novel in terms of placing stem cells into such devices and combining different organ systems, that the PIs also often didn't have solid answers.

After two years of trying to get the project to work, Jon felt that his PI was leaving him out to dry. Jon wanted to change projects to one that had a higher chance of publication, and work on this risky project on the side, but Dr. Targaryan didn't agree. She wanted this to work. Meanwhile, another grad student, Tyra, was having more success. Tyra rotated in the lab after Jon. Dr. Targaryan gave her a project that was part of her grant, and it had some promising preliminary data that was acquired by previous members of the lab involving engineering bacteria to supplement diabetes patients with insulin and to also serve as reporters for disease. The project had a clear direction with significant impact. Jon was unaware that this project was even available as it was not part of the initial discussion. It seemed that Dr. Targaryan had saved the project for Tyra, who seemed to have her project laid out for her for quick success. Dr. Targaryan was quickly taking Tyra to conferences and introducing her to the prominent PIs in the field. Jon and Tyra both went to top tier universities for bioengineering and were both awarded academic-based scholarships upon acceptance to grad school. Considering this, Jon wondered if it was because Tyra was Latina, while he is a white male, and Dr. Targaryan wanted to show that she could produce a successful scientist from her lab who is a minority and a woman. He approached Dr. Targaryan about going to conferences to

present his data as well, but she said that his project was not progressing enough to warrant giving a talk, leading Jon to think Dr. Targaryan was too worried about preserving her reputation than giving him opportunities to grow as a scientist.

Questions

1) What should Jon do?
2) Who should he go to?

Part 2: Frustrated, Jon goes to the Chair of the department, Dr. Thanos to express his concerns. Dr. Thanos sets up a meeting with Jon and Dr. Targaryan to have an honest discussion. Dr. Targaryan is surprised that Jon feels that she is unconsciously biased towards Tyra. She thinks that Jon is self-sufficient enough that he will eventually manage to get the project done and that Tyra's project is simply moving forward faster.

Questions

1) How should Dr. Targaryan respond?
2) What if things don't change?
3) How should Dr. Thanos be involved in helping the parties each address their concerns?

Vignette #4

Daenerys and Jon from the Lannister lab, who are in the same year of their PhD, applied for a travel grant to go to a conference in Westeros. The travel grant is highly competitive and intended only for senior graduate students with stellar academic records. After weeks of waiting, Daenerys was overjoyed to learn that she was awarded one of the travel grants, however, Jon was unsuccessful. Jon approached Daenerys to congratulate her on receiving the grant and says, "It's so fantastic to see they've started promoting women in computational neuroscience." Jon's comment made Daenerys instantly feel like she was given the travel award only because she was a woman, causing her to fall into a deep spiral of imposter syndrome. She feels frustrated that Jon made reference to her gender with respect to an award that was open to all applicants, although it did seem out of character.

Unknowingly to either Daenerys or Jon, their PI, Dr. Lannister, overheard the conversation as he was walking over to congratulate Daenerys for receiving the award. Sensing Daenerys's uneasiness, he wonders whether he should address Jon's comment.

Questions

1) How can Daenerys address the situation?
2) As a witness of the encounter, how Dr. Lannister address this situation?
3) What do you think were Jon's intentions? How can he respond if Daenerys or Dr. Lannister question his comment?

Vignette #5 (Hypothesis Myopia)

Theon is a 5th year PhD student. His previous project did not pan out, so he started working on a new project in the last year looking at receptor signaling in a particular neuronal subtype. His boss, Dr. Bolton, asks him to determine whether a particular protein that the lab has been working on for a long time called Flayin interacts with his receptor of interest. While there's no previous evidence to suggest this might be the case, Dr. Bolton is writing a grant on Flayin and would like to tie in Theon's research as preliminary data. Theon performs a co-immunoprecipitation on his receptor and Flayin. The first time he tries he finds that his positive control works but he cannot detect any Flayin pulling down with his receptor. He repeats the experiment with a new set of samples. This time he is able to see a faint band when he enhances the contrast of his blot. In order to back up this finding, he also performs immunostaining for the Flayin protein and his receptor in neuronal cultures, however he finds that he cannot see significant colocalization of the two. Theon doesn't know how to interpret this result, so he shows all of his raw data to Dr. Bolton. Dr. Bolton decides to show only the successful Co-IP in his R01 grant submission. He assigns a post-doc, Ramsey, to repeat the immunostaining. Within a few days, Ramsey comes back with new data showing that the 2 proteins do colocalize in culture, but when Theon asks to see the raw images, Ramsey refuses. Dr. Bolton does not ask to see Ramsey's raw data. Theon feels that the results of his research are being presented to the public incorrectly, but when he expresses his feelings to Ramsey, Ramsey cuts him off, saying "Its only preliminary data for a grant."

Questions

1) Should Theon tell anyone else about this issue? If so, who should he turn to?
2) Is Dr. Bolton responsible for verifying the validity of Ramsey's findings by examining the raw data?
3) What are the implications of publishing this research without showing all of the technical replicates?
4) Theon is focused on hypothesis-driven research. Would it be better for Theon to perform a more unbiased screen of all potential proteins that interact with his receptor? Why or why not?
5) How could this example of hypothesis myopia be prevented?

Vignette #6 (Texas Sharpshooter)

Larry Lackwit is a graduate student in a neuroscience lab trying to discover sex differences in rats to get preliminary data for his NRSA grant. To do so, he performs a large number of locomotor and cognitive assays. He takes measurements of hormone concentrations after every assay, then, after the whole session, kills the rats (N of 3 of each sex) and labels immediate early genes. After doing this, he runs an RNA-Seq analysis that shows sex-dependent increased early gene activity in the agranular cortex, and one cluster correlates to an understudied interneuron population, which he happened to work on in his previous lab. He also finds increased leptin concentrations, and a

decrease in anxiety metrics, although the significance is just under .05. Thrilled that this cell population might be functionally relevant, he starts to write his grant around this data. He then wants to present a poster at a conference so that he can present his data to not only claim the topic, but to rebuttal the many skeptics in the field who think that the interneuron population are either simply variability in the mouse strain, or a result of the way that these interneurons are classified. His PI tells Larry to take a step back and develop a specific hypothesis, since some of his results may have been due to chance in classification or experimental variability.

Larry is eager to get the data out and believes that the risk needs to be taken to advance the field. He wants to combine this data with data from his old lab where he ran a subset of the locomotor and cognitive assays and immediate early gene staining, but without the RNA-Seq data because of a lack of funding.

Questions

1) What's the difference between "exploratory" science and the sharpshooter fallacy?
2) What safeguards can we put into our experimental design to avoid committing the sharpshooter fallacy?
3) How can we rescue studies that have fallen prey to the sharpshooter fallacy?

Vignette #7 (Asymmetric Attention)

Your lab has created a novel descriptive model for how sleep regulates axon regeneration. You've included this model in a recent manuscript submission. The model is the focal point of the paper. You receive reviewer comments that are positive but two additional experiments pertaining to predictions of the model are requested. You perform these experiments and analyze the results, all in accordance with standard lab protocol.

Upon analyzing the results you find that experiment 1's results fit with the model predictions but experiment 2's results do not. To try to understand why experiment 2's results did not meet expectations, you review the protocol and reagents used. You discover that one of the reagents used in both experiments was expired at the time of use and may have contributed to the unexpected result.

You decide to re-run experiment 2 before writing and submitting your rebuttal. You also plan additional experiments to address the reviewer's concern in case the result from experiment 2 remains as it was.

Questions:

- Are these actions appropriate?
- Are there additional actions that should be taken?
- What should have been done when the expired reagent was found?
- What protocols can be put in place for future experiments?
- How should the author(s) address the results from the reviewer-requested experiments in their rebuttal/resubmission?
- If the results from experiment 2 ultimately do not agree with the model, does the model need to be revised or investigated further before it is publishable?

Vignette #8 ("Just So" story telling)

Ned is a seventh year PhD student in the Baratheon lab who is hoping to complete his final experiments and defend his thesis soon. In his last set of experiments, Ned is testing a drug in cohorts of five rats. He finds that two out of the five rats respond to the drug, and he is convinced the drug potency failed in the remaining three animals since they were injected last and the drug lost its potency once exposed to the room temperature. He reasoned that because he has seen drug's effects in vitro cell culture electrophysiology experiments, thus he should have seen the drug effects in the other animals in vivo.

Ned needs drug-naive adult animals of a particular genotype that he no longer has in order to redo these experiments. Ned questions how these unexpected results can fit into his broader hypothesis and is nervous that his expected defense date will need to be pushed back by at least six months. Additionally, Dr. Baratheon is planning on applying for grants and needs a publication over Ned's thesis work to strengthen the application.

