

HUMAN TISSUE ROUNDTABLE: INCREASE THE AVAILABILITY AND QUALITY OF HUMAN TISSUES IN SCIENCE

Roundtable Flash Report

On Oct. 25, 2018, the Physicians Committee for Responsible Medicine gathered 23 stakeholders including scientists, policy experts, physicians, and leaders from U.S. federal agencies and nongovernment organizations at its Washington, D.C., headquarters. Participants were charged with identifying the challenges of using human tissues in research and to cultivate a strategy to help meet the needs of the basic and translational research communities to increase the availability and quality of human tissues in biomedical and translational research.

The roundtable discussion highlighted the need for an augmented tissue donation process through streamlining donation consent forms and improving the communication pathways between donors, medical personnel, and Organ Procurement Organizations (OPOs). Additional key recommendations are outline below.



Session 1: Setting the Stage

Speaker: Edward LeCluyse, LifeNet Health

It's becoming more recognized that animals do not accurately represent human diseases and biologically and physiologically relevant models are necessary for scientific advancement. Human tissues and cells from healthy and diseased donors have become a critical part of research; they are

invaluable resources for medical research, disease modeling, diagnostic tests, biomarker discovery, drug development, product testing, chemical exposure, and much more. Fresh tissue samples are, for many applications, the preferred model environment to conduct in-depth analyses of human biological processes. However, access to high-quality human tissues and cells isn't always feasible, consequently many researchers turn to using animal tissue instead.

The main objective of the first roundtable is to identify the challenges faced by tissue procurers and users and provide recommendations for overcoming them.

Ongoing Objectives Include

- Establish standardized methods and quality control metrics for the recovery and provision of human tissues and cells
- Improve policies and regulation to increase donation and availability of human tissues for research
- Coordinate efforts amongst all principal stakeholders
- Develop a roadmap with recommendations for future scientific advancement and education
- Increase donation rates of tissues for research to meet a growing demand

Session 2: Addressing the Challenges

Speakers: Timothy Pruett, UMN; Thomas Buersmeyer, Lifenet Health; Gina Dunne Smith, IIAM; Sharon Presnell, Samsara Sciences; G. Sitta Sittampalam, NIH/NCATS; Scott Brubaker, FDA/DHT, Jean-Louis Klein, GSK

The use of human tissues in scientific research has improved health care by leading to numerous new discoveries in disease progression, drug development, and medical procedures. Presenters discussed the benefits of using human tissues; the primary benefit being that results more directly translate to outcomes that are applicable to human health. A growing number of researchers are recognizing that studies in animals do not provide them with relevant results.

Accessibility and quality are often cited as the main barriers of using human tissues and cells for scientific advancement. Frequently, researchers express that they simply do not have enough



tissues to carry out their studies or that the tissues are not of high quality, which hinders their results and reproducibility.

The Human Tissue Roundtable had seven presenters who represented the full spectrum of this topic, from a transplant surgeon who initiates the cycle of tissue recovery in the operating room to a scientist who uses human cells to study drug development for preclinical trials. The speakers presented on the context and magnitude of human tissues in research in their respective fields. Common themes included challenges of human tissues research, issues with using animals in research, difficulty in recovering tissues and cells, unknown variability in tissues that can impede a scientist's research, lack of oversight on the sourcing of human biomaterial, and absence of medical history with tissues.

Timothy Pruett, M.D., a transplant surgeon at the University of Minnesota, provided an overview of the lessons learned from transplantation, including some of the key measures and assessments of cellular function that are vital in assuring the beneficiary gets the best organs, tissues, or cells. Dr. Pruett discussed the intrinsic and extrinsic variables of organ quality and the role they play in transplantation. Intrinsic variables can include donors' stress, age, and body mass index, while extrinsic variables may include delayed donation, ischemia time, and preservation techniques.

Thomas Buersmeyer, M.H.A., the vice president of partner relations at LifeNet Health, described the role of an OPO, how they operate, and how each OPO's approach to securing tissues for research is different. In the hierarchy of donation, organ transplant is the driving use, followed by tissue recovery, and tissues and cells for research applications follow. Some of the challenges Mr. Buersmeyer expressed in recovery of tissues for research include requests for specific diseases, the quantity of tissues researchers request, the time at which donations take place (e.g., nights, weekends, holidays), and the operational constraints many OPOs face. He also shared that many families of recently deceased patients with chronic diseases are motivated to donate their relative's tissues to research to help others suffering from the disease.

Gina Dunne Smith, the director of the International Institute for the Advancement of Medicine, provided a deeper understanding into the world of organ donation and research tissue organizations. Ms. Dunne Smith compared the idealistic versus realistic expectations of available human tissues for medical research and therapeutic development, highlighted the many applications for human tissues in research, and described the need for the involved parties to recognize opportunities and resources to acquire human tissues. Unfortunately, only 10 percent of available organs are placed with researchers each year because of challenges connecting the right tissues with the right researchers.

Sharon Presnell, Ph.D., the chief scientific officer and president of Samsara Science, discussed the company's role as the "intermediary" of the tissue and cell supply industry. Samsara obtains tissues from the OPOs, processes the tissues for cell isolation, and generates primary cells that are subsequently used by end-users for in vitro models and regenerative medicine applications. Dr.

