CELL AND MOLECULAR BIOLOGY STUDENT NEWSLETTER

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IN THIS ISSUE

LETTER FROM THE EDITORS

Dear CAMB students, faculty, and alumni,

We'd like to extend a warm welcome to our newest CAMB 2017 matriculates. Orientation begins Monday, August 28th, with the CAMB happy hour on Thursday, September 7th, at 4:30 pm in the Biomedical Research Building lobby. We hope that you enjoy meeting your new classmates and faculty members, and we are excited to have you as members of the CAMB community.

In this issue we highlight two exciting CAMB student research projects from recent Genetics and Epigenetics (GE, formerly GGR) alumnus and 2017 Kadesch Prize in Genetics recipient Dr. Philipp Mews, and current GE student Suzi Shapira. We also catch up with two CAMB alumni and learn about their careers in science outreach and industry. Finally, we introduce new CAMB-er Dr. Andrew Vaughan and also provide tips for navigating scientific conferences in our Special Interest section.

For additional articles, past publications, and to learn more about the CAMB Newsletter team, visit our blog at **cambnewsletter.wix.com/blog**. Current students, including our 2017 matriculates, interested in contributing to the CAMB Newsletter can contact us at **camb.studentnews@gmail.com**. We hope you enjoy the August 2017 Issue!

Sincerely,

Camille Syrett and Iryna Shakhmantsir

Editors-in-chief

RESEARCH SPOTLIGHT

Connecting Neuronal Dots: Linking Metabolism to Synaptic Restructuring in Memory Formation

Lindsey Weed

Hippocampal memory formation requires neuroplasticity, which is produced by the orchestrated expression of neuronal genes through chromatin modification[1,2]. Histone acetylation is a post-translational modification of histone proteins that helps to restructure chromatin and regulate the ability to store and recall previously acquired information[3]. Histone acetyltransferases (HATs) transfer acetyl groups (-$COCH_3$) to the lysine residues of histone tails, thus neutralizing the positive charges and decreasing their affinity for negatively charged DNA that is wound around the nucleosome. This process allows the condensed chromatin structure to relax and local gene expression to increase. For this process to occur, metabolic production of the acetyl-group donor, acetyl coenzyme A (acetyl-CoA), is indispensable, but the precise mechanisms remain poorly understood.

Previous investigations have shown that manipulating the concentration of intracellular acetyl-CoA can alter histone acetylation and gene expression[4,5]. With this knowledge, GE alumnus Dr. Philipp Mews, who completed this thesis work in Dr. Shelley Berger's lab, set out to determine whether the metabolic enzymes that generate acetyl-CoA from intermediary metabolites might directly control the epigenetic modifications necessary for neuronal development and memory storage. In a recent *Nature* publication, he demonstrates that acetyl-CoA synthetase 2 (ACSS2) directly regulates histone acetylation in post-mitotic neuronal cultures and gene expression changes that affect

Philipp Mews, GE (formerly GGR)

spatial memory in mammals. Philipp recalls that at the time he conceived the project, metabolic enzymes participating in precise gene regulation of the nucleus was a highly controversial notion.

"The idea that key metabolic enzymes could bind directly to chromatin to fuel the local chromatin modification machinery was bold and novel, and to see it borne out so clearly in my data was really exciting," said Philipp.

Philipp used the Cath.-a-differentiated (CAD) cell line to investigate the function of ACSS2. CAD cells are derived from mouse catecholaminergic cells and differentiate to express neuronal properties upon serum deprivation. He observed that ACSS2 shifted from cytoplasmic localization in undifferentiated CAD cells to nuclear localization upon differentiation, suggesting ACSS2 may have a role in the neuronal development of these cells. Transcriptome analysis of differentiated CAD cells revealed upregulation of neuron-specific genes as well as increased acetylation of these genes compared to the surrounding genome. Additionally, knockdown of ACSS2 abolished this induction of neuronal gene expression upon differentiation. Philipp concluded that ACSS2 is critical for the upregulation of genes implicated in neuronal differentiation.

