iSLB

SOCIETY FOR LEUKOCYTE BIOLOGY

Vol 1 2026

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A Message from the President


Cindy Leifer

It is my honor to step into my role as president of the society for leukocyte biology. I joined SLB as an early career faculty member. That first meeting I attended was exciting and intimidating at first, but there was a vibe that made me feel so welcomed. That's what is so special about SLB, it's like a big science family. Early on, I joined the membership committee and later chaired that committee. Giving back to the society was important to me and gave me leadership experience along the way. Now, you, the members SLB, have put your faith in me as president at a challenging time for science and scientific societies. We are experiencing an uncertain federal funding landscape, reduced admissions at many graduate programs, changes in leadership and messaging from federal institutions, and reduced trust in science. Yet there is much to be optimistic about. Each day immunology discoveries move from bench to bedside, and advances in technology allow us to visualize and interrogate immune responses in greater detail than ever before. Scientific societies like SLB play a key role in this scientific ecosystem by providing a space for trainees and researchers to share their work and develop new collaborations, and to support each other.

Looking back on the past few years, I need to thank Lou Justement for his excellent leadership and leaving the society in such great shape; however, he won't go far because he remains part of the leadership team as past-president. I also need to thank David Underhill as he finishes his role as past president and Michelle Visser as she continues her role as treasurer. I look forward to working with our president-elect Ann Periera, the entire council and all the committee chairs and members as we move into the next few years.

Looking to the future, SLB is in solid financial standing and our membership remains strong. The Journal of Leukocyte Biology is our society's journal and revenue from the journal helps support society activities. JLB is highly regarded and has undergone some amazing changes under Michael Schnoor, editor-in-chief, to make it even more widely read. There are new types of articles, accepted articles are available online right away, and on average a manuscript goes from submission to first decision in under a month. Consider publishing your next paper in JLB.

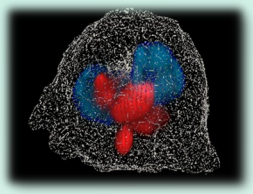
There are many activities throughout the year including the building bridges webinars, the annual meeting, and iSLB. Many thanks to Laura Sly and Vidula Vachharajani who organized an outstanding meeting in 2025 with excellent research and many awards to a broad range of trainees and early and mid-career faculty. iSLB continues to be the main source of updates and exciting new initiatives like the one Jean Scholz and Chad Markert are planning for iSLB. This new feature—the "UG Corner", will be an opportunity for undergraduate trainees to develop and practice science communication skills with mentoring while writing an article for iSLB. All the committees are hard at work behind the scenes planning activities for the annual meeting and new initiatives to engage the membership.

All of the activities that sustain SLB's vibrant community depend on volunteers. Please consider giving back to the society by joining a committee and attending our annual meeting. Mark your calendars now for SLB 2026 "Leukocytes, it's all about location" that will be held at the Blackwell Hotel and Conference Center at Ohio State University in Columbus Ohio September 14-17. The meeting co-organizers Andrew Taylor and Michelle Visser have prepared an impressive lineup of speakers for the meeting. They received a record number of proposals for special interest group (SIG) sessions so the first day will be packed with exciting science. There are also double the number of flash talk opportunities and single tracking of the sessions to everyone can see all the great science at the meeting. Don't forget, SLB gives a generous number of different awards, so be sure to apply before the deadline!

Most importantly, spread the word about the wonderful and welcoming community of SLB and encourage your colleagues and trainees to join.

SLB's Annual Image Contest

April 29th is the International Day of Immunology! SLB welcomes members to participate in a little fun. Submit an original, self-made, unpublished image in any of these categories and be entered into a prize drawing. Formats accepted include jpegs, gifs, pngs, and pdfs. Entries are being accepted **now through 5pm eastern Friday, May 1st**. Winners to be announced in early May. Learn more and submit today!


2025 Winner: Stephania Libreros

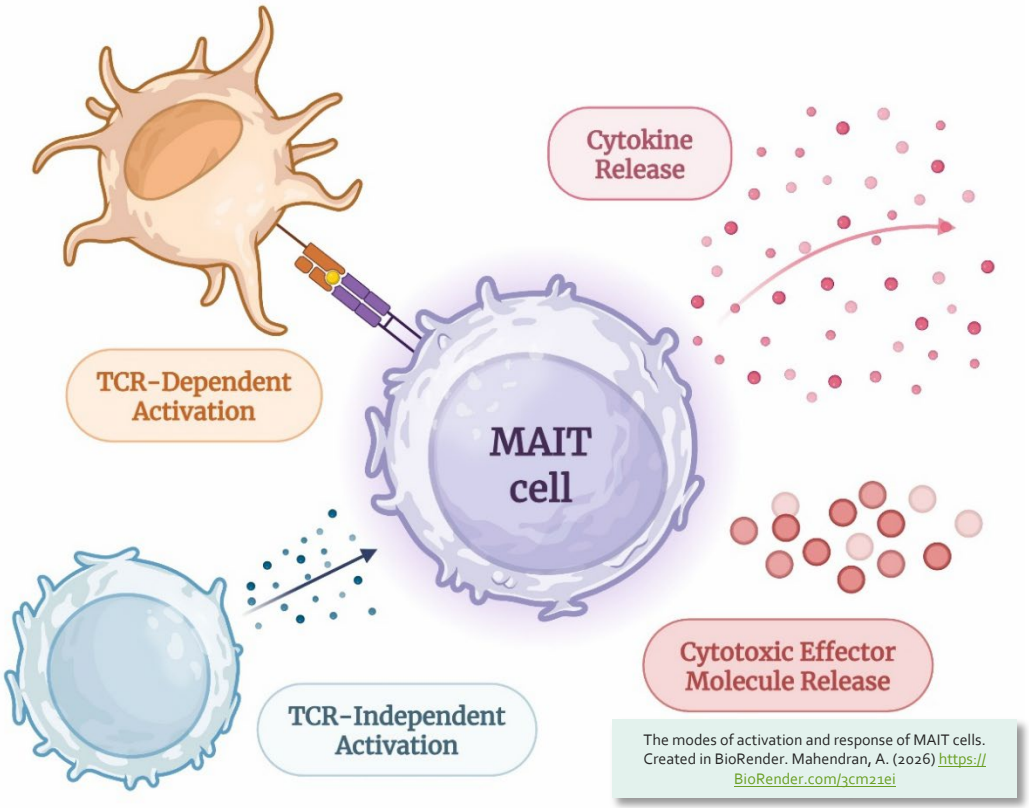
By submitting your image and caption, you give SLB permission to include the images (with credit) in the next issue of iSLB and on the society website.

