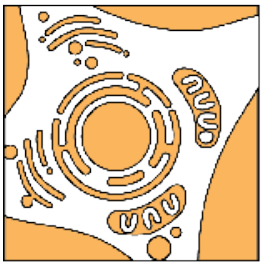

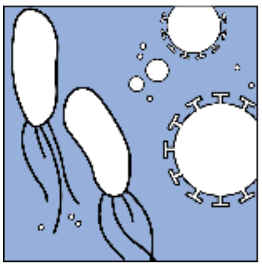

CAMB Student Newsletter

Volume 9 | Issue 4 | November 2024

In this issue

Letter from the Editors

Dear CAMB Students, Faculty, and Alumni,

We are excited to share with you the November 2024 edition of the CAMB student Newsletter!

In this issue we do a deep dive into the ongoing negotiations between the recently formed graduate student union (GET-UP/UAW) and the Penn Administration. Next, we highlight some of the incredible programing of the Penn Science Policy and Diplomacy Group (PSPDG). Our student research spotlight focuses on CAMB GTV student Vi Pham's latest paper on gene therapy treatments for Multiple Sulfatase Deficiency. Finally, we interview recent CAMB GTV alumnus Jesse Weber about his new job as a scientist at Scribe Therapeutics.

For additional articles, past publications, and to learn more about the CAMB Student Newsletter team, visit our blog at https://camb- newsletter.wixsite.com/blog or follow us on Twitter at @CambNewsletter.

The CAMB Student Newsletter is always looking for new writers and editors to join our team. Current students interested in contributing to the CAMB Student Newsletter can reach out to Kay Labella (klabella@pennmedicine.upenn.edu) or Ariana Majer (majerar@pennmedicine.upenn.edu) to learn more! You can also check us out in person – our brainstorming issue for the February 2025 issue will be on Tuesday, December 10th, at 3 PM. Join us in BRB 701 to pitch ideas over snacks!

Sincerely,
James Gesualdi, Kay Labella, and Ariana Majer

Special Interest

Everything You Need to Know About the Unionization of Penn Graduate Students

Eva Agostino
Peer Edited by James Gesualdi

This past May, thousands of Penn graduate students voted to form a union with over 95% voting in favor. This union at Penn (GETUP-UAW) will soon be the latest in a wave of graduate student unions formed over the past few years. As of 2023, over a third of all graduate students in the US (38.2%) are under union representation with a 133% increase in representation since 2012 (1). The continuous stream of information throughout the unionization process has been hard to keep straight, and the updates and legal jargon will only increase as contract negotiations continue. Therefore, we have put all the information you need to know about the unionization movement at Penn in one place. Here, we hope to answer some of the most pressing questions about the union, what's happening now, and the next steps.

What is GETUP-UAW?
GETUP-UAW stands for Graduate Employees Together - University of Pennsylvania / International Union, United Automobile, Aerospace and Agricultural Implement Workers of America. **GETUP-UAW is a group of graduate student teaching and research employees across the University of Pennsylvania who have unionized** to "improve our working conditions at Penn and to strengthen our collective voice as teaching and research assistants locally and nationally" (2). GET-UP is the local union lead by and made up of Penn graduate students while UAW is the international union that GET-UP has affiliated with.

Why is GET-UP joining UAW?
UAW is one of the biggest and most diverse unions in the US. Importantly, **UAW has successfully supported many graduate student unionization movements and therefore has expertise and a framework that GET-UP can rely on.** As of 2023, UAW represents nearly half (42.6%) of all graduate student unions nationwide (1).

As a CAMB student, am I required to join the union?
No, membership in the union is not required and cannot be required by law. The decision on whether to join GETUP-UAW or not is entirely up to you.

Who can join the union?
First, we must distinguish between being in the union and in the "unit". The union is a group coming together to support the unionization effort. The unit includes those in a job position protected by the union contract. **You can be part of and active in the union without being in the unit. You also can be in the unit without being a member of the union.**

As of the date of this publication, **Teaching or Research Fellowship Recipients are currently in the unit while Educational Fellowship Recipients (EFRs), which include pre-preliminary exam first and second year BGS students, are not.** While the Penn administration is trying to exclude EFRs from the unit, GET-UP is negotiating a contract to cover all graduate students who perform teaching or research labor, including EFRs**.**

Unsure whether you are in the unit? Check your official title on your Workday account.

Can international students join the union?
Yes. **International students have the same rights as US citizens under the National Labor Relations Act to participate in union activities** regardless of immigration status (4,5). For more information, please refer to GET-UP's international student FAQ page (5).

How do I join the union?
Any graduate student, whether in unit or not, can participate in union activities. Formal union membership will occur after Penn graduate students agree to a contract with Penn administration. **Until then, you can sign up for a GETUP-UAW authorization card without a fee which will allow you to vote in any union elections.** This can be done through the GET-UP website here.