Presnell addressed the need for standardization of definitions and measures (e.g., how to define “normal tissue”) and the ability to identify and regulate the controllable factors, while at the same time accepting that human donors are inherently heterogeneous.

G. Sitta Sittampalam, Ph.D., the senior advisor to the National Center for Advancing Translational Sciences Director at the National Institutes of Health (NIH), stressed the challenges of using human primary cells of varying quality and inadequate standardization, which results in inconsistent performance and research results. Dr. Sittampalam also emphasized the need for establishing rigorous standards for human tissue procurement to ensure a constant supply of high-quality cells. One challenge NIH is tackling is related to collecting and processing patient data related to tissues and cells collected. Privacy laws sometimes prevent researcher access to this data, and NIH is investigating how artificial intelligence such as neural networks can help to collect, process, and interpret data related to the health status of research tissues.

Scott Brubaker, the director of the Division of Human Tissues at the Food and Drug Administration (FDA), focused on tissues intended for therapeutic use; however, he emphasized some available FDA guidance and best practices which may be useful, if adapted, for tissues intended for research use.

Jean-Louis Klein, Ph.D., the scientific director at GlaxoSmithKline, summed up the sources of variability in human cells as “the good, the bad, and the ignored.” Dr. Klein discussed the benefits of having a diverse pool of tissue donors and that the biological variability of cells needs to be preserved from humans to the dish, emphasizing that when a reductionist approach to complexity is the wrong approach. The major challenges he faces as an end-user result from the lack of standardization and documented methodologies for the collection and processing of the tissues and cells, the lack of technical information on the cells he receives, and the lack of characterization of the original organ or tissue.

Overall, the presentations and associated discussion accentuated the need to address the availability and quality of human tissues and cells for research. Participants learned that better connections should be made between procurement organizations and end users, as it’s likely that some available cells and tissues go unused.

Session 3: Breakout Group Discussions and Recommendations

Breakout Groups: Scientific and Technical; Legal and Policy; Education and Training

The roundtable concluded with the team forming three breakout groups, followed by a group discussion of the critical factors hindering the availability and quality of human tissues for research and what steps need to be taken to make improvements.

Major Recommendations

- To increase the availability of human tissues, streamlining of donation consent forms to single-approval “check boxes” is recommended.
- There is an immediate need for education and improved communication pathways between donors and medical personnel: All parties need to better understand the importance of human tissue research, dispelling negative connotations around “laboratory research,” and the need for fresh tissues.
- Training and communication related to the collection of research tissues for OPOs is needed.
- Metrics are important to assess quality and adequacy of tissues: Standard definitions of quality and minimum quality specifications should be established.
- An overarching priority is the need for standardization of use, language, characterization, cell type, and recovery and procurement practices.
- Funding should be prioritized for human tissue research and promoting open access data.
- Revise federal agency policies that “prescribe” research or tests using animals as the preferred method.

There was a general agreement between roundtable attendees that a collaborative approach is required—this should include all relevant parties, including OPOs, industry, U.S. federal agencies, governing organizations like the American Association of Tissue Banks and the Association of Organ Procurement Organizations, and patient advocacy groups, among others. Cross-sector communication is going to be vital in order to implement and enforce changes to the current state of human tissue research. There are best practices documents already in existence for biospecimen resources and biorepositories; we are working to build upon what is already in place and build efforts to address the gaps and limitations in the available resources.



The Physicians Committee is working to build relationships with fundamental stakeholders and continue the momentum that has resulted from the Human Tissue Roundtable. We will be holding

follow-up meetings in the future to engage with our colleagues on this topic and continue working towards our objectives; we will also publish a manuscript on our findings and recommendations. We are confident that the pursuit of these activities will facilitate greater access to and use of high-quality human tissues for biomedical and translational research.

Participants

Emily Anderson, M.S., Physicians Committee for Responsible Medicine
Elizabeth Baker, Esq., Physicians Committee for Responsible Medicine
Christopher Black, Ph.D., BioIVT
Scott Brubaker, Food and Drug Administration
Thomas Buersmeyer, M.H.A., LifeNet Health
Murat Cirit, Ph.D., Massachusetts Institute of Technology
Kerrie Copelin, M.B.A., National Disease Research Interchange
Nancy Dock, Ph.D., Lonza
Dan Dryden, BioIVT
Jean-Louis Klein, Ph.D., GlaxoSmithKline
Ann Lam, Ph.D., Physicians Committee for Responsible Medicine
Edward LeCluyse, Ph.D., LifeNet Health
Feng-Yen Li, Ph.D., Physicians Committee for Responsible Medicine
Jason LoVerdi, M.H.A., Lonza
Janine McCarthy, M.P.H., Physicians Committee for Responsible Medicine
Elijah Petersen, Ph.D., National Institute of Standards and Technology
Sharon Presnell, Ph.D., Samsara Sciences
Timothy Pruett, M.D., University of Minnesota
G. Sitta Sittampalam, Ph.D., National Institutes of Health
Gina Dunne Smith, International Institute for the Advancement of Medicine
Valerie Soldatow, M.S., LifeNet Health
Kristie Sullivan, M.P.H., Physicians Committee for Responsible Medicine
Donald Tweedie, Ph.D., Merck