Spotlight on MAIT Cells

by Agetha Mahendran, Department of Microbiology and Immunology at Western University (London, Ontario, Canada)

Mucosa-associated invariant T (MAIT) cells are an evolutionarily conserved subset of unconventional, innate-like T cells that possess unique immunomodulatory properties. Unlike conventional T cells, MAIT cells express a semi-invariant T cell receptor (TCR), recognize non-peptide antigens and are not major histocompatibility complex (MHC) restricted. MAIT cells have recently become a focal point of immunological research due to their emerging roles in several diseases and malignancies. Here, we briefly review the history and future trajectory of MAIT cell research.

Porcelli *et al.* (1993) was the first to report the discovery of a T cell subset with a *TRAV1-2-TRAJ33* TCRα chain enriched in the $CD4^-CD8^-$ (DN) T cell population of human peripheral blood[1]. The Lantz group (1999) similarly identified a phylogenetically conserved human T cell population that expressed an invariant Vα7.2-Jα33 TCRα chain, with homologous populations in mouse and bovine tissues[2]. Human Vα7.2-Jα33 $TCR\alpha^+$ cells were found to be predominantly DN or $CD8^+$ and represent ~0.1-0.2% of all peripheral blood leukocytes[2]. In contrast to the α-chain of the TCR, the Lantz group found that the β-chain was variable but limited to Vβ2 and Vβ13 in humans, and Vβ6 and Vβ8 in mice[2]. These semi-invariant Vα7.2-Jα33 $TCR\alpha^+$ cells were finally coined the name MAIT cells in 2003 due to their high abundance in mucosal tissues[3]. MAIT cells comprise 2-5% of T cells in the gut lamina propria, up to 40% of T cells in the liver and ~15% of T cells lungs [4,5].



The modes of activation and response of MAIT cells. Created in BioRender. Mahendran, A. (2026) https://BioRender.com/3cm21ei

MAIT cells recognize antigens presented by the monomorphic MHC Class I-related molecule (MR1)[3], however, the nature of MR1-presented antigens remained undefined until 2012. While it was known that MAIT cells were activated by antigens of bacterial and fungal organisms such as *Klebsiella pneumoniae*, *Staphylococcus aureus, Candida glabrata* and *Candida albicans*[6], attempts at isolating specific MAIT cell activating ligands were unsuccessful. Kjer-Nielsen *et al.* (2012) finally made a pivotal breakthrough, demonstrating that MR1 presents metabolites derived from the microbial vitamin B2 biosynthesis pathway[7,8]. Unstable small-molecule derivatives of 5-A-RU (5-amino-6-d-ribitylaminouracil), such as 5-OE-RU (5-(2-oxoethylideneamino)-6-d-ribitylaminouracil) and 5-OP-RU (5-(2-oxopropylideneamino)-6-d-ribitylaminouracil), form MR1 ligands capable of activating MAIT cells[9,10]. This discovery not only differentiated MAIT cells as a unique T cell subset but also revealed that T cells can detect microbial metabolites in addition to peptide and lipid antigens.

Interestingly, subsequent work found MAIT cells are also capable of TCR-independent activation through stimulation by interleukin (IL)-7, IL-12, IL-15, IL-18, IL-33 and the type 1 interferons (IFN)[11–14]. Responsiveness to cytokines allows MAIT cells to participate in immune responses even in the absence of cognate antigen presentation, broadening their functional scope beyond the anti-bacterial and anti-fungal response. Upon activation, MAIT cells swiftly release cytokines and/or cytotoxic effector molecules such as IFNγ, tumor necrosis factor (TNF)-α, IL-4, IL-5, IL-13, IL-17, IL-22, granzymes, perforin and granulysin [4,5]. Their innate-like characteristics are largely attributed to this rapid secretion of effector molecules even in the absence of TCR signalling, allowing them to function as early responders of the adaptive immune system.

