CELL AND MOLECULAR BIOLOGY STUDENT NEWSLETTER

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RESEARCH SPOTLIGHT

Overshooting the Bookmark: A Spike in RNA Pol II Binding at Mitotic Exit

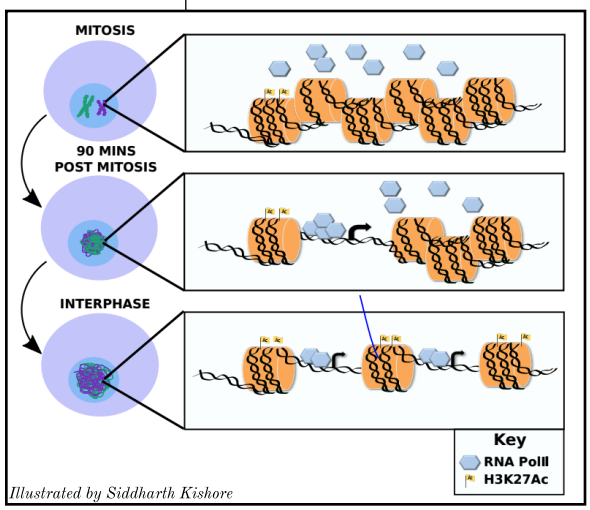
Katherine Palozola

As early as the 19th century, Walther Flemming and other biologists knew that a complex of genetic material and proteins—what we now refer to as chromatin—condenses during cell division. In fact, it was the condensed nature of mitotic chromosomes that enabled their visualization under a standard light microscope. Fast forward to the mid 20th century during the era of molecular genetics: early biochemical assays showed a severe reduction in RNA production during mitosis. More recently, antibody-based protein localization assays have indicated that most proteins involved in gene expression, such as RNA polymerase II and transcription factors (TFs), are largely absent from mitotic chromatin. Given this apparent cessation of RNA synthesis during division, the mystery that remains is how transcriptional machinery is properly recruited and reassembled in G1 so that the cell type-specific gene expression program is reestablished, and the cell's functional identity is maintained. This concept of transcriptional memory, of how phenotype is inherited, is the heart of epigenetics.

Several studies have shown that general transcriptional regulators, including polycomb (PRC1), trithorax (MLL), and TATA-binding protein (TBP) remain bound to a subset of their interphase binding sites, thus providing a bookmark of the cell's interphase transcriptome. A study from the Blobel lab led by recent GGR alumnus Chris Hsiung found that the macromolecular accessibility of promoters is overall maintained during mitosis, despite the microscopic compaction of chromatin. In addition, many histone modifications, which are indicative of transcriptional state, are also maintained on mitotic chromatin. Given the role of tissue-specific TFs in establishing cell identity during development, it was hypothesized that they play an important role in this process. Several studies conducted at Penn by Stephan Kadauke (GTV alumnus in Blobel lab), Juanma Caravaca (former Zaret lab member) and Robert Lake (Fan lab member) have shown that certain tissue- specific TFs in several different cell types indeed bookmark select regions of the mitotic genome.

Despite these insightful studies, there remained a lack of comprehensive analysis of whether transcription of the genome immediately after mitosis is in any way different from later in interphase. Early in his Ph.D., Chris decided to tackle this problem through a co-mentorship by Dr. Arjun Raj and Dr. Gerd Blobel. To do so, Chris performed chromatin immunoprecipitation coupled with DNA sequencing (ChIP- Seq) for RNA Pol II on G1E cells (a murine erythroid cell line) arrested in mitosis and at time points after the cells were released from the arrest and entered G1. Chris found that the bulk of RNA Pol II is recruited to promoters and intergenic enhancers after 90 minutes of mitotic exit, in strong agreement with previous cytological approaches. Interestingly, RNA Pol II at promoters and intergenic enhancers was more abundant earlier in mitotic exit compared to later in interphase. Based on this observation, Chris suggests that there is a "spike" in genome-wide RNA Pol II recruitment. This spike in RNA Pol II recruitment occurs when the promoter-enhancers loops are first reestablished after mitosis, though there is no concomitant spike in promoter-enhancer contacts. Chris says that his favorite part of the Pol II ChIP-Seq was when he saw the signal progressing from the 5' to 3' end of genes as cells transitioned from mitosis to G1. He says that this