Can I be punished by Penn for joining the union?
No. The right to unionize is protected by the National Labor Relations Act. Under the law, an **employer is forbidden from punishing employees who join a union** (5). Employers may not threaten the loss of job or benefits nor fire or otherwise punish employees due to their union engagement (4). Therefore, **neither Penn nor your PI can kick you out of the program, withdraw your healthcare, or otherwise punish you for joining the union or participating in union activities.** Additionally, neither Penn nor your PI can ask if you are a union member or actively discourage you from becoming a member or participating in union activities.

What's happened so far?
See the timeline below to get caught up.

- **Spring 2023** — The GETUP-UAW unionization campaign went public.
- **October 2023** — GETUP-UAW filed for an election with the National Labor Relations Board (NLRB).
  Penn administration responded to the petition for a union election, asserting that certain students, including EFRs, should be excluded from the proposed unit.
- **November 2023** — GETUP-UAW testified in NLRB hearings as to why EFRs should be included in the unit after Penn's attempt to exclude those students.
- **March 2024** — NLRB directed that an election be held for graduate students to decide on the formation of a union (GET-UP).
  NLRB defined the unit, ruling with Penn administration's request to exclude EFRs from the vote.
  GETUP-UAW requested that the NLRB conduct an expedited review of the exclusion of EFRs from the vote.
- **April 2024** — The NLRB ruled that EFRs could vote in the election, but those votes would be "subject to challenge" as EFR eligibility had not been formally agreed upon by all parties.
  The union election was postponed after Penn administration claimed they needed additional time to accommodate the inclusion of ERFs in the election.
- **May 2024** — Over 2,300 Penn graduate students voted in the union election.
  The NLRB certified the GETUP-UAW union following the 95% supermajority of Penn graduate students voting to form a union.
- **July 2024** — Penn graduate students elected 19 of their peers to serve as the 2024 GETUP-UAW Bargaining Committee.
- **August 2024** — Over 1,400 Penn graduate students completed the bargaining survey, allowing the Bargaining Committee to understand which issues to prioritize in their drafts of the Initial Bargaining Demands (IBDs).
- **September 2024** — The Bargaining Committee released the IBDs for ratification by Penn graduate students.
- **October 2024** — Negotiations over a union contract began between the Bargaining Committee and the Penn administration.

So, what happens next?

Throughout the past several months, the elected GET-UP Bargaining Committee incorporated feedback from over 1,400 bargaining surveys and graduate student working groups to draft IBDs for the Penn administration. Following ratification of those IBDs by over 2,000 students, the Bargaining Committee began contract negotiations with the Penn administration on October 17th. **Negotiation dates have been scheduled through the end of the year and will be added as needed until an agreement is reached.**

Negotiation Dates

1. October 17
2. October 30
3. November 6
4. November 21
5. December 5
6. December 9

How does bargaining work?

The bargaining process, formally called collective bargaining, involves negotiation between elected peer representatives (the Bargaining Committee) and their employer (the Penn administration). **The Bargaining Committee and Penn will bring forward demands and negotiate on their inclusion and language in the pending union contract. Both GETUP-UAW and Penn are legally obligated to bargain in "good faith",** meaning active participation in negotiations with the intent to reach an agreement or find common ground (6). While neither party can be forced to compromise, refusal of either party to bargain would violate the legal obligation to bargain in good faith as just one example (6,8,9). Any accusations of bad faith on either side are brought before the NLRB for a ruling (6).

If the Bargaining Committee and the Penn administration reach an agreement, a contract called a tentative agreement will be put forward to all Penn graduate students for a ratification vote. **If a majority vote in favor, the tentative agreement becomes a legally binding union contract with Penn.** If a majority oppose the tentative agreement, negotiations continue and the process repeats (3).

If the Bargaining Committee and the Penn administration cannot reach an agreement, an impasse could be declared (6). **This result is extremely unlikely** and would require months of no progress in negotiations despite good faith being upheld as determined by an NLRB review.

Who is on the Bargaining Committee?

The 2024 GETUP-UAW Bargaining Committee is made up of 19 Penn graduate students elected by their peers as representatives for negotiations. The diverse collection of members includes representatives from graduate programs across Penn, including the following schools:

- Perelman School of Medicine Biomedical Graduate Studies (including 2 CAMB students)
- Annenberg School of Communication
- Carey School of Law
- Graduate School of Education
- School of Arts and Sciences
- School of Engineering and Applied Science
- The Wharton School

What are the Initial Bargaining Demands?

The Initial Bargaining Demands (IBDs) are **a list of union contract demands aimed to improve the well-fair and working conditions of Penn graduate students.** The Bargaining Committee drafted these IBDs to reflect concerns expressed by current graduate students and will present these demands to the Penn administration during negotiations. **The IBDs released by the Bargaining Committee can be read here.** Keep in mind that GETUP-UAW has stated that these IBDs are intentionally broad and do not reflect the exact wording that has been brought forward during contract negotiations.

Are there any important takeaways from the first three negotiation sessions?

The first three negotiation sessions took place on October 17th, October 30th, and November 6th. **You can follow the progress of negotiations through the document linked here,** including PDFs with the proposals and tentative agreements from each meeting.

How long is this going to take?

No one can say for sure. Negotiations will continue until GETUP-UAW and Penn administration can reach an agreement. While the typical time to reach an agreement is around one year, this process could take as little as a few months or could extend beyond a year.