Questions

1) What conversations should happen between Ned and Dr. Baratheon?
2) How should Dr. Baratheon, respond to the situation regarding the requirement of Ned to repeat the experiments? What factors will affect Dr. Baratheon's response?
3) Is it acceptable to move forward to publication by excluding the drug experiments? What factors should be considered when preparing a manuscript for publication?
4) What actions could be taken to prevent this situation?

Wine Tasting

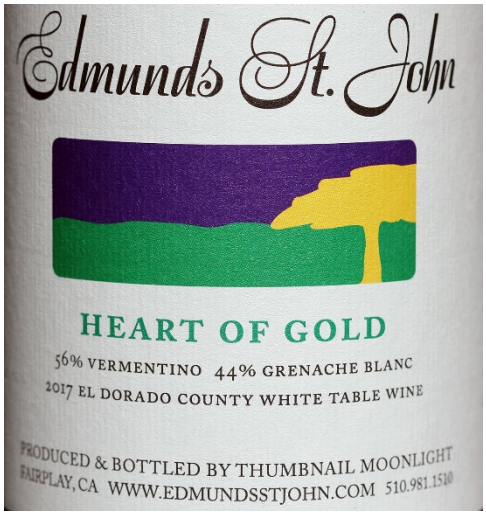
Welcome to the 2019 Neuroscience Retreat wine tasting event. Thanks to the adventurous selections of the wine committee, we have a very interesting mix of wines for all to try. These include: an unusual blending of Vermentino and Grenache Blanc grapes; a still red wine from Germany made entirely from the Pinot Meunier grape, typically a contributing component of champagne; and an Italian red wine of remarkable finesse from Calabria, made from a blend of little known grape varieties normally used to produce local, rather rustic, wines. We have not neglected to include at least one classic-style Old World wine, a luscious red blend exemplifying the Southern Rhone. Lastly, this year to really mix things up, we have included a wine not made from grapes but from rice. This particular sake, a Shiboritate Nama Genshu, may well be a type you have not experienced, fresher and much more flavorful and complex than those most often consumed by the North American market.

We have once again accompanying food bites, two contrasting ones for each wine, intended to provide different perspectives on the characteristics of each wine. There are more warm food items this year such as grilled vegetables and shrimp, Andouille sausage and steamed dumplings, and look for some very interesting pairings such as hot buffalo chicken with sake, or boquerones with a wine made from Prie Blanc grapes.

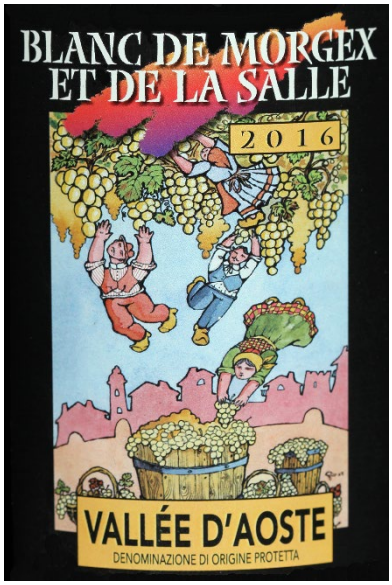
Two mystery wines also await for you to try, outcompete your colleagues' prowess in identifying them, and earn yourself a bottle.

I thank the wonderful group of members of the Wine Committee, including some three-year veterans and newcomers, that contributed to wine selection, the wine descriptions to follow, ideas for food pairings, setting up for the event, and most importantly of course, pouring wine into your glass. The members are: Ariel Vitenzon, Selina Solomon, Stacy Roudabush, Noelie Cayla, Heather Snell, Ilaria Carta, Sarah Goebel, Victoria Lovallo, Alexandra Quezada, Robyn Anderson, Kelsey McDermott, Kristin Palarz, Jacob Ratliff, Alison Xu, and Aida Davila.

Cheers,
Kostantin Dobrenis



1. Californian White Blend
Producer: Edmunds St John
Grapes: 56% Vermentino and 44% Grenache Blanc
Vintage: 2017
Pairings: Grilled lemon and garlic shrimp; roasted vegetable
Edmunds St. John's 2017 Heart of Gold is a refreshing and novel blend of Vermentino and Grenache Blanc. Winemaker and musician Steve Edmunds, working out of Berkeley, sourced the grapes from the Fenaughty Vineyards located in El Dorado County, California, that are elevated at 2800 feet and bear a dark red, well-drained volcanic origin soil called Aiken-Loam. This pale gold wine gives off a citrus and fruity aroma, with particular notes of pear. Interestingly, its fruity nature does not carry to the taste as much as one would expect. Instead, it is more mineral in the mouth, with bright acidity. Heart of Gold pairs well with almonds, manchego cheese, and salmon. (R. Anderson)



2. Italian White
Producer: Ermes Pavese
Grape: Prie Blanc
Vintage: 2016
Pairings: Vallé d'Aoste fontina cheese; boquerones
The life of Blanc de Morgex et de la Salle begins as a cluster of Prie Blanc dangling from a pergola in the mountainous terrain of Italy's Valley d'Aoste, near the summit of Mount Blanc. After surviving winter frost and conquering the summer months, each grape is picked by hand on the Pavese vineyard before undergoing the chemical process of becoming an intoxicating beverage. The aroma greets the nose with fresh scents of the outdoors and brisk mountain air, all to be expected from a wine produced at one of the highest elevation known in the winemaking community. What masterful tasters would call green and flinty, Blanc de Morgex et la Salle presents a lemony and chilled minerality ending with a gentle energy reminiscent of the close of a quiet hike. (V. Lovallo)

3. Japanese Sake
Producer: Hakkaisan
Rice: Yamadanishiki (koji); Gohyakumangoku and Koshiibuki (brewing)
Yeast: Kyokai No. 701, M310
Vintage: Brewed November 2018
Pairings: Buffalo chicken; steamed vegetable dumplings
Hakkaisan is well-known high quality brewery located in the Niigata prefecture of the Chubu region of Japan, an area with a reputation for its high quality rice. Hakkaissan uses spring water for all their sake production from Niigata's Mount Hakkai. This particular sake, "Echigo de Soro", is a Shiboritate Nama Genshu sake, in other words, freshly pressed, unpasteurized and undiluted, respectively. Along with a polishing ratio of only 60%, such sakes can be especially favorable and complex, and are only sold seasonally soon after production and must be stored cold at all times. However to best enjoy this "wine" allow it to warm up at least a few minutes in your glass. Once swirled awake, it conveys a subtle yeasty nose of fresh bread dough and sunflower seeds, along with light floral fragrances. It quickly warms the mouth in the attack, developing more fruity qualities and notes of mild caramel, white chocolate and agave nectar on the midpalate, which very nicely partner with the textural plump feel of the brew, yet still delivering an underlying clean and refreshingly bright element. The pleasantly rich and balanced flavors and texture then continue to notably linger on the tongue and throat as if being coated, and hints of coffee bean and bananas arise. (K. Dobrenis)

4. German Red
Producer: Darting Winery
Grape: Pinot Meunier
Vintage: 2016
Pairings: Roasted butternut squash; Danish blue cheese
This wine comes from the Pfalz region in Germany, west of the Rhine river and not far from the Haardt mountain range. The pinot meunier grape is best known for its common use in making sparkling wine, most famously in Champagne, France. Grapes are grown on marl and limestone hills, and the philosophy of the Darting Vineyard is to minimize handling of the grapes during the winemaking process. This wine is suggestive of fall. Intense red-brownish color, pomegranate and musk on the nose. Smooth on the palate, with moderate acidity. Mildly spicy with bay and pepper notes. Some suggested pairings are butternut squash, caramelized walnuts, and herb flavored cheese. (I. Carta)

5. French Red Blend

Producer: Domaine-de-Fenouillet

Grapes: ~50% Grenache, 40% Syrah, 10% Mourvedre

Vintage: 2016

Pairings: Smoked Andouille sausage; grilled Portobello mushroom

The Beaumes de Venise Rouge, Les Terres Blanches, is the "the most important wine of domaine" due to its value and exceptional quality (https://madrose.com/producers/france/cotes-du-rhone-south/domaine-de-fenouillet/). The winery is run by the Soard brothers, and has been in the family since the early 1900's. The winery is situated in the village of Beaumes de Venise in the Southern portion of the Rhone region of France, where the temperate Mediterranean soil adds an earthy quality to the wines produced. This particular wine is a blend of Grenache, and Syrah, with a splash of Mourvedre, which contributes to its complexity. Just like the intense color, its flavor is bold and strong, with notes of dark berries and spice. Smooth, with a hint of leather on the nose and a subtly dry finish, this wine pairs well with gamey meats such as lamb and beef. (S. Solomon, H. Snell, and A. Vitenzon)