Chris Hsiung, GGR



During mitosis, RNA Pol II is evicted from the DNA, though some histone modifications indicative of active chromatin, such as histone 3 lysine 27 acetylation (H3K27Ac), are retained at some sites more than others. Chris Hsiung found that when cells exit mitosis, the earliest rounds of transcription are unexpectedly higher in output than that later in G1. This spike in transcriptional activity can be observed at about half of the genes and intergenic enhancers, and correlates with the local level of H3K27Ac during mitosis. Chris's results from single-molecule RNA FISH suggest that this transcriptional spike during mitotic exit contributes to population heterogeneity.

made it clear to him that they had mapped the first round of transcription.

One important technique that allows for visualization of primary transcripts is single-molecule RNA fluorescence in situ hybridization (RNA-FISH), a method developed by Chris's co-advisor Dr. Arjun Raj. Using spectrally distinct probes for introns and exons, Chris quantified primary transcripts during mitotic exit and found that not all of the cells experience a spike in transcription. However, the cells that did display a spike in transcription produced more mRNA than those that did not. From this observation, Chris proposed a model in which the spike in transcription during mitotic exit contributes to population heterogeneity. "It is still not clear what causes this phenomenon, but we identified the localized levels of a histone modification (histone 3 lysine 27 acetylation) during mitosis as, so far, the best predictor of the mitosis-G1 transcriptional spike. We observed the mitosis-G1 transcriptional spike in two different cell types, suggesting it is a generalizable property of dividing cells."

As for the overall experience, Chris says, "We tested many hypotheses about the potential mechanism underlying the phenomenon we observed. They were either wrong or inconclusive, and never made it in the paper despite all the efforts. Most conclusions we drew from the data are far from some of the hypotheses we started with. I enjoyed how the data led to fresh conclusions rather than being limited to addressing pre-existing hypotheses. I learned a tremendous amount about experimental and data analytical approaches from the different scientific backgrounds of my advisors and lab mates."

Chris defended his thesis in November 2015 and is currently completing medical school as part of the MD-Ph.D. program at Penn.

Hsiung, C.C.-S., Morrissey, C.S., Udugama, M., Frank, C.L., Keller, C.A., Baek, S., Giardine, B., Crawford, G.E., Sung, M.-H., Hardison, R.C., and Blobel, G.A. Genome accessibility is widely preserved and locally modulated during mitosis. ***Genome Research*****, 2015; 25(2): 213-225.**

Crash Test for B7-H4 CARs

Iryna Shakhmantsir

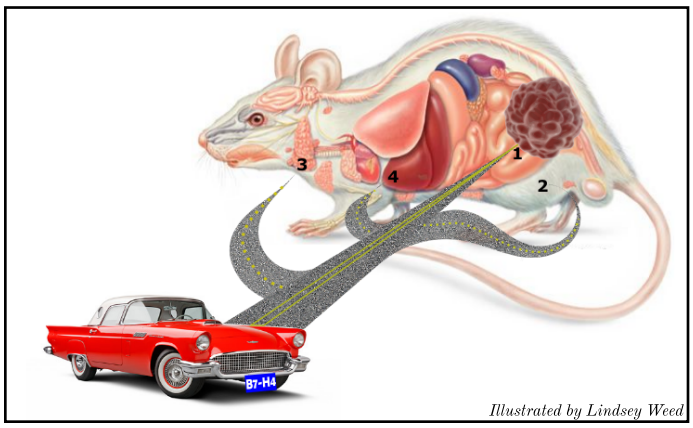
The University of Pennsylvania is a leader in chimeric antigen receptor (CAR) T cell research and in translating basic research findings into successful clinical trials. CAR T cell therapies are designed to attack and destroy cancer by harnessing a patient's own immune system. Researchers extract the patient's T cells, modify them outside of the body so that they recognize tumor cells, and reintroduce the modified T cells back into the patient's blood. The goal of this therapy is to provide a safe, highly specific, and long-term anti-tumorigenic system to prevent cancer relapse. Unprecedented clinical responses to CD19-specific CAR T cell therapy in patients with aggressive blood cancers have generated public awareness of T cell engineering and provide much future promise. One of the goals for T cell immunotherapy is to treat solid tumor cancers, which are more difficult to target with T cells than blood cancers.

