CAMB Student Newsletter

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In this issue

Letter from the Editors

Dear CAMB Students, Faculty, and Alumni,

We are excited to share with you the December 2023 installment of the CAMB student Newsletter! In this month's issue, we highlight the work of recent MVP graduate **Dr. Katie Marquis**, recapping her latest findings on the impact of vaginal microbiome composition on HIV transmission rates. We speak with recently hired professor of pharmacology **Dr. Caroline Bartman** and hear about her research on metabolic flux in cancer cells and leukocytes and hear about her goals for her newly established lab.

We also sat down with **Mara Davis** of the LTBGS student group regarding their advocacy for LGBT+ students and allies in BGS and their upcoming events. Finally, we go over some fun local activities to check out during the holiday season while working with a graduate student budget.

For additional articles, past publications, and to learn more about the CAMB Student Newsletter team, visit our blog at cambnewsletter.wix.com/blog or follow us on Twitter at @CambNewsletter. Current students interested in contributing to the CAMB Student Newsletter can reach out to jamesges@pennmedicine.upenn.edu and/or klabella@pennmedicine.upenn.edu.

Sincerely,
Kay Labella and James Gesualdi
Editors-in-Chief

Research Spotlight
Dr. Katie Marquis

Kay Labella

Peer Edited by Mara Davis

Historically, human immunodeficiency virus (HIV) has been stigmatized as a disease solely affecting the community of men who have sex with men. Amongst many negative outcomes of this stereotyped association, this has led to a dearth of studies on how HIV impacts other communities. For example, the host factors influencing HIV transmission in cisgender women remain poorly understood. Recent CAMB graduate ***Dr. Kaitlin Marquis*** *(MVP, Bushman Lab) aimed to identify some of the compounds that cause increased HIV infection susceptibility in women in her paper "2-Hydroxyisovalerate Is Produced During Bacterial Vaginosis and Boosts HIV Infection in Resting T Cells (1)."*

Previous research has indicated that the composition of the vaginal microbiome can impact HIV transmission risk (2). Significantly increased rates of HIV acquisition have been shown in women with microbiomes deficient in *Lactobacillus* bacteria but otherwise colonized with high diversity microbial communities (HDCs) when compared to women with microbiomes that are low in diversity (LDCs) (3). HDCs can be comprised of any array of bacterial types, while LDCs are typically dominated by a single species of *Lactobacillus* bacteria such as *L. crispatus* or *L. iners*.

Currently, it is hypothesized that HDCs play a role in impairing vaginal epithelial barrier integrity, decreasing its efficacy as a protector against infection (4). Furthermore, HDCs' lack of *Lactobacilli* is thought to result in reduced expression of protective lactic acid (5-8). Additional studies have shown that HDC colonization increases HIV burden relative to both LDC and

Dr. Katie Marquis

uncolonized controls, which supports the theory that both the lack of *Lactobacillus* and the prevalence of HDC-associated bacteria contribute to increased HIV transmission (9).

Dr. Marquis hypothesized that bacterially-derived metabolites from HDCs modulate T cell susceptibility to HIV-1 infection, and sought to identify these metabolites and define their influence on CD4+ T cells, the main targets of HIV infection. To start, Dr. Marquis utilized four publicly available datasets on vaginal bacterial abundance linked to metabolomic data. Samples were grouped as HDCs or LDCs, and the metabolomic data for these two groups were compared. Three metabolites were robustly enriched in HDC samples across all four datasets: 2-hydroxyisovalerate (2-HV), cadaverine, and tyramine.

To interrogate whether these metabolites increased T cell susceptibility to HIV infection, TZM-bl cells were treated with HIV in the presence or absence of each metabolite. TZM-bl cells are HeLa cells engineered to express CD4, CCR5, and CXCR4, the surface receptors necessary for HIV entry. Additionally, these cells contain a B-galactosidase reporter that is expressed only when the HIV genome is being actively transcribed. Therefore, these cells facilitate accurate quantification of HIV infectious titer after treatment with a viral challenge (10). While there was no significant increase in infection in cells cultured in cadaverine or tyramine, HIV-infected TZM-bl cells treated with 2-HV showed an increase in HIV replication. Though 2-HV has been identified as a biomarker in other diseases, such as maple syrup urine disease and endometriosis, the role it plays as an HDC biomarker and in HIV transmission is only beginning to be elucidated (11-12).

