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AABB News

Advancing Antibody Therapies

Association for the Advancement of Blood & Biotherapies

Transfusion's Monthly Podcast

Tune into *Transfusion's* free monthly podcast, which examines questions big and small about transfusion medicine and its role in supporting patients and society. This podcast highlights new manuscripts published in *Transfusion*, along with broader topics that relate to transfusion and biotherapies.

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- Predicting vasovagal reactions
- Following up with low-iron donors
- Prehospital blood transfusion
- Components for patients with sickle cell disease
- And many more

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Looking to the Future

Brian Gannon, BA, MBA

It's been three years since the COVID-19 pandemic swept across the globe, upending our personal and professional lives and routines. The public health crisis plagued the health care system and exacerbated the strains to the nation's blood supply. But in that difficult time, our community came together and faced unprecedented challenges head on, from blood supply shortages and canceled blood drives to staffing shortages and limited resources. We became more resilient.

"No matter how much falls on us, we keep plowing ahead. That's the only way to keep the roads clear." –Greg Kincaid

This quote accurately reflects our community. In the face of adversity, we refused to give up. Instead, we forged ahead. We adapted and upheld our mission to improve lives by making transfusion medicine and biotherapies safe, available and effective worldwide. The camaraderie and support found within our community and the Association remind us that we are better together. And the lessons learned during the crisis leave us better prepared for the future.

Exciting Developments

This issue of *AABB News* focuses on antibody therapies. Our first feature article examines the past, present and future of COVID-19 convalescent plasma (CCP) as a viable treatment. The second highlights AABB's PLasma Antibody Network (PLAN), which was established at the height of the pandemic, and the group's efforts to advance the development of antibody therapies and strengthen the nation's preparedness and response. The third feature discusses a newly funded initiative to develop a field-deployable, shelf-stable whole blood equivalent that can be used to resuscitate trauma patients when donated blood products are not available.

In addition, *AABB News* debuts a new wellness column in this issue. "Be Well" will cover stress management, burnout and other pertinent wellness topics for your overall wellbeing. The last three years have taken a toll on many AABB members physically, mentally and emotionally. It is vital to make our wellness a priority to ensure the wellbeing of our community—another valuable lesson learned during COVID-19.

As we enter a new season this month, I hope you take a moment to reflect on our community's accomplishments, as well as your personal growth. We have made a lot of progress, and I am excited about what is ahead. ■

Brian Gannon, BA, MBA
AABB President

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Marie Hollenhorst: AABB Foundation Supports Critical Research in Transfusion Medicine

By Kendra Y. Applewhite, MFA
Managing Editor

Since its inception in 1983, the AABB Foundation has awarded more than $11 million to early-career investigators and supported investigator-initiated original research in all aspects of blood banking, transfusion medicine and biotherapies. *AABB News* recently spoke to Marie Hollenhorst, MD, PhD, a 2019 Foundation grant recipient, about the Foundation's mission to advance the field through scientific research and provide funding for early-stage investigators.

Hollenhorst is a scientist and physician with expertise in non-malignant hematology, transfusion medicine and chemical biology. Her research interests include the biology of platelets and coagulation factors, and her laboratory at Brigham and Women's Hospital and Harvard Medical School focuses on glycoproteins that play critical roles in hemostasis and thrombosis. Hollenhorst received her early-career scientific research grant from the AABB Foundation in 2019 for her research project titled "CMP-Neu5Ac: A Central Molecule in Bleeding Diseases and Mediator of a Novel Platelet Effector Function." She credits the Foundation for helping her advance in her career and establish the Hollenhorst Lab, which officially opened in January 2023.

"The AABB Foundation's research funding helped me obtain this position, which provides the opportunity to set up my own research lab; the lab will be devoted to platelet and coagulation factor glycobiology," she stated. "I'm particularly excited about launching my lab at Brigham and Women's Hospital because there is a robust community of glycobiologists here, including past AABB Foundation grant recipient Sean Stowell, who has done foundational work. There's also an outstanding platelet research community in Boston, so it is a rich environment for someone working at the interface between glycobiology and platelet biology/hemostasis and thrombosis."

Hollenhorst told *AABB News* that she took a non-traditional route into the field. She pursued combined MD and PhD training at Harvard University. During her residency in internal medicine at Brigham and Women's Hospital, she developed an interest in transfusion medicine while treating patients with complicated transfusion issues.

"I was drawn to taking care of patients with hematologic issues during my residency, and I interfaced closely with the transfusion medicine service on a number of cases," Hollenhorst said. "I realized that the transfusion medicine service does many interesting things, and that it is essential to deeply understand transfusion medicine to take care of some hematology patients. I wasn't learning about these issues in my internal medicine residency, so I sought out additional training in this area."

She subsequently completed a fellowship in transfusion medicine at Harvard Medical School and then a fellowship in hematology at Stanford. "My transfusion medicine knowledge helps me to take care of hematology patients. I really appreciate having the dual training," Hollenhorst said.