Jenessa Smith, GTV

From a young age, recent GTV alumna Jenessa Smith has been fascinated with science. Having close family members affected by cancer motivated Jenessa to pursue translational research and to join the laboratory of Dr. Daniel Powell at Penn. In a paper recently published in *Molecular Therapy*, Jenessa and colleagues examined the *in vivo* efficacy of a novel B7-H4 CAR T cell therapy designed to treat ovarian cancer. B7-H4 is a transmembrane protein that negatively regulates T cell immunity and is overexpressed in a number of malignancies, particularly in ovarian cancers. Previous scientific reports provided evidence, albeit controversial, for the absence or relatively low expression of B7-H4 protein in non-oncogenic tissues, making B7-H4 a promising target for CARs. Anti-B7-H4 antibody-drug conjugates did not cause overt toxicity in previous murine studies, which further motivated the preclinical research of B7-H4 CAR T cell therapy spearheaded by Jenessa.

Jenessa and colleagues generated B7-H4 CAR constructs by cloning anti-B7-H4 single chain variable fragments into available CAR lentiviral vectors. These newly generated CAR vectors were efficiently transduced into primary T cells and selectively bound both murine and human recombinant B7-H4 proteins. Subsequent *in vitro* studies confirmed the capability of B7-H4 CARs to properly target and lyse B7-H4-expressing cells. Following these results, Jenessa and colleagues proceeded to test the efficacy of their CAR T vectors in an established mouse model of ovarian cancer. Nude mice bearing human ovarian tumor xenografts received either B7-H4 CAR T cell therapy or were treated with control CAR T cells. Supporting the team's hypothesis, the B7-H4 CAR treatment resulted in a significant reduction of ovarian tumor burden and spoke to the promise of B7-H4 treatment as a novel therapy to treat ovarian cancer. Further observations, however, revealed some negative side effects. While the mice with B7-H4 CAR T cell treatment had a positive anti-oncogenic response, they exhibited clear signs of overall toxicity: mice were underweight, lethargic, and dehydrated. What could account for such lethal side effects? Jenessa and colleagues excluded the graft-versus-host-disease-like pathology as the cause of the observed toxicity, and speculated that B7-H4 CAR T cells might have targeted non-cancerous tissues in mice.

To test that hypothesis, the team examined B7-H4 expression in cancerous and normal cells using a new B7-H4 antibody to verify previous reports of B7-H4 expression in both murine and human tissues. As expected, B7-H4



B7-H4 protein is frequently overexpressed in ovarian cancer, making it an attractive target for therapy. Although B7-H4 CAR T cells display anti-tumor reactivity against B7-H4(+) human ovarian tumor xenografts (1) *in vivo*, treatment reproducibly showed lethal toxicity 6-8 weeks after therapy. Assessment of B7-H4 protein distribution uncovered widespread expression in ductal and mucosal epithelial cells in normal mouse tissue, including haired skin (2), salivary gland (3), and liver (4). B7-H4 protein was found to also be expressed in the esophagus, trachea, mammary, gallbladder, kidney, and uterus. Expression patterns of B7-H4 protein in normal human tissue are comparable to the distribution in mice. Therefore, while B7-H4 CAR therapy mediates control of cancer outgrowth, long-term engraftment produces lethal, off-tumor toxicity.

was overexpressed in engrafted ovarian tumor xenografts. However, Jenessa and colleagues also observed widespread expression of endogenous B7-H4 in non-cancerous mouse and human tissues, contrary to previous reports. B7-H4 was mostly enriched in ductal and mucosal epithelial cells of multiple tissues, including esophagus, trachea, salivary gland, and liver. Additionally, B7-H4 was localized at or near sites of tissue damage and lymphocytic infiltration in mice receiving B7-H4 CAR T cell treatment. The latter finding further suggested that the CAR-induced toxicity likely occurred as the result of inauspicious attack mounted against B7-H4 expressed in non-cancerous tissues. This posed safety concerns, so B7-H4-specific CAR T cells in their current design could not be pursued in clinical applications.