Will graduate students have to go on strike during negotiations?

No, a strike is not necessarily required to reach an agreement as many graduate student unions have reached a tentative agreement without resorting to a strike. However, **the Bargaining Committee could call for a strike during negotiations** if they conclude that the Penn administration is acting in bad faith or has committed an Unfair Labor Practice. **The formal decision to strike is made democratically through an election and requires a supermajority of graduate students to vote in favor**. Thousands of graduate students would have to agree that a strike is the only path forward. A representative of GETUP-UAW has stated that **the decision to call for a strike will not be taken lightly**.

For more information on strikes, please refer to our blog.

What happens once negotiations are done and a contract is reached?

Once the tentative agreement reached by the Bargaining Committee and the Penn administration has been ratified by a union vote, GETUP-UAW will become an official union.

After a contract has been negotiated, all authorization card holders will be asked to sign an official membership contract for their union card, pay the initiation fee, and begin paying union dues. **Those who currently hold authorization cards do not automatically become union members and must sign the membership contract to become an official union member.** All members with union cards must begin paying union dues and all non-members must begin paying the negotiated agency fee.

What are union dues and do I need to pay them?

Union dues are monthly fees paid to the union by union members. As independent institutions, unions require such dues to maintain the ability to negotiate against well-resourced employers like Penn. **Members of GETUP-UAW will be required to pay dues once the first contract is ratified by a majority vote and they have received a membership card.** Additionally, a one-time initiation fee will be required for new union members.

As of the date of this publication, **UAW membership dues are between 1.15%–1.44% of your gross monthly income** (3,7). So, assuming our current annual CAMB stipend of $41,500, union dues at 1.44% would be **approximately $50 per month for a total of $600 per year**. The cost of union dues is typically accounted for in the negotiated stipend raise during bargaining. While UAW sets a minimum dues percentage, any increase in membership dues is decided democratically at the local level.

The initiation fee is set by each local union. While not yet decided for GET-UP, many other UAW graduate student unions have an initiation fee of around $10 for new members (3).

Will students who are not union members be required to pay union dues?

Only union members are required to pay union dues. However, **non-members that are in the unit are typically required to pay an agency fee (AKA a "fair share" fee) to the union.** This fee would account for the universally improved working conditions and benefits for all in-unit graduate students at Penn resulting from the union's efforts. Agency fees are subject to negotiation between the union and the employer.

Agency fees are usually comparable to union dues and would be accounted for in the negotiated stipend raise during collective bargaining**.** The exact amount of this fee will be determined by GETUP-UAW in the by-laws once a contract has been secured. A GETUP-UAW representative has stated that the agency fee will not be any higher than union dues.

What are union dues/fees used for?

Union dues are used for a variety of efforts at the local and national level. Dues are allocated to the local union (GETUP-UAW) or the international union (UAW) as follows (3,7):

- 28 - 38% Local union
- 25 - 32% UAW General Fund
- 30 - 44% UAW Strike and Defense Fund
- 2.5% Community Action Programs

The use of local GET-UP funds is democratically decided through the approval of an annual budget (3). Some examples of local initiatives include union education and recruitment, advising members filing grievances, and local events (3).

Dues allocated to UAW fall into three categories. The General Fund supports contract negotiation of future unions, advocacy for federal policies, and guidance during arbitrations with an employer (3). For example, the UAW lawyers that helped GET-

UP during this process were paid for through the General Fund. The Strike and Defense Fund is used for legal arbitration and aid, strike pay, and strike benefits for local unions on strike (10). Finally, the UAW Community Action Program is a non-partisan, community engagement effort to improve general welfare (7).

I still have questions. Who do I talk to?

If you have any more questions or want to get involved with GET-UP, you can reach out to either of the CAMB graduate students currently serving on the Bargaining Committee. You also can reach out to GET-UP through the interest form found here.

Emily Aunis (MVP): Emily.Aunins@Pennmedicine.upenn.edu
Austin King (G&E): Austin.King@Pennmedicine.upenn.edu; 301-906-1812

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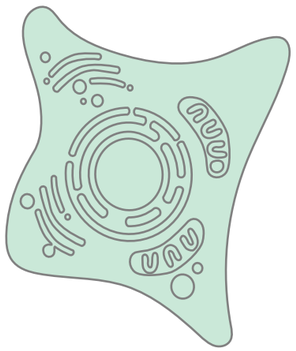


Student Group Spotlight:

The Penn Science Policy and Diplomacy Group

James Gesualdi
Peer Edited by Katey Stone

Are you interested in learning about career options for PhDs in government or scientific communication? Do you have a passion for helping broader audiences understand the importance of primary research studies? If so, the Penn Science Policy and Diplomacy Group (PSPDG) may be the student group for you! Read on to learn more about PSPDG's goals and activities from the group's student leaders in the CAMB community.

What is PSPDG? When and why was this student group founded?

