The University of Chicago
Medical Scientist Training Program

2016 Annual Retreat

Starved Rock Lodge & Conference Center
Oglesby, IL
June 24-25, 2016
TABLE OF CONTENTS

SCHEDULE OF EVENTS ................................................................. 4-5

KEYNOTE SPEAKERS

DEBORAH LENSCHOW, MD, PHD ......................................................... 6

SEAN CROSSON, PHD ......................................................................... 7

YOAV GILAD, PHD ............................................................................ 7

STUDENT PRESENTATIONS ......................................................... 8

RANGARAJAN NADADUR ................................................................. 8

GABRIEL SALZMAN ......................................................................... 8

STUDENT POSTER ABSTRACTS ................................................. 9-17

UNIVERSITY OF CHICAGO MSTP STUDENTS 2016-17 ................... 18

MEET THE INCOMING STUDENTS! ........................................... 19-21

LEISURE ACTIVITIES .................................................................. 22

RESORT INFORMATION AND RETREAT CONTACTS ............... 23
Friday, June 24, 2016

3:00 p.m. – 5:00 p.m.  Poster Session, Great Hall

5:30 p.m. – 5:45 p.m.  MSTP Retreat Welcome, Starved Rock Room
from Alison Anastasio, PhD

5:45 p.m. – 6:00 p.m. MSTP Student Presentation I
Rangarajan Nadadur
“Defining transcription factor-dependent gene regulatory networks by noncoding RNA Sequencing”

6:00 p.m. – 6:15 p.m. MSTP Student Presentation II
Gabriel Salzman
“Adhesion GPCRs couple extracellular interactions to Intracellular signaling”

6:30 p.m. – 7:00 p.m. Cocktails and hors d’oeuvres, Great Hall

7:00 p.m. Dinner, Great Hall

9:00 p.m. Team Trivia, Starved Rock Room
Saturday, June 25, 2016

8:30 a.m. - 9:30 a.m.  Breakfast, Great Hall  
(and check out of rooms)

9:30 a.m. - 10:00 a.m.  “State of the Program” address, Starved Rock Room  
from Marcus Clark, MD

10:00 a.m. – 10:45 a.m.  Keynote Speaker  
Deborah Lenschow, MD, PhD  
MSTP Co-Director, Washington University  
“Bench to Bedside, Bedside to Bench: My journey as a physician scientist”

10:45 a.m. – 11:15 a.m.  Featured Faculty Presentation I  
Sean Crosson, PhD  
“Bacterial sensory transduction”

11:15 a.m. – 11:45 p.m.  Featured Faculty Presentation II  
Yoav Gilad, PhD  
“Genomic variation Impact of regulatory variation from RNA to protein”

12:00 p.m. – 1:15 p.m.  Lunch, Pool Patio  
Informal Information Sessions

1:30 p.m. – 4:30 p.m.  Free Time/Activities

5:00 p.m.  Return to Chicago
Deborah Lenschow, MD, PhD is an Associate Professor of Medicine, Associate Professor of Pathology and Immunology at Washington University where she is a practicing Rheumatologist and also serves as the co-director of the Physician Scientist Training Program. She graduated from the University of Chicago in 1998 obtaining both an MD and PhD in immunology, performing her thesis work in the laboratory of Dr. Jeffrey Bluestone. She continued her clinical training at Washington University in St. Louis in Internal Medicine followed by a Rheumatology fellowship. During her fellowship she completed postdoctoral studies in the laboratory of Dr. Herbert “Skip” Virgin in the area of viral pathogenesis. She joined the faculty at Washington University in 2006. Her research program is focused on the area of host-pathogen interactions with an emphasis on understanding the role of the type I interferon response through the analysis of interferon subtypes and the functions of downstream interferon induced genes. In addition to her work on type I interferons, her research group has recently worked to understand the pathogenesis of the re-emerging alphavirus, Chikungunya virus. Through the utilization of patient cohorts, clinical samples, and mouse models her lab is working to identify the immune factors that regulate disease pathogenesis and to identify novel therapeutic targets.
Sean Crosson, PhD

Sean Crosson is from Grayson County, Texas. He received his B.A. in Biology in 1996 from Earlham College and Ph.D. in Biochemistry and Molecular Biophysics from the University of Chicago in 2002. From 2003 to 2005 he was a postdoctoral fellow at Stanford University School of Medicine, where he began to investigate mechanisms bacterial sensory transduction. He is currently Professor of Biochemistry and Molecular Biology and Chair of the Committee on Microbiology at the University of Chicago. Since joining the Chicago faculty in 2006, he has developed an interdisciplinary research program focused on understanding regulatory mechanisms that control bacterial cell physiology and infection biology. His studies center on the Alphaproteobacteria, including the freshwater bacterium Caulobacter crescentus, the marine photosynthetic bacterium Erythrobacter litoralis, and the mammalian pathogen Brucella abortus, which is a causative agent of brucellosis.

Yoav Gilad, PhD

Dr. Yoav Gilad completed his B.Sc. in Molecular Genetics and Biochemistry from the Ben Gurion University in Israel in 1998, his Ph.D in Molecular and Population Genetics from the Weizmann Institute of Science in Israel in 2003, and his Post-doctoral fellowship (which was funded by the European Molecular Biology Organization; EMBO) at Yale Medical School in 2005. In 2005, Dr. Gilad joined the faculty of the University of Chicago at the department of Human Genetics as an Assistant Professor. He was promoted to a tenured Associate Professor in 2009 and to a Full Professor of Human Genetics, Genomics, and Systems Biology in 2013. In 2016 Dr. Gilad was appointed a Professor of Medicine, and the Chief of the section of Genetic Medicine.

