Addressing Ethics in Cellular Therapies and Transfusion Medicine
Optimize blood and plasma management across collection operation, region, division and enterprise with InVita.

Our platform connects the people, information and processes to ensure the availability of blood products when they are needed. Integrating data from hospital orders, demand planning, staffing, mobile drives, donor recruitment, product quality control and equipment maintenance into one platform makes it easier to oversee compliance, quality and cost.

Real-time data provides visibility into issues across the supply chain, empowering staff to make dynamic, proactive adjustments. InVita’s integrated solution provides the tools that drive automated processes and efficiencies in all areas:

- HemaControl: Hospital order entry
- HemaConnect: Donor recruitment and engagement
- HemaCollect: Mobile drive and collections staffing
- HemaComply-Lab: Product QC
- HemaComply-Equipment Manager: Equipment maintenance

Want to learn more? We’re here to help.
Info@invitahealth.com / InVitaHealth.com / 904.288.5999

Our blood and plasma platform is based on a legacy of excellence started by HemaTerra Technologies. Now, under InVita Healthcare, expect more great things.
The Ethical Considerations of Cellular Therapies

As the potential uses of cellular therapies expand, ethical issues are emerging with respect to the use of unproven treatments, informed consent and access to clinical trials.

Ethics in Transfusion Medicine

Clinicians are using frameworks and consulting bioethicists to address ethical dilemmas.
Reflections on the Past Year

I t’s hard to believe that my tenure as AABB president will soon come to an end. Last year at the AABB Annual Meeting in San Antonio, when I picked up the president’s gavel, I never imagined that much of my term would be spent helping our community navigate a deadly pandemic nor envisioned the sacrifices that COVID-19 would demand of us. But that has been the reality of 2020, and I’m proud of how we have responded to the hardships and uncertainties of this unprecedented time.

Despite the challenges of the past year, our community has stayed focused on our mission. Those of us in transfusion medicine and in biotherapies called on to give 100% have given 110%. Those working in donor centers began collecting convalescent plasma at breakneck speed. We have had to adjust to numerous changes to meet guidelines to ensure the safety of our donors, our patients and ourselves. And we have responded by becoming experts in Zoom meetings, face masks and social distancing. Throughout it all, we have united as never before, and our community is stronger now for our efforts. And because the pandemic is ongoing, we continue to adapt, and we will continue to adapt for as long as it takes, as that’s what we’ve always done to meet the needs of the patients who depend on us.

**A Changing Association During Challenging Times**

During this period of intense transition, AABB has also changed. After we launched our new strategic plan at last year’s Annual Meeting, we began making some changes to the Association to better serve you — our members. The strategic plan’s renewed focus on fostering a connected community came just before the pandemic required us to forego in-person meetings, and we expanded our platforms to better communicate with our members. We also increased transparency.

This will be my final column as AABB president. I will truly miss seeing everyone, and I hope you will continue to connect with me on an individual basis. I thank everyone I worked with during this unprecedented year: my fellow Board members, my colleagues at New York Blood Center and Duke University, AABB staff and, most importantly, our members. Although I won’t be able to hand David Green the president’s gavel in person, I wish him all the best as he assumes the presidency and we continue to navigate this pandemic together.

Beth Shaz, MD
AABB President
NEW! UltraCW II Automatic Cell Washer

Exceptional performance and consistent, reproducible results for high performance automated cell washing

» Intuitive programming makes creating streamlined workflows a breeze
» Designed to provide consistent, reproducible results with precise saline fills
» Safe and easy to use with time saving performance

Reliable, safe, and effective solutions help you provide the highest standard of patient care.

For more information:
info.helmerinc.com/ultracwII

TrueBlue™

© 2018 Helmer Inc. All rights reserved.
Angelo D’Alessandro Receives 2020 NBF Award for Innovative Research

By Jerilyn Schweitzer, MA
Managing Editor

The National Blood Foundation has named Angelo D’Alessandro, PhD, as the recipient of the 2020 NBF Award for Innovative Research. D’Alessandro is a tenured associate professor and director of the Metabolomics Core of the School of Medicine and Colorado Cancer Center in the Department of Biochemistry and Molecular Genetics at the University of Colorado Denver’s Anschutz Medical Campus.