6. Italian Red Blend

Producer: Cantina Odoardi

Grapes: Gaglioppo, Magliocco Canino, Nerello Cappuccio and Greco Nero

Vintage: 2015

Pairings: Dark chocolate with blueberries/raspberries; Soft goat cheese

These wines come from an estate in Calabria, Southern Italy, which has been cultivated by the Odoardi family since 1480. The vineyard is located in the mouth of the Savuto River and ranges in altitudes up to 610 meters above sea level. The warmer climate of Calabria allows for riper grapes, contributing to the wine's full-bodied, smooth taste, and higher alcohol content. This wine is a rare and unusual blend of mainly local grape varieties: Gaglioppo, Magliocco, Nerello Cappuccio and Greco Nero. Gaglioppo is known for producing soft red wines, containing berry flavors with secondary notes of cherry and spices. Magliocco, similar to Gaglioppo grapes, produces wines of high alcohol content with soft flavors, but with a deeper burgundy color. Greco Nero is commonly blended with Gaglioppo wines, adding to the wines' plum, cherry and black fruit notes. Nerello Cappuccio grapes, mainly grown in Sicily, provide this wine with a subtle earthy essence with notes of woodyness, vanilla, and cherry. Overall, this unique blend of grape varieties allow for a smooth, structured, and elegant wine with a lingering tannic finish. This full-bodied red wine is hot on the nose with notes of anise, spiced oakiness and a tinge of various black fruits. It can be enjoyed with blueberries which accentuate the dark berry flavors or spaghetti with chili, beef, or lamb to complement its smooth and tannic finish. (A. Davila and J. Ratliff)

Attendees

B. Abdelmesih
M. Akabas
J. Alpert
A. Alves Francisco
R. Anderson
J. Arezzo
A. Aschner
A. Autry
P. Ballabh
S. Barkley
T. Bassett
R. Batista Brito
S. Beker
M. Bennett
C. Berthoux
R. Birnbaum
K. Brace
H. Buelow
H. Byun
A. Carbonell
I. Carta
P. Castillo
N. Cayla
C. Cho
J. Chung
A. Cibelli
K. Clemenza
R. Coen-Cagli
B. Court Vazquez
N. Cuevas
A. Davila
E. de Oliveira
C. De Sanctis
P. De Sanctis
I. Deyneko
K. Dobrenis
F. Echeverry
D. Faber
R. Ferger
D. Festa
K. Fisher
A. Francesconi
M. Frechou
J. Freund
B. Galinski
S. Gokhan
T. Goncalves
M. Gronska-Peski
J. Guarque-Chabrera
M. Gulfo
M. Gulinello
D. Hall
C. Hans
H. Hatch
J. Hebert
D. Herrera
K. Hiciano
C. Hodelin
K. Jensen
B. Jordan
J. Jordan
M. Kazmierczak
S. Kharod
K. Khodakhah
N. Killian
A. Kohn
A. Krishna
J. Krzyspiak
P. Kurshan
G. Lee
P. Lituma
R. Lo Bu
V. Lovallo
S. Lutzu
I. Maroto
A. Martin
S. McCutcheon
K. McDermott
M. Mehler
M. Miah
M. Miquel
S. Molholm
H. Monday
V. Mudragel
K. Nasrallah
S. Nicola
J. Norena
M. Onate
K. Palarz
A. Pavuluri
D. Perez Vazquez
S. Poser
B. Poulos
A. Quezada
M. Rahman
C. Ramos
J. Ratliff
C. Reyes
J. Reynolds
F. Rivera
S. Roudabush
T. Rubin
C. Saqcena
J. Secombe
V. Sedwick
K. Shadron
D. Sharma
L. Sjulson
H. Snell
F. Soldner
S. Solomon
D. Spray
R. Stout
E. Sussman
O. Sysoeva
Y. Tai
S. Tikir
J. Tindi
B. Tricomi
M. Trivedi
J. Vacher
M. Vega Villar
J. Vera
V. Verselis
A. Vitenzon
S. Walkley
C. Ward
S. Washburn
N. Wazeed
D. Wilson
E. Wood
Q. Xing
A. Xu
J. Yan
H. Yang
Y. Yang
J. Yoshida
S. Zukin

Faculty Publications 2018

Joseph Arezzo:

- Pardo ID, Rao DB, Butt MT, Jortner B, Valentine WM, **Arezzo JC**, Sharma AK, and Bolon B. Toxicologic Pathology of the Peripheral Nervous System (PNS): Overview, Challenges, and Current Practices. Toxicol Pathol. 46(8):1028-1036 (2018).
- Antoine MW, Zhu X, Dieterich M, Brandt T, Vijayakumar S, McKeehan N, **Arezzo JC**, **Zukin RS**, Borkholder DA, Jones SM, Frisina RD, **Hébert JM**. Early uneven ear input induces long-lasting differences in left-right motor function. PLoS Biol. 2018 Mar 13;16(3):e2002988. doi: 10.1371/journal.pbio.2002988 (2018).

Anita Autry:

- Kohl, J., Babayan, B. M., Rubinstein, N.D., **Autry, A. E.**, Marin-Rodriguez, B., Kapoor, V., Miyamaishi, K., Zweifel, L. S., Luo, L., Uchida, N., Dulac, C. Functional circuit architecture underlying parental behavior. Nature, 556 (7701) 326-331. 2 (2018).

Renata Batista-Brito:

- **Batista-Brito R**, Zagha E, Ratliff JM, Vinck M. Modulation of cortical circuits by top-down processing and arousal state in health and disease. Curr Opin Neurobiol. 52:172-181 (2018).
- Mayer C, Hafemeister C, Bandler RC, Machold R, **Batista Brito R**, Jaglin X, Allaway K, Butler A, Fishell G, Satija R. Developmental diversification of cortical inhibitory interneurons. Nature. 555(7697):457-462 (2018).

Michael V.L. Bennett:

- Xia Y, Pu H, Leak RK, Shi Y, Mu H, Hu X, Lu Z, Foley LM, Hitchens TK, Dixon CE, **Bennett MVL**, Chen J. Tissue plasminogen activator promotes white matter integrity and functional recovery in a murine model of traumatic brain injury. Proc Natl Acad Sci USA. 115:E9230-E9238, https://doi.org/10.1073/pnas.1810693115 (2018).
- Yan J, Porch MW, Court-Vazquez B, **Bennett MVL**, **Zukin RS.** Activation of autophagy rescues synaptic and cognitive deficits in fragile X mice. Proc Natl Acad Sci USA. 115:E9707-E9716 (2018).

Pablo Castillo:

- Weng FJ, Garcia RI, Lutzu S, Alviña K, Zhang Y, Dushko M, Ku T, Zemoura K, Rich D, Garcia-Dominguez D, Hung M, Yelhekar TD, Sørensen AT, Xu W, Chung K, **Castillo PE**, Lin Y. Npas4 Is a Critical Regulator of Learning-Induced Plasticity at Mossy Fiber-CA3 Synapses during Contextual Memory Formation. Neuron 97:1137-1152 (2018).
- Monday HR, Younts TJ, **Castillo PE**. Long-Term Plasticity of Neurotransmitter Release: Emerging Mechanisms and Contributions to Brain Function and Disease. Annu Rev Neurosci. 41:299-322 (2018).
- Nandi S, Alviña K, Lituma PJ, **Castillo PE**, **Hébert JM**. Neurotrophin and FGF Signaling Adapter Proteins, FRS2 and FRS3, Regulate Dentate Granule Cell Maturation and Excitatory Synaptogenesis. Neuroscience. 369:192-201. doi: 10.1016/j.neuroscience.2017.11.017 (2018).

Kostantin Dobrenis:

- Boutry M, Branchu J, Lustremant C, Pujol C, Pernelle J, Matusiak R, Seyer A, Poirel M, Chu-Van E, Pierga A, **Dobrenis K,** Puech JP, Caillaud C, Durr A, Brice A, Colsch B, Mochel F, El Hachimi KH, Stevanin G, Darios F. Inhibition of Lysosome Membrane Recycling Causes Accumulation of Gangliosides that Contribute to Neurodegeneration. Cell Rep. 23(13):3813-3826 (2018).
- Kerner-Rossi M, **Gulinello M, Walkley S**, **Dobrenis K.** Pathobiology of Christianson syndrome: Linking disrupted endosomal-lysosomal function with intellectual disability and sensory impairments. Neurobiol Learn Mem. pii: S1074-7427(18)30114-X. doi: 10.1016/j.nlm.2018.05.004 (2018).

Donald Faber:

- **Faber DS** and **Pereda A**. Two forms of electrical transmission between neurons. Front Mol Neurosci. 11:427. doi: 10.3389/fnmol.2018.00427. (2018).

Tiago Gonçalves:

- An in vivo model of functional and vascularized human brain organoids. Mansour AA, **Gonçalves JT**, Bloyd CW, Li H, Fernandes S, Quang D, Johnston S, Parylak SL, Jin X, Gage FH. Nat Biotechnol. 36(5):432-441. doi: 10.1038/nbt.4127 (2018).