In 2010, Dr. Gilad was also appointed as the Director of the Functional Genomics facility at the University of Chicago (a core facility that provides empirical and computational genomic services, including next generation sequencing, microarrays, and bioinformatics). Dr. Gilad also holds an appointment at the University of Chicago Institute for Genomics and Systems Biology, the committee on Genetics, Genomics, and Systems Biology, the committee on Immunology, and the committee on Developmental Biology and Stem Cell Research. Dr. Gilad is the recipient of multiple federal grants to study human disease and human evolution using cutting edge empirical and computational genomic techniques. His lab’s research focuses on understanding the genetics of complex phenotypes and the potential for Personalized Medicine by using Next-Generation Sequencing, Genome Informatics, and Functional Genomics tools.
Rangarajan Nadadur
Graduate Student, Year 5

You wouldn't ask why the rose that grew from the concrete had damaged petals. When growing up on the streets (of the suburbs) of LA, I knew there were only three ways out: slinging crack rock, declaring for the NBA draft, or getting an MD/PhD. So I here I am. After attending MIT, I moved to Chicago where I study gene regulatory networks of heart development under Dr. Ivan Moskowitz. Don't ask me why. Ask me how.

Gabriel Salzman
Graduate Student, Year 5

I grew up in New York City and got my BA in Biophysics at Johns Hopkins University in 2012. After completing M1 at Pritzker, I joined the UChicago Biophysical Sciences program and was encouraged to pursue a dual-mentored PhD. I joined the labs of Shohei Koide and Demet Araç (both in the Department of Biochemistry and Molecular Biology) and have since attempted to apply the cutting-edge protein engineering techniques developed by the Koide Lab to investigate the biological roles of Adhesion G protein-coupled receptors studied by the Araç Lab.
Specificity of IgA Responses

Jeffrey J. Bunker, Theodore M. Flynn, Steven A. Erickson, Jason C. Koval, Dustin G. Shaw, Marlies Meisel, Benjamin D. McDonald, Isabel E. Ishizuka, Alexander L. Dent, Patrick C. Wilson, Bana Jabri, Dionysios A. Antonopoulos, and Albert Bendelac

Immunoglobulin A (IgA) is prominently secreted at mucosal surfaces and coats a fraction of the intestinal microbiota. However, the commensal bacteria bound by IgA are poorly characterized and the type of humoral immunity they elicit remains elusive. We used bacterial flow cytometry coupled with 16S rRNA gene sequencing (IgA-Seq) in murine models of immunodeficiency to identify IgA-bound bacteria and elucidate mechanisms of commensal IgA targeting. We found that residence in the small intestine, rather than bacterial identity, dictated induction of specific IgA. Most commensals elicited strong T-independent (TI) responses that originated from the orphan B1b lineage and from B2 cells, but excluded natural antibacterial B1a specificities. Atypical commensals including segmented filamentous bacteria and Mucispirillum evaded TI responses but elicited T-dependent IgA. These data demonstrate exquisite targeting of distinct commensal bacteria by multiple layers of humoral immunity and reveal a specialized function of the B1b lineage in TI mucosal IgA responses.

To define the origins and molecular targets of IgA responses, we derived hundreds of recombinant monoclonal IgA antibodies from single IgA plasma cells in intestinal and extraintestinal tissues of various mouse models and assessed their reactivity toward commensal microbiota using bacterial flow cytometry, monoclonal IgA-Seq, and biochemical methods. These approaches led to unexpected insights into the origins and properties of IgA antibodies, the consequences of somatic hypermutation in the intestine, and the molecular and bacterial targets of homeostatic IgA responses. Further, our commensal-reactive monoclonal antibodies may enable for the first time manipulation of specific members of the microbiota for research, diagnostic, or therapeutic purposes.

Dan Camacho (G3, Immunology)

FcγRIII signaling promotes IL-33-dependent monocyte migration to the lung extravascular space

Daniel F. Camacho, Melissa Y. Tjota, Heth R. Turnquist, and Anne I. Sperling

IL-33 is implicated in type 2 inflammatory processes, including allergic asthma. Our group previously demonstrated that two Th2 stimuli, allergen-specific IgG immune complexes (ICs) and house dust mite extract (HDM), signal through Fcγ-associated receptors on antigen presenting cells to upregulate IL-33 and induce type 2 allergic airway inflammation. In this study, we investigated the role of IL-33 in regulating type 2 responses by comparing localization of allergen-positive monocytes in IL-33-deficient and IL-33-sufficient mice. We found that IL-33 is necessary for optimal monocyte accumulation in the lung extravascular space after allergen challenge and that treatment with pertussis toxin abolishes this migration. Our findings suggest that during allergic sensitization, activation of the Fcγ signaling pathway promotes IL-33- and GPCR-dependent monocyte migration into the lung extravascular space, where monocytes may then contribute to type 2 allergic inflammation.
**Sofija Canavan (G3, Computational Neuroscience)**

*Regulation of sleep replay in the songbird motor system*

Sofija V Canavan and Daniel Margoliash

Memory benefits from, and may require, sleep. One key mechanism whereby sleep influences learning is thought to be neural replay of memories. During sleep, the songbird brain replays sequences of motor activity that correspond to learned song. What remains unknown is how this replay is regulated with respect to sleep architecture. Replay of spatial memories in the mammalian hippocampus has been shown to co-occur with slow waves, aiding in declarative learning. However, studies in humans have demonstrated that sleep also benefits the consolidation of nondeclarative memories, and that this effect may be mediated by either REM sleep or stage 2 sleep.