It is clear that safety remains a paramount concern for the advancement of CAR T cell research. Yet, CAR T cell therapy holds promise for academic

and medical communities. Jenessa, among many, has hope, and her work at Penn is a valuable contribution to the field. She explains that "in the future [B7-H4 CAR T cell therapy] could provide a unique opportunity for pre-clinical evaluation of safety approaches that limit CAR-mediated toxicity after tumor destruction *in vivo*." Overall, Jenessa's research provides a promising yet sobering view of both the current advances and ongoing challenges that the booming field of T cell immunotherapy faces.

Jenessa continues to study CAR T cells as a research scientist at Poseida Therapeutics and feels "extremely lucky to be a part of this very exciting and groundbreaking field."

Smith, J.B., Lanitis, E., Dangaj, D., Buza, E., Poussin, M., Stashwick, C., Scholler, N., and Powell, D.J. Jr. Tumor regression and delayed onset toxicity following B7-H4 CAR T cell Therapy. *Molecular Therapy*, 2016.

SPECIAL INTEREST

Student Groups Promote Diversity in Biomedical Sciences

Arwa Abbas and Francesca Tuazon

An inclusive and diverse community is the cornerstone for an adaptable, creative, and sustainable academic center. The Penn community itself includes many diverse populations, comprised of students from broad and varied backgrounds. Yet while various ethnic minorities and women are successfully recruited to biomedical graduate programs, these populations remain noticeably underrepresented in the general scientific community. Here, we highlight two Penn groups that address this problem. Both groups are student-initiated and student-led and support graduate students through the completion of their degrees. They also cultivate future careers in biomedical science through discussions, events, collaboration with other groups, and community outreach.

EE Just

While there are many efforts to recruit underrepresented ethnic minorities, there is a lack of support networks to ensure their retention and success. To address this problem, the Ernest E. Just Biomedical Society (EE Just) was founded at Penn in 1997 to foster the personal and professional development of biomedical graduate students, medical students, and post-doctoral fellows from traditionally underrepresented populations in science and medicine. The group was named after the early twentieth century biologist Ernest Everett Just, a pioneering African American scientist who made significant contributions to genetics and embryology.

EE Just organizes programs that span academic, social, and professional topics and consolidates and disseminates important resources. A vital aspect of EE Just is its focus on building community. There are monthly General Assembly meetings over lunch with discussions on specific themes, such as public speaking, fellowship applications, and social justice issues. These meetings offer the opportunity to share personal experiences and serve as a forum for meaningful discussion among peers. Current president Brenda Salantes (GTV) expressed gratitude for finding a support system like EE Just, explaining, "Students really know what you're going through; it's invaluable to have a shared cultural or ethnic background."

EE Just members left to right: Annie Chen, Niambi Brewer, Brenda Salantes, Ernest Monahan-Vargas, Julienne Rieders, and Arwa Abbas

Other EE Just programs uphold their commitment to community, both on and off campus. At Penn, EE Just partners with PennPREP – a group for recent undergraduates involved in research – to guide students applying to graduate school. EE Just also co-sponsors the annual Cell 600 Happy Hour with the Biomedical Graduate Student Association after the first Cell 600 exam. Beyond the immediate Penn community, EE Just sponsors events that bring science and public health concerns, such as vaccine education, to the public. To participate in the national conversation, EE Just also participated in a Black Lives Matter photo campaign. Goals for future partnerships include expanding outreach to Penn undergraduates, fostering closer relationships with existing on-campus cultural centers like Makuu and La Casa Latina, and working with the STEM POSSE program at Bryn Mawr. Past president Seleeke Flingai (GTV) affirms EE Just's dedication to "figuring out…what the community needs for support to make it as strong for other students as possible."