Collaboration

Hollenhorst recently co-authored a research article published in the *Journal of Thrombosis and Haemostasis*. The purpose of the study was to comprehensively analyze GPIbα amino acid sites of glycosylation (glycosites) and glycan structures. GPIbα is heavily glycosylated, and its glycans have been proposed to play key roles in platelet clearance, von Willebrand factor binding and as target antigens in immune thrombocytopenia syndromes.[1] Although the hemostatic protein is central to the bleeding and clotting process and important in platelet biology, the glycosylation profile of GPIbα was not well characterized, Hollenhorst noted.

"This protein is essential for platelets to bind to the endothelium, and without a proper interaction between platelets and the endothelium, we don't have

normal blood clotting," she explained. "There's a lot of interest in what the biological implications of GPIbα glycosylation may be. We think GPIbα glycans may be important for clearance of platelets in the context of thrombocytopenia and possibly following cold storage in the blood bank. There are all these different interesting ramifications of GPIbα glycosylation, but we have been unable to study them in any fine-tuned way because we haven't had the tools available previously to characterize these carbohydrate structures."

Hollenhorst first became interested in conducting research to understand the glycosylation of GPIbα while working with her colleague Stacy Malaker in Professor Carolyn Bertozzi's laboratory at Stanford University in 2019. She noted Malaker had pioneered a novel strategy that allowed them to study heavily glycosylated proteins and biochemically characterize different carbohydrate structures. "I was inspired that she figured out how to use bacterial enzymes as tools to chop up proteins that otherwise couldn't be analyzed. We started examining how we could use the methods she developed to study GPIbα," she said. "Our collaboration began there."

Throughout the duration of three years, Hollenhorst and her colleagues used mass spectrometry (MS) glycomics and glycopeptide analysis to perform a site-specific analysis of GPIbα purified from human platelets. Upon conclusion of their study, they identified 48 O-glycosites and 1 N-glycosite and determined that GPIbα carries diverse N- and O-glycans, including sialoglycans, Tn antigen, T antigen and ABO(H) antigens.[1]

"The biggest surprise to me about our data was the diversity of different glycan structures that we identified. The glycan diversity was stunning and much more than I would have predicted," she added.

Mentorship

When reflecting on her career, Hollenhorst expressed a deep appreciation for her mentors, noting their key role in her professional growth and development. She received a PhD in Chemical Biology under the mentorship of the late Professor Christopher T. Walsh, a "truly exceptional mentor" who inspired her to think about medical questions at a chemical and biochemical level and pursue a career at the interface of chemistry, biology and medicine. She also credited her recent mentor, Nobel laureate Carolyn Bertozzi, for helping her become more expansive and creative in her thought process.

"Carolyn has a passion for science. She likes to think about many different kinds of questions, and she's creative. I admire her ability to communicate complex scientific concepts clearly. I try to emulate that as much as I can," she said. "I have had great mentors at every phase of my career. I feel lucky that I had the opportunity to work with Chris and Carolyn, and also many wonderful clinical mentors in hematology and transfusion. I've had role models that have shown me how to do rigorous science, and cheerleaders who made me feel like I could do science at a high level."

The most rewarding aspects of her career, she stated, are taking care of her patients and mentoring the next generation. She looks forward to recruiting young scientists and hopes she can pay it forward through mentorship. "I'm excited that I can help members of my lab develop their own careers, and that I may be able to spark their interest in some of the scientific questions that fascinate me. I'm able to do this because of the Foundation award," she said. "I hope I can live up to the standard that my mentors have set as I start to mentor members of my own lab."

Giving Back

The AABB Foundation has helped to advance the careers of more than 200 researchers in the blood and biotherapies community. Contributions from the community help to enable the AABB Foundation to continue its support for early-career research and education initiatives. To that end, Hollenhorst encourages her colleagues to give back to ensure the Foundation can keep providing critical funding and mentorship opportunities for scientists in the transfusion medicine and biotherapies field.

"It is evident from the careers of investigators who have been supported by the AABB Foundation in the past that this funding mechanism helps to accelerate people's careers and supports research that is urgently needed and often under-appreciated by other funding agencies," Hollenhorst noted. "Many of the conditions we are studying are not recognized or funded to the same degree as other diseases, so it is important to foster our research in this area.

"The AABB Foundation's grant programs have a strong track record of supporting researchers who go on to be successful long after the award," she added. "I hope this will stimulate people to give back in support of the AABB Foundation's mission." ■

To learn more about the AABB Foundation and support its mission, visit *https://www.aabb.org/foundation*.

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Hollenhorst M, Tiemeyer K, Mahoney K., et al. "Comprehensive Analysis of Platelet Glycoprotein Ibα Ectodomain Glycosylation." *Journal of Thrombosis and Haemostasis*. January 13, 2023. https://www.jthjournal.org/article/S1538-7836(23)00037-5/fulltext