David Hall:

- Clark JF, Meade M, Ranepura G, **Hall DH**, Savage-Dunn C. Caenorhabditis elegans DBL-1/BMP Regulates Lipid Accumulation via Interaction with Insulin Signaling. G3 (Bethesda). 8(1):343-351 (2018).
- Gibson CL, Balbona JT, Niedzwiecki A, Rodriguez P, Nguyen KCQ, **Hall DH**, Blakely RD. Glial loss of the metallo β-lactamase domain containing protein, SWIP-10, induces age- and glutamate-signaling dependent, dopamine neuron degeneration. PLoS Genet. 14(3):e1007269 (2018).
- Soulavie F, **Hall DH**, Sundaram MV. The AFF-1 exoplasmic fusogen is required for endocytic scission and seamless tube elongation. Nat Commun. 9(1):1741 (2018).
- Al-Hashimi H, **Hall DH**, Ackley BD, Lundquist EA, Buechner M. Tubular Excretory Canal Structure Depends on Intermediate Filaments EXC-2 and IFA-4 in Caenorhabditis elegans. Genetics. 210(2):637-652 (2018).
- Mutlu B, Chen HM, Moresco JJ, Orelo BD, Yang B, Gaspar JM, Keppler-Ross S, Yates JR 3rd, **Hall DH**, Maine EM, Mango SE. Regulated nuclear accumulation of a histone methyltransferase times the onset of heterochromatin formation in C. elegans embryos. Sci Adv. 4(8):eaat6224 (2018).

Jean Hébert:

- **Hébert JM**, Vijg J. Cell Replacement to Reverse Brain Aging: Challenges, Pitfalls, and Opportunities. Trends Neurosci. 41(5):267-279. doi: 10.1016/j.tins.2018.02.008. (2018).
- Antoine MW, Zhu X, Dieterich M, Brandt T, Vijayakumar S, McKeehan N, **Arezzo JC, Zukin RS,** Borkholder DA, Jones SM, Frisina RD, **Hébert JM.** Early uneven ear input induces long-lasting differences in left-right motor function. PLoS Biol. 16(3):e2002988. doi: 10.1371/journal.pbio.2002988. (2018).
- Nandi S, Alviña K, Lituma PJ, **Castillo PE**, **Hébert JM**. Neurotrophin and FGF Signaling Adapter Proteins, FRS2 and FRS3, Regulate Dentate Granule Cell Maturation and Excitatory Synaptogenesis. Neuroscience. 369:192-201. doi: 10.1016/j.neuroscience.2017.11.017. (2018).

Kamran Khodakhah:

- Tara E, Vitenzon A, Hess E, **Khodakhah K.** Aberrant cerebellar Purkinje cell activity as the cause of motor attacks in a mouse model of episodic ataxia type 2. Dis Model Mech. 11(9). pii: dmm034181 (2018).
- Kros L, Lykke-Hartmann K, **Khodakhah K.** Increased susceptibility to cortical spreading depression and epileptiform activity in a mouse model for FHM2. Sci Rep. 8(1):16959. doi: 10.1038/s41598-018-35285-8 (2018).
- Kros L, Angueyra Aristizábal CA, **Khodakhah K**., Cerebellar involvement in migraine. Cephalalgia. 38(11):1782-1791. doi: 10.1177/0333102417752120 (2018).

Adam Kohn:

- Aschner A, Solomon SG, Landy MS, Heeger DJ, **Kohn A**. Temporal Contingencies Determine Whether Adaptation Strengthens or Weakens Normalization. J Neurosci. 38(47):10129-10142 (2018).
- Russo AA, Bittner SR, Perkins SM, Seely JS, London BM, Lara AH, Miri A, Marshall NJ, **Kohn A**, Jessell TM, Abbott LF, Cunningham JP, Churchland MM. Motor Cortex Embeds Muscle-like Commands in an Untangled Population Response. Neuron. 97(4):953-966.e8. doi: 10.1016/j.neuron.2018.01.004. (2018).

Saleem Nicola:

- Caref K and **Nicola SM.** Endogenous opioids in the nucleus accumbens promote approach to high-fat food in the absence of caloric need. eLife, 7:e34955 (2018).

José Luis Peña:

- Cazettes F, Fischer BJ, Beckert MV, **Pena JL** Emergence of an adaptive command for orienting behavior in premotor brainstem neurons of barn owls. Featured article, Journal of Neuroscience, 38: 7270-7279 (2018).
- Batista G, Johnson JL, Dominguez E, Costa-Mattioli M, **Pena JL.** Regulation of filial imprinting and structural plasticity by mTORC1 in newborn chickens. Scientific Reports, 8:8044 | DOI:10.1038/s41598-018-26479-1 (2018).
- Fischer BJ, Wydick JL, Köppl C, **Pena JL.** Multidimensional stimulus encoding in the auditory nerve of the barn owl. J. Acoustical Society of America, 144(4): 2016-2027 (2018).

Alberto Pereda:

- Marsden K.C., Jain R.A., Wolman M., Echeverry F.A., Nelson J.C., Hayer K.E., Miltenberg. B., **Pereda A.E.**, and Granato M. A Cyfip2-dependent excitatory interneuron pathway establishes the innate startle threshold. Cell Rep. 23(3):878-887 (2018).
- Jain R.A., Wolman M.A., Marsden K.C., Nelson J.C., Shoenhard H., Echeverry F.A., Szi C., Bell H., Skinner J., Cobbs E.N., Sawada K., Zamora A., **Pereda A.E.**, Granato M. A forward genetic screen in zebrafish identifies the G-protein coupled receptor CaSR as a modulator of sensorimotor decision-making. *Current Biology*, 28:1357-1369 (2018).
- **Faber D.S.** and **Pereda A**. Two forms of electrical transmission between neurons. Front Mol Neurosci. 11:427. doi: 10.3389/fnmol.2018.00427. (2018).

Lucas Sjulson:

- Cocaine Place Conditioning Strengthens Location-Specific Hippocampal Coupling to the Nucleus Accumbens. **Sjulson L**, Peyrache A, Cumpelik A, Cassataro D, Buzsáki G. Neuron. 98(5):926-934.e5. doi: 10.1016/j.neuron.2018.04.015 (2018).

David Spray:

- Zhao R, Najmi M, Aluri S, **Spray DC**, Goldman ID. Concentrative Transport of Antifolates Mediated by the Proton-Coupled Folate Transporter (SLC46A1); Augmentation by a HEPES Buffer. Mol Pharmacol. 93(3):208-215 (2018).
- Iacobas DA, Iacobas S, Tanowitz HB, Campos de Carvalho A, **Spray DC**. Functional genomicfabrics are remodeled in a mouse model of Chagasic cardiomyopathy and restored following cell therapy. Microbes Infect. 20(3):185-195 (2018).
- Cabahug-Zuckerman P, Stout RF Jr, Majeska RJ, Thi MM, **Spray DC**, Weinbaum S, SchafflerMB Potential role for a specialized β3 integrin-based structure on osteocyte processes in bone mechanosensation. J Orthop Res. 36(2):642-652 (2018).

Elyse Sussman:

- Yu YH, Shafer VL, **Sussman ES.** The duration of auditory sensory memory for vowel processing: Evidence from neurophysiological and behavioral measures. Frontiers in Psychology Auditory Cognitive Neuroscience. doi.org/10.3389/fpsyg.2018.00335 (2018).

Vytautas Verselis:

- Srinivas M, **Verselis VK** and White TW. 2018. Human disease associated with connexin mutations. Biochim. Biophys Acta Biomembr. 1860:192-201 (2018).
  Delmar M, Laird DW, NAus CCm Nielson MS, **Verselis VK** and White TW. Connexins and disease. Cold Spring Harb Persepct Biol. 4: 1-18.5 (2018).

Steven U. Walkley:

- Kerner-Rossi M, **Gulinello M**, **Walkley S**, **Dobrenis K.**, Pathobiology of Christianson syndrome: Linking disrupted endosomal-lysosomal function with intellectual disability and sensory impairments. Neurobiol Learn Mem. pii: S1074-7427(18)30114-X. doi: 10.1016/j.nlm.2018.05.004 (2018).
- Boudewyn LC, **Walkley SU**., Current concepts in the neuropathogenesis of mucolipidosis type IV. J. Neurochem. doi: 10.1111/jnc.14462 (2018).

R. Suzanne Zukin:

- Yan J, Porch MW, Court-Vazquez B, **Bennett MVL**, **Zukin RS.** Activation of autophagy rescues synaptic and cognitive deficits in fragile X mice. Proc Natl Acad Sci USA, 115(41):E9707-E9716 (2018).
- Hwang J-Y. and **Zukin RS.** REST, a master transcriptional regulator in neurodegenerative disease. Curr. Opin. Neurobiol. 48:193-200, (2018).
- Hwang JY, Aromolaran KA, **Zukin RS**. Author Correction: The emerging field of epigenetics in neurodegeneration and neuroprotection. Nat Rev Neurosci. (12):771. doi: 10.1038/s41583-018-0065-5. (2018).

