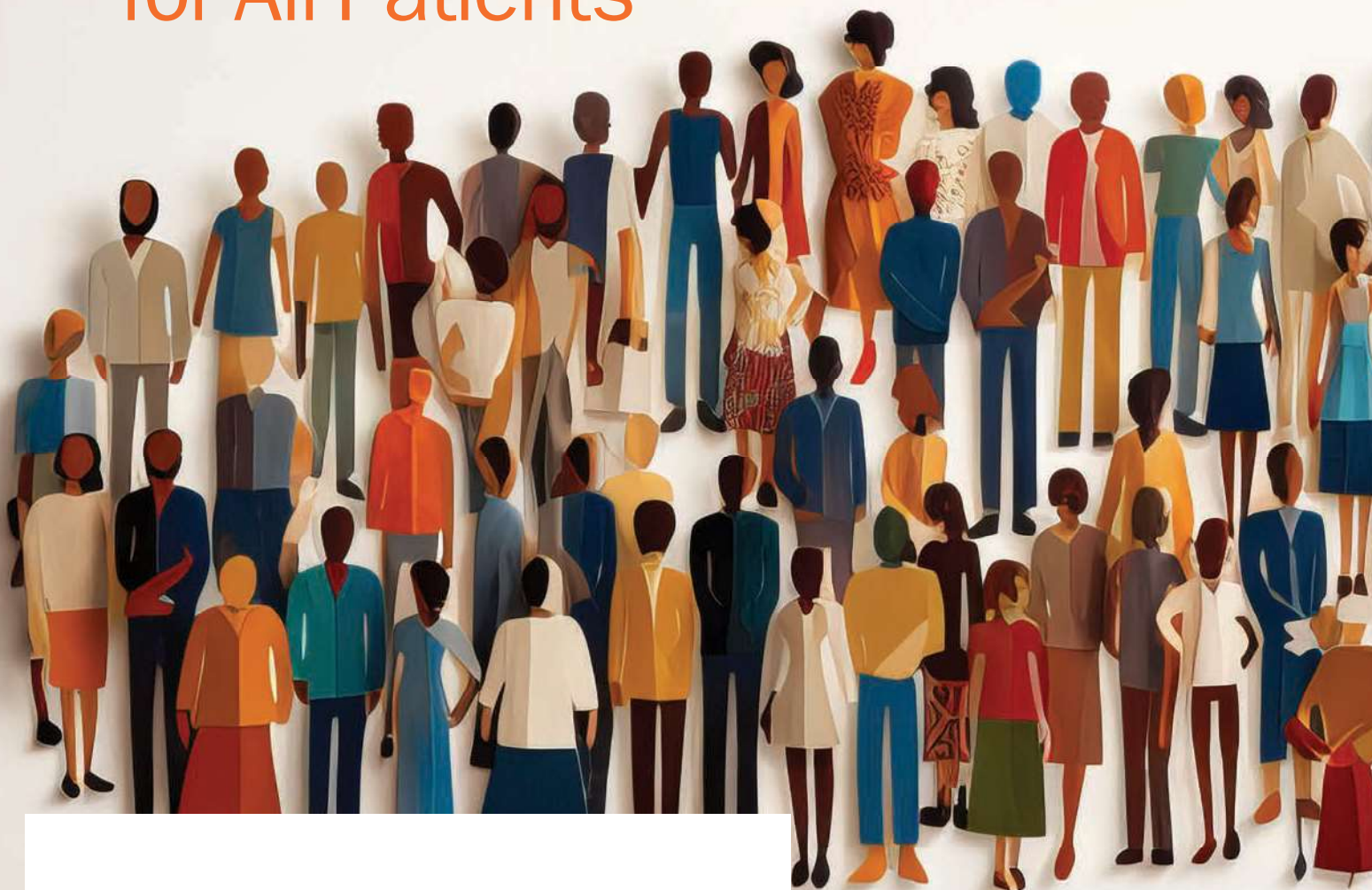


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Reaching Diverse Donor Populations

A closer look at strategies for increasing blood donations in underserved communities.



