Each month MD/PhD scholars and other NIH trainees interested in clinical research can participate in a series of events similar to those available at traditional MD/PhD programs. The Clinical Case Studies and Translational Research Seminars were created to provide these trainees a chance to brush up on their clinical knowledge and to speak with experienced physician-scientists.

Steve Witte, NIH MD/PhD Student and OxCam Scholar, and Dr. Rick Fairhurst, Director of the NIH MD/PhD Partnership Training Program, organize each event to ensure that MD/PhD students at the NIH have unique opportunities that rival those available at US medical schools.

In 2012, while completing the PhD portion of his dual-degree training, Dr. Geoff Lynn (OxCam Class of 2010) started the Clinical Case Studies to create a forum for students to hone their medical knowledge while taking time out of their busy schedule to network with other clinical scholars and graduate students on the NIH campus. These events encourage scholars to apply their critical thinking skills through the presentation and analysis of clinical cases. The role of moderator rotates amongst the scholars, who present different cases, generally adopted from New England Journal of Medicine Clinical Cases; moderators provide an interactive discussion of patient history, diagnosis, and work-up, while explaining technical jargon and walking students through clinical reasoning.

The Translational Research Seminars afford scholars an opportunity to interact with a diverse array of physician-scientists. Guests are selected from internal NIH investigators and external researchers in industry and academia who represent different areas of research as well as various career stages. Unlike the larger-scale seminars that are available in medical school, the intimate environment of this event promotes an active dialogue between scholars and guest speakers, which allows for a more engaging and informative interaction.
**NOTABLE EVENTS**

**DIRECTOR NAMED HIGHLY CITED RESEARCHER**

Dr. Tom Wynn (pictured with his graduate students Trey Gieseck and Casey Rimland), was named a 2015 Thomson Reuters Highly Cited Researcher. After careful analysis of citation data over an 11-year period, Dr. Wynn was selected and named in the list of 2015 World’s Most Influential Scientific Minds.

**THE CURE PARKINSON’S TRUST GRANT AWARDED TO SCHOLAR AND MENTOR TEAM**

Sabrina Heman-Ackah and her mentor, Professor Matthew Wood, were awarded £45,000 from the Freemasons’ Grand Charity, represented by Roger Hampshire of the Oxfordshire Freemasons, and the Cure Parkinson’s Trust, represented by COO Helen Matthews (pictured above from Left to Right) in December 2015.

The Freemasons’ Grand Charity is a grant-making charity designed to support people in need; they have previously donated funds to the Cure Parkinson’s Trust in support of research. The Cure Parkinson’s Trust is a private organization dedicated to funding and supporting research efforts into the cure for Parkinson’s. They are currently funding and supporting a number of lines of investigation into mitochondrial function and dysfunction, including Sabrina and Professor Wood’s research.

**SCIENIST SPOTLIGHT**

In 2015, the NIH welcomed back Dr. Ilyas Singeç as the Director of the Stem Cell Translation Laboratory in the National Center for Advancing Translational Sciences (NCATS). Previously a postdoc at the National Institute of Neurological Disorders and Stroke (NINDS), Dr. Singeç moved to the Sanford Burnham Prebys Medical Discovery Institute, where he served as staff scientist and director of cell reprogramming.

The OxCam Program was fortunate to have Dr. Singeç present his research to program interviewees in February 2016. When we reached out to Dr. Singeç in the spring, he provided us with details on his current research (below):

Reprogramming adult somatic cells into induced pluripotent stem cells (iPSCs) allows the generation of unlimited numbers of patient- and disease-specific cell types for laboratory research, drug discovery and regenerative medicine. However, to bring this technology closer to clinical applications, it is necessary to work on key scientific and technical challenges that currently impede the therapeutic use of iPSCs. The Stem Cell Translation Laboratory (SCTL) at NIH’s NCATS represents a multidisciplinary team approach aimed at providing novel biological insights and innovative solutions to iPSC research.

To achieve these goals, the following topics are currently investigated:

1. Establish quality control standards to define pluripotency and differentiated cell types
2. Develop methods to assess heterogeneity in iPSC-derived cells
3. Develop standardized methods to produce mature cells meeting the QC standards above
4. Discover, validate, and disseminate small molecule reagents to replace expensive recombinant proteins, xenogenic material, and undefined media components in cell differentiation protocol

The SCTL has access to cutting-edge equipment and resources including quantitative high-throughput small molecule screening, robotic automation of cell culture workflows, multi-scale assay development, 3D bioprinting, and integrated platforms to profile gene and protein expression and measure functional endpoints in standard cultures as well as on the single cell level.