PGWISE

The Penn Graduate Women in Science and Engineering (PGWISE) was established to combat the underrepresentation of women in leadership positions in STEM fields. Although over half of all biological Ph.Ds are awarded to women, less than a third of biological professorships are held by women in the United States. Thus, PGWISE's mission is to provide resources to students at Penn (in BGS and other science and engineering-related departments) and the surrounding community to recruit and retain women in the sciences. By helping foster a support system that begins in primary school and continues to post-doctoral positions, PGWISE aims to change the culture of science education to promote growth and innovation of the nation.

PGWISE members left to right: Stephen Goldstein, Seleeke Flingai, Elisabet Bjanes, Alexandra Delaney, Ruby O'Lexy, and Sarah Sneed

Rochelle Sadeghi, a third year CB graduate student, is the Co-Chair of Academic Affairs for PGWISE. She detailed the plethora of resources the organization provides to graduate students. These include career-building workshops, community-building social events, seminar speakers, and mentoring and community service opportunities. Their most valuable resource, Rochelle says, is the opportunity for graduate students to interact with and solicit advice from women outside of Penn. To this end, PGWISE brought women representatives from academia, government research, medical writing, and the pharmaceutical industry to their spring career panel. In Rochelle's opinion, this was their most successful event in the past year. Reflecting on how PGWISE could augment their impact, Rochelle says that they plan to incorporate women representatives from engineering and mathematics fields to their career panels as well.

PGWISE also steps off campus to provide support to the larger Philadelphia community. Their members put on science demonstrations at local schools,

volunteer at the Philadelphia Science Festival, and mentor high school students on the college application process.

A common theme in organizing these events is leveraging expertise already on Penn's campus. For example, a recent CV-writing workshop was led by Career Services, while a speaker from the School of Communication gave tips on how to give a good presentation. Indeed, Rochelle counts off the various groups PGWISE has collaborated with such as the Biomedical Postdoctoral Council and Women in Chemistry. PGWISE also collaborated with the Philadelphia chapter of the Association of Women in Science to showcase a lecture from the female CEO of Addgene.

When asked to provide a sneak peek of what the organization will be doing next year, Rochelle exclaimed, "We definitely want to focus this year on outreach…So I don't want to give away too much…but we have a lot of really good ideas for this year."

Get involved!

For students interested in learning more about EE Just, Seleeke and Brenda suggest attending the next monthly meeting and visiting the EE Just website (http://upenneejust.com) to subscribe to their email list and connect on social media. EE Just welcomes all biomedical graduate students to its meetings and events, underscoring its commitment to fostering an inclusive, diverse, and supportive community.

For students interested in PGWISE, Rochelle suggests visiting their website (http://pgwise-upenn.squarespace.com/) and social media pages on Facebook (UPenn- Graduate- Women- in- Science- Engineering) and Twitter (pgwise_upenn) to join their mailing listserv. A biweekly newsletter keeps members abreast of upcoming events and recaps the successes of previous ones. Rochelle also emphasizes that you do not have to be a woman to join. There are many men in the group and on the executive board, and they encourage more men to join.

For students interested in the other affinity groups on campus, they are encouraged to visit the GAPSA website (http://www.gapsa.upenn.edu/affinity-groups/).

Catching Up with the Coordinators: A Behind the Scenes Look at the CAMB Office

Ellie Tarlow

When was the last time that you went to the CAMB office? If you can run a PCR faster than you can recall your last visit, it's time to consider making the trip.

Tucked away on the 4th floor of the Anatomy/Chemistry building, room 404 houses the all-star team that is integral to the success of the CAMB program. The dynamic trio of CAMB coordinators Meagan Schofer, Anna Kline, and Kathy O'Connor-Cooley has been functioning seamlessly for over 10 years. Their calm demeanor and the expedience with which they respond to a daily barrage of emails belie the multitude of responsibilities that each coordinator handles. These tasks range from organizing faculty mini talks to event planning. Each coordinator has a designated focus, but the open layout of the office underscores the importance of teamwork and collaboration. In fact, the coordinators traded in their cubicles for adjoining desks when the CAMB office was renovated a few years ago.