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Creative Campaigns Drive Awareness for Blood Donations

In honor of National Blood Donor Month, this issue highlights two unique and successful blood donation campaigns.



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Greetings and Happy New Year! I hope your 2025 is off to a great start. As we enter a new year, I want to take a moment to reflect on the significant progress we have made in our field. Our community and Association worked tirelessly last year to advance transfusion medicine and biotherapies. Your dedication, support and unwavering commitment to our profession have been instrumental in transforming patient care and improving lives worldwide.

The month of January is designated as National Blood Donor Month in the United States—a time to celebrate blood donors and remind people of the importance of donating blood. This month, we celebrate the extraordinary generosity of nearly 7 million individuals nationwide who selflessly donate blood every year. Moreover, we also laud and recognize the efforts of the blood and biotherapies community to preserve and maintain a safe and adequate blood supply.

Reaching Diverse Donor Populations

In 2023, we witnessed a monumental change as we implemented individual donor assessments (IDA) to determine blood donor eligibility, which marked the beginning of a new era in the blood community and helped to expand the donor pool.

Recruiting and retaining diverse blood donors, particularly donors of color, remains an ongoing challenge in our field. More work needs to be done to ensure the donor pool reflects diversity and meets the needs of patients from all backgrounds.



Meghan Delaney,
DO, MPH

This issue of *AABB News* focuses on building a diverse donor base and addresses the challenges of reaching diverse donor populations. The first feature highlights three organizations on a mission to address donor disparities and increase blood donations, particularly in historically underrepresented communities. The second feature explores two successful blood donor campaigns that used storytelling and community engagement to attract new donors.

In addition, this issue also honors the life of pioneering scientist Dana Devine, PhD, one of my predecessors as AABB president, and a personal friend and colleague. Dr. Devine left behind an incredible legacy, and her mentorship shaped the careers of countless emerging scientists. She will be missed, but certainly never forgotten. May her life's work continue to inspire us and future generations of transfusion professionals. ■

Meghan Delaney, DO, MPH
AABB President

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Foundation Grant Recipient Developed Tool to Aid in RH Genotyping

By Leah Lawrence
Contributing Writer



Yan Zheng, MD, PhD

Anyone even vaguely familiar with blood typing and blood donation knows that there are four main blood types—A, B, AB and O. Those with a little bit more knowledge may also be familiar with RhD, a protein on the surface of red blood cells that defines someone as “positive”—presence of the protein—or “negative”—absence of the protein.

However, Yan Zheng, MD, PhD, associate member at St. Jude Children’s Hospital in Memphis, Tenn., knows

that Rh antigens are much more than “positive” or “negative.”

“When we do blood transfusions you have to match the blood type; if someone is type A, you give them type A,” Zheng said. “But for Rh, it is a bit more complicated.”

Rh blood group is characterized by two proteins, RhD and RhCE, which express five main antigens—D, C, c, E and e—called “D,” “Big C,” “little c,” “Big E” and “little e.” These antigens are encoded by two genes called “*RHD*” and “*RHCE*.”¹

“Just like with ABO blood type, if someone is D-positive, we give them D-positive red cells,” Zheng said. “Somehow though some patients can start making D antibodies. It was very confusing.”

Rh alloimmunization is not benign and can cause hemolysis. The resulting Rh antibodies limit compatible red blood cells and can affect the care and survival of patients in need of transfusion, like those with sickle cell disease (SCD). The conundrum is caused by the presence of diverse *RH* variant alleles that exhibit various single nucleotide polymorphisms (SNPs), insertions/deletions, and complex structural variations. The variant alleles encode proteins that lack certain epitopes or express new epitopes, leading to increased

risk of Rh alloimmunization. Since routine serology typing cannot distinguish most Rh variants, RH genotyping and consideration of *RH* genotype matching can help to prevent *RH* alloimmunization.