For more information, visit [https://ncats.nih.gov/stemcell](https://ncats.nih.gov/stemcell).

**OXCAM SCHOLAR ON COVER OF JOURNAL**

An image from Joshua Bernstock’s research was featured on the cover of the February issue of the *Journal of Cerebral Blood Flow & Metabolism*. Within the paper entitled “a novel quantitative high-throughput screen identifies drugs that both activate SUMO conjugation via the inhibition of microRNAs 182 and 183 and facilitate neuroprotection in a model of oxygen and glucose deprivation,” the authors described work completed in the laboratory of Dr. John Hallenbeck, a senior investigator at the National Institute of Neurological Disorders and Stroke (NINDS) and the director of its Stroke Branch.

During the course of this project Bernstock and his colleagues engineered a human neuroblastoma cell line in an effort to identify small molecule inhibitors of several classes of microRNAs that cause the upregulation of global SUMOylation. Several of the identified compounds were in fact capable of upregulating SUMO-conjugation and in so doing facilitated neuroprotection when cell systems were challenged by oxygen/glucose deprivation followed by the restoration of oxygen/glucose (i.e. an in vitro model of ischemic stroke). It is expected that this novel high-throughput screening modality will help facilitate the development of drugs aimed at reducing the morbidity/mortality currently associated with ischemic stroke. Further, the technology may ultimately be repurposed in an effort to target microRNAs relevant to other CNS diseases/disorders in need of novel therapeutics.

It is the hope of Bernstock and his colleagues that this work will ultimately improve the lives of both patients and their families.
APPLYING INNOVATION ACROSS DISCIPLINES

By: Huayu Ding

The direction selective (DS) circuit in the mammalian retina, which gives the eye the ability to discern object motion, is an excellent model network to study neural computation because it engages just a few well-characterized cell types. In particular, directionally tuned signaling from starburst amacrine cells (SACs), the main participating inhibitory interneurons, lies at the heart of direction computation. By using two-photon calcium imaging, I study how dendritic branches of a single SAC are able to transform and output signals independently of one another. By examining the angular tuning properties and mapping the receptive fields of individual outputs on a SAC, I found that lateral inhibition from neighboring SACs plays a key role in decorrelating the signals transmitted. In collaboration with other labs, we explored the wiring patterns of the SAC network in different species. We performed a detailed connectomics reconstruction of SAC circuitry in the mouse retina and found subtle differences in the synaptic connectivity compared to previous studies in rabbits. Then, we built an anatomically constrained model that offered predictions we tested experimentally. We found that minute shifts in the location of inhibitory inputs onto a SAC enabled mouse retina to encode for lower linear velocities than rabbit retina, thereby conserving angular velocity tuning so that both animals detect a similar range of visual motion.

I believe that the OxCam program provides a unique opportunity for scientific and personal development. I was introduced to a wide variety of techniques and ideas by spending time in two different labs. For example, I was able to incorporate the method we developed in Cambridge for ganglion cell receptive mapping on a multielectrode array into the research I do now at NIH on amacrine cells with microscopy. Both of my mentors encouraged me to learn as much as possible and provided opportunities for coursework, including graduate level neuroscience classes and an advanced course in computational neuroscience at Cambridge. I gained valuable interpersonal skills through building collaborations and mentoring summer students. Due to the multidisciplinary nature of this program, I have had rich interactions with both PhD and MD students in different fields. The communities in college and at NIH provide great support for work/life balance. For example, rowing at Cambridge has completely changed my perspective on fitness. Overall, OxCam has helped me to grow as a scientist and as an individual, and I am certain the knowledge I have gained through this program will serve me well in the future.

MEET THE WELLCOME TRUST

Sarah Watters

Human immunodeficiency virus (HIV) infection is controlled, but not cured, by combination antiretroviral therapy (ART). As part of the viral life cycle, HIV integrates a DNA copy of itself into the host genome where it can remain latent until the cell is activated. The ability of HIV to persist in long-lived, infected immune cells, despite ART, represents one of the major barriers to HIV eradication. Understanding the mechanisms of viral persistence, within these cellular reservoirs, is essential to decipher how they can be perturbed and the virus eradicated. Recent attempts to cure HIV-infected individuals have utilized chemotherapy alongside haematopoietic stem cell transplants and thus far the Berlin Patient (1) remains the only known individual to have been cured of HIV. Although additional potential cases have been reported, these individuals experienced rebound viraemia, highlighting the substantial gaps in our understanding of viral persistence (2).