- Antoine MW, Zhu X, Dieterich M, Brandt T, Vijayakumar S, McKeehan N, **Arezzo JC**, **Zukin RS**, Borkholder DA, Jones SM, Frisina RD, **Hébert JM**. Early uneven ear input induces long-lasting differences in left-right motor function. PLoS Biol. 2018 Mar 13;16(3):e2002988. doi: 10.1371/journal.pbio.2002988 (2018).

Faculty Seminars and Talks 2018

Joseph Arezzo:

- "Assessment and training of neuropathy in children", DPPOS, Maryland (February 2018).
- "Outlining procedures for the assessment of peripheral neuropathy", Zafgen (February 2018).
- "Novel work targeting peripheral nerve damage in ongoing human clinical studies", Regeneron, (March 2018)
- "Outlining the methods and analysis of novel approaches to the assessment of seizures in experimental animal models", Merck (June 2018).
- "Exploring procedures for the assessment of deficits in auditory processing", Pfizer, (September 2018).
- "Outlining novel approaches to the assessment of peripheral neuropathy", AbbVie, (October 2018).
- "Outlining the strengths and limitations of various measures of the assessment of nerve damage" American College of Toxicology (November 2018).

Renata Batista-Brito:

- "Developmental dysfunction of VIP interneurons impairs cortical circuits", Developing Brains – The Nobel Forum, Stockholm, Sweden (September 2018).
- "Cortical inhibition in health and disease", Einstein Internal Faculty Seminar, Albert Einstein College of Medicine, N.Y. (October 2018).
- "Cortical inhibition in health and disease", Seeds for collaboration, Albert Einstein College of Medicine, N.Y. (October 2018).
- "Cortical inhibition in health and disease", the Sixth Annual Isabelle Rapin Conference on Communication Disorders, Albert Einstein College of Medicine, N.Y. (November 2018).
  "Cortical inhibition in health and disease", Allen Institute showcase, Seattle, WA (December 2018).

Pablo Castillo:

- "Presynaptic Plasticity: Novel Functions and Mechanisms" - Centre for Integrative Neuroscience, University of Tübingen, Germany (March 2018).
- "Presynaptic Plasticity: Novel Functions and Mechanisms" - Texas Tech University Health Sciences Center, Lubbock, TX, (April 2018).
- "Presynaptic plasticity at an associative circuit in the dentate gyrus" - 5th International Symposium on Synaptic Transmission and Plasticity, Guangzhou, China (April 2018).
- "Presynaptic Plasticity: Novel Functions and Mechanisms" - National Institute of Mental Health, Bethesda, MD (May 2018).
- "Presynaptic plasticity at an associative circuit in the dentate gyrus" - 11th Forum of Neuroscience, Fens, Berlin, Germany (July 2018).
- "Presynaptic plasticity at an associative circuit in the dentate gyrus" - BonnBrain3, Bonn, Germany (2018).

- "Presynaptic plasticity at an associative circuit in the dentate gyrus" - University of California, Irvine, CA (October 2018).
- "Long-term Presynaptic Plasticity: Novel Functions and Mechanisms" - Northwestern University, Chicago, IL (October 2018).
- "Presynaptic plasticity at an associative circuit in the dentate gyrus" - Autonomous University of Madrid, Spain (December 2018).

Kostantin Dobrenis:

- "Cyclodextrins in the Therapy of Niemann Pick C Disease", Derek Horton Award Session, 255th American Chemical Society National Meeting, New Orleans, Louisiana (March 2018).
- "Science of Salla Disease", Rare Disease Day 2018: Living with a Rare Disease—the Family-Clinician-Scientist Partnership, Einstein-Montefiore, Bronx, N.Y. (February 2018).
- "Perspectives on Treatment of Neurologic Lysosomal Storage Diseases", Center for Dementia Research, Nathan S. Kline Institute, Orangeburg, N.Y. (March 21, 2019).

J. Tiago Goncalves:

- "In vivo 2-photon imaging of neuronal development", Universidad Autonoma de Barcelona, Spain (January 2018).
- "Adult neurogenesis in the hippocampus: from stem cells to behavior", City University of New York (October 2018).
- "An In vivo model of functional and vascularized human brain organoids" Einstein Stem Cell Retreat, New Paltz, NY (October 2018).
- "Adult neurogenesis in the hippocampus: from stem cells to behavior", Fordham University (October 2018).
- "Adult neurogenesis in the hippocampus: from stem cells to behavior", Einstein Cancer Center Advances Meeting, New Rochelle, NY (October 2018).

David Hall:

- "Electron microscopy of nematode neurons: origin and future of connectomics", Fudan University, Shanghai, China (April, 2018).
- "Gap junctions in C. elegans", Fudan University (April 2018).
  "New methods for 3D anatomy of the nematode, C. elegans", Fudan University (April 2018).

Jean Hébert:

- "Replacement as an approach to undo aging - even for the brain?", SENS Research Foundation/Forever Healthy Foundation Conference on Undoing Aging, Berlin, Germany (March 2018).
- "Replacement as an approach to undo aging – even for the brain?", Gordon Conference - FGFs in Development and Disease, Ventura California (March 2018).
- "Distinct FGFR functions depending on the adult neural stem cell niche", Neurosurgery Grand Rounds, Montefiore Hospital (December 2018).

Bryen Jordan:

- “Signaling to the nucleus and back”, Neuroscience Seminar Series, St. John's University (October 2018).
- “RNA Binding Proteins in Local Synaptic Function”, Neuroscience Symposium, NYU Langone School of Medicine (November 2018).
- “Signaling from Synapses to the Nucleus and Back”, Neuroscience Seminar Series, Universitat Autonoma de Barcelona (November 2018).

Kamran Khodakhah:

- “Cerebellar Modulation of Addictive and Social Behavior”, Johns Hopkins Neuroscience Retreat (September 2018).
- The Brain Sciences Initiative, Basic Science Chairs Meeting, Albert Einstein College of Medicine (November 2018).
- “Cerebellar modulation of the reward circuitry: implications for addictive & social behaviors”, New Jersey Institute for Technology (November 2018).
- “Cerebellar modulation of the brain's dopaminergic pathways, on the Cerebellum motor and non-motor functions”, University of Minho (November 2018).
- “Cerebellar dysfunction in ataxias and Dystonias”, IBRO-APRC 5th Tehran School of Neuroscience (November 2018).
- “The motor & non-motor functions of the Cerebellum”, NeRD Retreat, Portugal (November 2018).
- “Cerebellar Modulation of the Reward Circuitry: Implications for Addictive & Social Behaviors”, Internal Faculty Seminar, Albert Einstein College of Medicine (December 2018).

Adam Kohn:

- "Corticocortical signaling between populations of neurons", Brown University, (April 2018).

Saleem Nicola:

- “Cued approach learning requires an NMDA receptor-dependent increase in cue-evoked excitation in the nucleus accumbens”, Universidade Federal do Paraná, Curitiba, Brazil (July 2018).
  “Cued approach learning requires an NMDA receptor-dependent increase in cue-evoked excitation in the nucleus accumbens”, National Institute on Alcohol Abuse and Alcoholism (April 2018).

Jose Luis Peña:

- "Anticipated ITD statistics built-in human sound localization", Eastern Auditory Retreat, City College, New York (June 2018).
- "Emergence of an adaptive behavioral command for sound localization", Hearing and Communication in Neuroscience Seminar Series, University of Southern California (March 2018).
- "Emergence of an adaptive behavioral command for sound-orienting behavior in owls and translation to humans", Kresge Hearing Research Institute, University of Michigan, Ann Arbor (February 2018).

Alberto Pereda:

- "Electrical synapses and their interactions with chemical synapses", Universitat de Barcelona, Barcelona (March 2018).
- "Dynamic properties of synaptic transmission mediated by gap junctions", Hospital Ramón y Cajal, Madrid (March 2018).

Lucas Sjulson:

- "Neural circuitry of addiction", Albert Einstein College of Medicine, Psychiatry Grand Rounds (March 2018).
- "Cocaine place conditioning strengthens location-specific hippocampal inputs to nucleus accumbens", National Institute on Drug Abuse (April 2018).
- "Cocaine place conditioning strengthens location-specific hippocampal inputs to nucleus accumbens", Rockefeller University (June 2018).
- "Cocaine place conditioning strengthens location-specific hippocampal inputs to nucleus accumbens", Columbia University School of Engineering and Applied Sciences (October 2018).