The Penn Science Policy and Diplomacy Group (PSPDG) is a graduate student-led organization creating opportunities for Penn trainees to gain hands-on experience in science policy, diplomacy, and communication. STEM trainees often lack formal training in communicating to lay audiences, advocating for science in policy, and incorporating science into global diplomacy.

PSPDG was formed in 2017 after the Penn Science Policy Group merged with the Penn Science Diplomacy Group. Since then, PSPDG has continued to grow, with student members across the graduate schools and partnerships with numerous campus, community, and national policy organizations.

Why did you decide to get involved with PSPDG? How has it impacted your grad school experience?

Rose Albert (Vice President): My background is in environmental justice advocacy, and I chose to pursue a PhD with the goal of providing scientific support to communities most impacted by the climate crisis. I quickly realized that my day-to-day work lacked training in certain scientific writing (memos, whitepapers, media), and I also needed to better understand policy processes to advocate for environmentally just decision making. My favorite aspect of PSPDG is that our initiatives are highly student interest-driven, and the leadership team has been extremely supportive of me developing programming related to my career goals, including an Environmental Justice and Policy Panel in Spring 2024 and our current Media Training Series for Scientists. I've learned of many policy opportunities and careers I hadn't previously considered, and I'm now completing a FASEB Advocacy Fellowship that I heard of through the PSPDG network. PSPDG is also an amazing community of graduate students, and I've enjoyed the new friendships I've made through the group!

How can PSPDG help graduate students in terms of professional development and networking? What are some of the post-graduate roles that PSPDG can help prepare students for?

Miles Arnett (Science Policy Chair): One of the things I've appreciated most about being part of PSPDG is that it has opened the door to a whole field of connections and job opportunities that I might never have learned about otherwise. When you're pursuing a STEM degree, and especially while you're still an undergraduate, most of the career conversation is based around the dichotomy of academia and industry, with the assumption that almost everyone will fall into one of those two categories. But a scientific background, and especially a scientific PhD, prepares you for a lot more options than just those, including the ones we focus on in our club. In my branch of science policy, we've met scientific advisors to legislative offices, people working for executive branch agencies like the National Institutes of Health, consultants at scientifically-minded advocacy nonprofits, and many others, all of whom started their careers with a STEM graduate degree. And that's just in science policy, science communication features important jobs in media and education, and science diplomacy career options are expanding with each passing year. In PSPDG, we try to both inform our members about these opportunities and help them develop the expertise

they need to pursue them.

The main way we do this is by helping our members gain practical skills, writing samples, and contacts they can carry with them into the next stages of their career or training. We put on an extensive training series of workshops each year and have previously hosted external speakers such as Judy Swann for scientific writing and a variety of career and fellowship panels. Each year, PSPDG members travel to DC to meet with legislators and network at the AAAS conference. We also have working relationships with national organizations such as the Union of Concerned Scientists and campus entities such as the Perry World House.

Our alumni have gone on to pursue the Eagleton Science and Politics Fellowship, Science and Technology Policy Fellowships at USAID, and a variety of policy related roles including analysts and commissioners.

Has your involvement in PSPDG helped you to become more confident when communicating your research? What are some situations in which you have practiced communicating your (or other) research to a non-scientist audience?

Kaeri Martinez Medina (President): Yes, my involvement in PSPDG has helped me communicate my research. I think that a wonderful part of this group is that you interact with other scientists in completely different fields who share a common interest in policy, diplomacy, or communication. This kind of scientific diversity pushes me to better my communication skills so I can convey how important my research is and how much I believe in the power of science. As president, I have had the privilege of meeting policy and diplomacy experts on campus and at the AAAS conference. Often, these individuals do not have an advanced degree in my field of research but are still curious about what I do. I have had to condense my background and thesis project into a few quick sentences that are still understandable and interesting. This is challenging but still enjoyable.

What strategies have you used to balance your leadership position in PSPDG with your research responsibilities? Do you have any advice for other students considering becoming more involved in student groups?

Dimitris Boufidis (Science Diplomacy Chair): Balancing a leadership role in PSPDG with PhD research is challenging, but the group's flexible time commitment helps. Some members only attend workshops, while others take on organizing roles, which is often the best way to learn. Those seeking deeper involvement can step into leadership positions. It's an exciting time for science policy, diplomacy, and communication, and that excitement motivates us to create meaningful programs. One challenge is that many advisors aren't aware of science policy, diplomacy, and communication as a career path for STEM PhDs, with most focused on the academia vs. industry debate. To address this, we're developing a guide to inform PIs and help students engage in these fields without compromising their research progress.

What are some of your goals for the future of PSPDG?

Kaeri Martinez Medina (President): PSPDG has been consistently creating programming for STEM graduate students for the past 10 years. We're incredibly proud of the knowledge base we have built up and imparted onto curious students. As we continue to teach our members of SciPol, SciDip, and SciCom, we would also like to grow as an organization. For us, this means making Penn leadership aware of our activities, increasing our funding, maintaining our member numbers, and building connections with professors, non-profits, and other experts inside and outside of Penn.

What is the best way for interested students to get involved in PSPDG?