Chemotherapy is used to successfully treat a variety of cancers and autoimmune disorders. Chemotherapy includes agents that can be either cytotoxic or immunomodulatory (IMiDs) to cells. Cytotoxic drugs kill cancer cells and decrease immune cells, including CD4+ T cells, which are the primary targets of HIV. Conversely, IMiDs have been shown to activate immune cells and therefore expansion or reduction of infected CD4+ T cells is possible.

My PhD thesis attempts to address if, and how, chemotherapy agents affect the HIV reservoir by longitudinally sequencing viruses from within HIV-infected individuals who also have cancer. We sequence viruses from blood samples obtained before, during and after individuals have received chemotherapy. In this way we hope to be able to address the effect that chemotherapy is having on the persistence of viral populations, as well as to deduce whether or not these agents may be of benefit in future HIV functional cure strategies.

Greetings from the OxCam Office! We are looking forward to seeing everyone at the upcoming Annual Workshop hosted by the University of Oxford. Our Oxford collaborators have planned a diverse and dynamic agenda for this event and we are excited to come together in this multidisciplinary forum to exchange scientific ideas and discuss current and future research.

The OxCam Class of 2016 and the MD/PhD Class of 2018 will be joining us, so please be sure to welcome them! Also be sure to follow us on Twitter @NIHOxCam.

Current students and mentors, quick reminder, Progress Reports are due September 1st. Best of luck to those who are finishing up and preparing for thesis defense. Please send us some of your graduation photos for our Facebook page (facebook.com/NIHOxCam).

Best wishes for a happy and safe summer!

Katie Soucy

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FAMILIAR FACES

OxCam alumnus, Dr. Justin Lathia (Class of 2003), is currently working as an Assistant Professor of Molecular Medicine at the Cleveland Clinic Lerner College of Medicine.

Dr. Lathia received an R01 grant for his research on novel adhesion mechanisms in glioblastoma stem cells. The average age for R01 grant recipients is 42; however, Dr. Lathia was awarded his first R01 grant before the age of 35.

After his recent visit to the NIH, we reached out to Dr. Lathia and he was more than happy to share some information on his current research:

While efforts have been focused on activating anti-tumor immune responses for immunotherapies, they are confounded by immune cell populations that suppress immune system function, including myeloid-derived suppressor cells (MDSCs). We identified MDSCs in the brains of glioblastoma patients and found them in close proximity to self-renewing cancer stem cells (CSCs). We uncovered a signaling axis by which CSCs amplify the function of MDSCs via macrophage migration inhibitory factor; targeting MDSCs directly, or via this axis, increases immune response and decreases glioblastoma growth. These findings are the basis for a clinical trial we have opened targeting MDSCs in glioblastoma.

During his time in the program, Dr. Lathia worked with Dr. Mark Mattson in the National Institute on Aging (NIA) and Prof. Charles ffrench-Constant at the University of Cambridge.

WELCOME BACK

DR. BASSETT

Former OxCam Scholar, Dr. Danielle Bassett, returned to the NIH to give a seminar as part of the NIH BSSR Lecture Series on May 5, 2016. Her talk, entitled “The Network of Human Thought”, focused on studying the brain as a social network and different interdisciplinary questions that come from exploring neural networks.

During her visit, Dr. Bassett also took time to sit down with a few of our scholars to offer advice based on her experiences in the program and her career path. While discussing the program and her current work, she said that a lot of her early success and her interest and pursuit of interdisciplinary and collaborative research is due to her time in the OxCam Program.

Dr. Bassett is currently a tenured Skirkanich Assistant Professor of Innovation in the Department of Bioengineering at the University of Pennsylvania. She was awarded the MacArthur Fellowship, often called the ‘Genius Grant’, in 2014 for her research on understanding how the brain is connected and how learning new skills and different disease states affect that connectivity pattern. She was also awarded the 2016 NSF CAREER Award.

As a member of the OxCam Class of 2004, Dr. Bassett’s primary mentors were Dr. Daniel Weinberger in the National Institute of Mental Health (NIMH) and Professor Edward Bullmore at the University of Cambridge.

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LETTER FROM

THE MANAGING DIRECTOR

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