Functionally, MAIT cells are classified as either MAIT1 or MAIT17 cells – which induce a T helper (T_H)1- or T_H17-type response, respectively[15,16]. MAIT1 cells are defined through the expression of the master transcriptional regulator of T_H1 cell differentiation, T-box expressed in T cells (T-bet)[15,16]. MAIT17 cells are identified through the expression of the transcription factor retinoic acid receptor-related orphan receptor γt (RORγt)[15,16]. The majority of MAIT cells are comprised of MAIT17 cells, allowing them to maintain homeostasis at mucosal barriers and protect against extracellular pathogens.

Since the late 1990s and early 2000s, interest in MAIT cells has intensified through increased associations with a broad range of diseases and conditions. Clinical and pre-clinical MAIT cell research initially focused on diseases of bacterial origin due to their antigen reactivity. Patients with pulmonary bacterial pathologies such as tuberculosis had decreased MAIT cell frequency in their peripheral blood, thought to be caused by MAIT cells migrating to the site of infection from the blood[6]. Human MAIT cell frequencies also dropped in the peripheral blood of patients with critical illnesses including severe bacterial infections and sepsis[17–19]. MAIT cells were observed to be impacted by viral infections as early as 2013, when several independent studies demonstrated the persistent decrease and functional impairment of MAIT cells in patients with chronic HIV infection[20–22]. Aside from illnesses of microbial origin, MAIT cells have also been implicated in various malignancies where their role is complex and context dependent. MAIT cells can function in both a tumor-promoting and tumor-suppressive capacity, typically linked to MAIT17 and MAIT1 phenotypes, respectively. A growing body of literature reveal MAIT cells contribute to the progression and severity of lung[23,24], liver[25,26], colon[27–29], bladder[30] and ovarian cancer[31], underscoring the importance of defining their cancer specific roles.

Despite the long history of immunological research, MAIT cells and other innate-like T cells have been overlooked, frequently mistaken for conventional T cells. Their high frequency, rapid responsiveness, and their restriction to the monomorphic MR1 molecule highlights their unique role in the adaptive immune response, depicting MAIT cells as attractive therapeutic targets. Future research will likely be focused on uncovering novel MR1 ligands, developing signatures to better define MAIT cells in multi-omics analyses and continuing to investigate MAIT cell involvement in various conditions, which will ultimately inform efforts aimed at leveraging MAIT cells in disease.

References

UG Corner: A New iSLB Column Dedicated to Undergraduate Researchers

By Chad Markert, Amali E Samarasinghe, and Jean L Scholz

Many SLB members host undergraduate (UG) students in their labs to assist with ongoing projects or conduct an independent study. Some of these experiences ultimately lead to contributing authorship on a poster or paper, affording the UG a citable reference in an indexed scientific journal. Others turn to journals dedicated to the publication of undergraduate articles, such as the Undergraduate Journal of Experimental Microbiology and Immunology (UJEMI) (jemi.microbiology.ubc.ca/). This and other similar journals publish undergraduate research or research-in-progress, methods and troubleshooting, and perspectives.

Here we launch **UG Corner** as a regular iSLB column for articles by students pursuing Bachelor's degrees. To include UGs at non-research intensive institutions, we will begin with short, educational perspectives on topics related to leukocyte biology / immunology. Examples might include NETosis and autoimmunity, vaccine development or efficacy, a "favorite" leukocyte, or the gut-brain axis. We seek research-based, thoughtful articles consistent with the scientific method, as opposed to simplistic recitals of facts. Because some undergraduate institutions (whether in the US or internationally) may not offer immunology courses, we also invite articles where students share the commonalities between their coursework in disparate disciplines, and immunology. Our vision is to afford UGs an early opportunity to articulate and publish accounts of their nascent interest in immunology.

Article length is up to 1500 words. Include 1-3 scientific literature references and, optionally, links to 1-2 relevant videos or websites that are publicly accessible at no cost. In addition, faculty mentor or other scientists may be cited with their permission by name and affiliation (up to 3 such references).

To make a start and provide an exemplar, the first **UG Corner** article will appear in iSLB Volume 2 (summer 2026). Please contact Jean Scholz (jeanl@pennmedicine.upenn.edu) or Chad Markert (markertcd@wssu.edu) about submissions for Volume 3 and beyond. In addition, we are developing webinars on pathways to undergraduate publishing in immunology, so please feel free to contact us with suggestions for topics and potential speakers!

2026 Legacy Awardee, Anna Huttenlocher, M.D.,Ph.D.

Anna Huttenlocher, M.D, Ph.D.

Anna Ruth Brummett and Vilas distinguished Research Professor of Pediatrics and Medical Microbiology and Immunology at University of Wisconsin-Madison

For this issue, I had the distinct pleasure to interview Dr. Anna Huttenlocher, physician–scientist and pioneering leader in live imaging of immune cell behavior, as this year's Society for Leukocyte Biology Legacy Awardee. Dr. Huttenlocher, based at the University of Wisconsin–Madison, has transformed the way we understand leukocyte migration by bringing immune cells into view, quite literally, through elegant in vivo imaging approaches in zebrafish and complementary mammalian systems.

Her work on neutrophil reverse migration, immune cell interactions within tissues, and the contextual regulation of inflammation has reshaped long-standing assumptions in the field. In this conversation, she reflects on the clinical spark that launched her career, the risks that led to breakthrough discoveries, and why resilience, and joy, remain essential ingredients in scientific life.