David Spray:

- "Role of the Gap Junction Nexus in establishment and maintenance of Blood-Brain-Barrier- Department of Molecular Psychiatry", University of Bonn (June 14, 2018).
- "What holds the brain together: Adhesive and communicating junctions in the nervous system and their regulation", Department of Bioscience, University of Bari (June 18, 2018).
- "Glia, neuronal and glial-neuronal gap junctions: What they are, how they work and how dysfunction causes disease", Department of Neuropathology, University of Bari College of Medicine, (June 19, 2018).

Elyse Sussman:

- "Attention, Expectation, and Awareness: Contributions from MMN" and "Stimulus expectations and implicit learning: implications for MMN". Mismatch Negativity conference, Helsinki, Finland (Symposium Co-chair, June 2018).
- "Influences on Typical and Atypical Language Development", Society for Psychophysical Research, Quebec, Canada (Symposium Chair, October 2018).

Steven U. Walkley:

- "Normal Lysosomal Function", Lysosomal Disease Network meeting, San Diego, CA (February 2018)
- "Lysosomal Storage Diseases", Lysosomal Disease Network meeting, San Diego, CA (February 2018).
- "Niemann-Pick Disease Type C: A neurodegenerative disease" 10th Scientific Symposium on Niemann-Pick disease Type C (NP-C): Continuing our 10-year voyage of discovery, Amsterdam, The Netherlands (Keynote speaker, March 2018).
- "Niemann-Pick C in 2018 and Beyond: Quo vadis NP-C?" 10th Scientific Symposium on Niemann-Pick disease Type C (NP-C): Continuing our 10-year voyage of discovery, Amsterdam, The Netherlands (March 2018).
- "Neurometabolic Disease: A new era is upon us", National Tay-Sachs and Allied Diseases Foundation meeting, Jacksonville FL, (April 13, 2018.
- "The Art of the Soluble: Charting the journey to develop a therapy for the rare genetic brain disease, Niemann-Pick type C", Department of Molecular & Human Genetics, Baylor College of Medicine (April 2018).

- "The Art of the Soluble: Charting the journey to develop a therapy for the rare genetic brain disease, Niemann-Pick type C", Johns Hopkins School of Medicine (May 2018).

R. Suzanne Zukin:

- "Activation of autophagy rescues cognitive deficits in Fragile X mice", Winter Brain Conference, Vancouver, BC, (January 2018).
- "The memory protein CPEB3 coordinates AMPA receptor mRNA targeting to dendrites and transcription in neurons of Fragile X mice", UC Irvine, (May 2018).
- "The memory protein CPEB3 coordinates AMPA receptor mRNA targeting to dendrites and transcription in neurons of Fragile X mice", UC Irvine (Oct 2018).
- "Global ischemia induces lysosomal-mediated degradation of mTOR and activation of autophagy in hippocampal neurons destined to die", Fudan Conference on Brain Injury, Shanghai, (Nov 2018).

Grant Review Panels and NIH Study Sections 2018

Pablo Castillo:

- Ad Hoc member, Special Emphasis Panel ZRG1 MDCN-P-57, Cellular and Molecular Biology of Complex Brain Disorders (October 2018).
- Ad Hoc member, Special Emphasis Panel ZRG1 MDCN-P-57, Cellular and Molecular Biology of Complex Brain Disorders (June 2018).
- Ad Hoc member, NIDA Research "Center of Excellence" Grant Program (P50) ZDA1GXM-A-02, (March 2018).
- Ad Hoc member, NIDA Research "Core Center of Excellence" Grant Program (P30) ZDA1GXM-A-01 (March 2018).

Kostantin Dobrenis:

- Member, NIH ZNS1 SRG-J 18 Special Emphasis Panel (February 2018).
- Ad-hoc member, NIH NSDB Study section (February 2018).
- Member, NIH ZNS1 SRB-J(23) Special Emphasis Panel (Oct. 2018).
- Member, NIH ZRG1 MDCN-G (04) M Special Emphasis Panel (December 2018).

Anna Francesconi:

- Ad hoc reviewer, University of Strasbourg Institute for Advanced Study (USIAS), Strasbourg Fr.

J. Tiago Gonçalves:

- Reviewer for Grad Women in Science Fellowships (March 2018).
- Grant reviewer for Neurological Foundation of New Zealand (October 2018).

David Hall:

- Fund for Scientific Research, FNRS. Brussels, Belgium. 4 reviews during 2018.
- BBSRC, Royal College, UK. One review in 2018.

Jean Hébert:

- NIH, NCF Study Section. Hong Kong Research Grant Council, Biology and Medicine Panel.

Bryen Jordan:

- NIH CSR special emphasis panel MDCN-P-03.
- NIH CSR special emphasis panel ZRG1-MDCN-N-52.
- NIH CSR special emphasis panel ZRG1-MDCN-Q-50.
- Standing member: NIH Synapses and cytoskeleton (SYN) study section.

Kamran Khodakhah:

- Chair, SMI NIH Study Section
- Simons Foundation Bridge to Independence
- NWO, Netherlands
- Grass Fellowship Program
- Neurological Foundation of NZ
- National Ataxia Foundation

Adam Kohn:

- ZRG1 IFCN-T, BRAIN Initiative Special Emphasis Panel, NIH.
- ZRG1 IFCN-Y, Special Emphasis Panel, NIH.

Saleem Nicola:

- National Institute on Drug Abuse Cutting Edge Basic Research Awards (CEBRA).
- National Institutes of Health Integrative, Functional and Cognitive Neuroscience Integrated Review Group Special Emphasis Panel.
- National Institute on Drug Abuse K99 Special Emphasis Panel.
- National Institutes of Health Neurobiology of Motivated Behavior (NMB) study section.

Jose Luis Peña:

- AUD NIH study section – permanent member.
- Brain Initiative – K99/diversity panel.

David Spray:

- Standing member, FO3B Fellowships: Biophysical, Physiological, Pharmacological and Bioengineering Neuroscience (Winter, Spring, Fall meetings 2018).
- Ad hoc, Intercellular Interaction (Summer 2018).
- Ad hoc, French Telethon.
- Ad hoc, Italian ministry.
- JINRA grant review mock study section.

Elyse Sussman:

- National Institute of Deafness and other Communication Disorders, Special Emphasis Panel for Voice, Speech and Language Fellowship Application Review (ZDC1 SRB Y54), (February 2018).

Vytautas Verselis:

- Action of Hearing Loss (Ad Hoc Reviewer).
- Einstein IDDRC Pilot Grant Review Panel (Internal).

Steven U. Walkley:

- Permanent Member, Developmental Brain and Disease Study Section, National Institutes of Health (Winter, Spring, Fall meetings, 2018).
- Ad hoc reviewer for BSC Site Visit (intramural) review for the National Heart Lung & Blood Institute, NIH, Bethesda, MD (April 2018).
- Million Dollar Bike Ride Rare Disease Research Center Grant Review, University of Pennsylvania, (November 2018).
- Special NIH teleconference review, Developmental Brain and Disease Study Section, NIH (December 2018).

R. Suzanne Zukin:

- Cellular and Molecular Biology of Neurodegeneration (CMND) Study Section.

Advisory and Editorial Boards 2018

Joseph Arezzo:

- BluePrint Medicines Cognitive Effects Advisory Board.
- Merck Pharmaceuticals - Advisory Board.
- Hoffman La Roche- Advisory Board.

Renata Batista-Brito:

- Next Generation Leadership Council.
- The Allen Brain Institute Board of Directors.

Pablo Castillo:

- Editorial Board member of Physiological Reviews.
- Editorial Board member of eNEURO.
- Editorial Board member Neuroscience, IBRO Journal.

Donald Faber:

- New York State Injury Research Board, Vice-Chair.

David Hall:

- Editorial Board, Journal of Histochemistry & Cytochemistry.
- Board of Directors, New Jersey Audubon. Board of Directors, Bergen County Audubon Society.

Kamran Khodakhah:

- Scientific Review Board, Simons Foundation Autism Research Initiative.
- Grass Foundation Trustee.
- SfN Neuroscience Training Committee.
- External Scientific Advisory Board, Institute for Neuroscience, University Autonoma de Barcelona.

Adam Kohn:

- Member, Editorial Board, PLOS Biology.

Alberto Pereda:

- Editorial Board Member, Developmental Neurobiology.

David Spray:

- Editorial Board, Glia. Editorial Board, American Journal of Pathology.
- Editorial Board, Journal of Pharmacology and Therapeutics.
- Editorial Board, American Journal of Physiology – Cell Physiology.
- Editorial Board, Journal of Neuroscience Research.
- Editorial Board, Brazilian Academy of Sciences.
- Editorial Board, Journal of Integrative Neuroscience.

Elyse Sussman:

- Editorial Board Member, International Journal of Psychophysiology.
- Editorial Board Member, Scientific Reports, Nature publishing group.

