CELL AND MOLECULAR BIOLOGY STUDENT NEWSLETTER

Volume 4, Issue 1
February 2019

IN THIS ISSUE

LETTER FROM THE EDITORS

Dear CAMB students, faculty, and alumni,

Happy (belated) New Year! In this issue of the CAMB Student Newsletter, we showcase activities that CAMB students partake in outside of the lab as a way to balance doing full time research. We highlight several students who participate in various sports and athletic activities. Additionally, we talk with students who express their creativity through dancing, playing music, and other artistic pursuits. We also highlight the Public Health Certificate Program, which BGS students can complete. We spoke with Elizabeth Loy (Microbiology, Virology, and Parasitology) about her research tracking the evolution of the parasite *Plasmodium vivax*. Finally, we catch up with Microbiology, Virology, and Parasitology alumna Rachel Liebman who talks about her path to becoming a Clinical Scientist at a biotech startup.

For additional articles, past publications, and to learn more about the CAMB Newsletter team, visit our blog at **cambnewsletter.wix.com/blog**. Current students interested in contributing to the CAMB Newsletter can contact us at **camb.studentnews@gmail.com**. We hope you enjoy the February 2019 Issue!

Sincerely,

Lexy Stanley and Somdutta Mukherjee

Editors-in-chief

RESEARCH SPOTLIGHT

Novel Insights into the Evolutionary History of *Plasmodium vivax*

James Gesualdi

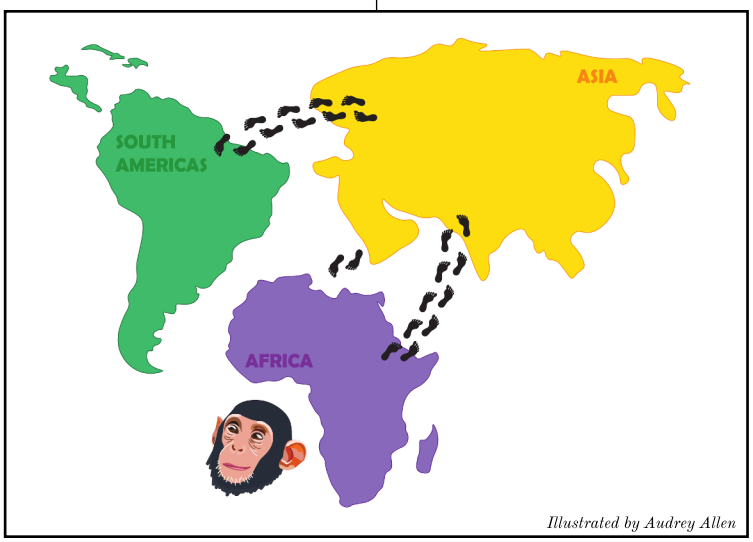
Malaria remains one of the world's most devastating diseases. Campaigns to eradicate transmission have yielded encouraging results in recent years. However, expansion of vector habitats has resulted in substantial increases in disease burden in the Americas, South-East Asia, and Africa, with over 2 million new cases and 445,000 deaths reported in 2016.

While *Plasmodium falciparum* is responsible for most malaria cases in Africa, *Plasmodium vivax* is the leading cause of malaria elsewhere in the world, particularly in Southeast Asia and South America. *P. vivax* is thought to have originated as a human pathogen by zoonoses of ape parasites; the long-standing dogma in the field stated that human *P. vivax* emerged through a cross-species transmission event from macaque parasites in Asia. However, recent sequencing analysis revealed that wild-living apes throughout Africa harbor numerous strains closely related to human *P. vivax*. Because of the possibility of cross-species transmission between humans and apes, a complete understanding of the evolutionary history of *P. vivax* and its related strains is critical, as apes susceptible to infection by similar parasites could serve as reservoirs and hamper eradication efforts. Elizabeth Loy, a former MVP student in Beatrice Hahn's lab, has been working on further characterizing the relationship

Elizabeth Loy, MVP

between human *P. vivax* and related non-human primate strains. Her recent findings have helped to articulate a more complete model of the ancestry and dissemination of *P. vivax*.