An Interview by Julia Bohannon

From Clinic to Cell Migration: An Origin Story

Dr. Huttenlocher's path into neutrophil biology began at the bedside.

"As a fellow at UCSF, I cared for a patient with a rare inflammatory disease," she recalls. "She had fevers from birth and neutrophil-rich skin rashes. When we studied her cells, we found something surprising: her neutrophils had impaired motility."

This paradox, profound inflammation coupled with defective migration, captured her imagination. Why would cells central to inflammation move poorly? What is the true relationship between migration and inflammatory disease?

Years later, the patient was found to harbor an NLRP3 inflammasome mutation. More recently, others have shown that NLRP3 regulates neutrophil motility. "But at the time," she says, "it simply sparked my curiosity about how neutrophil movement relates to the onset and resolution of inflammation."

She went on to train in cell motility in the laboratory of Rick Horwitz, focusing on integrin regulation and fundamental mechanisms of migration, training that, notably, was not centered on immunology. When she launched her own lab, she returned to neutrophils with a new toolkit.

Early work *in vitro* quickly revealed a limitation: to truly understand leukocyte behavior, she needed to see cells in their native environment.

Mice proved technically challenging for dynamic imaging at the time. So, in a bold move as a newly funded assistant professor, she pivoted to zebrafish.

"It was a risky time to switch directions," she says. "But once I had my first R01, I felt I could take that risk. Collaboration was absolutely key."

Developing transgenic zebrafish that fluorescently labeled neutrophils took years and required extensive collaboration, including with Tom Look's lab at Harvard. The tools available today did not yet exist. But the effort paid off. For the first time, neutrophils could be watched migrating to and from sites of tissue damage in real time.

"I've never looked back," she says. "It's been such a blast."

Reverse Migration: A Field Evolves

Asked which discovery still excites her most, she does not hesitate: neutrophil reverse migration.

The concept – that neutrophils can leave inflamed tissues and re-enter circulation – challenged dogma when first described. Early attempts to publish the findings were met with skepticism. The *Journal of Leukocyte Biology*, however, recognized the significance immediately.

"That openness to ideas that challenge dogma is incredibly important," she notes.

Today, reverse migration remains an active frontier. Zebrafish allow direct visualization of the process; mouse models provide powerful genetic tools to dissect mechanisms. Her lab now uses single-cell sequencing to profile reverse-migrated neutrophils and determine how they are reprogrammed by their inflammatory experience.

"The clinical implications are enormous," she explains. "Reverse-migrated neutrophils have been implicated in tumors, infection, pancreatitis, acute respiratory distress syndrome. There's still so much to learn."

Migration in Context

Looking forward, Dr. Huttenlocher sees the next major advances coming from studying migration in context.

"It's not enough to just track neutrophils," she says. "We have to understand what's happening around them."

Her lab is now dissecting how neutrophils interact with epithelium, fibroblasts, macrophages, T cells, and the extracellular matrix within intact tissues. The same cell can behave very differently depending on its microenvironment.

Macrophage–neutrophil interactions, in particular, illustrate this complexity. In sterile injury, macrophages can cloak tissue damage and limit neutrophil recruitment. In infection, they act as powerful attractants.

"And it goes both ways," she emphasizes. "We've thought a lot about how macrophages influence neutrophils, but neutrophils also shape macrophage behavior."

This bidirectional communication, embedded within tissue architecture, represents one of the most exciting and nuanced areas of modern leukocyte biology.

Trained Immunity and Reprogramming

The expanding field of trained immunity also holds promise.

"The idea that prior inflammatory experiences can reprogram innate immune cells is fascinating," she says. Her group is exploring these questions using human iPSC-derived neutrophils alongside zebrafish and mouse systems.

Like many innovative approaches, iPSC-derived neutrophils initially faced skepticism. "People say, 'Those aren't real neutrophils.' But we're at the beginning of this field."

Here again, persistence matters. New models open new questions, even when they challenge convention.

Huttenlocher Lab Reunion

A Lab Built on Curiosity

Dr. Huttenlocher's laboratory reflects her belief in intellectual freedom.

"When postdocs join the lab, I want them to pursue what excites them," she explains. As a result, the lab's portfolio has evolved with its people.

Current projects span adaptive immune cell imaging in zebrafish, comparative genomics of neutrophil heterogeneity, fungal infection, burn injury and fibroblast–neutrophil interactions, inflammatory regulation of motility, aging, and cancer invasion.

"It's broad," she acknowledges, "but it depends on the group of people who are there."

Watching trainees launch independent careers is among her greatest joys. "That's one of the biggest pleasures of science, seeing people go off and do great things."

The Role of SLB

Dr. Huttenlocher's connection to the Society for Leukocyte Biology dates back nearly two decades, beginning with that first reverse migration paper.

"SLB has been such an important home for trainees," she says. "The meetings foster a collaborative dynamic that's really focused on helping younger investigators."

Receiving the Legacy Award is deeply meaningful. "I can't imagine a bigger honor than this community recognition."

Advice for the Next Generation

Her advice to early-career scientists is both simple and hard-won:

"Have fun. Follow what excites you. Take risks. And don't get discouraged."

Resilience, she says, is essential. Papers will face resistance. Grants may hinge on a single reviewer. Funding climates fluctuate.

"If you know what you're doing is important and you're excited about it, just keep at it."