To determine whether ACSS2 enrichment correlated with histone acetylation, Philipp performed ChIP-seq analyses in undifferentiated and differentiated CAD cells. Areas bound by ACSS2 were proximal to genes linked to neuronal differentiation and 80% of these ACSS2 peaks overlapped an acetylation peak or had an acetylation peak at downstream targeted transcription start sites. The co-occupancy of ACSS2 and acetylation marks suggests ACSS2 may have a role in providing acetyl-CoA for HAT enzymes. To investigate this, Philipp measured the levels of acetyl-CoA in ACSS2 knockdown cells and cells treated with ACSS2 siRNA and found significant reduction of the metabolite in both cases. Global transcription-linked acetylation marks were similarly reduced upon ACSS2 knockdown. Experiments with primary mouse hippocampal neurons corroborated these findings, supporting the hypothesis that ACSS2 functions in neuronal histone acetylation.

Previous studies have shown that there is a strong link between histone acetylation in neurons and memory formation[3]. ACSS2 co-immunoprecipitated with H3K9ac and H3K27ac, which are key substrates of transcriptional coactivators CBP and p300 that have roles in long-term memory[6]. ACSS2 also co-immunoprecipitated with CBP in differentiated CAD cells, correlating with data showing colocalization of the two proteins in the mouse hippocampus. To examine the function of ACSS2 in hippocampus-dependent spatial memory, ACSS2 expression was attenuated in the dorsal hippocampus of adult mice by shRNA. An object-location memory paradigm revealed impaired long-term spatial memory upon ACSS2 knockdown. mRNA-seq of the dorsal hippocampus of untreated control mice exposed a small number of upregulated genes which encode proteins that mediate the strength of neural connections immediately after learned behavior. Upregulation was reduced by ACSS2 knockdown, as was induction of memory retrieval-associated genes. Together, the *in vitro* and *in vivo* findings are the first evidence linking metabolic signaling to chromatin restructuring in the brain and memory consolidation.

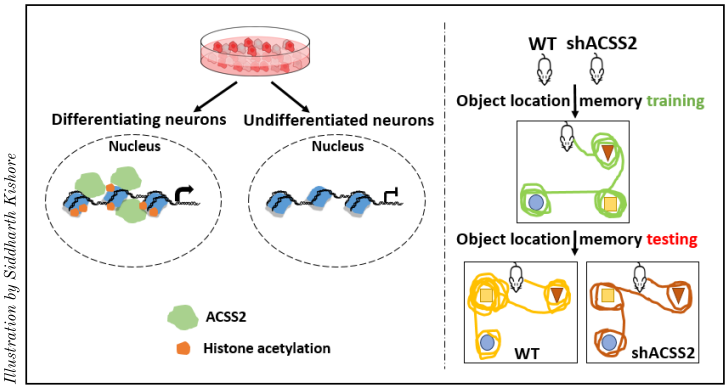


Illustration by Siddharth Kishore

ACSS2 is a chromatin-bound source of acetyl Co-A for histone acetylation in neurons and is essential for memory formation in mammals. **(A) ACSS2 binding correlates with histone acetylation and gene expression of differentiation-linked genes in neuronal cultures. The co-occupancy of ACSS2 and acetylation marks suggests ACS22 may have a role in providing acetyl Co-A for histone acetyltransferase (HAT) enzymes (B) In an object-location memory paradigm, mice explore three different objects during a training period. After 24 hours, the mice are re-exposed to the objects with one object changed to a new location. The amount of time spent exploring the novel object-location corresponds with spatial object memory; the ACSS2 knockdown mice had reduced total object exploration, suggesting ACSS2 is critical for long-term memory formation.**

Philipp's work establishes an association between cellular metabolism, gene regulation, and neuroplasticity by elucidating the neuronal function of ACSS2 as a chromatin-bound source of acetyl-CoA for histone acetylation. Localization of ACSS2 is linked to the increased histone acetylation and transcription of neuronal genes required for spatial memory formation and retrieval. Understanding this metabolic pathway and other epigenetic mechanisms brings us one step closer to unraveling the complex functions and behaviors of the brain and how these may become dysregulated in neuropsychiatric disorders, such as anxiety or depression. ACSS2 is now a novel enzymatic target for developing therapies to restore histone acetylation due to its critical role at the interface of neural metabolism and chromatin restructuring.