Obtaining genome sequences from ape *P. vivax* strains has historically been challenging. Primate hosts are endangered species, and the infection involves low levels of parasitemia. To circumvent these hurdles, Elizabeth and colleagues adapted a selective-whole genome sequencing amplification (SWGA) method, which amplifies parasite sequences from complex mixtures of host and pathogen DNA. This approach allowed for detection and sequencing of *P. vivax* in unprocessed blood samples from both chimpanzees and gorillas from multiple regions in Africa, yielding significantly more complete data than previous studies. Comparison of sequences from six different ape *P. vivax* strains to human strains from both Southeast Asia and Latin America demonstrated that ape and human parasites were highly similar, with 98% sequence identity observed in protein coding regions. However, the diversity among the ape strains was nearly an order of magnitude higher than that of the human strains. Further, the nature of the nucleotide polymorphisms in human and ape parasites was substantially different. Most polymorphisms among ape *P. vivax* strains were synonymous whereas those among human strains were largely nonsynonymous. This relative excess of nonsynonymous mutations was present broadly across the entire parasite genome, rather than concentrated in any particular subsets of genes, suggesting that these mutations are indicative of population expansion under relatively low selective pressure as opposed to a consequence of directional selection.



Human *P. vivax* is hypothesized to have left Africa in a wave of human migration, spreading through Asia and Europe and probably from Europe into the Americas. Strains of *P. vivax* now present in Madagascar and East Africa likely reflect human re-introductions from Asia.

Elizabeth and colleagues also observed that several red blood cell binding proteins (RBPs) – which are critical for the parasite entry into red blood cells during the intraerythrocytic phase of malaria infection – are pseudogenized in the human parasites, whereas their ape counterparts maintain intact transcripts. Elizabeth reasoned that ape *P. vivax* strains maintain these proteins in order to more efficiently invade host cells by binding to receptors that are present only on ape erythrocytes, or that are highly divergent in apes and humans, and that the loss of function mutations in human *P. vivax* represent adaptations to a novel host devoid of these receptors. To test this hypothesis, she constructed recombinant versions of the three RBPs pseudogenized in human parasites and examined their ability to bind erythrocytes from humans, gorillas, and chimpanzees. Surprisingly, the recombinant constructs showed no increased affinity for ape erythrocytes, demonstrating that there are no ape specific receptors to which these proteins bind in vivo. This suggests that these loss of function mutations do not confer increased fitness to parasites within the human host, and in fact may be slightly deleterious to parasite virulence. Therefore, the maintenance of these mutations in human *P. vivax* strains again indicates that expansion of these parasites has largely occurred under comparatively mild selective pressures.

Taken together, Elizabeth's findings support a model of *P. vivax* evolutionary history in which there was a universal ancestor capable of infecting both apes and humans, as evidenced by the near identity of all protein coding regions observed between human and ape parasites. This ancestral parasite is likely to have moved out of Africa during a large-scale migration of its human hosts, and subsequently undergone a severe genetic bottleneck, explaining the substantially reduced diversity among human *P. vivax* strains compared to their ape counterparts. Finally, in the time following this bottleneck, *P. vivax* has undergone rapid population expansion under relaxed selective pressure, resulting in an enrichment of nonsynonymous mutations, as well as the pseudogenization of several genes considered to be key virulence factors. Elizabeth's work illuminates some of the genetic changes that the *Plasmodium* parasite undergoes as it crosses a species barrier and may possibly be generalized to other instances of pathogens expanding their host range. As such, other members of the Hahn lab are currently investigating whether similar differences in human and ape strains are also observable in *P. malariae* and *P. ovale*.

Loy, D.E., Liu, W., Li, Y., Learn, G.H., Plenderleith, L.J., Sundararaman, S.A., Sharp, P.M., Hahn, B.H. Out of Africa: origins and evolution of the human malaria parasites falciparum and Plasmodium vivax. *Int J Parasitol* 2017; 47:87-97.