PSPDG has opportunities at different levels of commitment and prior experience for all students to get involved. We host monthly meetings with dinner and drinks where we provide updates from each of our branches, share upcoming opportunities, and discuss current policy and diplomacy events. We also host monthly social events that are open to all members of the Penn community, and these have included mini golf, picnics, movie nights, game nights, and more! The monthly meetings and social events are especially great, low commitment ways for new members to learn more about our team and work.

Our branch chairs lead a variety of training workshops, such as Science Policy 101, Science Diplomacy 101, Media Training with Scientists, and How to Meet with Legislators. We also hold reading discussions and foreign policy analyses on topics such as the Paris Agreement.

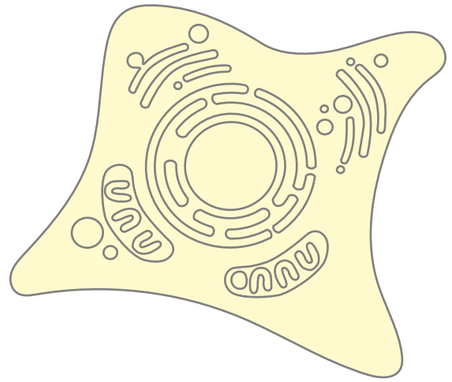
Students who are interested in gaining more leadership with the group can join or lead working groups that facilitate these workshops. The working groups are short-term commitments of 2-3 hours a week leading up to the event. We also have a variety of ongoing teams for memo writing, our blog, our podcast (Penn Talks Science- listen to us on Spotify!), and our Science Shorts Series. Students can connect with us on Slack, Twitter, Instagram, and our Website.

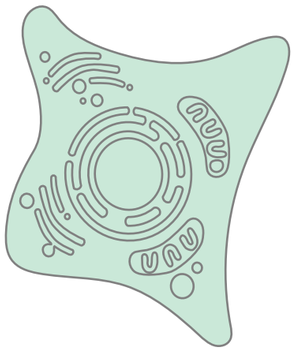
What are some upcoming group events that you are most excited about?

Kaeri Martinez Medina (President): My favorite events from PSPDG are the "Science Diplomacy 101" workshop and the "Science Diplomacy Simulation." I feel like they are the two best attended SciDip events that actually show students how interesting and impactful science can be in a diplomatic setting. It gives participants a chance to consider careers outside of academia or industry. It encourages them to think about how they want to use their expertise in the world. Both events are built to be engaging and teach students no matter their level of experience with SciDip.

Miles Arnett (Science Policy Chair): I'm most excited by how much the group has been expanding in recent years, and how we've managed to incorporate larger, more elaborate events into our programming. The Science Diplomacy Simulation is a great example of one such event from last year, and this year we have even higher ambitions, including trips to DC and Harrisburg, a Penn Science Policy Symposium, and a Science Policy Simulation. I think all of these could become fixtures of our programming for years to come.

If you are interested in learning more about PSPDG, check out their website here or connect via slack.





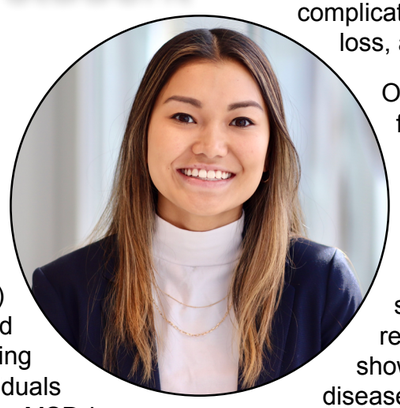
Research Spotlight

Vi Pham, GTV student

Ariana Majer

Peer Edited by Kay Labella

See page 12 for a glossary of key terms.



Multiple sulfatase deficiency (MSD) is a devastating, ultra-rare inherited lysosomal storage disorder affecting an estimated 1 in 500,000 individuals (2). Like many other rare diseases, MSD is chronic, degenerative, and debilitating. Individuals with MSD have a significantly shortened life expectancy, averaging around 13 years, and experience poor quality of life in that time. Like many other rare diseases, MSD has historically been understudied and consequently lacks effective treatment options (3,4). Currently, there are no approved therapies to slow or reverse MSD disease progression. Recognizing this unmet need for effective MSD treatment, fifth year CAMB-GTV PhD candidate Vi Pham from Rebecca Ahrens-Nicklas' lab sought to develop an *ex vivo* gene therapy approach for MSD (5).

Abbreviations
MSD: multiple sulfatase deficiency
FGE: formylglycine-generating enzyme
GAG: glycosaminoglycan
AAV: adeno-associated virus
HSCT-GT: hematopoietic stem cell transplantation - gene therapy
HSC: hematopoietic stem cell
ARSA: arylsulfatase A

MSD results from pathogenic germline variants in the gene *SUMF1*, which lead to diminished activity of the *SUMF1* protein product formylglycine-generating enzyme (FGE). FGE is required for activation and subsequent activity of all cellular sulfatases, and individuals with MSD are therefore functionally deficient in all cellular sulfatases. In the absence of functioning sulfatases, toxic sulfated molecules like glycosaminoglycans (GAGs) accumulate in lysosomes throughout the body, leading to multiple debilitating symptoms that include bone abnormalities, hepatomegaly, respiratory complications, cardiac dysfunction, hearing loss, and neurologic regression (6).