Steven U. Walkley:

- Scientific Advisory Board, International Society for Mannosidosis and Related Diseases.
- Scientific Advisory Board, National MPS Society.
- Scientific Advisory Board, National Tay-Sachs and Allied Diseases Foundation.
- Scientific Advisory Board, A STAR for Ben Foundation.
- Scientific Advisory Board, ML4 Foundation.
- Scientific Advisor, Hide and Seek Foundation for Research on lysosomal diseases.
- Scientific Advisor, Dana's Angels Research Trust.

Edith Macy Maps and Floor Plans

Edith Macy Conference Center
Guest Rooms Layout

321	320	319	318	317	316	Top Lobby	311	312	313	314	315
2 D	2 D	2S - 1D	2S - 1D	2D	2D		2D	2S - 1D	2S - 1D	2D	2D

North Building

310	309	308	307	306	305	Lobby	304	303	302	301	300
2D	2D	2D	2D	2D	2D		2D	2D	2D	2D	2D

212	211	210	209	208	Top Lobby	207
2 D	2 D	2S - 1D	2D	2D		2S - 1D

West Building

206	205	204	203	202	Lobby	201	200
2D	2D	2D	2D	2D		2D - H	2D-H

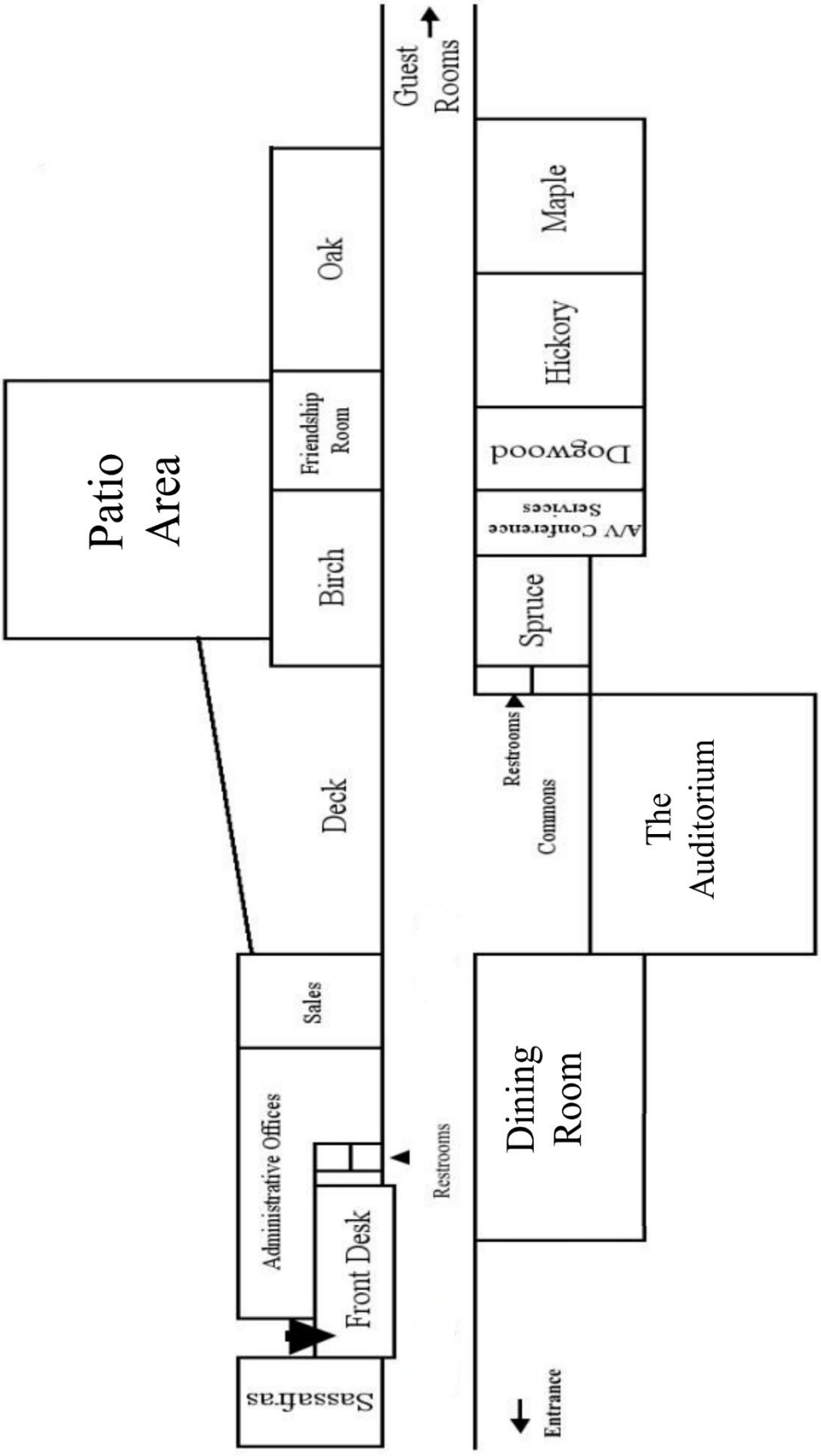
110	109	Top Lobby	106	107	108
2S - 1D	2D		2S - 1D	2D	2D

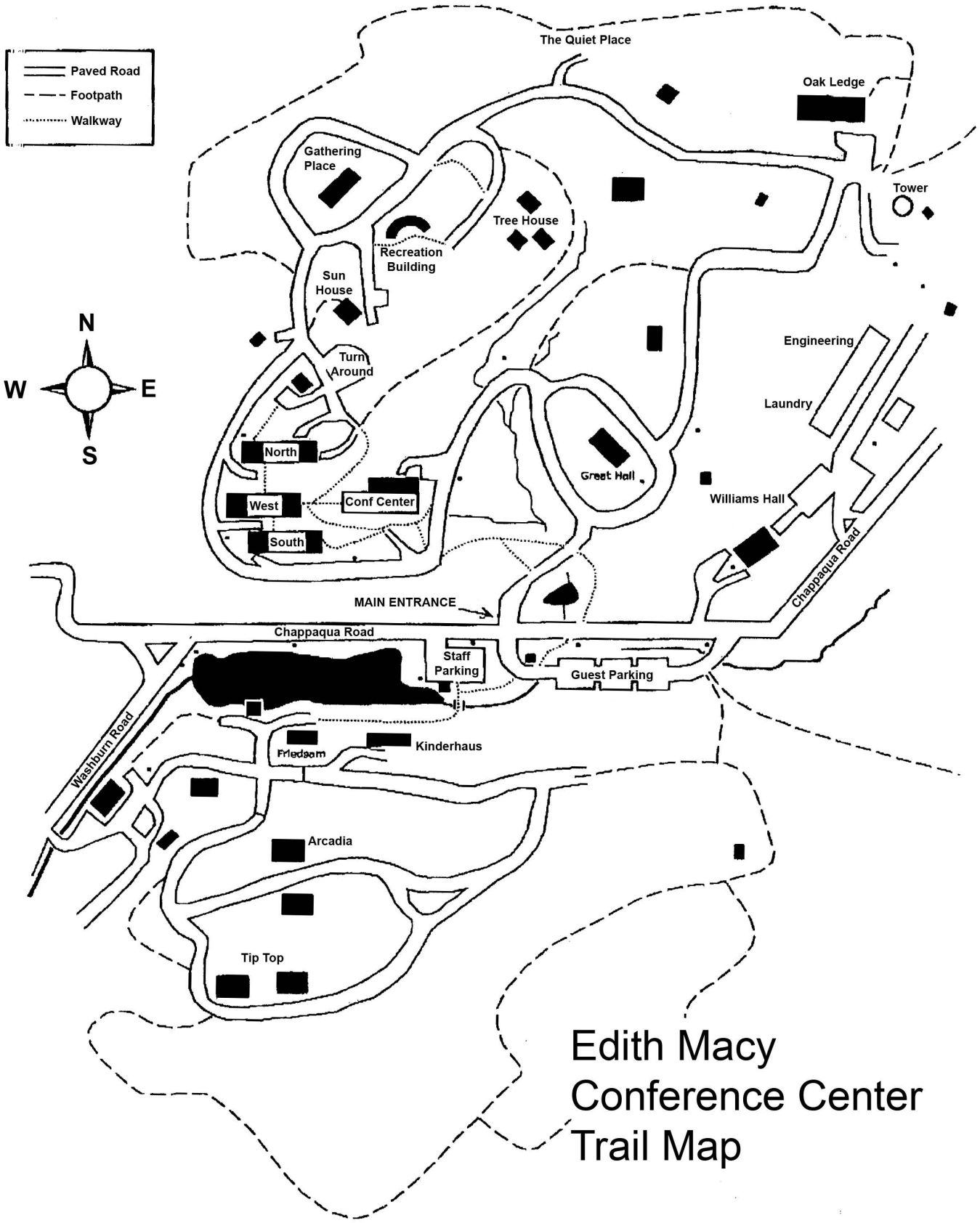
South Building

105	104	Lobby	103	102	101	100
2D	2D		2D	2D	2D-H	2D - H

⟺ = Ramp

Conference Center Map




Paved Road
Footpath
Walkway
The Quiet Place
Oak Ledge
Gathering Place
Tower
Tree House
Recreation Building
Sun House
N
W
E
S
Turn Around
Engineering
Laundry
North
West
Conf Center
South
Great Hall
Williams Hall
Chappaqua Road
MAIN ENTRANCE
Chappaqua Road
Staff Parking
Guest Parking
Washburn Road
Friedsam
Kinderhaus
Arcadia
Tip Top
Edith Macy
Conference Center
Trail Map