SPECIAL INTEREST

Public Health Certificate Program

Felicia Peng

The field of public health goes hand in hand with biomedical research to keep people healthy and safe through disease prevention. Doctoral students in Biomedical Graduate Studies (BGS) looking to form a bridge between their research and public health can do so through the Public Health Certificate Program (PHCP), which is offered through the Master of Public Health Program (MPH Program). Founded in 2006, PHCP complements graduate studies by teaching students population-based approaches to research that allow them to think broadly about the effect of biomedical research on public health. Training biomedical scientists from a public health perspective is of critical importance. Hillary Nelson, a co-director of PHCP, emphasizes that epidemiology provides graduate students with a broader context for their research, priming them to "better understand disease incidence and disease prevalence in a way that [they] aren't trained in [during their Ph.D. programs]." Part of this broader context includes placing biomedical research within a social context.

Dan Ju, a second year CAMB student in the certificate program explains that "public health considers both environmental and social issues, which allows for appropriate sensitivity when performing population studies." As biomedical research does not occur in a

vacuum, it needs to consider the wide range of problems that society faces in order to be as effective as possible.

PHCP requires students to take public health courses, attend a PHCP seminar series, and complete a public health project. Required courses include "Introduction to Principles and Methods of Epidemiology", a biostatistics course, and three elective courses in public health. Although most of the coursework is typically completed in the first two years of graduate school, the certificate program allows students to take one public health course per semester during later years.

Central to PHCP is its bi- weekly seminar series. In this series, speakers both within and outside of Penn are invited to discuss their research and careers, exposing students to a wide variety of public health issues. To highlight the diversity of research presented in the PHCP seminar series, Ju recalls a particularly fascinating talk given by Michelle Kondo, a scientist with the USDA Forest Service, Philadelphia Field Station, that related urban planning to gun violence. Thus, students can expect to learn about public health issues that are both biological and social in nature.

In addition to hearing invited speakers discuss their research, students present their project in progress reports and, ultimately in a final presentation as a part of the seminar series. Students decide on their public health projects at the end of the second year. While the public health project is encouraged to address a question related to one's Ph.D. thesis, it can also be more open-ended and separate from one's thesis work. Projects may range from focusing on a public health issue from an epidemiological perspective, to being based in social or community service work. This flexibility allows students to work on a public health project that is tailored to their interests. As an example of a community-based approach, Nelson highlights the work of Prioty Sarwar, a third year CAMB student, who works to provide sex education to local schools through a program that both the MPH Program and Center for Public Health Initiatives conduct.

PHCP students can expect to finish the program equipped with key skills that will serve them well in their careers. The public health courses expose students to a different kind of teamwork not seen in their graduate programs, and students also gain new writing and presentation skills. Nelson has served as a reference for numerous PHCP students, and she observes that "[these skills] give students an edge, especially those going into industry." Additionally, the certificate program provides a jump-start to students who go on to pursue public health fellowships or master of public health degrees.

While PHCP is competitive and primarily accepts students who applied to the certificate program in concurrence with their graduate programs, the PHCP seminars and MPH courses are open to all students. Overall, PHCP provides a supportive environment for students interested in public health, and participants of the program leave well prepared for the next phases of their careers

More information about PHCP and the application can be found at https://www.med.upenn.edu/phcp/. The PHCP seminar schedule is listed on the website, and attendance is open to all. Registration is required for MPH courses. Students interested in taking MPH courses may contact Hillary Nelson about enrollment. Dr. Nelson can be contacted at hnelson@pennmedicine.upenn.edu.

Scientists by Day, Artists by Night

Sam Sander Effron

Creativity is, "the process of generating new information", states Dr. Tina Seelig, professor at Stanford University and author on innovation entrepreneurship and creativity[1]. She continues to explain that, "[creativity] at the core is the ability to look at problems from different angles, to connect and combine concepts, and the ability to challenge traditional assumptions. These are skills that require practice to master." Historically oversimplified as a property of the brain's right-side hemisphere, creativity is a neurologically complex process involving the flow of mental connections across multiple brain networks[2,3]. This makes it clear that creativity is much more than the ability to produce artwork, but rather is a paradigm through which one interacts with the world[4]. Here at Penn, there are many creative scientists at different stages of their graduate studies, who pursue hobbies across all types of creative media including music, visual arts, and dance[5].