To answer this question, we used chronic extracellular recording to track sleep and replay in freely behaving animals. We targeted the nucleus RA, the avian analogue of the laryngeal motor cortex. Adult zebra finches were implanted with high impedance electrodes loaded onto a moveable microdrive, along with EEG and EOG electrodes to obtain sleep architecture measurements. Singing and sleep/wake behavior was monitored with acoustic and infrared video recordings. With this method we were able to isolate several RA units for long time periods (9-11 hours).

During both song and replay, RA neurons fire a series of precise bursts. Preliminary analysis of the dataset showed that bursting activity during sleep most often co-occurs with slow waves. This suggests that slow waves universally function in both birds and mammals to coordinate replay events, and extends our understanding of the mechanisms that underlie sleep’s role in procedural learning in humans.

**Ben Casterline (G3, Immunology/Microbiology)**

*Early life acquisition and adult pathogenesis of Bacteroides fragilis*

Benjamin W. Casterline, Aaron L. Hecht, Juliane Bubeck Wardenburg

Maternally acquired microbes may predispose to disease later in life; however, the determinants of maternal inheritance and their contributions to disease are poorly understood. We have developed a mouse model of vertical transmission in which the common human commensal enterotoxigenic *Bacteroides fragilis* (ETBF), carried by the dam, is stably incorporated into the neonatal microbiota. Surprisingly, *Bacteroides fragilis* toxin (BFT), a carbohydrate-regulated metalloprotease associated with E-cadherin cleavage, is a key determinant of maternal inheritance, as BFT-deficient ETBF shows impaired persistence in juvenile mice. Enteric disease in adulthood can be induced by antibiotics and is characterized by ETBF outgrowth, elevated bft expression, and loss of colonic mucus. We propose a model in which antibiotic treatment favors expansion of the mucolytic ETBF population and depletion of mucus-associated sugars, leading to BFT derepression and host injury.
**Justin Chew (G4, Genetics, Genomics and Systems Biology)**

*Investigating the Effects of Molecular Noise on Cyanobacterial Clock Function by Varying Kai Protein Copy Number*

Justin Chew and Michael Rust

Circadian clocks drive the 24-hour oscillations in gene expression and behavior that allow an organism to anticipate the day/night cycle, and its disruption has been implicated in the pathogenesis of cancer, metabolic syndrome, and cardiovascular disease. However, our understanding of conditions where the clock fails remains poor, making it crucial to understand how clocks keep accurate timing over a range of physiological conditions despite being composed of stochastic biochemical reactions. How does the cell achieve a noise-free clock, and does noise from limited molecular copy number impose a significant physical constraint on clock robustness? This project utilizes the model cyanobacterium *Synechococcus elongatus*, in which core clock behavior is generated entirely by three proteins, KaiA, KaiB, and KaiC, allowing for investigation of clock molecular noise by manipulating Kai expression levels in vivo. Stochastic modeling suggests that reduction of Kai protein copy number will lead to a loss in accuracy of clock timing that ultimately imposes a cellular fitness penalty. Here, I have successfully engineered a strain of *S. elongatus* with tunable Kai expression, and I have confirmed with time lapse microscopy that clock noise increases as Kai copy number is reduced. Current work focuses on investigating the mechanistic role of cell division in the observed increase in noise. Future measurements of single-cell growth rates will assess whether noisy rhythms induced by low Kai copy number reduce cellular fitness in cyclic environments. Altogether, this study will elucidate basic principles of the relationship between noise suppression and molecular copy numbers within the cell.

**Alexander Guzzetta (G3, Genetics, Genomics and Systems Biology)**

*Hedgehog signaling controls gene regulatory networks for early cardiovasculogenesis*

Alexander Guzzetta, Megan Rowton, Jeff Steimle, Andrew Hoffman, Junghun Kweon, Ivan P. Moskowitz

Congenital heart disease (CHD) is the most common birth defect—occurring in as many as 3 in every 100 live births. In this study, we uncover a gene regulatory network essential for the proper development of cardiovascular lineages downstream of hedgehog (hh) signaling—a crucial pathway in cardiac development. Using Genetic Inducible Fate Mapping, we observed that late labeling of cardiac progenitors (E8.5 and later) marked only second heart field structures while early labeling of cardiac progenitors (E6.5) additionally marked first heart field derived structures. Germline removal of all hh signaling, through ablation of a key membrane-bound receptor, smoothened (*smo*), caused hypoplasia of the linear heart tube, a failure of chamber expansion, and early embryonic lethality. Conditional *smo* removal using a cardiogenic mesoderm marker, Mesp1-Cre, recapitulated the germline phenotype whereas *smo* removal in specified cardiac lineages via Nxk2-5-Cre supported chamber formation, restricting the requirement for hh signaling to early mesoderm. RNA-seq of Mesp1*+* cells overexpressing Gli3R, the primary transcriptional repressor downstream of hh revealed upregulation of lineage-determining transcriptional programs for both cardiac, blood, and vascular endothelial lineages at embryonic day 7.5 (E7.5) but down-regulation of factors involved with maintenance of progenitor identity. In accordance with this model, RNA-seq of Mesp1*+* cells at E8.5 shows marked dysregulation of genes that mark the identity of cardiovascular lineages. Based on these data we hypothesize that hedgehog signaling controls a gene regulatory network required for the proper establishment of cardiovascular system lineages by controlling the timing for differentiation of mesodermal progenitors.
Jennifer Jacobsen (G4, Immunology)