Above all, she emphasizes perspective: "We are so privileged to have this career. I can't imagine doing anything else."

Life Beyond the Lab

Outside of science, Dr. Huttenlocher recharges through reading, hiking in the woods with her husband and dog, spending time with her children and grandchildren, and playing the viola.

Acknowledgments

Finally, she is quick to credit the many trainees and collaborators who have shaped her journey.

"What has happened wouldn't have happened without them."

In honoring Dr. Huttenlocher, the Society for Leukocyte Biology celebrates not only a body of transformative discoveries but a career defined by curiosity, courage, collaboration, and joy in science.

Coming FREE FOR ALL Building Bridges Webinar

Join on March 25, 2026, 1pm ET to hear Shruti Rawal, *BWH Harvard* present "**A microRNA mediated regulation of macrophage immunometabolism in diabetes-associated atherosclerosis**". Learn more and register.

And look for more great speakers scheduled in 2026...

- Andres Hidalgo, *Yale University, Immunology Department* - May 27th
- Carlos Rosales, *Universidad Nacional Autonoma de Mexico* - June 24th
- Ronen Sumagin, *Northwestern Feinberg School of Medicine* - July 22nd
- Chyna Lovell, *MASS General / Harvard* - August 26th
- Manjari Trivedi, *Harvard Medical School* - October 28th
- Amali Samarasinghe, *UW Madison* - November 18th

SLB Members Who's Who

Dr. David Underhill: Scientist, Leader, and Steward of the Community

By Elsa Bou Ghanem, SLB Membership Committee

Dr. David Underhill is Professor and Chair of the Department of Biomedical Sciences at Cedars-Sinai in Los Angeles. His involvement with the Society for Leukocyte Biology (SLB) started after attending an annual meeting and grew into a long-term commitment to SLB's mission. Since joining SLB in 2006 as a member, he has contributed to several levels of leadership, first serving as a Counselor then President of the society. He views these roles as a way of giving back to the society. Of all his roles, the one he enjoyed the most was organizing the 2018 joint SLB and International Endotoxin and Innate Immunity Society meeting in Phoenix Arizona. He considers SLB meetings as the flagship method of interacting with other people in the society and enjoyed "putting his own stamp" on the event, from shaping the scientific program to importantly creating space for meaningful interactions. Such thoughtful contributions have been a signature of Dr. Underhill's time in SLB. What he values most about being part of SLB is the stable set of relationships and recurring connections that followed him throughout his career.

Dr. Underhill's career has been driven by his scientific curiosity, collaborations, and openness to unexpected research directions. He began with a PhD in cell biology, studying basic ion transport in cells. He didn't start working on leukocytes till his postdoctoral training, where he joined a macrophage laboratory to study phagocytosis and mechanisms of vesicle maturation. This eventually led him to study Zymosan where he discovered it activated Toll-like receptor 2 signaling and launched his career in pattern recognition receptors and their functions as initiators of innate immunity and inflammation. His research evolved again after getting recruited to Cedars-Sinai, that had an institute focused on inflammatory bowel disease. Given his work on immune responses to fungal products, this led him to question the existence of a fungal microbiome, which was another turning point in his career and launched his research into defining the fungal microbiome and its interaction with the immune system in health and disease. Going back to his original focus, his group had developed a technology for labeling proteins inside a phagosome, allowing them to examine the interactome within these compartments. This led to an unexpected foray into neuroimmunology, examining how microglial cells process amyloid beta plaques, a project that started by chatting with colleagues who work on Alzheimer's disease. For David, there is no one way to have a successful research career, but what has worked for him is following the science that interests him, focusing on compelling discoveries, and embracing collaborations.

Apart from research, Dr. Underhill's career has focused on training the next generation of scientists. When he joined Cedars-Sinai, he did so with the ambition of helping grow its research enterprise. He founded the institution's PhD program, helping transform Cedars-Sinai into a degree-granting institution. For more than a decade, he led the program, overseeing its growth and expansion into multiple master's degrees and new PhD tracks. Eventually, he stepped into the role of Chair of the Department of Biomedical Sciences. David views administration not as management, but as stewardship. He finds great satisfaction in advancing the academic community and creating opportunities for the next generation of scientists. When asked about what advice he would give early career scientists, he emphasized the importance of joy. He acknowledges that academic science comes with a lot pressures, from funding challenges to administrative demands, and external stressors. However, he urges young scientists not to let these stressors define their careers or reduce their love of discovery. He believes that genuine enjoyment of one's work is key for long-term success. He encourages scientists to communicate the joy of scientific discovery with colleagues and importantly trainees, and to always celebrate the successes of others.

Dr. Underhill's wish for SLB is continued activity, engagement, and growth. He admires the society's stability and its strong and loyal membership and would like to see it grow while maintaining its close-knit character. He sees that engagement of newer members who will shape SLB in the decades ahead as key to the society's future. He is a strong supporter of the Associate Counselor position, which gives the chance for mid- and early-career scientists to become a part of SLB's future leadership. He believes that maintaining vibrancy requires trying new ideas, welcoming fresh perspectives, and invites the community to be part of SLB's growth.