Illustrated by Rebecca Windmueller

Playing music has been shown to be beneficial for your brain, as it helps to maintain alertness, increase reaction time, and integrate multi-sensory input[6]. Improvising with fellow musicians, or jamming, can also sharpen 'soft skills' which are important to us both as individuals and scientists. "Communication is a big part of it. Jamming is the ultimate dialogue-less, application-less conversation that is nothing but has everything", says Hooman Hamedani, a bioengineering Ph.D. candidate who sings and plays the cross-harp harmonica and keyboard. He has been a student-musician for the past two decades, and recognizes creativity in science and art as, "a balance between doing useful beautiful things and useless beautiful things."

These benefits are not restricted to playing in a group, as there is much to be gained from playing music solo. Brian Keith, Ph.D., of the Wistar Institute has been playing classical guitar for years, and maintains it as an individual retreat. "Playing music is a mental vacation, even if it's just 15 minutes that I can sit down and play in the morning. It takes you away from all the day-to-day stuff." Practicing music helps his scientific process too, as, "doing something that takes me out of the problem always makes me think better". Indeed, it has been shown that individuals are more successful at creatively solving problems that they have seen before when they take a break with an activity that requires less working memory and promotes mind-wandering[7,8].

Qu Deng Ph.D., is a post-doc who practices photography as her medium of choice, which allows her to get some fresh air. "I like to be in nature, so it allows me to go outside and explore new places,

since 90% of our time is in the lab." In particular, this art form is a mode for her to explore alternative perspectives[9]. "Just as in science, in photography you need to discover some new aspect [of your subject]. Even if it's the same landscape, you can always find different angles to take a picture."

Creative arts as a hobby can also be a profound source of liberation from the rigidity and high stakes of science research. "Science requires rationale, importance, and a translational impact on people. Art is different— the rationale is because it is beautiful," says Shaun Egolf, a doctoral student in CAMB who sang with the Penn chorus last year. He appreciates the different paradigm that art exists in. "[Creative] success isn't so dependent on quantitative measures, like significance value. You simply entertain people and bring them joy."

Former MVP Ph.D. candidate Arwa Abbas recognizes that her science skills can inform how she makes her illustrations. "My science training in grad school has influenced my art because I'm more open to trying new things. In my art, I used to not go outside of the boundaries of what I was good at. Now, if there's something that I don't know how to do, I do the research and learn how to do it."

Although many people are exposed to their artistic endeavors from a young age, it's never too late to try something new. Kathy Huang, a GCB doctoral student, recently started taking introductory ballet classes for the first time, to break out of her comfort zone. "It's refreshing as a form of physical discipline after I spend most of my day practicing mental discipline [with science]". The class setting provides an element of motivation too. "I paid for it, which keeps me on track, since I feel like I have to go, to make every penny worth it."

While it certainly looks different for all of us, Qu stresses, "it's important to find something that you're really passionate about outside of the lab." The way in which we integrate artistic creation into our lives is also a personal choice. Hooman enjoys it leisurely by, "not taking it too seriously." That's not to say though, that you're stuck at amateur status. Kathy reminds us that, "you don't have to be singular with what you're good at. You don't need to put all of your time towards your art, but don't think of it as just a distraction, since you really can get better." Arwa emphasizes how appropriate critique is vital in both disciplines. "Don't compare yourself to other people. The only thing you should compare to is what you were doing a year ago. You're the only person that is doing your thing, and as long as it makes you happy to do it, that's all that matters." Creative hobbies come in all shapes and sizes, across various mediums that satisfy diverse goals and spans interests. We can all benefit from bringing a little creativity into our lives, however we see fit.

For a full list of citations from this article please see our blog.

GRAthletes in CAMB

A Sports Enthusiast

Little League. High School Sports. NCAA College Athletics. The Super Bowl. The Olympic Games. Athletics are an important pillar throughout all stages of society. The Eagles are playing on everyone's TV on most Sundays of the school year. Yet, student athletes seem to be forgotten in graduate school. Many CAMB students are still highly involved in athletics, from the social intramural level up through the professional level. These students have a passion competing in athletics that their fellow students and PIs alike are unaware of. This article spotlights four graduate student athletes, or "GRAthletes," who participate in in a variety of sports to compete, stay healthy, release stress, and importantly to have fun.