Philipp is currently a postdoctoral fellow in Dr. Eric Nestler's lab at the Friedman Brain Institute at the Icahn School of Medicine at Mount Sinai in NYC. His long-term goal is to understand the complex interplay between epigenetic gene regulation and neuronal circuit connectivity.

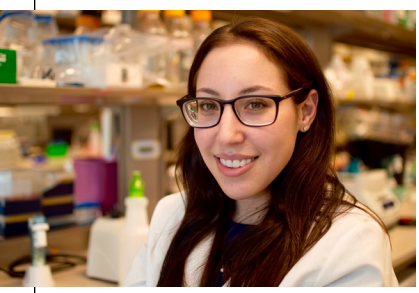
Mews, P., Donahue, G., Drake A.M., Luczak, V., Abel, T. and Berger, S.L. Acetyl-CoA synthetase regulates histone acetylation and hippoccampal memory. ***Nature*** **2017;546:381-6.**

For a full list of citations, please visit our blog.

Ebf2 Puts the "Brown" in Brown Fat

Lexy Stanley

Fat has a bad reputation for its negative contribution to a host of diseases such as cardiovascular disease, diabetes, and obesity. However, not all fat is created equally. The study of brown adipose tissue (BAT) is becoming a hot topic in the world of gene regulation, metabolic diseases, and in the exercise industry. Rising interest in brown adipose tissue research parallels the growing efforts to combat rising obesity rates in America. The exercise industry is interested in understanding BAT for weight loss and healthy lifestyle maintenance. BAT is a highly metabolically active tissue that converts food energy into heat, which subsequently regulates thermogenesis. In contrast, white adipose tissue (WAT) stores food energy as triglyceride deposits and is a dreaded enemy of anyone trying to achieve a "beach body". While a healthy amount of WAT is critical to cushion vital organs and provide insulation to maintain body temperature, too much WAT adversely affects metabolic functions and leads to disease, such as obesity and heart disease. Luckily, cold exposure or β-adrenergic stimulation can increase brown fat mass to counteract the negative effects of WAT. Part of appreciating how BAT functions is understanding its genetic regulation at the core of its biologic function. Insights into genetic regulation of BAT could uncover potential therapeutic targets for weight loss and disease management.



Suzi Shapira, GE (formerly GGR)

Dr. Patrick Seale's laboratory focuses on elucidating the regulatory pathways that control the development, differentiation, and function of adipose cells. Dr. Seale identified *Prdm16* (protein domain 16) as a vital cell-autonomous regulator of brown adipose cell fate. Recently, the lab identified

Ebf2 (Early B-Cell Factor 2) as an upstream regulator of *Prdm16*. *Ebf2* is required for the differentiation and function of BAT, with *Ebf2* knockout mice developing WAT-like tissue where BAT usually is. *Ebf2* is necessary for binding of a key adipogenic transcription factor, *Pparα*, to *Ucp1*. Uncoupling protein 1 (*Ucp1*) regulates energy transfer in BAT by uncoupling of the respiratory chain mitochondria and allowing for fast glucose oxidation with a low rate of ATP production. However, it remained unclear how EBF2 facilitated this PPARα/UCP1 interaction on a molecular level. Suzi Shapira, a GE student in the Seale lab, took on the enormous task of unpacking the details of BAT fate commitment using ChIP (chromatin immunoprecipitation) followed by deep sequencing (ChIP- seq). She discovered that *Ebf2* binds directly to lineage- specific enhancer regions to regulate brown fat differentiation and homeostasis (Figure 1A). Her work uncovered a novel molecular mechanism of adipocyte fate regulation, and BAT function at the chromatin level.