EZH2 restricts expression of effectors of the pre-BCR and pre-TCR checkpoints in early B and T cell progenitors

Jennifer Jacobsen, Jennifer Woodard, Elizabeth Bartom, Mikael Sigvardsson, and Barbara Kee

The histone methyltransferase EZH2 catalyzes the repressive histone modification, H3K27me3. EZH2 is frequently mutated in blood and epithelial tumors and increased EZH2 activity enhances tumorigenicity. EZH2 is required for both B and T cell development, but its specific role in these lineages is not clear. Here we used an Il7ra<sup>cre</sup> to delete Ezh2 in all lymphocytes. We confirmed that EZH2 was required in B and T cell progenitors to promote development beyond the pre-antigen receptor checkpoints, but found that EZH2 was dispensable for NK and ILC2 development. EZH2-deficient pro-B cells failed to expand in vitro, which was associated with increased apoptosis and cell cycle defects. In EZH2-deficient pro-B and DN3 cells expressed increased mRNA of the cell cycle regulators, p16<sup>INK4a</sup> and p19<sup>ARF</sup>, which are encoded at the Cdkn2a locus and are known targets of EZH2 in other tissues. ARF prevents ubiquitin-mediated degradation of the tumor suppressor p53 leading to cell cycle defects and apoptosis. p53 and several canonical p53 target genes were increased in EZH2-deficient pro-B cells and DN3 cells. p53 is a critical effector of the pre-BCR and pre-TCR checkpoints and developing B and T cells that fail to express a pre-antigen receptor at the cell surface undergo p53-induced cell death. Genetic ablation of Cdkn2a rescued B and T lineage maturation, but not expansion in EZH2-deficient mice. In summary, we found that there is a lineage specific role for EZH2 during early lymphocyte development to repress effectors of the pre-antigen receptor checkpoints.

Ellis Kim (GDDTP G3, Molecular Pathogenesis and Molecular Medicine)

A model of human skeletal muscle using urine cells

Ellis Kim, Eugene Wyatt, Patrick Page, Lisa Castillo, and Elizabeth McNally

Cellular models of muscle disease are increasingly important for studying disease mechanisms and testing potential treatments. Accessing muscle cells to model disease requires an invasive biopsy, which may be challenging in muscle mass-limiting disorders. Dermal fibroblasts are a useful source for generating in vitro models, where direct reprogramming with transcription factor MyoD induces myogenesis. However, isolating fibroblasts requires skin biopsies, which can pose limitations, especially for pediatric populations. An alternative cell source comes from urine samples, which are easily collected non-invasively. Urine cells are thought to be from renal epithelium and have previously been used for stem cell generation. We show that urine cells can be directly reprogrammed to skeletal muscle with MyoD delivered by a tamoxifen-inducible lentiviral vector (iMyoD). Urine-derived cells were transduced with the iMyoD lentivirus, treated with tamoxifen to induce nuclear translocation of MyoD, and cultured in differentiation media. When analyzed at different time points (7, 14, and 28 days), cells fused and elongated to form myotube-like structures. By RT-PCR and immunofluorescence analyses, myotubes expressed muscle markers such as dystrophin, myogenin, and fetal and mature myosin heavy chains. This method was used to model two forms of muscular dystrophy, Limb Girdle Muscular Dystrophy Type 2C and Duchenne Muscular Dystrophy. Urine cells isolated from patients formed myotubes and expressed transcripts of expected sizes. Further, these myotubes showed absence of γ-sarcoglycan and dystrophin, respectively, recapitulating patient disease phenotypes. This demonstrates the potential utility of this model in studying disease mechanisms and developing therapies in a non-invasive, patient-specific manner.
David Koren (G4, Neurobiology)

Metabotropic signaling supports retinal direction selectivity

David Koren, James C. Grove, and Wei Wei

Starburst amacrine cells (SACs) are required for direction selectivity in the mouse retina. Precise GABAergic connectivity between individual SAC dendritic processes and direction-selective ganglion cells (DSGCs) enables DSGCs to fire action potentials during motion in their preferred direction, but not during motion in their anti-preferred (null) direction. Although glutamatergic inputs to SACs are non-direction-selective, SAC processes preferentially depolarize and release GABA during motion in the centrifugal direction. Several mechanisms underlying this emergent direction selectivity in SACs have been proposed, potentially implicating both intrinsic membrane properties and patterns of presynaptic inputs. However, it is unknown how direction selectivity is maintained for a broad range of stimulus speed and contrast conditions. We find that signaling through metabotropic glutamate receptor 2 (mGluR2), localized to SACs, is crucial for direction selectivity. Using two-photon calcium imaging and whole-cell patch clamp recording and visual stimulation, we find that pharmacological mGluR2 blockade leads to altered dendritic processing of motion stimuli in the SAC dendrites, impairing direction selectivity of SACs and DSGCs in a speed-dependent manner. Our data suggest that the rules of motion processing in SACs are not static, but instead can be dynamically regulated by modulatory synaptic transmission.