Exercising is an important part of leading a healthy life. And, even if you are not a top athlete, there are many opportunities at Penn for grad students and faculty to exercise and play sports. There are many intramural leagues, club sports teams, social leagues, pickup games, and gyms in and around Penn to choose from. We hope telling these students' stories will encourage students and faculty to participate and support others in athletic endeavors

Pro GRAthlete: Coral Kasden, 1st year GTV student

Sport: Rowing

Team: Men's High Performance Group for the New York Athletic Club (NYAC)

Position: Coxswain

Goal: To be selected as coxswain for the United States boat in the 2019 Pan American Games in Lima, Peru.

Fun fact: Coral was a coxswain at UC Santa Barbara during undergraduate years. Her NYAC team won the Head of the Schuylkill Regatta in October 2018.

Coral's Thoughts: "You really have to be dedicated to be a competitive athlete in grad school. Whenever we are not in class or studying we are expected to be in lab, which makes fitting in practices difficult. This means early morning and late evening training is the only way to do it, and an hour incubation can be easily turned into a quick workout at the gym! My PI thinks it's really cool that I have this other life outside of school, as long as I'm getting my work done. It's fun. It keeps me sane!"

Coral and her NYAC team winning the Head of the Schuylkill.

Pro GRAthlete: Corey Holman, 1st year CPM student

Sport: Obstacle Course Racing (OCR)

Category: Elite

Goals: To win the 2019 Spartan US Stadion Series and place at the 2019 OCR World Championships in London, England.

Fun Fact: Corey was a gymnast at Brown as an undergraduate and has since translated that love of flipping over things into OCR. She had a top 3 podium finish in seven out of nine of her competitive

Corey jumping over a wall during a Spartan race at Citi Field in NYC.

races in 2018. As a fun, new challenge, she is also branching out into triathlons this coming season!

Corey's Thoughts: "Competing at such a high level against professional athletes while being a Ph.D. student is tough. Making your own training schedule and keeping yourself accountable is the hardest part – it's easy to skip a workout when school gets busy. Working efficiently is key to fit in morning workouts, classes, lab work, and studying. I love racing on weekends because it is a way to get out of Philly to do something totally different and thrilling. Plus, the people I meet through this sport are some of the best individuals around."

Club GRAthlete: Matt Pine, 1st year GTV student

Sport: Division I Club Volleyball

Team: Penn Men's Club Volleyball

Position: Outside Hitter

Goals: To qualify for the national tournament in Denver, CO in April 2019 and to improve as an individual player in general.

Fun Fact: Matt played Club Volleyball during his undergrad at Franciscan University. Penn Club Volleyball is currently ranked 5th in the nation, and Matt helped beat Lehigh at the Palestra three games to none in November 2018.

Matt (#33) in a Club Volleyball match.

Matt's Thoughts: "This is how I maintain a healthy lifestyle outside of lab. My availability for volleyball practice is dependent on my grad schedule, so I try to plan ahead with assignments to make it to my two-hour practices, three times a week. Managing the workload means I can both travel to weekend tournaments and stay on top of my lab work. I've loved the support I've gotten from my fellow students that are excited to see me play."

Intramural GRAthlete: Jake Hoffman, 1st year GTV student

Sport: Intramural (IM) volleyball - Grad/Faculty/Staff league

Team: Gene Gnomes

Position: Team Captain

Goals: Play some volleyball, have some fun, and meet some cool people who you normally wouldn't meet.

Fun Fact: Jake has played everything IM from ultimate frisbee to broomball and is an avid runner. Jake led the Gene Gnomes to qualify for the playoffs this season, where they finished in a comfortable 4th place, which was "better than expected!"

Jake and the Gene Gnomes battling in the playoffs - while having fun!

Jake's Thoughts: "Sports are something that I enjoy doing, and at the IM level it's very social. They are fun way to release the stresses of grad school. You can have the simulated drama of a sports movie without the high stakes when you play IM. You also get really good at giving motivational speeches with gnome puns intended!"

WHERE ARE THEY NOW?