Next, Dr. Marquis examined the impact of 2-HV directly on CD4+ T cells. After 24 – 48 hours pretreatment with increasing concentrations of 2-HV, CD4+ T cells from seven donors were infected with HIV BaL. After eight days, viability and both cell-free and cell-associated ***p24*** content were determined for each sample. Average intracellular p24 increased threefold on average at the highest dosage of 2-HV, with cell viability unimpacted, suggesting that 2-HV increased HIV susceptibility. Dr. Marquis suggested that 2-HV may therefore play a role in activating T cells.

p24: *a structural protein distinctive to HIV. Assays to detect p24 are used both for clinical diagnosis and in laboratory.*

For more information about p24 and its detection methods, see https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6005050/

To further interrogate the role 2-HV plays in modulating the immune environment in the context of vaginal transmission, Dr. Marquis performed a ***Luminex assay*** to interrogate changes in cytokine production. Upon treatment of vaginal epithelial VK2 cells with 2-HV, Dr. Marquis observed an unexpected decrease in pro-inflammatory cytokines such as IL-6, IL-8, MIP-3a, RANTES, and IP-10, along with a corresponding increase in anti-inflammatory cytokine IL-1RA. This secretion profile was similar to that seen upon treatment with

Luminex assay: *This bead-based assay detects and quantifies secreted proteins similar to an ELISA. However, it is considered higher efficiency and throughput.*

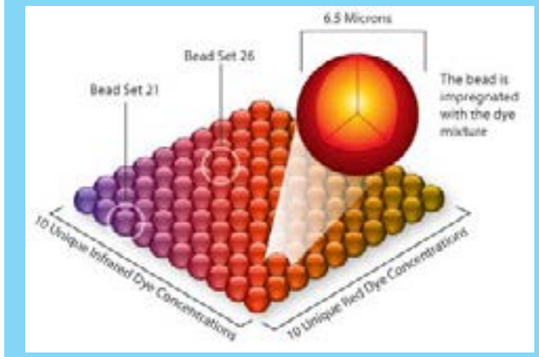

Image from ThermoFisher

lactic acid, which provides a protective effect to the vaginal epithelium. Dr. Marquis concluded that 2-HV does not induce a pro-inflammatory cytokine profile. As such, it may be modulating activation by other, mechanism-of-action independent, means, such as acting directly on the T cells themselves.

Dr. Marquis then interrogated vaginal culture supernatants using untargeted ***gas chromatography-time of flight (GC-TOF) mass spectrometry*** to ascertain which bacterial species of the cervicovaginal microbiome might produce 2-HV. She identified three HDC-associated bacterial species that secrete 2-HV, and no species associated with LDCs. Upon quantifying 2-HV in cultures of *Gardnerella vaginalis, Atopobium parvulum*, and *Veillonella montpellierensis*, it was found that *G. vaginalis* and *A. parvulum* secrete significantly increased 2-HV compared to other bacterial strains. Furthermore, Dr. Marquis noted that no *Lactobacillus* strains secreted significant quantities of 2-HV, indicating that robust 2-HV production is a trait unique to HDCs. Further study showed that *G. vaginalis, A. parvulum*, and *V. montpellierensis* all contain the necessary enzymes to produce 2-HV, while the studied *Lactobacillus* strains did not have detectable levels of these enzymes. Dr. Marquis therefore concluded that

To learn about ***gas chromatography-time of flight (GC-TOF) mass spectrometry***, please see https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4123969/

high-level production of 2-HV is common to HDC but not LDC microbiomes.