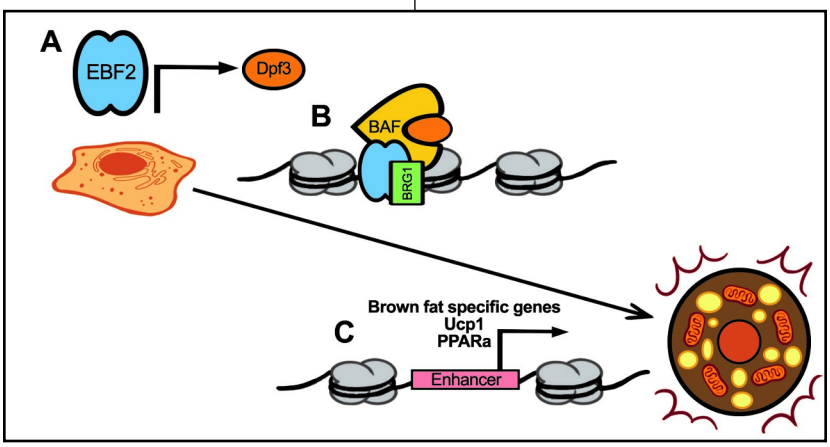


Illustration by Arwa Abbas

EBF2 physically interacts with the chromatin remodeler BRG1 and the BAF chromatin remodeling complex in brown adipocytes. The histone reader protein DPF3 is the brown fat-selective component of the BAF complex required for brown fat gene programming. EBF2 recruits DPF3/BAF to *Ucp1*, *PPARα*, etc. These results reveal a novel mechanism by which EBF2 cooperates with a tissue-specific chromatin remodeling complex to activate brown fat identity genes.

Suzi first assessed whether EBF2 directly binds chromatin or indirectly regulates PPARα/UCP1 interactions. Among the 28,000 binding-site hits were genes controlling fatty acid/glucose metabolism and BAT-specific differentiation. Using an *Ebf2* knockout mouse, she found that EBF2 binding at brown-fat genes enhancer sites was reduced, but binding was not altered at enhancers shared by both WAT and BAT. This confirms *Ebf2*'s specificity as a transcriptional activator for BAT fate.

Co-immunoprecipitation experiments showed a physical interaction between EBF2 and the BAF (BRG1-associated factor) chromatin remodeling complex in mature brown adipocytes (Figure 1B). The BAF complex is an epigenetic regulator of several cell types, including adipocytes. Suzi identified *Dpf3* (double Ph.D. fingers 3), a regulatory subunit of the BAF DNA remodeling complex, as specifically required for brown fat induction in WAT, both in basal conditions and in response to β-adrenergic stimulation (Figure 1A). Similar to *Ebf2* knockouts, her *Dpf3* knockout mice showed decreased accessibility at *Pparα* and *Ucp1* enhancer regions in both basal conditions and with β-adrenergic stimulation. This finding established that *Dpf3* is required to promote permissive chromatin state at brown- fat specific enhancers to allow for differentiation (Figure 1C). The *Dpf3* knockout also showed it is required for recruitment of other BAF complex subunits, but not *Ebf2*, to enhancer sites of brown fat specific genes. Therefore, *Dpf3* functions downstream from *Ebf2* to regulate the BAT genetic program.

In conclusion, *Ebf2* is an indispensable lineage-specific enhancer activator for the genes that control the BAT cell lineage program. *Dpf3* expression downstream of *Ebf2* is necessary for *Ebf2* to facilitate *Pparα* and *Ucp1* interactions in BAT. Taken together, Suzi's paper identifies a molecular mechanism that orchestrates the BAT genetic program, shedding light on *Dpf3* as a key downstream target of *Ebf2*-mediated *Pparα* and *Ucp1* activity. By identifying both *Ebf2* and *Dpf3* as particular regulators of the BAT lineage, she has presented two points of possible therapeutic modulation to treat metabolic disease.

Suzi is currently writing her thesis manuscript and is defending this fall. She aims to do a post-doctoral fellowship that continues to focus on genetics and epigenetics. She says, "I really enjoy bench science and my long-term goal is to pursue drug discovery/therapeutics development based on the skills I gained during my Ph.D. work and future training." We are excited to see what she does next.

Shapira, S.N., Lim, H.-W., Rajakumari S., Sakers, A.P., Ishibashi, J. Harms, M.J., Won, K.-J., and Seale, P. EBF2 transcriptionally regulates brown adipogenesis via the histone reader DPF3 and the BAF chromatin remodeling complex. *Genes Dev*. 2017 Apr 1;31(7):660-673.