Left to right: Christina Strathearn, Kathy O'Connor-Cooley, Anna Kline, and Meagan Schofer

The camaraderie between the CAMB coordinators is apparent instantly. Throughout the interview, they completed each other's sentences and constantly reiterated how much they genuinely enjoy working together. They share many common interests and are the proud mothers of a combined total of five children aged 4-19. Perhaps the most striking commonality was the enthusiasm with which they explained why they love their job. All three coordinators asserted that it is incredibly rewarding to watch students grow and flourish in the CAMB program. The coordinators are in a unique position to observe the transformation that students make as they gain a sense of confidence and ownership of their project. In this article we will delve into resources and advice for CAMB students and become better acquainted with the CAMB coordinators.

Relevant Resources

The CAMB office contains a wealth of underutilized resources for students. Notably, the free access to black-and-white and color printers make the CAMB office the perfect place to print documents ranging from Cell 600 slides to an entire thesis. There is also an adjacent conference room that can be scheduled to hold study sessions and meetings. Since refreshments make any meeting worth attending, there is a full refrigerator and freezer conveniently located inside the CAMB office. This EHRS-friendly alternative provides a better place to stash birthday cakes and beverages than the closest cold room. Last, but certainly not least, there are boxes of free CAMB t-shirts in several sizes and colors that are always up for grabs. Stop by for the swag or just to say hello. The CAMB coordinators relish the opportunity to interact with students.

Words of Wisdom

With annual enrollment approaching 300 students, the CAMB coordinators have dealt with nearly every possible scenario and have spectacular advice to offer about how to ensure success. First and foremost, the resounding consensus among the coordinators is that communication is key. Often, students are too afraid to ask questions and seek help. However, no question is too trivial and even if the coordinators don't know the answer, they are more than happy to troubleshoot and point students in the right direction. It is important to keep each program specific coordinator in the loop, especially when correspondence pertains to academic inquiries and thesis committee meetings. To streamline all information and communication that concerns academic milestones and thesis progress, the trio has become a quartet. Christina Strathearn just joined the team as a fourth coordinator. Her primary focus will be to track the academic affairs of current students to ensure successful progress throughout the stages of the CAMB program.

Another important point that the coordinators raised is that students should not enroll themselves in classes. While the Penn InTouch platform interface is simple to navigate, course registration for CAMB students involves complicated logistics. Finally, the coordinators explicitly want to emphasize that one of their main roles is to facilitate interactions between students. Students can access records of where every student has rotated, which is a great resource for first year students deliberating between different labs. The

CAMB coordinators also have an extensive database of alumni affiliations and contact information. This archive is a fantastic tool to initiate communication with CAMB alumni that have chosen a wide variety of career paths.

Meet Meagan

Sub Programs: DSRB, GGR
Primary Focus: Schedules faculty interviews and facilitates logistics for admissions and recruitment.
Favorite Philly Attractions: While it is difficult for her to choose a favorite place, Meagan appreciates Philly's vibrant, affordable restaurant scene. She loves how approachable and fun the city is and enjoys dining out.
Fun fact: Before her arrival at Penn, Meagan was a preschool teacher. Her experience managing three year olds likely instilled in her many of the traits that enable her to oversee large groups of scientists.

All About Anna

Sub Programs: GTV, MVP
Primary Focus: Orchestrates the annual CAMB symposium and organizes combined degree (MD-Ph.D.) recruitment.
Favorite Philly Attractions: Anna's top picks are Wissahickon Creek, Frankford Avenue, and the multitude of festivals held throughout the city. All of these attractions are free, which is a price point that any Ph.D. student can get behind.
Fun fact: Anna earned degrees in art and art education. She has lived in a multitude of places, including Alaska.

Get to Know Kathy

Sub Programs: CPM, CB
Primary Focus: Spearheads course registration, monitors faculty and student participation, and facilitates new faculty joining.
Favorite Philly Attraction: The Italian Market, especially Tortillaria San Roman. Located on 9th and Christian, this establishment serves up the perfect combination of authentic, affordable Mexican fare.
Fun fact: Kathy enlisted in the United States Air Force at the age of 18 and served for a total of nine years. Her experiences span geographical boundaries, as she lived abroad in Europe for five years.