Early in her career, Zheng took an interest in further characterizing these Rh variants. In 2019, Zheng received an AABB Foundation Early-Career Scientific Research Grant for her project, “Comprehensive Characterization of RH Loci by Whole Genome Sequencing and Long-read Genome Sequencing.” The project was designed to provide more comprehensive Rh blood genotyping.

Looking Deeper

“RH genotyping at that time was not widely used,” Zheng said, adding that the RH genotyping platforms that did exist only looked at the most prevalent *RH* alleles.

Zheng noted that in addition to being a children’s cancer hospital, St. Jude also treats several hundred patients with SCD. Together in a collaboration with hematology from St. Jude and Texas Children’s Hospital, Zheng was able to access whole genome sequencing (WGS) data for about 800 patients with SCD.

A colleague asked whether Zheng would be able to extract blood type from the WGS data, to avoid the need for serology typing. Use of WGS would also provide more information on *RH* genotype than the existing molecular tests could, including identification of rare and new alleles.

With the support of the grant, Zheng and colleagues developed a computation algorithm called RHtyper for accurate and high throughput RH genotyping from existing WGS data.² RHtyper was able to determine *RH* genotypes in about 3 minutes per patient.

The algorithm identified diverse RH genetic variations—38 *RHD* and 28 *RHCE* distinct alleles, and one

novel allele in the 800s patients with SCD. The results were published in 2020 in *Blood Advances*.

“More and more people are realizing that genotyping has really helped to improve transfusion safety,” Zheng said. “At my center, we have more and more relied on genotype for red cell antibody identification and red cell matching.”

Zheng said she has also seen that more blood donor centers are adopting genotyping technology for their donors as well to improve resource allocation.

More to Learn

Zheng’s original research funded by the grant has evolved into more projects.

“Whole exome sequencing [WES] is more popular than WGS because of its lower cost,” Zheng said. “Our next step was to modify our RHtyper to see if we can genotype using WES data.”

Despite its lower cost, WES data presented challenges because of “uneven sequencing coverage and exacerbated sequencing read misalignment.”³

In order to adapt RHtyper to WES, Zheng and colleagues had to harness the power of machine learning models. The resulting work was published in 2024 in *Blood Advances*. RHtyper was able to predict RHD and RHCE genotypes using WES with high concordance rates with WGS data in two large cohorts, patients with SCD and cancer survivors. Use of machine learning improved accuracy of RH prediction with WES data.

However, Zheng said a limitation of her original research was the use of short-read sequencing data. She explained that RHD and RHCE are duplicated genes with high homology and short-read sequencing can be difficult in detecting complex structural variations.

Her most recent project used long-read sequencing technology. Unlike short-read sequencing, which breaks DNA into pieces of 150-300 base pairs long, Zheng explained, long-read sequencing can generate reads more than 10,000 base pairs long.

In another study, Zheng and colleagues performed long-read sequencing in order to identify breakpoints of hybrid RHD alleles, which are structural variants and consist of sequences originating from both RHD and RHCE. Using this long-read technology, they were able to define precise breakpoints and, more importantly, discover three unique intronic SNPs for one of the most common hybrid alleles in patients with SCD, RHD*03N.01 or RHD*DIIIa-CEVS(4-7)-D.

“Since RHD*DIIIa-CEVS(4-7)-D encodes variant C that may result in anti-C,” Zheng said. “The intronic



SNPs provide a simple and low-cost method for detection, facilitating red cell matching and lowering the risk for alloimmunization.”⁴

“We have developed one more tool in our toolbox for red cell typing,” Zheng said. “I imagine in the future that most healthy people may have their sequencing data, like a fingerprint. In that case, we have provided a way to look for blood type from that sequencing data without having to do serology testing.” ■

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To learn more about the AABB Foundation grant program and how you can donate to help further critical research like Zheng's, visit aabb.org/foundation.

Reaching **DIVERSE** Donor Populations

Three organizations share strategies for increasing blood donation in underrepresented communities.

By Kendra Y. Applewhite, MFA
Managing Editor