Leader in a New Field of Study

Dominick Purpura arrived on the Einstein campus in 1967, recruited from the College of Physicians and Surgeons at Columbia, to be professor and chair of anatomy. In 1969, he was appointed scientific director of Einstein's Rose F. Kennedy Center, which focuses on research of the causes of intellectual and developmental disabilities; he was named the center's director in 1972. Two years later, he founded and was named professor and chair of neuroscience—a new department and field of study that he helped to establish. Under Dr. Purpura's direction, Einstein's Kennedy Center and neuroscience department achieved international renown for pioneering interdisciplinary research in the brain sciences. (The department at the College of Medicine has borne his name since his retirement in 2006, a tribute to his leadership and influence in neuroscience at Einstein and beyond.)

In presenting Dr. Purpura with the 1996 Presidential Award from the Society for Neuroscience, Dr. Pasko Rakic noted that Dr. Purpura "was a neuroscientist before the word neuroscience was invented to denote our multidisciplinary field." When he was leaving Einstein in 1982, having been recruited to the deanship at Stanford University School of Medicine, a colleague observed, "Dom has shepherded and fostered and sustained the growth of neuroscience at Einstein during its critical early years… and leaves behind an interdisciplinary and multifaceted structure of people and programs that is one of the major strengths of this institution."

His exceptional contributions span the field of neuroscience. While initial work focused on neurophysiology, his research on the origin of brain waves and on the effects of hallucinogenic agents had a great impact on research of epilepsy—which, in 1992, led the American Epilepsy Society to present him with its Clinical Science Research Award. Turning his interests to developmental neuroscience and developmental neuropathology, he used state-of-the-art neuroanatomical techniques to demonstrate that structural abnormalities of nerve cells in the brain are fundamentally involved in intellectual disabilities and other disorders of cognitive development. His pioneering work on an animal model of the rare genetic disorder Tay-Sachs disease and articles on the abnormal development of dendritic spines on cortical neurons in congenital formations offered

early examples that demonstrated the power of neuroscience to address clinically important issues. He was author of more than 200 scientific papers and chapters during his distinguished career.

Visionary Leadership

Dr. Purpura opted not to pursue a career in neurosurgery, focusing on research instead, because he realized he could reach more people through his scientific investigations. He also stepped into the administrative realm—first as a department chair and center director, and later as dean—so that he could help younger generations reach their potential. In addition to these roles at Einstein—and two years as dean at Stanford—Dr. Purpura served 30 years (1970 to 2000) as editor-in-chief of *Brain Research*, a multidisciplinary journal established in 1966 that has become the largest storehouse of information for neuroscientists worldwide.

He also held leadership roles in numerous professional organizations, including president of the Eastern Association of Encephalographs, the American Epilepsy Society, the Society for Neuroscience, and the International Brain Research Organization. He also served as member and/or chair of the Neurology A Study Section of the National Institutes of Health (NIH), and was elected to the National Academy of Sciences and its Institute of Medicine.

At the academy, he chaired the committee that produced the first *Guidance for Research in Animals*, which has served as the starting point for subsequent versions that have followed. He also advised Congress on issues related to neuroscience as a representative to the National Research Council, and he was one of just two scientists in the nation to receive the inaugural National Medical Research Award bestowed by the council at a White House ceremony in September, 1988. And, he received New York City's highest honor, the Mayor's Award for Excellence in Science and Technology in recognition of his numerous achievements and contributions.

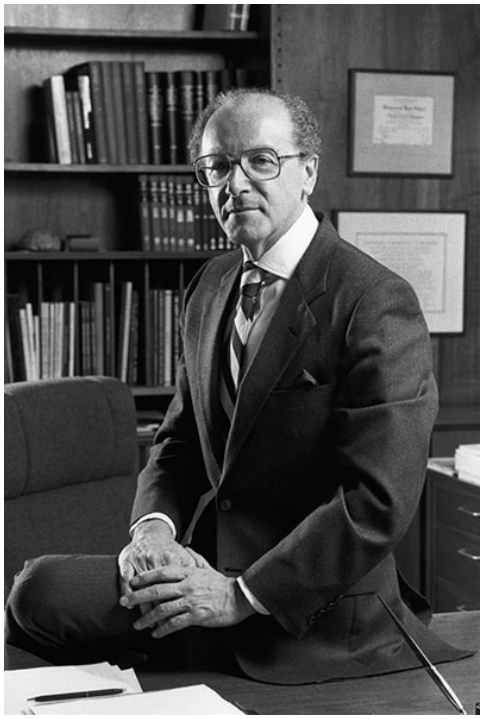
In further recognition of his influence and leadership, he was among the candidates considered for directorship of the NIH during George H.W. Bush's presidency. In a newsletter to the Einstein community he shared:

"On June 27th I was interviewed by Secretary Louis J. Sullivan as a candidate for the Directorship of the National Institutes of Health… Secretary Sullivan requested that I notify him within two weeks of that date as to my willingness to accept the position of Director if it was offered to me by the President. After much deliberation, I informed the Secretary on July 5th of my decision to withdraw my candidacy… I came to Einstein in 1967 to build my career and departed to Stanford 15 years later. In 1984, I enjoyed the transcendental experience of a 'second coming' upon my return. My first going was a lesson not a mistake. A second going, now, would suggest a serious learning disability."

Deanship at Einstein

The College of Medicine recruited Dr. Purpura back to the Bronx as its dean in 1984. Commenting on the appointment, Dr. Norman Lamm, then president of Yeshiva University, said, "…he is a brilliant

scientist, a skillful administrator, and an inspiring educator whose talents enriched Einstein for nearly 15 years. He is the right person for the right job at the right time."



"Dr. Purpura revolutionized the way medical education was taught," said Edward R. Burns, M.D., executive dean at Einstein—who has served in that capacity for 19 years, and worked hand in glove with Dr. Purpura through 6 of his last 22 years as dean. "He recognized that students could more successfully retrieve long-term memories of the science they learned when it was taught by great teachers who informed them broadly, rather than by research experts who focused more narrowly on their own particular lab work, as was the tradition at medical schools at the time." This approach was adopted by medical schools across the nation.

Dr. Burns added, "Dom was universally recognized as an extraordinary teacher. Generations of neuroscientists, neurologists, and neurosurgeons achieved their own successes after experiencing Purpura's command and love of neuroscience.

In 1985, during a period of dramatic realignments in healthcare, he coined the term "healthquake." During that time, his vision and leadership positioned the College of Medicine as the educational hub of a network of major hospitals throughout the New York metropolitan area. This assured Einstein's leadership position in education, clinical research, and patient care.

During the early 1990s, the College of Medicine was the first private medical school in New York City to establish a department of family medicine (now family and social medicine). Under Dr. Purpura's guidance, Einstein also established an academic department of emergency medicine to complement the existing clinical department at its University Hospital, Montefiore Medical Center.

In the commencement address he gave in May 2005, he told the graduates, "It is no secret that Einstein graduates are among the most effective and skilled interns and residents in any program. I've known this for four decades and I pass it on to you to strengthen your resolve and dispel doubts of deficiencies…You have been privileged to experience the rigors of our basic science and clerkship and sub-internship programs and I predict you will be a joy to your attendings and a savior to your patients."

He also reminded them of the advice he offered each class of entering first-year medical students as they navigated the demands of their education: "Pressure makes diamonds." Through two decades of his vision and guidance, he took his own advice to heart, assuring that Einstein could be a Hope diamond of the Bronx—an institution that, through its teaching and research endeavors, sought to foster social justice and equity in care, while producing caring, curing physicians and competent scientists.

Life, In General

Dr. Purpura was born in Manhattan on April 2, 1927 and grew up on the Upper East Side. He served in the United States Air Force following World War II, and later earned his bachelor's degree at

Columbia College (1949) and his medical degree magna cum laude at Harvard Medical School (1953). He then completed his internship at Presbyterian Hospital and his residency in neurology at the Neurological Institute. He married Florence “Penny” Williams in 1948; she survives him, along with their four children, Craig, Kent, Keith, and Allyson, and four grandchildren.