Dr. Marquis's work has further enhanced our understanding of how metabolites influence HIV transmission in cisgender women. Her research established 2-HV as a potential biomarker for increased risk of HIV transmission, as well as identified three bacterial strains, *G. vaginalis, A. parvulum*, and *V. montpellierensis*, that produce this metabolite. Dr. Marquis noted, however, that the complete mechanism by which 2-HV influences HIV transmission in HDC-colonized women remains open to further investigation. Future avenues of exploration will include the physiological levels of 2-HV in vaginal fluid, influence of 2-HV on the HIV viral life cycle, and potential synergistic effects of 2-HV with other metabolites. Understanding these factors together, and the impact of HDCs on HIV transmission more generally, may in the future provide a means of interfering with transmission via microbiome modulation.

References

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Faculty Spotlight
Dr. Caroline Bartman

Nivitha Murali

Peer Edited by Ariana Majer

Dr. Caroline Bartman is an Assistant Professor of Pharmacology at the University of Pennsylvania. She completed her PhD training with Dr. Gerd Blobel and Dr. Arjun Raj at Penn studying transcriptional regulation. Her thesis work revealed that transcriptional regulation is mainly governed by changes in rates of burst initiation and polymerase pause release. Later, she completed postdoctoral work with Dr. Josh Rabinowitz on tumor metabolic fluxes. Here she compared metabolic rates of primary and late stage/metastatic tumors with a focus on TCA flux and ATP production. She returned to Penn in October 2023 to launch her own lab, to further investigate metabolic fluxes in cancer cells and immune cells. Her lab aims to measure and manipulate immune cell metabolism to increase anti-tumor responses.

Dr. Caroline Bartman

Hello Dr. Bartman! Thank you for taking the time to speak with the CAMB Newsletter Team today. To start off, can you tell me a little bit about your doctoral thesis training and how that went?

I actually did my PhD at Penn! It was in a totally different field than I work in now. I was in Arjun Raj and Gerd Blobel's labs jointly and started in 2013. And I studied transcriptional regulation in red blood cell precursors. They were both fantastic mentors, and I really wanted PhD training that was very basic science but also had a quantitative aspect to it. I think those are the aspects I carried forward even though I did not stay in the transcription field.

What type of difficulties did you face in your PhD training? Did you have a "eureka moment"?

Goodness, difficulties. I think so. My first project went very smoothly. That was kind of why I joined those labs, because my rotation project was going very well. Everything seemed great, so that was fine. And then I had to start a second project, and that went horribly. I had all these ideas that did not work out. At one point, I had this idea that I was working on, and my PIs both told me it was a bad idea. My whole committee was like, no, it's really a bad idea. I had to drop that one. I guess you see this sometimes when people are lucky early on, and then they're like, oh no, not everything works the way you envision it. So that was hard.

And it looks like you liked Penn enough to return as faculty! What is it about Penn that won you over?

Just lots of things! I think there's a lot of excellent science, but I find people are very collaborative and not too competitive. Also, I did my postdoc at Princeton, which is so great, but there's no hospital. And there's not a whole lot of biomedical

research. There are a lot fewer labs in general, so it's very excellent basic science. But for my own work, I really wanted to have some more translational relevance, and I'm hoping to eventually do some human studies. So, Penn is a perfect place for that.

I understand that your current research interest is on immune cells' metabolism in the tumor microenvironment space. What made you pivot?

I guess there are two pivots, right? When I went to do my postdoc, I switched to cancer metabolism away from transcription. And I found a lab that I really, really liked and work that had relevance to disease, but also strong quantitative aspects. Metabolism—if one glucose goes in, six carbons must come out somewhere. Either CO_2, lactate, whatever. So, it makes it nice for quantitative modeling. You get very accurate measurements, and you can make predictions, which is much harder to do in transcription and gene regulation. I have loved that about the field.

And I think in general, in metabolism, people did a lot of it in the first half of the 20th century, which was amazing, but they did not have knockout genetics, and they did not have mouse models of a lot of diseases that we have these days. But it is nice that we now can go back and do a lot of the same types of experiments, but with better mass spec, better mouse models, and learn new things.