Victoria Lee (G3, Immunology)

Defining tolerance mechanisms regulating self-specific T cells

Victoria Lee, Jaime Chao, and Peter A. Savage

The adaptive immune system relies on stringent immune tolerance mechanisms to ensure that self tissues are protected from autoimmune attack. The failure and success of such immune regulation have important implications for the prevention of autoimmune diseases and the efficacy of anti-tumor immune therapies. Thus, there is great interest in defining the prevailing mechanisms that regulate T cell responses specific for self antigens, in the hopes that these processes can be manipulated for clinical benefit. Whereas many autoreactive T cells are thought to be purged from the conventional T (Tconv) cell repertoire by clonal deletion, substantial evidence suggests that this process is imperfect. In this regard, little is known about the nature of self-specific T cells present in the endogenous repertoire. Moreover, in the context of cancer, it has been difficult to define whether self-specific T cells contribute to the repertoire of tumor-infiltrating lymphocytes (TILs), or whether most TILs are non-specific T cells that are recruited to the tumor by TCR-independent inflammatory signals. Here, we identified CD4+ T cell clones in the endogenous T cell repertoire that infiltrate the prostate following Treg cell ablation. By tracking the fate of these prostate-infiltrating Tconv clonotypes in TCR retrogenic mice, we aim to determine the nature of the self antigens recognized by these cells, and define the tolerance mechanisms regulating these cells. Additionally, we aim to determine the contribution of these clonotypes to the tumor infiltrate in oncogene-driven mouse prostate tumors. This study is expected to yield new insights into the mechanisms underlying immune tolerance and anti-tumor immunity.
**Ramya Parameswaran (G4, Biophysical Sciences)**

*Optical modulation of neuronal activity with novel silicon-gold nanowires*

Ramya Parameswaran, Joao L. Carvalho-de-Souza, Ektor Acaron Ledesma, Michael J. Burke, Erin Adams, Francisco Bezanilla, Bozhi Tian

The development of minimally invasive methods to modulate electrical activity in cellular systems with high spatiotemporal resolution has been a significant challenge for many years now. Shapiro et al. and Carvalho-de-Souza et al. have recently demonstrated that IR light and gold nanoparticles can stimulate neurons photothermally. Here, we explore an inorganic platform that when interfaced with neurons, can modulate neural activity via a photovoltaic effect. We demonstrate that coaxial pin Silicon nanowires consist of both a radial p-n diode component and an axial Au-Si diode component caused by the diffusion of the gold nanoparticle catalyst along the nanowire side-walls during growth. In culturing these nanowires with primary rat dorsal root ganglion cells, we show that upon localized laser stimulation at the cell-nanowire interface, they can efficiently induce action potentials in individual neurons. These findings provide us with a novel method to optically modulate neuronal activity in a wireless manner and thus a potential therapeutic strategy for patients suffering from neurodegenerative diseases.

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**Sylvia Ranjeva (G4, Ecology and Evolution)**

*Modeling the dynamics of human papillomavirus: mechanistic inference from longitudinal data*

Sylvia Ranjeva, Edward Baskerville, Anna Giuliano, Sarah Cobey, and Greg Dwyer

There are over 200 types of human papillomavirus (HPV), the most common sexually-transmitted infection. Optimizing HPV vaccination requires understanding HPV ecology in human populations. To understand the factors that promote HPV diversity, we fit mechanistic models to a longitudinal clinical dataset. The data span 37 HPV types in over 4,000 men and include information about patient demographics and sexual practices. We infer the contributions of host-specific risk factors, type-specific immunity, and type interactions to HPV dynamics.
Ian Roundtree (G4, Chemistry/Biochemistry and Molecular Biology)

N6-methyladenosine promotes processing and export of nuclear messenger RNAs

Ian Roundtree

N6-methyladenosine (m6A) is the most abundant internal modification in eukaryotic messenger RNA (mRNA), and plays many fundamental roles in RNA biology. In mammalian cells the function of this reversible chemical modification is mediated in part by m6A ‘reader’ proteins of the YTH family. Despite the critical step of nuclear mRNA export in regulating gene expression, little is known about how m6A affects translocation of mRNA to the cytoplasm. Here we report the function of the essential nuclear m6A ‘reader’ protein YTHDC1 in mediating export of methylated mRNAs from the nucleus to the cytoplasm. We show that knockdown of YTHDC1 in HeLa cells results in a nuclear accumulation and cytoplasmic depletion of methylated mRNAs, along with an extended nuclear half-life time and reduced loading onto the canonical nuclear export factor NXF1. The adaptor protein SRSF3 mediates this function, linking pre-mRNA splicing to nuclear export by interacting directly with NXF1. Additionally, we show that m6A-dependent export of mRNA is dynamic and involved in the cellular response to oxidative stress. Together with functions of YTHDF1 and YTHDF2, this work indicates that the YTH proteins act as mediators of an accelerated lifetime by promoting nuclear processing and export, translation, and decay of methylated mRNA transcripts.

Nicelio Sanchez-Luege (G4, Development, Regeneration, Stem Cell Biology)

The role of Abl kinase in stabilizing photoreceptor cell fate during terminal differentiation

Nicelio Sanchez-Luege and Ilaria Rebay

The signals and mechanisms that maintain neuronal identity in the retina remain elusive and poorly understood. We have uncovered a novel paradigm in the Drosophila eye, in which a cytoplasmic kinase actively silences signals that normally antagonize gene expression programs associated with neuronal specification and development. The foundational observation is that loss of the Abelson kinase (Abl) causes differentiating photoreceptors to lose expression of neuronal genes. Interestingly, some of these former photoreceptors appear to transdifferentiate and activate the program of an alternative pigment cell type, suggesting both reversibility and plasticity among retinal cell types even days after specification. How does Abl mechanistically coordinate neuronal maintenance? Our model is that Abl actively silences signaling pathways, such as Notch, that normally antagonize expression of neuronal programs. Supporting this model, we have found upregulation of Notch transcriptional targets, and accumulation of the Notch (N) receptor itself into large endocytic puncta in abl mutant tissue. Consistent with prior work from other labs showing that Notch signaling can be ectopically activated by aberrant trafficking, genetically reducing Notch dominantly suppresses the loss of photoreceptor marker expression phenotype in abl mutant tissue. We are also investigating what happens to the former photoreceptors as their fate is destabilized and they activate a new cell fate program. We have found that shortly after they lose expression of neuronal and photoreceptor-specific markers, many cells gain expression of markers associated with interommatidial pigment (IOP) cells. In addition to more in depth characterization of the cellular morphology and function of these transdifferentiated cells, we are also using G-TRACE to lineage trace and purify abl mutant cells at several developmental stages in order to profile their transcriptome. We expect that the detailed molecular view of the gene expression changes that accompany photoreceptor specification, differentiation, dedifferentiation and transdifferentiation that emerges from our work in the fly eye will produce novel insights broadly relevant to visual system development, degeneration and regeneration in vertebrates.
Sophia Uddin (G3, Computational Neuroscience)