D’Alessandro received the prestigious award in recognition of his 2016 National Blood Foundation-funded research on the role of adenosine signaling in the preservation of energy metabolism in stored erythrocytes. For the study, he used and integrated metabolomics and proteomics with a functional approach to investigate the role of adenosine signaling through the ADORA2B/AMPK axis in both mouse and human red blood cells during storage. In order to conduct this research, D’Alessandro developed high throughput omics methodologies that have had an impact on the most diverse fields of biomedical research, from cancer metabolism to inflammation, and high-altitude hypoxia to hibernation, and — most relevant to AABB — personalized transfusion medicine applications.

He told AABB News that receiving the NBF’s early-career Scientific Research Grant was instrumental in helping him secure federal funding.

Overall, D’Alessandro has supported research projects involving more than 70 international colleagues. Since completing his NBF grant-funded project in 2017, he has authored approximately 150 papers in peer reviewed journals, including Cell, Nature Medicine, Cancer Cell, Cell Stem Cell, Cancer Discovery and Blood. He is currently the Principal Investigator in projects funded by three R01 and one R21 research program grants sponsored by the National Heart, Lung, and Blood Institute.

D’Alessandro noted that the underlying hypotheses for all of these projects were generated as a result of observations he made during his NBF-funded research.

Research funded through the NBF early-career grant also earned D’Alessandro the 2020 Jean Julliard Prize from the International Society of Blood Transfusion and fostered critical collaborations that led to the funded research projects on which he is currently working.

“In this era of social media, social science is an essential strategy to coalesce complementary expertise to mechanistically dissect specific hypotheses,” he said, “I couldn’t be luckier than I am to have the collaborators I get to learn from on a daily basis, most of whom are NBF grant recipients, Scholars or Hall of Fame inductees themselves.”

D’Alessandro will be recognized as this year’s recipient of the NBF Award for Innovative Research during the NBF Research Symposium, an exclusive premier showcase of innovative research impacting the field. This invitation-only event will take place on Monday, Oct. 5 at 12:30-2 p.m. ET.
BRINGING FLOW CYTOMETRY TO LIFE
Applications in Cellular Therapies

AABB’s newest online education course, “Bringing Flow Cytometry to Life: Applications in Cellular Therapies” introduces students to flow cytometry and how it is applied to characterize many of the cells used in cellular therapies today. The course includes interactive examples to simulate real-world experience – bringing flow cytometry to life!

The course is divided into 3 sections that highlight important aspects of flow cytometry practice. Students will test and apply knowledge in a series of exercises. A glossary and list of supporting reference material is included.

WHAT IS COVERED:

SECTION 1 Foundational Concepts in Flow Cytometry
SECTION 2 Cell Therapy Applications Using Flow Cytometry in the Cell Processing Laboratory
SECTION 3 Review of Concepts – Applying What You Have Learned

MEMBER: $395 | NONMEMBER: $450

A 15% discount is available for institutions purchasing the program for 4 or more people.

aabb.org/flowcytometry
The Ethical Considerations of Cellular Therapies

By Leah Lawrence
Contributing Writer

listed first among the ethical and professional principles in the AABB Code of Ethics is to “Apply available evidence and ethical principles to provide products and services that optimize the delivery of safe and efficacious care to patients and donors.” However, the expansiveness of the field of “cell-based research” and the experimental nature of most cell-based therapies have led to a plethora of ethical issues related to their use.

Stem cell and other cell-based therapies offer the potential to treat a variety of diseases and conditions for which few — if any — treatments exist.