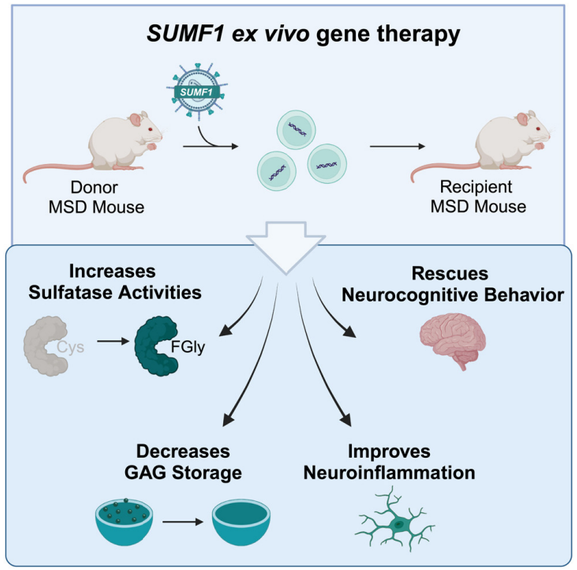
One attractive therapeutic strategy for monogenic diseases like MSD is gene therapy (7). Clinical trials are starting for *in vivo* adeno-associated virus (AAV)-mediated gene therapy for MSD, and gene therapy in combination with hematopoietic stem cell transplantation (hereafter referred to as HSCT-GT) has been shown to alleviate symptoms and slow disease progression in preclinical models and early phase clinical trials for other lysosomal storage disorders. Vi therefore hypothesized that using HSCT-GT to deliver functional copies of *SUMF1* to hematopoietic stem cells derived from individuals with MSD may similarly benefit individuals suffering from MSD.

To begin testing her hypothesis, Vi designed a clinically translatable lentiviral vector expressing a functional copy of human *SUMF1*. Transducing immortalized patient-derived primary fibroblasts with the *SUMF1* lentiviral vector resulted in robust expression of FGE, with increasing vector copy number integrations correlating with higher FGE expression. Importantly, cells transduced with the *SUMF1* lentiviral vector exhibited increased activity of three different sulfatases, with one of the three sulfatases exhibiting activity comparable to cells lacking a *SUMF1* mutation (wild-type). Cells transduced with the *SUMF1* lentiviral vector also exhibited decreased lysosomal accumulation of GAGs. As GAG accumulation is a key factor contributing to the tissue damage and organ dysfunction observed in MSD, this suggests that *SUMF1* gene therapy can effectively increase FGE expression and sulfatase activity in FGE-deficient cells.

Given her promising *in vitro* findings, Vi next assessed the safety, durability, and efficacy of her *SUMF1* lentiviral vector *in vivo* using a mouse model harboring a clinically relevant pathogenic mutation in the *Sumf1* gene. Vi performed primary and secondary transplants of hematopoietic stem cells (HSCs) transduced *ex vivo* with the *SUMF1* lentiviral vector. Transplanted *SUMF1* HSCs engrafted with high efficiency and differentiated into both erythroid and lymphoid populations, in proportions similar to those observed in untreated wild-type mice. This suggests that exogenous expression of *SUMF1* in HSCs does not alter normal hematopoiesis. Importantly, all mice survived to study endpoint without any signs of transplant-related morbidity, indicating that *SUMF1* HSCT-GT is well-tolerated and safe. To assess the stability of the *SUMF1* lentiviral vector, vector copy number was determined four months post-transplant for both primary and secondary transplant recipient mice and was found to fall within the clinically relevant range for *SUMF1*. These data lead to the conclusion that the vector stably integrates into the transduced HSCs, resulting in robust FGE expression that is not lost with progressive cell divisions.

To assess the efficacy of her *SUMF1* HSCT-GT approach, Vi then investigated the effects of *SUMF1* HSCT-GT on sulfatase activity and GAG accumulation in MSD mice. *SUMF1* HSCT-GT significantly increased the activity of the sulfatase arylsulfatase A (ARSA) in the spleen, which had a high vector copy number. In contrast, there was no effect in the brain, heart, lung, and liver, which had significantly lower vector copy numbers compared to the spleen. Despite the tissue-specific restoration of sulfatase activity, however, *SUMF1* HSCT-GT reduced accumulation of multiple GAG subspecies relative to untreated MSD mice in all five tissues, with the brain, liver, and spleen exhibiting the greatest reductions. Notably, MSD mice receiving non-transduced HSCs exhibited increased GAG levels compared to untreated MSD mice, and the *SUMF1* HSCT-GT was able to significantly reduce this transplant-associated GAG accumulation in all five tissues. These data indicate that, while transduced HSCs preferentially localize to some organs, *SUMF1* HSCT-GT is effective at reducing the accumulation of some GAG species in multiple organs.