SPECIAL INTEREST

Scientific Conference Survival Guide

Lexy Stanley and Somdutta Mukherjee

Going to a scientific conference can be exciting and informative, but also stressful and overwhelming. Since conferences are vital components to a successful graduate student's progress and future career, we thought a breakdown of the do's and don'ts of a conference, along with some other tips, were in order.

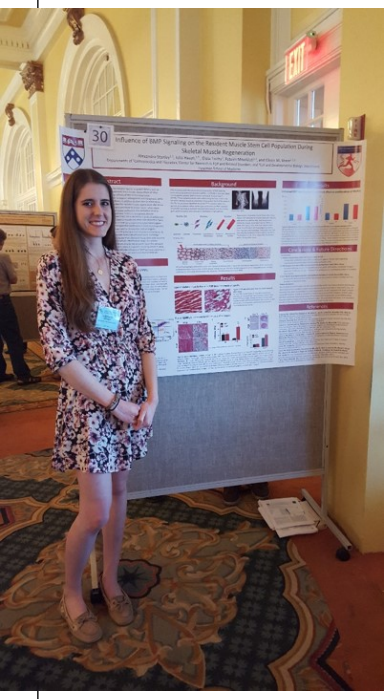
Before you go: The first step is obvious: find a conference you want to go to. Some big meetings to search through are Keystone Symposia, the Gordon series, Cold Spring Harbor, and FASEB. The research should be intellectually stimulating and relevant to your own work. It is also important that you go to a conference where you can present a poster or give an oral presentation (or both!). Next, talk to your mentor! Mentors want their students to go to conferences because it gets the lab's work out into the scientific community. That being said, they will not say 'yes' to any and every conference you want to go to. Ask them respectfully, and listen to their reasons if they say 'no'.

Conferences are a great way to go somewhere new, so if you can, book your trip for an extra day or two and do something fun. While a lot more expensive, international conferences can often bring you into contact with some bigger names in science, and they can also offer great vacation experiences after the conference is over (just remember this will be at your own expense, not your PIs). If the conference is not in an instantly-obvious exciting place, still consider it. These conferences may be cheaper and no less intellectually prestigious.

It is important to factor the size of a meeting into your decision when choosing a conference to attend. Smaller conferences are better for hearing about other people's research, getting direct feedback on your work, and making personal connections. Larger meetings are good for getting a general overview of what other people in the field are working on. You should also consider the best time to attend a conference. It may be more beneficial to wait until you have a better idea of what you are working on, and how to communicate your research to others before going to a meeting. However, you do not want to wait until you are about to graduate, as you may miss out on important networking opportunities.

Conferences can get pretty expensive depending on the location, size, length, and amenities provided. You may have a PI who is able and willing

to pay for all of it out of their grant(s), in which case a nice thank you note is in order. If you are on a training grant or have an individual NRSA grant, find out what sort of travel funds are available through these channels. There are several other sources to apply for travel funds. GAPSA at Penn offers travel funds with a maximum award up to $800 and BGS also awards small travel grants ($500 maximum, visit this article on our blog for specific links). Both have deadlines and require a letter of recommendation from your PI. Your individual CAMB subgroup group might also have some funds set aside for small travel grants for its students. Ask your group chair if this is the case. Some conferences also offer small reimbursements for speakers/presenters, which is something else to consider during your conference research.



Author Lexy Stanley ready to present her work during a poster session

The next step is to make a plan to maximize your conference experience. Look over the schedule of speakers, posters, and/or workshops and note when events of interest are scheduled. You may not be able to make every talk depending on how the conference is set up, but you will at least ensure you can attend the critical sessions. You should also prepare to network, so that you can get input on your research, and also make connections for future collaborations or jobs. Many conferences have a list of all the attendees. Look it over and make note of anyone or any companies you would like to talk to. You should be prepared to give a quick informal summary of your research to pique their interest. Lastly, don't forget to dress for the occasion. Check the conference website or email the organizers if you are unsure of the dress code. Being too dressed up is just as awkward as being too casual.

During the conference: Now that you have prepared for your conference and are finally there, use your time as efficiently as possible. Firstly, take notes on the sessions you attend. Importantly, take breaks during the day. Conferences may have talks that go on throughout the whole day, and listening to hours of talks can get exhausting.