ICYMI

SLB's on-demand library of scientific and professional development videos continues to grow! Available to society members anytime, check out the resources available. The latest additions include talks on **"Differential subversion of host immune signaling by tuberculous and non-tuberculous mycobacteria"** and **"Swimming into Neutrophil Heterogeneity: Lessons from Zebrafish".**

Watch now

Behind the Science: 3 Interviews with JLB Authors

by Ramizah Mohd Sabri

Daniel Kim, *Purdue University*, RABEP1 regulates neutrophil migration via endosomal recycling and actin polymerization

READ

Q: How would you summarize your key findings in plain language?

A: We discovered that Rabep1, a target gene of miR-190, is important in regulating neutrophil motility by controlling endosomal recycling for precise actin polymerization at the leading edge of migrating cells. The findings were determined using both the zebrafish *in vivo* system and the neutrophil-like HL-60 *in vitro* system.

Q: What initially sparked the idea for this study?

A: A previous screen of miRNA in zebrafish neutrophils showed a significant decrease in motility upon miR-190 overexpression. This led to trying to figure out which specific genes miR-190 targets and how they play a role in neutrophil migration.

Q: Was there a moment during the project when the data surprised you?

A: The endosomal recycling experiment was especially interesting to complete. We were able to demonstrate that Rabep1 knockdown did not impair the uptake of transferrin or wheat germ agglutinin (WGA), yet it significantly reduced their recycling, which is an outcome that was insightful to validate.

Q: What methods or approaches were especially important in allowing you to answer this question?

A: The use of zebrafish as an *in vivo* model and high-resolution confocal microscopy were an invaluable tool that allowed us to conceptualize, test and prove our hypotheses.

Q: What was the biggest challenge you faced during this study, and how did you overcome it?

A: The biggest challenge was the endosomal recycling experiment as there was extensive troubleshooting required, particularly because the experiment was structured as a time course. Our original plan to perform live imaging was not successful as endosomal recycling occurred faster than we anticipated, resulting in missed meaningful changes by the time samples were prepared and imaged. We addressed this by implementing a temporal fixation approach and imaging multiple defined time points to approximate live imaging. We are pleased to report that the results were consistent, insightful, and ultimately strengthened our hypothesis.

Q: What do you enjoy most about doing research?

A: When an experimental design is successful and gives definitive results that prove or disprove a hypothesis. At the end of the day,

I find it exciting when there is room to figure out what the crucial next steps are to progress the project.

Q: How do you approach creativity or problem-solving when you hit a scientific roadblock?

A: I would take a step back and go back to the basics by looking up literature and seeing where the missing pieces of the puzzle may be located. Then, I would consult my understanding and methods of solving a roadblock to my peers, mentees and mentors. Talking out loud with a group that has the same scientific goal always seemed to help.

Q: What part of working in science brings you the most satisfaction?

A: Determining a novel concept and uncovering a truth that has not been unveiled before. This incremental contributions to the field of science are, in my opinion, one of the greatest accomplishments a scientist can achieve.

Q: Looking ahead, what excites you most about where the field is heading in the next few years?

A: Personalized therapeutics is a direction the field is headed towards. To integrate differences between individuals with robust immunology-related therapy techniques to ensure a more efficient and safe recovery is an exciting future I am much looking forward to being a part of establishing.

Q: What advice would you give to those that are at the beginning of their scientific journey?

A: Don't waste time but do take your time.

Hannah Weppner & Laurel Hind, *University of Colorado Boulder*, Human M-MDSCs impair neutrophil migration in the infectious microenvironment

READ

Q: How would you summarize your key findings in plain language?

A: Our study was focused on how monocytic myeloid-derived suppressor cells (M-MDSCs) regulate neutrophil function during infection. M-MDSCs, a heterogenous population of immunosuppressive myeloid cells, are primarily studied in the context of cancer, but are also found in patients with severe infections. We found that M-MDSCs impair the innate immune response to *Pseudomonas aeruginosa* infection in an infection-on-a-chip model by reducing neutrophil extravasation and migration. Furthermore, we identified an increase in IL-10 in the presence of M-MDSCs and blocking IL-10 restored neutrophil extravasation, indicating one mechanism for M-MDSC-mediated suppression of the neutrophil response. This finding is novel because most research focuses on the ability of M-MDSCs to suppress T cell functions, especially in the tumor microenvironment, and the impact on other cells, including neutrophils, has not been explored.

Q: What initially sparked the idea for this study?

A: A significant portion of our lab is focused on understanding how multicellular interactions influence the innate immune response to infection. We had been investigating how M-MDSCs respond to infection and how that might contribute to immunosuppression. In learning more about these cells, we found the signals MDSCs release to suppress T cell function, including IL-10 and iNOS, were largely defined; however, these signals are not specific to T cells and the effect of MDSCs on other immune cell populations has not been thoroughly researched. Given the critical role of the innate immune response in protecting against infection, we wanted to determine how MDSCs might affect innate immune cells.


Laurel Hind

Q: Was there a moment during the project when the data surprised you?

A: We were surprised when we noticed decreased neutrophil extravasation to *P. aeruginosa* when MDSCs were embedded in the extracellular matrix. It was supposed to be a quick experiment to complement our study on the M-MDSC response to infection, but we were surprised by the magnitude of the change, and that experiment became the centerpiece of the study.

Q: What methods or approaches were especially important in allowing you to answer this question?

A: The infection-on-a-chip device was crucial. Our lab developed this device to investigate the human innate immune response in a physiologically relevant environment that includes a model blood vessel, a collagen extracellular matrix, primary human immune cells, and a live bacterial pathogen. Using this device for the present study allowed us to use all human cells and to mimic important aspects of an infection in a way that would not be possible with traditional *in vitro* approaches or an *in vivo* model.