To better understand the efficacy and therapeutic potential of her *SUMF1* HSCT-GT approach, Vi



next assessed the effects of *SUMF1* HSCT-GT on neuroinflammation and neurologic function, as neurological symptoms are a major source of morbidity in individuals with MSD. Importantly, transplanted *SUMF1*-expressing HSCs can cross the blood-brain barrier and differentiate into microglia-like cells with the potential to secrete activated sulfatases to neighboring cells lacking sulfatase function. *SUMF1* HSCT-GT partially reduced neuroinflammation by decreasing the presence of activated microglia, but was unable to improve motor coordination, balance, or muscular strength in MSD mice. *SUMF1* HSCT-GT did, however, improve spatial learning and memory, and also reduced neurodegenerative phenotypes in a subset of MSD mice. These data indicate that *SUMF1* HSCT-GT can improve spatial learning and reverse memory deficits associated with MSD, though further optimization of the HSCT-GT approach is needed to rescue neuromuscular deficits and slow neurodegeneration.

Collectively, Vi's data demonstrate that *ex vivo* lentiviral *SUMF1* HSCT-GT is a novel treatment strategy with the potential to improve symptoms and slow disease progression in individuals suffering from MSD. While further optimization is needed to improve the benefits of the *SUMF1* HSCT-GT approach in treating the neurological and motor deficits associated with MSD, Vi's findings serve as a proof of principle for using HSCT-GT to treat MSD and lay the groundwork for bringing *SUMF1* HSCT-

Key Terms

Formylglycine-generating enzyme: an enzyme present in the endoplasmic reticulum that catalyzes the conversion of cysteine to formylglycine. Its activity is required for the activation of all sulfatases in humans.

Gene therapy: a technique that seeks to modify the expression of a gene of interest in order to treat disorders resulting from problems in that gene's expression or function. In this article specifically, we are discussing a type of gene therapy that delivers functional copies of a gene of interest into cells with pathogenic mutations in that gene to promote functional activity of the gene's protein product.

Hematopoiesis: the process of producing blood cells in the bone marrow.

HSCT-GT: the transplantation of hematopoietic stem cells (HSCs) that have been transduced *ex vivo* to exogenously express a gene of interest. The process involves 1) deriving HSCs from the patient, 2) transducing patient-derived HSCs *ex vivo* with a lentiviral vector expressing the gene of interest, 3) irradiating the patient to deplete endogenous untransduced HSCs, and 4) reinfusing the edited HSCs into the patient.

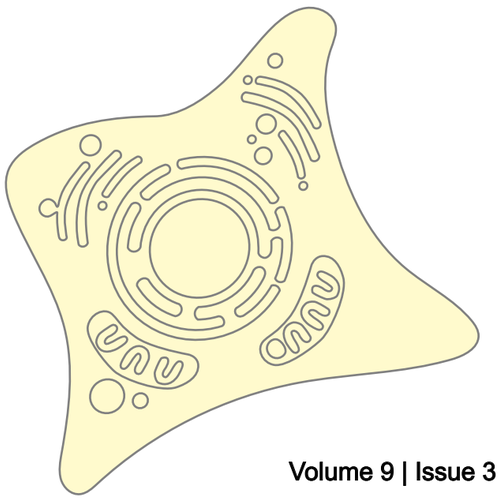
Monogenic disease: a genetic disorder resulting from pathogenic mutations in a single gene.

Neuroinflammation: inflammation of the brain and spinal cord primarily mediated by microglia, which are the resident innate immune cells of the central nervous system.

Sulfatase: an enzyme that catalyzes the hydrolysis of sulfate esters, thereby removing sulfate groups from a range of substrates. Sulfatases play a critical role in lysosomal degradation of sulfated molecules.

SUMF1: the gene encoding formylglycine-generating enzyme.

GT into clinical trials. Given the lack of therapies to slow or reverse MSD disease progression, Vi's findings offer hope to individuals living with MSD. Future studies investigating optimized vector constructs, including those expressing functional copies of downstream sulfatases in addition to FGE, as well as studies investigating the combination of *SUMF1* HSCT-GT with small molecules therapies currently in development for MSD, may reveal even more effective treatment options to significantly improve quality of life for individuals living with MSD.



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Alumni Interview

Jesse Weber, GTV alumnus

Kay Labella

Peer Edited by Mara Davis

Getting ready to graduate and looking further afield for your job prospects? Curious what your industry options are outside of Philadelphia? In this edition of the CAMB Student Newsletter, we sat down with former CAMB-GTVer Dr. Jesse Weber to discuss life after PhD, the job search process, and how to move on to your next great success! Dr. Weber completed his PhD in the lab of Dr. Beverly Davidson, and after his thesis defense this past March, he moved into a new role as a scientist at Scribe Therapeutics. There, he works as the platform lead for cargo engineering and delivery for several partnership programs the company has running.

What is your day-to-day like at your job?

Honestly, it's not entirely too different from my PhD! There's a good deal of freedom – not to the same degree as grad school, but it's certainly not as "red tape" as PIs often make industry sound. I have a lot more meetings than I did in grad school, but in turn, I also do a good bit less of lab work. They hire for your brain rather than your hands.

What are the key benefits/perks of your current role?