*Recognizing sounds in sentence context*

Sophia Uddin, Shannon LM Heald, Stephen C Van Hedger, Serena Klos, and Howard C Nusbaum

From one theoretic perspective, word recognition is facilitated by sentence context only after initial sound processing occurs. If the mechanisms that mediate the interaction of sentence context and lexical processing are specialized for language understanding, it could be predicted that the influence of sentence context on word recognition might be different from a more general cognitive system serving to use this contextual information. Stimuli such as environmental sounds can convey clear meaning, yet are not linguistic. We compared the effect of spoken sentence context on word and nonspeech sound recognition. In Experiment 1, sentence context significantly decreased recognition time for nonspeech sounds and spoken words, with a similar effect for both. In Experiment 2, sentence meaning decisions were significantly faster for high-constraint contexts for both nonspeech and speech. These results suggest that linguistic context may aid recognition for nonspeech sounds in a way that is the same as words.

Frank Wen (G2, Ecology and Evolution)

*Expected effects of vaccination on influenza evolution and the total burden of disease*

Frank Wen, Anup Malani, and Sarah Cobey

Vaccines against seasonal influenza are intended to protect hosts against infection, but may inadvertently select for non-targeted antigenic variants. To understand the effects of vaccination on such a fast-evolving pathogen, we simulated the dynamics of influenza in a host population in which vaccination occurs at some rate, confers some breadth of immunity (relative to natural immunity), and has some lag (relative to strain selection). Antigenic phenotypes were modeled as points in Euclidean space. Increasing vaccination rate usually decreases the average cumulative antigenic evolution of the viral population. However, the distribution of outcomes is clearly bimodal. Vaccination either drives the viral population extinct, or the population persists and evolves further than if vaccination had not taken place at all. The effects of vaccination rate are also mediated by breadth. Vaccines that confer broader immunity likewise decrease the probability of pathogen survival, but increase the antigenic evolution of surviving populations and the incidence among hosts. These results illustrate how vaccination against a pathogen whose evolution is driven by positive selection for rapidly emerging strains can simultaneously antagonize and enhance antigenic evolution to the respective detriment or benefit of hosts.
Alyson Yee (G2, Microbiology)

*Microbiome determinants of health outcomes in preterm infants*

Alyson Yee, Maureen Groer, Larry Dishaw, Ming Ji, and Jack Gilbert

Preterm infants are a unique population with abnormal early life microbiome colonization. Compared with term infants, those born preterm are at higher risk for microbial insult. First, they are often delivered via emergency Caesarean section, which reduces their exposure to maternal vaginal and enteric microbes. Furthermore, they are subject to higher rates of formula feeding, invasive procedures, antibiotics, and medications that alter gastrointestinal pH, all of which contribute to the assembly of the microbial community. Finally, preterm infants who stay in the NICU can develop a flora dominated by microbes associated with the NICU environment and high levels of antibiotic resistance. Few prospective studies focus on the preterm gut microbiome over the NICU stay. We enrolled 67 preterm infants (born <37 weeks’ gestational age) and collected stool microbiome samples over their NICU stay, up to six weeks. We analyzed the samples by 16S rRNA amplicon sequencing. For each infant, we also collected parental demographic data, characteristics such as gestational age, weight, APGAR scores, morbidities, and recorded volumes of milk consumed. Consistent with the literature, we found that preterm infants’ gut microbiomes increase in diversity and show reduced time-to-time variability over the course of their hospitalization. We hypothesize that microbial community structure can be predicted by birth mode, gestational age, weight gain, length of stay, feeding status, human milk cytokines, fecal calprotectin, and adverse prenatal events.

Katherine Zhou (G4, Biochemistry and Molecular Biology)

*N6-methyladenosine (m⁶A) dependent regulation of alternative splicing through interaction with a low-complexity region of hnRNP G protein*

Katherine Zhou, Nian Liu, Marc Parisien, Qing Dai, and Tao Pan

*N6-methyladenosine (m⁶A) is the most abundant internal mRNA and long noncoding RNA (lncRNA) modification in eukaryotes. m⁶A-dependent structural switches can promote protein binding by exposing single-stranded RNA binding motifs. Heterogeneous nuclear ribonucleoprotein G (hnRNP G) is a nuclear RNA binding protein with functions in DNA repair, transcriptional regulation, and alternative splicing. Both the globular RNA recognition motif at its N-terminus and a low-complexity region at its C-terminus are capable of binding RNA. We show that hnRNP G uses its C-terminal low-complexity region to bind purine-rich sequences in an m⁶A-dependent structural switch. Using PAR-CLIP and MeRIP-seq, we identify 16,200 m⁶A-modified hnRNP G binding sites. In addition, we show that hnRNP G knockdown influences the alternative splicing of thousands of transcripts. In transcripts that contain m⁶A-modified hnRNP G binding sites, over 1,000 alternatively spliced exons show the same splicing changes upon hnRNP G or m⁶A methyltransferase knockdown. Our results demonstrate that the low-complexity region of hnRNP G can recognize m⁶A-dependent structural switches to influence the alternative splicing of m⁶A-modified transcripts.*
# UofC MSTP Students 2016-17