The role of CAMB coordinator is certainly not a typical desk job. These impressive coordinators have to draw upon their troubleshooting, organizational, and interpersonal skills on a daily basis. Always focused on the big picture, the coordinators ensure that all aspects of the CAMB program function smoothly. We are so fortunate to have Meagan, Anna, and Kathy here at Penn.

WHERE ARE THEY NOW?

Steve Santoro

Siddharth Kishore

Astronomer Carl Sagan once said, "Every kid starts out as a natural-born scientist, and then we beat it out of them. A few trickle through the system with their wonder and enthusiasm for science intact." Recently, I had the opportunity to converse with one such natural-born scientist, Steve Santoro. Steve graduated with his Ph.D. from the Gene Therapy and Vaccine (GTV) program in 2014. He spent six years at Penn in Dr. George Coukos's lab, researching the interaction of chimeric antigen receptor bearing (CAR) T cells with tumor vasculature.

Steve recalls being drawn to science from a very young age. "I remember watching National Geographic videos on biology, astronomy, and paleontology as a kid and always being amazed by them." He pursued his love for science at the University of Colorado, where he got his dual Bachelor's degree in Geology and Molecular, Cell, and Developmental biology. He vividly recollects what drew him to Penn and the GTV program. "Penn's GTV program is arguably the best in the country. However, what really stood out for me was the fact that during the course of the interview weekend I felt like I had already made close friends and that was a really unique experience." He was particularly excited by the chance to work on CAR T cells and their potential to treat cancer, which at the time was a very nascent field.

Steve Santoro, GTV

While Steve enjoyed studying and researching this cutting edge technology, he realized fairly early on that he wasn't attracted to the academic career route. "A lot of professors may disagree with me, but if you look at facts about the competition for funding in academia, the math does not add up. After grad school, you would ideally do one or two post-docs and that's seven to eight years of life on hardly livable wages, just to have a relatively small chance of becoming a PI. A lot of qualified, high-caliber scientists see this and are smart enough to recognize that the odds of making it are just too small. This makes it a challenge to retain talented individuals in academia who possibly want more of a balance and financial security. Having done that math for myself a little earlier, I decided to pursue something more industry based." While wanting to continue doing science on a daily basis, he concluded that an industry post-doc was "the best of two worlds that did not completely cut off the academic route."

Steve advises current students to form meaningful relationships with people and highlights the important role it played in his job search. "These relationships will go a long way toward shaping your future," he adds. After graduating from Penn, Steve started working as a post-doc at Genentech with Dr. Shannon Turley, whom he met via Dr. Ira Mellman, an acquaintance of his PI. At Genentech he researched the interplay between immune cells and cancer-associated fibroblasts and other cells, collectively called the stroma, to uncover the consequences of such interactions. He gushes about the positives of industry post-docs, such as the ample funding available and having core facilities to do most of the technical experiments. He endorses Genentech by stating, "Intellectually, Genentech has some of the smartest people I've been around." However, Steve does highlight some drawbacks of an industry post-doc. "In academia, you can take a good theory from one lab and then build on it in your own lab, but that is hard to do in the industry with intellectual property laws and other such barriers."

After about a year at Genentech, Steve felt like he wanted to try something new and more challenging but decided to leave only if the right opening arose. That opportunity presented itself in the form of Cell Design Labs, a start-up company focused on harnessing synthetic biology to improve the specificity and efficiency of CAR T cells. Steve started working at Cell Design Labs in June 2016 and already feels like it's a perfect fit for him. "I love the start-up environment where I get a flavor of everything, from basic science and experiments to management meetings. It really feels great to be doing what I love and having my hands in multiple pots."

Steve eloquently brings to life his scientific journey and reiterates his dream to treat solid tumors using CAR T cells. He has maintained this passion from very early on in his career and will certainly be at the forefront of the field when his dream eventually becomes reality.

Jason Diaz

Arwa Abbas

How do you transition from being a graduate student sitting in the audience of a lecture hall to becoming a professor presenting at the lectern? One way is through the PENN-Postdoctoral Opportunities in Research and Teaching (PENN-PORT) program, which combines traditional post-doctoral training with an immersive teaching experience. It is one of 20 programs funded by the NIH under the Institutional Research and Career Development Award initiative. Each institution implements a unique blend of scientific and pedagogical training and STEM outreach. Here, we present the perspective of a current PENN-PORT fellow.