Conferences are a great way to network and put your name out there. You should use them as an opportunity to meet new people and make new connections. Once you start going to conferences regularly, you will begin to meet the same people. Talking to other students, postdoctoral fellows, and faculty who attend these meetings gives you an opportunity to discuss your work, and get new ideas and perspectives that can help move your project along. Additionally, the connections you make at conferences may be useful for your career after graduate school. You might work as a postdoctoral fellow with a faculty member that you connected with, or perhaps you will get a job at a company after meeting one of their employees.

Lastly, enjoy yourself! Don't forget to take pictures of yourself presenting your poster or on your mini vacation. A lot of conferences will have a disclaimer prohibiting photography of posters, slides, and notes, so you should never take pictures of someone else's presentation unless specifically given permission.

After the conference: Once you get back to lab, there are still a few things you should do. Go over your notes from the conference to review the information while it is still fresh in your mind and share what you've learned with other members of your lab. They are working in the same field as you, so it is likely that they will find this information useful as well. Furthermore, you should send out emails to people that you met at the conference to maintain those professional connections.

Lexy and fellow scientists enjoying the conference experience

Conferences are great ways to learn about all the exciting work that people are doing to advance your field of study. While conferences can be overwhelming and exhausting, they are easily one of the most fun things about graduate school, so go enjoy one!

WHERE ARE THEY NOW?

Wenny Lin

Clarissa Rous

"What do you want to do with your Ph.D.?" - both dreaded and inescapable, this question seems to crop up at every gathering of family, old friends, and new acquaintances. For those of us who mark "industry" in our tentative list of potential careers, it can seem a daunting path to an endpoint with uncertain responsibilities. What are some of the jobs available in industry? How does a Ph.D. student gain the experience and seek out opportunities that lead into those positions? The best way to answer these questions is to ask people who have walked that path before: people like Wenny Lin, a CAMB-GTV alumna who now works as a Senior Real World Data Scientist (or epidemiologist) at Genentech, a member of the Roche Group.

At Genentech, Wenny collaborates with teams that push drugs in late-stage development to market. This encompasses a range of activities, from designing and managing clinical trials (Clinical Development Team), to investigating potential side effects (Safety Science Team), to educating the medical community (Medical Affairs Team), and demonstrating the value of drugs to achieve insurance coverage (Payer Evidence Team). Wenny's main role on these teams is to provide strategies for utilizing evidence from "real world-data" such as insurance/administrative claims, cancer registries, and electronic medical records. When an observational research study is needed, Wenny forms a study team to design and execute the study, and disseminate the results at conferences and in peer-reviewed publications.

Wenny's expertise in epidemiology stems from her work on HIV vaccines in the lab of Hildegund Ertl at the Wistar Institute, where she became interested in HIV prevention and gained bench skills. Early on at Penn, she audited a few public health and epidemiology courses, and at the end of her Ph.D. in 2008, she applied and was accepted to the Cancer Prevention Fellowship at the National Cancer Institute (NCI). The fellowship program sent her to Harvard's T.H. Chan School of Public Health for a one-year Master's of Public Health degree, concentrating in Quantitative Methods. While completing her Master's coursework, Wenny also worked as an intern at the

Massachusetts Department of Public Health, compiling the state's data on birth defects for annual reports and press releases. In 2009, she moved to the NCI for the second part of the fellowship program and joined a group in the Division of Cancer Epidemiology & Genetics. There, she learned statistical programming and combined epidemiological study design methods with her molecular biology background to identify immunological, nutritional, and genetic risk factors and early detection biomarkers in esophageal cancer patients. Towards the end of her fellowship in 2013, Wenny's husband decided to pursue a MD at Stanford, so she began a job search on the West Coast.

Wenny Lin, GTV

While she was submitting job applications, Wenny also checked LinkedIn to identify contacts who could connect her to hiring managers for any potential job opportunities. Then, if she was in the area, she would ask hiring managers for in- person informational interviews. These in- person informational interviews not only allowed her to learn more about the company and positions available, but also let Wenny make a direct impression of herself as a potential candidate. Having been involved on hiring committees at Genentech, she stresses the importance of building your network early, and making the most of it during your job search. If there is someone in the company who knows and can vouch for you, it can be just the edge needed to elevate you above other equally qualified candidates.