Hannah Weppner

Q: What was the biggest challenge you faced during this study, and how did you overcome it?

A: HKW: Confirming the phenotype of our differentiated M-MDSCs. I started working on the T cell suppression assay during my first months, and it took a long time to learn the protocol and teach myself flow cytometry. I read a lot of papers and watched a lot of videos to learn flow cytometry, and I was grateful to our collaborator, Dr. Richard Tobin, who provided valuable insight into the assay.

Q: What do you enjoy most about doing research?

A: HKW: I like collaborating with other researchers to solve problems. Maya Singh, an undergraduate student who worked with me, was so fun to collaborate with. She worked really hard and provided many valuable insights. I also really enjoy troubleshooting. My background is in engineering, so I think it's fun to find the root cause of scientific problems.

LEH: I love discovering new questions and determining the best approach to investigate them. It is especially exciting when these questions arise out of an unexpected finding. Working on answering these questions with collaborators and trainees is also extremely rewarding. The interdisciplinary nature of our work allows us to work closely with immunologists and engineers, combining different ways of thinking and areas of expertise means I am always learning something new.

Q: How do you approach creativity or problem-solving when you hit a scientific roadblock?

A: HKW: I try many approaches when I hit a roadblock. I often turn to online papers and protocols to see how other people are approaching the problem, and I will ask other researchers to see if they have ideas. I also like to call customer service lines to discuss troubleshooting with product experts. I try to look at a roadblock as an interesting problem rather than a frustration.

LEH: Hannah is fantastic at creative problem solving. I always try to see the project from a higher level to determine if the roadblock is instead a change in path, like we experienced with this project. Our initial experiments investigating M-MDSC function were hard to optimize but the creative idea to look at their effect on neutrophils changed our path and led us to these exciting findings.

Q: What part of working in science brings you the most satisfaction?

A: HKW: I like how working in science, and especially in immunology, helps me understand the world around me. For example, I started graduate school during the pandemic, and being able to understand the biology behind testing, viral mutation, and vaccine development allowed me to stay informed and to inform those around me.

LEH: Pushing science forward to improve human health is one of the most satisfying parts of this work – I love seeing one of our results be used by another group to answer a new question. Science really is a community effort, and I appreciate that I am part of that community. I also find that working with trainees and helping them develop into independent scientists is one of the most rewarding parts of my job. Seeing the growth in their understanding and interpretation of science over the course of their graduate school career is a very rewarding experience.

Q: Looking ahead, what excites you most about where the field is heading in the next few years?

A: HKW: I am excited for future discoveries about M-MDSCs. Monocyte-derived cells have an outsized impact on disease outcomes, and I hope that new research will help us to understand their roles and develop therapies to address medical challenges.

LEH: I agree with Hannah. I am also excited to see the field broadening to become more interdisciplinary. Along with this, the rapid expansion of human immune models with increased complexity. I cannot wait to see what we can learn from studying human cells in increasingly relevant systems.

Q: What advice would you give to those that are at the beginning of their scientific journey?

A: HKW: I would tell a young scientist that the people around them are just as important as their research project. Research is a long and tiring process, and no matter how interesting your project is, there will be days when it feels overwhelming and impossible. I am grateful to work with people who are helpful, collaborative, and supportive, and I think graduate school would have been much more difficult without them.

LEH: For the development of your research: continue to ask questions and don't be afraid of failed experiments, for your personal and professional development: create a network of mentors that can support you. Working in science is a process of constantly learning from others and from your work – failed experiments often lead to new areas of inquiry and discussing your ideas and findings with experts in many areas broadens your understanding and insight into scientific questions. Creating a network of senior and peer-mentors that can contribute to your learning, professional development, and support you when you have a hard day is critical for success.

Prasad Tongaonkar & Michael Selsted, *University of Southern California, Los Angeles*, The macrocyclic peptide rhesus theta defensin 1 activates interferon and antiviral pathways in human monocytes

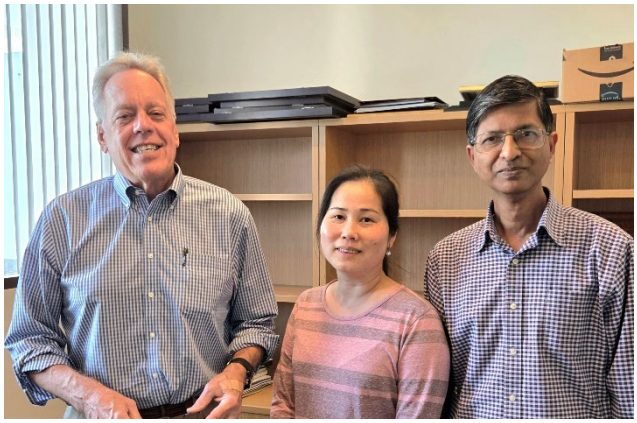
READ

Q: How would you summarize your key findings in plain language?