Beyond making a living wage compared to grad school? I'd say the ability to still make contributions to the scientific world without the headache that I felt academia was becoming for me. Scribe is unique, though, I will say. We still publish papers and present at conferences, so there's a push to still keep the positive aspects of academia, which I do love.

What's the best thing about your job?

Hands down the people. The company seemingly attracts like-minded individuals who enjoy creative thinking as well as a work-life balance, but are driven as all hell. Most of the company is from Jennifer Doudna's lab (she's a co-founder) and they're all absolute geniuses. I've been learning way more than expected, but not in an exhaustive manner. I feel energized and excited, since the education is coupled with an understanding and patience that did not really exist in grad school.

What have been the biggest differences between your time as a grad student and your current role?

Like I mentioned before, I think the shift toward meetings over lab work. Scribe in particular wants to hire scientists for their brain rather than hands – mostly. There's definitely some experiments that I've been able to help with, since I was the only one who had previously performed it!

How has your degree helped you in your current work?

Having my degree in gene therapy and gene editing was the most important thing for this role. Scribe is flying through with new projects, data, brainstorming sessions, and so on. If I hadn't had the niche experience I did, I don't think I'd be as successful in my role.

When did you start looking for jobs?

About a month after getting permission to defend! I'd recommend everyone to do this – the market is rough right now, and it cannot hurt to even just send one or two emails or apps out a week.

What was the job search process like for you? What was your experience job searching while preparing to defend?

It was shockingly easy on my end, but I do think this is a bit of an anomaly from what I've heard from peers. Scribe was the first job I applied to, and honestly, I only applied to another one because I had thought my interview went horribly. That turned out to not be the case – I just overthink things, especially when it's over Zoom. It actually coupled very well with defense prep. Writing my thesis prepared me for all the background information, while getting my slides together helped me whip up a presentation for my interview at Scribe.

What other career trajectories, if any, did you consider when job hunting?
None! I knew that I still wanted to be connected to science and be in the room when we plan experiments, just certainly not in the context of academia.

What were your considerations when looking at different possible job opportunities?
I wanted to make sure that the company had longevity. I spent a good bit of time looking at the science behind each company and evaluating their science itself as well as their funding. If you are applying to startups, make sure to take a look at their Series A/B funding and what their runway looks like. Also, make sure to see where the project(s) you'd be working under are funded, and if it's through a partnership versus internal. While I'd love to say I was searching for the best job that really felt right in my heart, I didn't really have that luxury in this current market. I'd rather my first job out of grad school be one that won't lead to me getting laid off in a year.

How did your previous connections or networking opportunities help your job search?
While I did reach out to my network, I didn't actually know anyone at Scribe. My network was supportive and reviewed my resume/CV, but other than that didn't really help with the search as much!

How did you find out about your current position?
I had made a list of gene editing/gene therapy companies that were not in Boston (that city isn't for me) and kept an eye on their websites. Eventually, I saw an opening for Scribe, with a description that fit my PhD very well. One thing I wanted to make sure of was that I would be successful at my role – so I avoided companies that were tangentially related to my experience or completely different. Maybe I just lack blind overconfidence, but part of me feared not being good at where I went next, so I really wanted to make sure it was a good fit that I could hop right into. By the way – this was a hit to say during my interview! Take notes!

Can you tell us about the interview process and how you prepared for it?
There were 4 components to the interview:
1. Phone interview with a recruiter for Scribe
2. Zoom interview with the hiring manager – typically the person you'd be working for/with
3. Long day of one-on-ones with people you'd be working with as well as an hour-long thesis-level presentation of your work.
4. A Whiteboard Session where you receive a prompt and have to give a talk/presentation (with minimal slides) on the topic. The whiteboard was by far the most stressful. I, admittedly, did not prepare much for these. HOWEVER, I do wish that I had asked my lab to listen to me give my talk first.

What are the key skills that companies look for during the hiring process?
Communication, confidence, and critical thinking. I've sat in on a lot of interviews and whiteboard sessions now, and one of the worst things is when someone can't get their point across and we're just lost for the rest of the presentation. Remember to walk people through your story in more simple terms rather than convoluted ones.

Do you have any tips for unwinding during the job search process?
Yes! Don't take a no personally, like at all. One position I helped run interviews for at Scribe came down to two people who were both incredible. There was only one spot though – and it solely landed on preferences. The other person was still amazing, and that may just be you in the future, unfortunately. Always easier said than done, but try your best to just shake off a rejection and keep powering through.

What advice do you have for current graduate students?
Learn every technique you can from your lab or nearby labs. Those techniques are checklists for a lot of companies. Yes, they want you more for your brain – but they also want to know which techniques you can talk about and perhaps train a research assistant that will work underneath you. The more techniques you know, the more powerful your application becomes.

Though the job search can be daunting, fellow students past and present have your back! If you'd like to get in touch with Dr. Weber, you can contact him on LinkedIn or email him at jaw5964@gmail.com. Dr. Weber encourages anyone to reach out, especially if they're in the Bay Area and want to grab coffee!

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
majerar@pennmedicine.upenn.edu
Check out our blog page!

Meet our team