Networking and communicating with people both in science and in other fields are skills that Wenny cultivated as a Graduate Associate (GA) in Penn's undergrad dorms and as a GAPSA executive board member. Beyond advancing skills useful for career preparation, her extracurricular activities also helped her stay grounded and engaged during grad school, which she admits can be a very isolating time when lab experiments continually fail. So for an individual who took advantage of many opportunities in grad school, is there anything that Wenny wishes she had done differently? She admits that her one regret is not making more connections with BGS faculty. Though it is easy to be intimidated by their "star power", faculty have much to share about their career and life experiences. Seizing opportunities to learn from others and to build your network, whether with faculty or other scientists, is a habit that will serve you well throughout your Ph.D. and beyond.

David Garbe

Somdutta Mukherjee

David Garbe, GE

Outreach programs are essential for sparking young students' interest in scientific research. Spreading the knowledge, importance, and awareness of biomedical research is a passion that CAMB-GE alumnus David Garbe has been pursuing as an outreach educator at the Pennsylvania Society for Biomedical Research (PSBR) for the past year.

David began his scientific training in the laboratory of Dr. Greg Bashaw, where he studied developmental axon guidance in the central nervous system of fruit flies. After defending his thesis in 2007, he worked for the pharmaceutical company Wyeth for three years. While he was there, Wyeth was acquired by Pfizer. During the merger, David decided that the corporate setting was not for him. He realized that he enjoyed doing experiments and interpreting the data in order to tell a story, so he returned to Penn for an academic postdoctoral fellowship in Dr. Amita Sehgal's laboratory. As a postdoc, David also taught as an adjunct professor at local colleges and universities because he loves teaching science and mentoring students.

David initially pursued a postdoc to obtain a faculty position, but for various reasons, he decided to focus on a different career path. He knew that he wanted to combine his passion for science and education, so he talked with Dr. Jamie Shuda, director of life science outreach at the BioEYES program. BioEYES is a successful science outreach program that started locally in Philadelphia, and has expanded its work both nationally and internationally. Dr. Shuda didn't have any available positions at BioEYES, but suggested that David look into to PSBR, which had job openings for outreach educators at the time. The mission of PSBR is to educate the public, specifically K-12 students, about the value of using animals in biomedical research. As an outreach educator, David's job is to engage and excite students about science and biomedical research. He teaches students about the importance of using animals in research by providing hands-on lessons using fruit flies. He is also working to bring zebrafish to classrooms to expand the types of model organisms students can work with. Additionally he provides factual information about why animals are necessary for biomedical research in order to fight negative information that some animal rights groups distribute. As an outreach educator, every day is different for David. Some days are spent in the office, while others are spent traveling to different parts of the state talking to many people and interacting with students.

David's teaching experience during his adjunct work helped ease the transition from a traditional academic setting to an informal science education environment at PSBR. Furthermore, he said that the many opportunities to present posters and give talks both as a Ph.D. student and a postdoc helped him improve his communication skills. The biggest challenge for David at his new job was learning to distill information for non-scientific audiences, and presenting it in an understandable way. David likes interacting with people and building networks, and now he is in a perfect position to reach out to others and contribute to the growth of his organization.

For graduate students looking to go into outreach, David's advice would be to join a group or organization on campus, such as BioEYES, that does outreach in the local community. David's experiences in both the pharmaceutical business and academia demonstrate that there are a variety of jobs that require a doctorate degree, even though it might take some extra effort to find them. On a broader note, David's advice to graduate students would be not to "feel like you have to pigeonhole yourself into a traditional academic postdoc and faculty path. There are a lot of opportunities to use your training for a wide number of jobs." David's career took many twists and turns, but ultimately led him to a rewarding and exciting job that he truly enjoys. He is more than happy to talk to anyone interested in learning more about non-traditional career paths similar to his own.

For more information about the Pennsylvania Society for Biomedical Research, visit http://www.psbr.org/. For those interested in speaking with David, he can be reached at david@psbr.org.