Jason Diaz is an MVP alumnus from Jianxin You's lab who defended his thesis work on Merkel cell polyomavirus in December 2014. Jason is in his second year of PENN-PORT and is only slightly frazzled at the prospect of teaching an introductory biology course at Delaware County Community College this semester. While the PENN-PORT program begins with a mix of laboratory work and teaching preparation, second year fellows are expected to teach at least one full course in both spring and fall. These assignments take place at partner institutions that serve underrepresented minorities such as community colleges and historically black universities. Following this bout of teaching, the fellows return to research and are well equipped to apply for jobs and grants.

Choosing this path was natural for Jason, who discovered his passion and talent for teaching while tutoring and being a teaching assistant (TA) during his undergraduate studies at Ithaca College. For Jason, graduate school was a means to an end; his goal is to be a college professor in a small liberal arts setting. The PENN-PORT program calls for candidates who are interested in teaching, have a strong research background, and who are dedicated to serving underrepresented minorities. Jason felt well qualified even though he was never a TA at Penn. When applying to PENN-PORT, he leveraged his extensive undergraduate teaching experience, his strong scientific training at Penn and many outreach efforts around the community in his application. Specifically, he volunteered with the Science Education Academy to bring hands-on science to elementary school children in West Philadelphia and was involved in the Philadelphia Science Festival.

For others with similar interests, Jason has a few tidbits of advice. First, he emphasizes that you will only know if you're meant for teaching until you actually do it. So if you have never been a TA, do it! Even that small taste is enough to determine if teaching is your cup of tea. Second, teaching positions at academic institutes will absolutely require prior experience that can be gained by teaching intensive post-doctoral fellowships like PENN-PORT and visiting assistant professor positions. Jason himself is preparing to apply for tenure-track positions with a contingency plan of a visiting professorship after completing the PENN-PORT program. Notably, visiting professors are given the same benefits and responsibilities as a first-year tenure track professor. Although visiting professors are usually given one year appointments, they can sometimes be streamlined into a formal faculty search pool.

Jason Diaz, MVP

Despite the new responsibilities, Jason regards life as a PENN-PORT fellow to be both similar and infinitely better than as graduate student. He particularly relishes the lack of tension that accumulates on the eve of thesis committee meetings. Just as in graduate school, Jason is free to set his own schedule and must still overcome challenges and be an independent learner. For example, for his post-doctoral research, Jason made the daring move to switch fields into plant biology. One reason for this was pragmatic - his current mentor, Kim Gallagher, confirmed that she would be highly supportive of Jason and the PENN-PORT program requirements and was also deeply involved in teaching undergraduate courses. However, Jason also wanted to become well versed in an area of research that would be easy to transplant to an institution that didn't necessarily have the same resources as Penn. Continuing his graduate work with human viruses, which require specialized equipment and containment, would have been more difficult.

Still, when asked to recall his favorite memory of Penn, Jason remembers how elated he felt when prominent virologist Beatrice Hahn asked an invested question during his presentation at Virology seminar. In this moment, Jason realized that he was an expert in the topic at hand, and how fruitful and interesting discussions with other scientists could be. He will certainly miss the array of exceptional virologists present at Penn and says that he could not have had such an amazing graduate school experience elsewhere.

CAMB SYMPOSIUM POSTER WINNERS

Congratulations!

CB: Caiyue Xu - *SirT1 downregulation through autophagy during aging*
CPM: Katelyn Miller - *Persistent measles virus in the brain after resolution of acute infection*
DSRB: Ben Tajer - *Distinct signaling roles for type I receptors Bmpr1 and Acvr1l, and the type II receptors Bmpr2 and Acvr2 within the BMP receptor complex*
GGR: Mischa Li - *TIP60 acetyltransferase activity regulates DNA double-strand break repair pathway choice*
GTV: Scott Dooley - *Harnessing the biology of AAV despite its physical limitations*
MVP: Stephen Goldstein - *MERS NS4b enzymatically modulates the host antiviral response in the nucleus*