“A lot of people desperately want these treatments, but the majority of them remain unproven in rigorous studies,” said Quentin Eichbaum, MD, PhD, MPH, professor of pathology, microbiology and immunology, and of medical education and administration at Vanderbilt University School of Medicine, Nashville, Tenn. “Even for proven treatments, outcomes can depend on disease background and patient and other factors, and procedures can have widely varying levels of success.”

Use of these treatments, both within the context of translational research and in the more harrowing world of direct-to-consumer clinics, brings with it a variety of ethical considerations.

Direct-To-Consumer Stem Cells

One ethical issue at the forefront of cellular therapies is the growing market for direct-to-consumer “stem cell-based” treatments. The market for unproven stem cell treatments started when overseas clinics began advertising stem cell-based treatments for conditions varying from orthopedics to issues associated with aging, to macular degeneration, stroke, spinal cord injuries and more.

“There was a company, for example, in San Diego that advertised treatments, claiming that 100% of customers were satisfied with injections of mesenchymal stem cells,” said Jeanne F. Loring, PhD, professor emeritus and director of The Center for Regenerative medicine at Scripps Research. “The work was not actually taking place in San Diego though, but over the border in Mexico.”

Between 2005 and 2010, this type of “stem cell tourism” was rampant, said Loring. More recently though, direct-to-consumer clinics have popped up in the U.S., as well. When these clinics were not shut down immediately or taken to court
by the Food and Drug Administration, many clinic owners assumed they were safe and expanded operations, she said.

The only stem cell-based products approved by FDA for use in the U.S. consist of hematopoietic progenitor cells derived from cord blood.2

Any other therapies being advertised as “miracle” treatments should be viewed with skepticism, according to Indira Guleria, PhD, assistant professor of medicine at Harvard Medical School.

A 2016 FDA workshop discussed several cases in which patients who received unapproved treatments experienced severe adverse events — such as blindness or spinal cord tumors.2 A 2018 study found 35 cases of acute or chronic complications or death after alleged stem cell administration.3

“People are often in search of a miracle. These clinics should be marketing only legitimate treatments, and any legitimate treatment would have gone through regulatory approval and the multiple phases of clinical trials,” Guleria said. “Instead, people are often left paying large amounts of money for unproven — and possibly dangerous — treatments as a result of misguided hope.”

FDA has the authority to regulate stem cell products in the U.S., but it does not have sufficient resources to investigate every clinic claiming “magical” cures, according to Abba C. Zubair, MD, PhD, a professor of laboratory medicine and pathology at Mayo Clinic, Jacksonville, FL, and a Foundation for the Accreditation of Cellular Therapy (FACT) inspector.

“Anyone who travels abroad is going outside of the safety net of the FDA,” Zubair said. “When dealing with these stem cell clinics, people are trusting them with their life and hoping that everything will be ok. If anything sounds too good to be true, it is likely just that.”

Informed Consent

Participants’ understanding of the risks and potential benefits of a trial is of critical importance. Even within the context of translational research conducted at a major academic center, the ethics surrounding informed consent are complex.

“Sometimes, for example, you have a mismatch in understanding between investigators conducting the clinical trial and the individuals approached to participate,” explained Leigh Turner, PhD, associate professor at the Center for Bioethics, School of Public Health & College of Pharmacy at the University of Minnesota.

The researchers view the experiment as one that will develop generalizable scientific knowledge but not necessarily benefit individual study participants.

“In contrast, the participants may participate in the trial because they think it will provide direct therapeutic benefit for them,” Turner said. “They sometimes think of it not as a clinical study, but as gaining access to the best treatment currently available.”

For example, a study of about 40 early phase gene transfer studies showed that the language used in principal investigators’ discussion and in the informed consent forms “was mostly vague, ambiguous and indeterminate about benefit, rather than clearly negative.”4

Even when the informed consents are very well written, it is not always enough to ensure that trial participants understand the nature of the research, according to Loring.

“Some people just go to the last page and sign it,” she said. “It is like reading a long legal document.”