## Med Year 4
- David Blair, PhD
- Adam Gasser, PhD
- Melissa Tjota, PhD
- Vivian Choi, PhD
- Ben McDonald, PhD
- Tony Tu, PhD

## Med Year 3
- Aaron Hecht
- Erin Mowers
- Jeremy Treger, PhD
- Megan Zilla, PhD
- Mark Lunderberg, PhD
- Arup Sarma, PhD
- Iboro Umana, PhD

## Grad Year 4
- Anya Bershad
- Justin Chew
- David Koren
- Ramya Parameswaran
- Ian Roundtree
- Nicelio Sanchez-Luege
- Katherine Zhou
- Jeffrey Bunker
- Jennifer Jacobsen
- Rajiv Nadadur
- Sylvia Ranjeva
- Gabriel Salzman

## Grad Year 3
- Dan Camacho
- Ben Casterline
- Alex Guzzetta
- Sophia Uddin
- Sofija Canavan
- Nina Gao
- Victoria Lee

## Grad Year 2
- Michael Clark
- Phillip Hsu
- Kaitlin McLean
- Mat Schnorenberg
- Alyson Yee
- Blake Flood
- Katie Long
- Victoria Okuneye
- Frank Wen

## Grad Year 1
- John Coukos
- Reem Elorbany
- Christine Miller
- Zaina Zayyad
- Wenli Dai
- Molly Imgruet
- Dustin Shaw

## Med Year 2
- Alan Hutchison
- Sammy Thomas

## Med Year 1 / Beginning Grad
- Rebecca Abraham
- Meytal Chernoff
- Grace Hansen
- Somin Lee
- Donald Rodriguez
- Caraline Sepich
- Allen Zhu
- Saara-Ann Azizi
- Emily Cullum
- Lakshmi Kirkire
- Maya Lozinski
- Kishan Sangani
- William Wagstaff
Meet the Incoming Students!

Rebecca Abraham
Rebecca (Reba) Abraham joins us from the University of Florida. She was born in Chicago and is excited to be making her way back home, although she is concerned about freezing to death and might miss Florida’s year round 1000% humidity (not really). She’ll have her love of hot tea and coffee to keep her warm—if you’re ever invited to her home, you can expect to be offered a pot or two of tea. And she can stay indoors if it gets frigid out, curled up with a good novel. Reba says, “The more magic, the better.” She’s an admirer of Oliver Sacks, Cuban food, and immunology/immunotherapy. Welcome, Rebecca!

Kishan Sangani
Originally hailing from Charlotte, NC, Kishan Sangani attended Indiana University to research endocannabinoids. He plans to study neurodevelopment, with an emphasis on signaling mechanisms. While his friends say he’s famous for his awkwardness, he’s not afraid to ask for help and take the initiative in learning new techniques. His goal for his first year is to find something meaningful to be involved in outside of this research, though. He loves camping, hiking, climbing, and outdoorsy activities, so that’s a good place to start! He backpacked through New Zealand on his study abroad. Welcome, Kishan!

Caraline Sepich
New Mexican Caraline Sepich also studied abroad in New Zealand, where she learned about global health and culture and got to swim with wild dolphins and go bungee jumping. As a biophysics major, Caraline probably understands the safety implications of that particular activity better than I’d care to. In her undergrad at Arizona State University, she co-founded a BIOMOD team that created antibodies out of DNA origami. On weekends you can find her hiking, camping, and kayaking. Should the occasion arise, Caraline can be bribed with authentic New Mexican green chile, but if it’s a chalk talk on a whiteboard, a bribe won’t even be necessary because “Whiteboards make everything better--they're remarkable!” (her friends have gotten used to her nerdy jokes). Welcome, Caraline!

Emily Cullum
Emily Cullum is an Illinois native from Grayslake and a graduate of UI-Urbana Champaign, where she majored in bioengineering. She’ll miss her dogs, but hopes to get a cat this year. Sounds like she’s an animal lover—she admits that the perfect way to bribe her is with puppies! (ex: “if you run my gel this afternoon I will let you play with my new puppy.”) Her favorite restaurant is Five Guys (so she’ll frequent 53rd St) and burger in hand, you can find her catching up on TV shows on the weekends. Emily says the best science advice she ever received was, “Don’t get a PhD,” but then again, she’s famous for her sarcasm. Her dream vacay is New Zealand (maybe she should talk to Kishan and Caraline, and Reba could tag along to look at some Hobbits). Welcome, Emily!
Grace Hansen
William and Mary grad and former NIH postbac Grace Hansen, of Portsmouth, VA, just got back from an incredible trip to Morocco and is ready to start applying her Cognitive Neuroscience major to researching schizophrenia and neuropsychiatric disorders at U of C! She loves Indian food, fancy coffee, and foraging (her skills will certainly be put to good use finding free food in grad school). She’ll miss living in Washington, DC because of its proximity to the Shenandoah mountains—maybe the Indiana Dunes will cut it? And maybe because of its politics. Her goal for this year is keeping Trump out of the presidency. On weekends you can find Grace pedaling her bike around to local breweries, something she’ll definitely be able to continue in Chicago, or jamming out to Santigold, Chet Faker, and Chance the Rapper. Welcome, Grace!