Having been in the labs of Dr. Raj, Dr. Blobel and Dr. Rubinowitz, I'm sure you've seen varied lab environments. What kind of a lab environment are you aiming to create in your lab? And what type of students do you hope to attract?

People who are interested in metabolism, I guess. I think sometimes when people think about glycolysis or the TCA cycle, they're like, oh God, biochemistry. But I think it's really interesting. I think on a more serious note, I'd like to run a lab that is really supportive, knowing that people are coming from different levels of training, different backgrounds, but trying to enable each other to do the best science and get to the next career step that they want. And in a similar way that people come from different backgrounds growing up, I'm also excited to have trainees from different academic backgrounds, like computational people and immunologists, because no one is going to come in able to do quantitative metabolism. As long as someone is enthusiastic to learn these different things, we can all learn from each other's expertise.

Could you tell us a little bit about your mentorship style?

Different students do well in different contexts, and a lot of it depends on their personality and their level of prior training. I think it's important as a PI to try to at least figure out what your students need. I guess that's the most important thing—try to establish good communication and have your students be willing to tell you when they need something or when something isn't working for them. Because I'm not a mind reader, but different people have different needs, and they'll find different things challenging. If we don't communicate about those problems, then problems can fester.

And do you have any advice for first year students? Anything that you would recommend they don't do?

This is what we were told, which I think is true: try not to worry too much about your classwork, because it's very time-consuming and it makes it tough to focus on rotations. It is true that when you finish your PhD, you're not going to remember that much from your classes, whereas the most important part of your first year is for sure your rotations. Find a place where you are happy and you can do good science. And it's challenging because you're very busy and you have these classes you have to keep going to and it's hard to get anything done.

It's fine if you don't make scientific progress during your rotations. That's also something people get very stressed about, including myself. I had a horrible first rotation. Nothing worked. But you just have to see if you like the type of science they're doing in the lab. Do you like the way that they work together, the type of experiments? You can get a sense for that even if none of your experiments work.

How do you like Philly? What do you enjoy doing outside of science?

I love Philly. It's so great. My gosh, I love the art museum. The river path is lovely. Just in general, all the Revolutionary War stuff. It's nice to have a city where you can walk everywhere easily and it's not that expensive.

I really like reading science fiction. Actually, some of the people I went to grad school with started a book club that is still going! That and running.

And I know that you really enjoy puns and bad jokes. What's your most favorite science joke?

Oh my God. I should have prepared. It's hard to bring one to mind. As a graduate student and postdoc, I feel like I thought of puns when I spent a lot of time waiting for things to happen. Like centrifuges or PCRs. We'll see. Now that I'm a PI, I probably still have boring things to do, haha!

Lastly, are you accepting rotation students this year?

Yes, I am! But since I start October 1, not for the fall, but starting in January.

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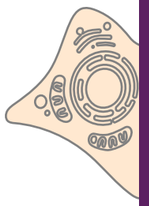
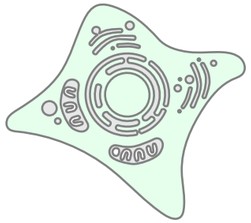
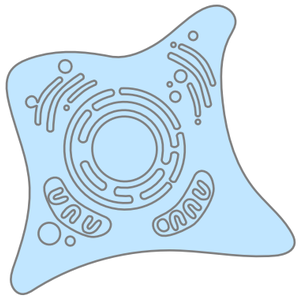
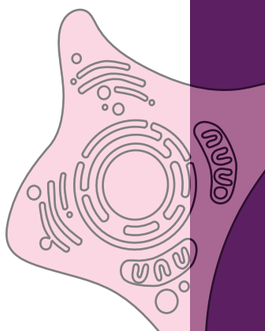
*Dr. Bartman's office is located at **Smilow 9-136.** Trainees interested in learning more about her work can reach her at cbartman@pennmedicine.upenn.edu.*









Special Interest:
LTBGS Spotlight with Mara Davis

Kay Labella
Peer Edited by Amber Abbott

What is LTBGS? Why was the group founded?