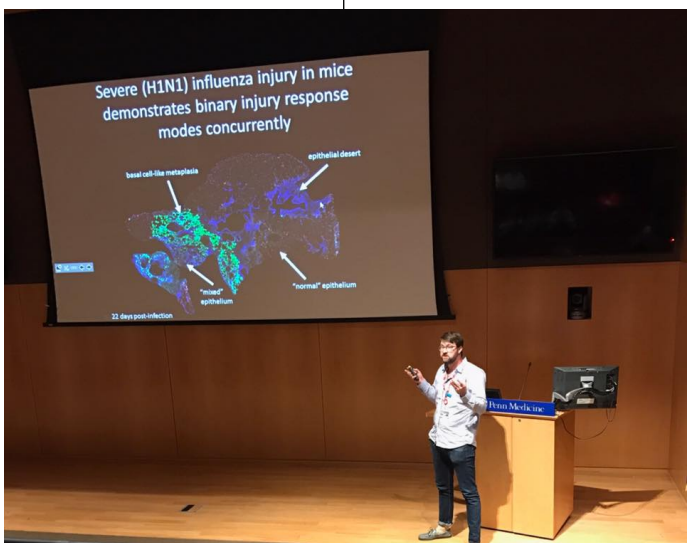
Welcoming New-CAMB-ers:

A Faculty Profile on Andrew E. Vaughan, Ph.D.

Camille Syrett

The UPenn School of Veterinary Medicine welcomed Dr. Andrew Vaughan in April 2017. As the newest assistant professor in the Department of Biomedical Sciences, Dr. Vaughan is currently seeking new graduate students to join his laboratory team. Dr. Vaughan is part of the CAMB (DSRB) graduate group, and is a member of the Penn Institute for Regenerative Medicine (IRM).

As a graduate student in the lab of gene therapy pioneer Dr. Dusty Miller at the Fred Hutchison Cancer Research Center, Andy was at the forefront of the fast-paced field of retrovirology. There, he took on multiple projects, first dabbling in AAV-mediated gene therapy, and then honing in on the role of cancer stem cells using a mouse model of a unique Jaagsiekte retroviral-driven lung cancer. Intriguingly, the envelope protein of this retrovirus alone is sufficient to induce pulmonary adenocarcinoma. As his thesis work developed, Andy became more and more interested in cancer stem cells and factors underlying differences in lung cell susceptibility to the Jaagsiekte envelope protein.



Andrew Vaughan, Ph.D., Assistant Professor of Biomedical Sciences

After completing his dissertation, Dr. Vaughan was ready to move on from the field of retrovirology. Guided by his passion for understanding the mechanisms of lung regeneration after epithelial injury, Andy joined the lab of Dr. Hal Chapman at The University of California San Francisco. During his postdoctoral research Dr. Vaughan focused on how tissues can respond to injury and undergo repair. He uncovered distinct stem and progenitor cell pools that contribute to epithelial regeneration, and demonstrated a novel role for Notch signaling in this dynamic process.

Lately the pulmonary field has been very excited about the influenza model of lung injury, and the robust regeneration observed after flu exposure. As this momentum continues, Andy remains enthusiastic about elucidating the mechanisms driving cell fate decisions after influenza-mediated injury. Questions such as "how do cell fate decisions influence the physiological function of the lung?" are a guiding force for his laboratory. Dr. Vaughan is also taking his research in new and exciting directions, and plans to investigate whether CRISPR and gene therapy approaches can be used to reprogram epigenetic states of lung cells.

Dr. Vaughan brings unmistakable energy and passion for mentoring to CAMB, and is likewise excited about being at Penn where there are "great collaborators and mentors in the field, with lots of great people to bounce ideas off of." While faced with many of the typical challenges new investigators encounter while setting up a lab, he remains elated with the "total freedom of possibilities to explore in projects, and the ability to pursue interesting tangents."

Dr. Vaughan's latest research titled "Local lung hypoxia determines epithelial fate decisions during alveolar regeneration" was recently published in *Nature Cell Biology* (doi: 10.1038/ncb3580). He welcomes inquiries for potential rotations from incoming students. Please contact him directly at andrewva@vet.upenn.edu for more information on his research.