Lakshmi Kirkire
Like Grace, Lakshmi Kirkire of Brookeville, MD, really hopes Trump doesn’t become president. She’s also from the DC area, joining us from University of Maryland College Park, where she studied cell biology, genetics, and Spanish. She worked in a lab studying developmental biology and the body plan of insects. Lakshmi is into baking—she’ll miss her Kitchenaid named “Clara”—and is known for making sarcastic comments during Food Network’s Diners, Drive-Ins, and Dives. She’s nutty for chocolate and Nutella—her goal this year is to keep a jar for longer than a week (good luck!) At UChicago, she plans to pursue research in bioinformatics and cancer biology. Fittingly, she idolizes Sidney Farber. Welcome, Lakshmi!

Somin Lee
Somin Lee, an Akron, OH native, joins us from Yale, where she studied cell bio. She’s now broadly interested in all things neuro. She hopes this year she won’t have to answer any more questions about why she wants the dual degree. Somin has a soft spot for fast food, especially McDonald’s and Taco Bell, and fun stickers. Her favorite science-related advice from Rick Sanchez of Rick & Morty is "Forget love, focus on science."—something her favorite singer, Taylor Swift, should probably keep in mind. Somin’s famous for her homemade yogurt and cake decorating artistry and spent a year in Japan climbing Mt. Fuji and eating noodles all day every day. Welcome, Somin!

Donald Rodriguez
Another Yale, Donald Rodriguez, hails from Worcester, MA (super logically pronounced “Wooster” or “Wuhster,” because, Massachusetts). He majored in psychology and biochemistry, and did research stints in neurobiology and biomedical engineering labs, but is not planning on doing any of those things at U of C. Instead, he wants to switch to cancer immunology. Donald’s role model is Edward Bouchet, the first African-American to graduate with a PhD in the sciences from an American university, who focused his career on teaching other minority students and helping them get to higher places in the realm of education. Donald’s ideal weekend involves hanging out with friends, watching TV, and good food. He thinks he’ll miss Yale’s architecture and its food trucks but I’m pretty sure Chicago will best it on both counts. Welcome, Donald!
Maya Lozinski
Maya Lozinski grew up in Menlo Park, CA (home to Facebook), before moving to Hyde Park for a BA in Economics from UofC. She’ll be doing her PhD in public policy at the Harris School and is interested in payment incentives, new methods of care delivery, and hospital markets. She’s been working at Epic since graduating, which probably reinforced her interest in health care economics. Upon leaving Madison, WI, she’ll miss those cheese curds, but is excited about all the vegetarian restaurants in Chicago (Native Foods, Chicago Diner, etc) and Vietnamese food. She’s a big fan of podcasts and studied abroad in India, France, and China. Welcome, Maya!

Allen Zhu
Also a UofC lifer, Allen Zhu already has a favorite Chicago pizza (Lou Malnati’s), hot dog (Jim’s Original), burger (Au Cheval), and ice cream (Jeni’s). And he’s already been to Starved Rock, where he recently enjoyed a hiking trip. But while joining our program should be a smooth transition, he misses the BBQ from his hometown of Overland Park, KS and he still hasn’t gotten used to walking in snow boots. In undergrad, he did computational chemistry research, specifically force field generation, fluorophore umbrella sampling, and parameterization of unnatural amino acids. Outside of lab, he hopes to find the time to read for fun (goal: 2 books a quarter), pick up guitar and piano, and make lip sync videos! Welcome, Allen!

Meytal Chernoff
Hailing from Evanston, Meytal Chernoff attended Washington University in St. Louis, where she studied anthropology and biology and minored in English. She is particularly interested in studying biomedical anthropology, epidemiology and public health through a biological lens. She wants to expand her interests and explore new realms in science and research, as well as bond with her cohort. She hopes to do so through movie nights and dinner parties—her friends say she’s famous for her cooking! Meytal has a weakness for all things Disney, and her favorite trip was a recent visit to Disney World, where she and her siblings unleashed their inner eight-year-olds. When she’s not cooking up a storm or watching The Lion King again, she can be found listening to country music or haunting The Blind Faith Café up in Evanston. Welcome, Meytal!

Saara-Anne Azizi
Last (but certainly not least), Saara-Anne Azizi of Philadelphia joins us from Dartmouth. In undergrad, she majored in chemistry and classical languages, and has traveled to Athens and Istanbul. If you want to learn some Ancient Greek, Saara-Anne can be bribed with sugared cardamom almonds (yum!) and pastries. She’s famous for wearing hole-y sweaters and spends weekends reading and making pancakes. This year she hopes to learn lots and make new friends, and she wants to avoid the often temporary but frustrating misplacement of her possessions. This girl is a field hockey player and loves singing along to music. Welcome, Saara-Anne!

Class summary: We need to watch out for the entering class’s sarcasm and shade, and should probably move the retreat to New Zealand next year. They’ll bond over home-cooked meals, Netflix, and hiking trips.

Compiled and written by Alyson Yee.
Saturday, June 25th

1:30 – 4:00pm
   Long Guided Hike

1:30 – 3:00pm
   Photo Scavenger Hunt

3:00 – 4:30pm
   Short Guided Hike

4:30pm
   Scavenger Hunt Results
Retreat Information/Contacts

Starved Rock Lodge & Conference Center
2668 East 873 Road
Oglesby, IL 61348
(815) 667-4211 or toll-free 1-(800) 868-7625
http://www.starvedrocklodge.com/

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