LTBGS is a group founded by and for LGBT+ students and allies in BGS. The group was founded to provide representation, support, and, overall, a safe community for queer BGS students where they can meet similar students and faculty and celebrate queerness, find refuge in their scientific struggles, and develop confidence in their academic and professional abilities.

How does LTBGS fit into the broader goal of increasing diversity and inclusion in our research community?

LTBGS functions to celebrate queer students doing research in BGS. Its existence allows queer folk to gather in a safe place and find people like them facing similar struggles. I think more importantly it acts to connect people to resources outside of LTBGS, like queer faculty on campus, the LGBT Center, which has many of its own events and resources, and even other student groups, some of which LTBGS co-hosts events with. In the past we have hosted events alongside BGSA and other queer grad groups through the LGBT center, and in the future we hope to connect more queer students with each other by hosting events with other queer grad groups.

How has the LTBGS community impacted your life?

It's made me feel safe and seen. I think many grad students, especially those just starting out, get overwhelmed by imposter syndrome. As a queer person who was raised in and went to undergrad in Alabama, where transphobic faculty faced no consequences, I felt the need to diminish the queer part of my existence. Joining LTBGS gave me a place to exist as I am, and a place to struggle as a scientist, without creating room for doubting my place in a prestigious academic community, because I know now that I belong here just as I am.

How do you hope LTBGS will impact BGS and our research community as a whole going forward?

I really think LTBGS will allow BGS students, as well as students and faculty outside of BGS, to exist comfortably and unapologetically as they are without fear. Creating a space for ourselves to celebrate who we are and meet others like us will, hopefully, mean others joining this community can come to Penn and feel only more comfortable with being who they are here. I want the whole research community at Penn to know that they can exist and thrive here amongst similar peers, and I think the growth of LTBGS will help facilitate that, because it facilitates meeting people within one's community, whether they be in BGS or possibly outside of BGS entirely, as well as faculty.

Why did you decide to take a leadership role with LTBGS? How has your leadership position enriched your professional experience here at Penn?

When I learned about LTBGS, it sounded like the group I had always wanted to join but that didn't exist back home at my undergrad institution. I knew I wanted to be a part of the group, and I knew I wanted more people to know about the group and the resources it could offer, so I took on a leadership role. The election process is simple; LTBGS provides students on our Listserv with a form to self-nominate or nominate others for two weeks before a two-week period of voting. My first year at Penn, I acted as external events chair, and I developed a deep appreciation for the opportunity to work with other queer groups at Penn and the LGBT center, and so I ran for chair the following year and won.

It has been more rewarding than I could have anticipated. I get to talk to queer faculty and staff at Penn, engage more with my community at Penn outside of BGS, and promote the wonderful community LTBGS cultivates to new students. The new connections to students and staff alike is invaluable and it's wonderful to know of so many queer people in so many walks of life and career paths.

What LTBGS events are you most excited about for this coming school year?

Our Queer in Steminar series! This series of hour-long informal talks over lunch highlights queer scientists both at and outside of Penn and their journey as queer scientists. Openly queer professors were not something easily found at my undergraduate university, and I love the opportunity to meet fellow queer scientists farther along in their career path and how they found success in their field. It brings a lot of hope and comfort to struggling graduate students to see people like them persevere and succeed, especially in an environment as traditionally exclusive as academia.

What goals, initiative, and programming does LTBGS hope to start in the future?

I'm looking forward to continuing our Halloween event collaboration with BGSA and organizing another joint LGBT Grad group event with the help of the LGBT Center for Pride week in June 2024! We are also looking to collaborate on more events with both other BGS grad groups as well as other LGBT student groups looking to host similar types of events. I think in the near future we are most excited to set up our Queer in Steminar series as a regular, yearly series. Additionally, we want to host more queer scientists that have pursued career paths outside of academia, in order to reflect the change in the types of careers being pursued by BGS alumni.