Rachel Leibman

Sylvia Stankov

Dr. Rachel Leibman graduated from CAMB (Microbiology, Virology, and Parasitology) in 2017 after completing her training in Dr. Jim Riley's laboratory. After two years in her current position as a Clinical Scientist, she is excited to share her experience with current students, and tell us how CAMB graduates are undoubtedly qualified for this translational-focused field.

Rachel works for Stemcentrx, an oncology biotech startup acquired by AbbVie, a global pharmaceutical company and spin-off of Abbott Laboratories. As a Clinical Scientist, she supports clinical trials and clinical program development. Rachel describes herself as the right-hand woman to the Medical Director (MD degree) or Scientific Director (Ph.D. or PharmD degree), the clinical leads within the company who are in charge of designing and overseeing clinical trials. During study start-up, her roles include helping to develop and write clinical protocols and informed consent forms, and contributing to regulatory documents like Investigator's Brochures, which summarize the available data and guidelines about a product or drug. Rachel also participates in regulatory responses to the FDA and other analogous international agencies. Once a study starts, her roles shift to training doctors and staff at the different participating trial sites on their clinical protocols, and analyzing the data generated. She then prepares presentations regarding trends in safety and efficacy for internal use, study doctors, and other stakeholders. Rachel also performs "data cleaning" to track individual subjects' clinical trial data and ensure that it is entered properly. Once a trial is over, she assists in writing study publications, including journal manuscripts, and the final clinical study report required by government agencies. Rachel also attends conferences pertinent to the diseases that she is working on.

Rachel knew early on in her graduate career that she was interested in translational research, and her thesis project on designing CAR T-cells for HIV- 1, within the Center for Cellular Immunotherapies (CCI), supported this goal. While training, she volunteered part-time and learned about clinical development jobs within the CCI and Penn. Over the 6 months as a volunteer, Rachel helped write Investigational New Drug reports containing initial trial proposals and pre- clinical information for FDA approval. Additionally, Rachel learned of Institutional Review Board (IRB) experience opportunities through a friend in the ITMAT Certificate Program. Rachel sat

on an IRB for 2 years, where she reviewed proposed and ongoing clinical trials to judge the benefit-risk profile, and clarity and transparency of the language for patients. These extracurricular experiences were critical additions to her clinical skillset.

While applying for jobs, Rachel broadly searched for various position titles related to her experience (Clinical Trial Manager, Clinical Science Manager, Clinical Trial Scientist, etc…) as companies tend to use different terms for very similar positions. Initially, she felt that the jobs for advanced degree candidates required more clinical trial experience than she had to offer. However, after searching via Google, LinkedIn, and individual company websites, Rachel secured a phone interview with AbbVie, was flown out for an in-person interview, and offered the position, all within a few weeks.

Rachel Leibman, MVP

Rachel believes her background in data analysis, ability to absorb complex information, and attention to detail have helped her excel greatly. In addition, the frequent presentations in graduate school prepared her for the presentations she now makes for study doctors and executives. She also cites her background in immunology and molecular biology as a foundation for her understanding of Stemcentrx's immune-based biologics, and for her fruitful interactions with pre-clinical and lab teams. Other transferrable skills that Rachel highlights include the ability to read scientific and medical journals about diseases, drug markets, and clinical issues, and the ability to work and communicate with multidisciplinary teams when managing projects. Rachel emphasizes that any clinical expertise can give you an edge when combined with your research background during the job search. She advises CAMB students interested in this field to get as much clinical experience as possible by sitting on an IRB, collaborating with anyone who does pre-clinical or clinical research, and volunteering to work with regulatory documents. She also suggests joining a clinical team at Penn as a part-time volunteer or after graduate school to work as a Clinical Research Coordinator, Clinical Research Associate, or Clinical Data Manager.

Overall, Rachel enjoys her job and encourages other Ph.D.s to explore this relatively unknown career path. While the hours can sometimes be intense when meeting deadlines or working with an international team, she typically works a regular schedule, is able to work remotely, and is paid well. After working as a Clinical Scientist for two years, Rachel feels that CAMB Ph.D.s can absolutely qualify for this position if they work hard and learn the skills required for the job.