One example where patient understanding and consent created an ethical issue was the Geron trial of human embryonic stem cells for spinal cord injury. Although initially approved by FDA, the trial was halted after only four patients received the intervention. The trial’s design was controversial partially because patients were enrolled so soon after a serious injury, making their consent in a first-in-human trial challenging.5

Even academic researchers have to be careful around the language and hyperbole that can be used when discussing stem cell treatments, said Turner.

“Hyperbole doesn’t just come from direct-to-consumer clinicians but also from academic medical centers and press offices for major research universities, and can even be baked into peer reviewed articles,” Turner said. “There is a whole lot of hype around stem cells, and that can lead to an increased chance for misunderstanding on the part of a research participant.”

Years ago, Loring wrote the informed consent statement for an experiment involving the use of cells from skin biopsies that were reprogrammed into induced pluripotent stem cells for research.

“I included everything that was known at the time about the topic, but I had the additional requirement that I make sure that every single patient heard from me and had all their questions answered,” said Loring. “That is unusual though. A lot of people don’t have time for that and it is simply not done.”

Loring also noted the importance of informed consent for cell and tissue donors. One area
commonly mentioned in any discussion of ethical considerations regarding donors’ rights is the use of umbilical cord blood. In many cases, cord blood is donated with altruistic intent. However, cord blood may also be used to develop commercial products to be sold for a profit. Ethically, the collector should disclose the potential for any type of commercial use of donated blood or tissue in informed consent documentation or provide an option to dispose of the donation in situations where altruistic or non-profit use is not possible.

For both donors and recipients, all of the uses of the product and potential risks and benefits must be clearly explained. Zubair emphasized.

“There should never be any coercion or remuneration offered to entice people, beyond compensation for the inconvenience of participation in a trial, like fees for parking or taxis,” Zubair said. “Use of money to entice creates many ethical issues.” For instance, offering payment could create an incentive for donors to lie to meet eligibility criteria.

Ethics of Access

The U.S. health care system also creates the ethical conundrum that only certain patients can afford some of the most advanced cell-based treatments, according to Eichbaum.

“How does one ask who deserves to get treated from an ethical point of view?” he said. “In reality, it is often wealthier people who have the most access.”

One of the most recent examples demonstrating difficulties with access to care relates to the use of chimeric antigen receptor (CAR) T-cell therapy. CAR T-cell therapy works by removing a patient’s own T cells and genetically engineering them to produce receptors on their surface called CARs. These CARs allow the T cells to recognize and attack specific proteins on tumor cells.6

There are currently two FDA-approved CAR T-cell therapies in the U.S.: axicabtagene ciloleucel (Yescarta, Kite Pharma, Inc.) for adults with relapsed or refractory large B-cell lymphoma and tisagenlecleucel (Kymriah, Novartis Pharmaceuticals Corp.) for certain pediatric patients with acute lymphoblastic leukemia (ALL) or adults with relapsed or refractory large B-cell lymphoma.7,8

Both of these treatments carry a high price tag ranging between $373,000 to $475,000 per infusion. Additionally, the price of the treatment does not include many other associated medical costs, such as post-infusion care for management of complications and associated out-of-pocket expenses, such as the cost of housing that is close to the treatment center and that may be needed for as long as 4 weeks.9

“CAR T cells are an example of a promising therapy that is worlds away from the types of scams seen in the stem cell direct-to-consumer arena but that is also in its own world in terms of costly therapeutics,” said Turner.

Even for a more established treatments, like allogeneic hematopoietic stem cell transplant, costs can be as high as $80,000 to $137,00 or more.10

“It raises the issue of do you want to have a world where people are desperate for care and going on things like GoFundMe to cobbled together small donations from friends, family and strangers?” Turner asked. “Or, should we have a better social arrangement, where products are more affordable or we have a publicly funded system to promote affordability and accessibility?”

As the potential uses of cell-based therapies continue to expand, these and emerging ethical issues related to consent, use and access will persist and take on increasing importance.

ENDNOTES


AABB.ORG OCTOBER 2020 AABB NEWS

9