Want to keep up-to-date on all the latest & best LTBGS news? Follow them on Twitter and Instagram, join the group Slack, and reach out to ltbgs@pennmedicine.upenn.edu to join their e-list!

LTBGS Board (Left to right): Thomas Zhang, Hannah Geller, Mara Davis, Taylor Miller-Ensminger, Melody Tan (Not pictured: Nicholas Cerda)

Special Interest:
End of Year CAMB Activities

Kay Labella and James Gesualdi

As the holiday season approaches, Dilworth Park will transform once again into Center City's Holiday Market! Located on the west side of City Hall, the Holiday Market will consist of an ice skating rink, a winter garden with a landscaped walking path and seating area, a ski-lodge inspired cabin with seasonal food and drinks, and an assortment of local craft stalls and vendors, perfect for some last minute holiday shopping. The Holiday Market will run this year from November 10th until January 1st and will be open from 12 - 8 pm. Admission to the Market is free, so a walk through the garden and some shopping can be a thrifty and grad-student friendly outing. The ice skating rink is affordable as well, with tickets going for just $8 for a 90 minute session and skate rentals available for $10. Your best bet is to order online ahead of time to avoid sellouts or long lines. After your stroll or your skate, the Cabin is a great place to grab a hot cider or seasonal cocktail to wrap up your trip. Dilworth park is about a 15 - 20 minute walk from the Grad Hospital area and a quick 34 trolley ride away from University City.

If you need a break from solving the usual scientific puzzles but want to give your brain some exercise, or are looking for a fun group activity for your cohort or lab, take a trip to Expedition Escape in King of Prussia. The deceptively small-seeming shop offers six different escape rooms where you and a gaggle of friends can test your mettle. Each charmingly themed room is fully stocked with clues, puzzles, and props to challenge, delight, and

Ice skating at Dilworth Park

LumiNature at Philadelphia Zoo

surprise anyone who tries their hand at them. Your CAMB Newsletter team has Quested for the Throne and found Aunt Edna's Inheritance, with plenty of laughs along the way. Rooms can be tested by anywhere from two to ten players, and you have an hour to complete your trial and make your way out! Good luck!

Aiming for adventure a little further afield? Don't mind a bit of a quest to get to your destination? Restless for a rousing joust? Pack your cloaks, don your armor, and head to the Pennsylvania Renaissance Faire any weekend from mid-August to the end of October to dive into a spectacular medieval-adjacent fantasy realm. Check out the fairgrounds at the Mount Hope Estate & Winery, home to noble knights, boisterous bards, mesmerizing merfolk, and many others. Spend your day taking in the spectacular shows and raucous revels set forth by the myriad performer, or amble about perusing the many wares made by accomplished artisans. Try your hand at archery or axe-throwing, and maybe a bit of dancing if you're feeling bold. And don't forget to try the faire's fare! Of course classics like turkey legs, bread bowls brimming with soup, and baked potatoes heaped with chili and cheese are featured; the menu options also include some frankly luscious ice creams, soft pretzels, sausages, and of course, a full range of wines, meads, and even absinthe from Mount Hope and other local establishments (your author is a particular fan of the elderflower lemonade!). If you're in need of a day away to play, the Pennsylvania Renaissance Faire is the place to be.

Finally, if you are looking to enjoy some holiday light displays, check out LumiNature at the Philadelphia zoo! Running from 11/17 to 1/6/24, the light show brings the zoo to life at night with over a million lights organized into 16 distinct displays. In addition to the show, the zoo offers seasonal snacks, hot chocolate, and alcoholic beverages. Tickets are $25 each and the zoo can easily be accessed via either the 38 bus or the 15 trolley. This is a great venue to check out if you have some family members visiting town over the holidays.

Thank you for reading.

For any questions, comments, concerns, or if you're interested in joining our team, please feel free to contact us at:

klabella@pennmedicine.upenn.edu

or

jamesges@pennmedicine.upenn.edu

Check out our blog and twitter page!

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