A: Theta (θ) defensins are the only known cyclic peptides in the animal kingdom. These are 18 amino acid residue, tri-disulfide linked peptides that are produced only in Old World monkeys such as rhesus macaques and baboons. In this study, using an RNAseq approach, we have shown that the θ -defensin, Rhesus Theta Defensin-1 (RTD-1), stimulates interferon and antiviral pathways in human monocytes and in THP-1 cells, a human monocytic cell line. RTD-1 stimulates activation of the Signal Transducer and Activator of Transcription Factor (STAT) 1 by phosphorylation at the tyrosine 701 (Y701) residue which plays a key role in these pathways. In a reporter-based assay, RTD-1 activated interferon-stimulated response element (ISRE) reporter, and this was inhibited by ruxolitinib, a Janus kinase inhibitor, and by neutralizing antibodies to IFNAR1, a type I interferon receptor, demonstrating a role for the interferon receptor pathway. Consistent with the stimulation of antiviral activity by RTD-1, RTD-1 inhibits infection of vesicular stomatitis virus (VSV) pseudotyped with either the VSV-G glycoprotein or with SARS-CoV-2 spike protein and inhibits infection of Calu3 2B4 cells by the SARS-CoV-2 virus.

Q: What initially sparked the idea for this study?

A: Though theta defensins were discovered due to their broad-spectrum antimicrobial activity *in vitro*, results from our lab have disclosed RTD-1 mediated regulation of host innate immune responses. RTD-1 inhibits secretion and gene expression of cytokines from immune stimulated cells by regulation of the NFκB and MAP kinase pathways. This raised the question of whether RTD-1 by itself had any effect on cellular gene expression and signaling pathways and if RTD-1 could induce an altered immune state in the cell.



Q: Was there a moment during the project when the data surprised you?

A: The revelation that RTD-1 treatment of monocytes stimulates expression of a large number of interferon stimulated genes (ISGs) was completely unexpected. This has opened a new area of research in our laboratory.

Q: What methods or approaches were especially important in allowing you to answer this question?

A: We used an unbiased RNAseq approach to evaluate the effect of RTD-1 on monocytic cell gene expression. This approach and the bioinformatics analysis of the differential gene expression was crucial in revealing the stimulatory effect of RTD-1 on interferon and antiviral pathways. Application of ISRE reporter cell line to demonstrate and analyze the role of RTD-1 in these pathways was the other pillar that supported this study.

Q: What was the biggest challenge you faced during this study, and how did you overcome it?

A: These studies were initiated before the COVID-19 pandemic, and we had to work within the restrictions during that time. However, this also provided us with a unique opportunity to study antiviral activity of the peptide against SARS-CoV-2 virus.

Q: What do you enjoy most about doing research?

A: PT: Being curious, asking *what* and *how* things work steered me towards research. I enjoy reading up on research topics; to me, framing a hypothesis and designing experiments to test it are the best parts in doing research.

MES: Discovery of the details that underpin regulation of physiology and pathology of biological systems is exceedingly rewarding.

Q: How do you approach creativity or problem-solving when you hit a scientific roadblock?

A: PT: By going over every step and by trying to identify potential issues with each step. Reading up on related topics and talking to people who are more knowledgeable plays a significant role in problem-solving. Sometimes taking a break from the problem at hand and getting back to it later gives a fresh perspective to the problem.

MES: Scientific roadblocks typically reveal something important, either about the system under study and/or limitations of the investigative tools being employed. In either case, creative solutions often emerge when pursued with rigor and without bias.

Q: What part of working in science brings you the most satisfaction?

A: PT: True satisfaction is when the discovery process, with all its struggles and challenges, finally leads to a published study.

MES: For me, integrating our findings with those of others, to build a greater understanding of biology is deeply satisfying.

Q: Looking ahead, what excites you most about where the field is heading in the next few years?

A: In the past few years there has been significant interest in using macrocyclic peptides as potential biotherapeutics. Theta defensins have therapeutic efficacy in murine models of polymicrobial sepsis, Candidiasis and rheumatoid arthritis and these peptides will likely serve as starting points for developing novel bioinspired macrocyclic peptides for treatment of diverse immune mediated diseases. The host directed nature of θ-defensin effects is a major advantage towards developing general purpose antivirals as a first line of defense against future pandemics. From an evolutionary standpoint, it is of interest why these unique peptides are produced only in Old World monkeys and not in human beings.

Q: What advice would you give to those that are at the beginning of their scientific journey?

A: PT: Keep an open mind and do not restrict yourself to your own area of research- read about diverse scientific topics. Discuss science with every researcher you meet. There will be failures along this journey, treat them as learning opportunities!

MES: I agree. And pay attention! Don't ignore a result because it seems to not make sense.

FASEB CORNER

FASEB
Federation of American Societies for Experimental Biology

A summary of the most recent science advocacy activity by FASEB

- FASEB Thanks Chairman Cassidy for Holding NIH Reform Hearing
- FASEB Issues Statement of Support for National Primate Research Centers
- FASEB Submits Feedback on NSF FY 2026-2030 Strategic Plan
- FASEB Submits Comments to OSTP on Accelerating the American Scientific Enterprise

COMING SOON! SLB 2027 ANNOUNCEMENTS

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contacts:
Membership
Meetings
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- Registration, abstract and award applications now being accepted through June 29th
- Volunteer to co-chair a concurrent session during abstract submissions – a great opportunity to network and get involved!
- Extended Special Interest Group offerings!
- Single tracked program – don't miss a thing!
- The t-shirts are back this year; complete your wardrobe!

Spotlight on MAIT Cells References

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