Published in final edited form as:
Clin Transl Sci. 2013 June ; 6(3): 226–231. doi:10.1111/cts.12032.

How to Build an Integrated Biobank: The Washington University Translational Cardiovascular Biobank & Repository Experience

Kathryn A. Yamada, Ph.D.[1,*], **Akshar Y. Patel, B.A.**[1], **Gregory A. Ewald, M.D.**[1], **Donna S. Whitehead, R.N.**[1], **Michael K. Pasque, M.D.**[2], **Scott C. Silvestry, M.D.**[2], **Deborah L. Janks, Ph.D.**[3], **Douglas L. Mann, M.D.**[1], and **Jeanne M. Nerbonne, Ph.D.**[3]

[1]Department of Medicine (Cardiovascular Division), Washington University School of Medicine, St. Louis, MO

[2]Department of Surgery (Cardiothoracic), Washington University School of Medicine, St. Louis, MO

[3]Department of Developmental Biology, Washington University School of Medicine, St. Louis, MO

Introduction

Biomedical research has undergone a paradigm shift since sequencing of the human genome opened the door to a deeper understanding of the molecular basis of human disease and spawned an explosion in cutting edge technologies applied to elucidating mechanisms specifically relevant to human disease states. Despite the enormous and invaluable contribution that experimental animals have made to our understanding of both physiology and disease pathogenesis in humans, it has become increasingly clear that pathogenesis, development of potential treatment strategies and therapeutic efficacy would, at some point in the preclinical investigatory pathway, be best assessed in human, as opposed to animal, tissues. Human tissue sampling is also imperative for fulfilling the potential promise of personalized medicine realized from advances and insights generated from next-generation sequencing[1] and disease- and patient-specific induced pluripotent stem cells.[2]

Biospecimen science is an emerging multidisciplinary field dedicated to establishing procedures for the collection, processing, shipping and storage of biospecimens that have been experimentally tested and rigorously validated to limit alterations in the quality, composition and consistency of the collected samples.[3, 4] Several outstanding reports emanating from organizations such as the International Society for Biological and Environmental Repositories (ISBER)[5] and the National Cancer Institute's (NCI's) Office of Biorepositories and Biospecimen Research (OBBR)[6] have delineated published methods and best practices for sample processing, quality control and documentation and should be consulted for their wealth of requisite considerations.[7,8]

The purpose of this article is to detail the parameters that we have found to be critical for success in the development and maintenance of an integrated cardiovascular biospecimen repository, the **Translational Cardiovascular Biobank & Repository (TCBR)**, established at Washington University School of Medicine. The TCBR was founded for the acquisition (using standardized, validated procedures), utilization and storage of human cardiovascular tissues for detailed phenotypic (electrophysiological, structural, molecular and biochemical) and genotypic (genomic, epigenetic and somatic) analyses. Our repository houses a

[*]Address correspondence to: Kathryn A. Yamada, Ph.D., Cardiovascular Division, Campus Box 8086, Washington University School of Medicine, 660 South Euclid Avenue, St. Louis, MO 63110, U.S.A., Telephone: 314-362-8901, FAX: 314-362-8957, kyamada@dom.wustl.edu.

collection of cardiovascular tissues, including blood products, that is fully integrated with clinical information from the patients or the individuals who have donated the tissue, as well as experimental data emanating from the tissue samples.

A number of institutions have established human heart tissue biobanks and these include the Harvard Human Cardiovascular Tissue Bank (http://cardiogenomics.med.harvard.edu/component-detail?project_id=236), the University of Pennsylvania Human Heart Tissue Bank (http://somapps.med.upenn.edu/ohr/card/viewpub.php?rc=N&type=display&pub=Y&sqlstr=protocol%20*%20802781), and the Vanderbilt Human Heart Tissue Bank (http://www.vanderbilthealth.com/cardiovascular/23792); the most mature entity is the pediatric Heart Centre Biobank at the Hospital for Sick Children in Toronto (http://www.heartcentrebiobank.ca/home/index.php). However, despite the increasing number of human heart tissue banks being established, a specific, practical "instruction manual" outlining each of the required elements of a successful biobank replete with regulatory considerations, specific infrastructure recommendations, as well as pitfalls and problems to avoid, does not exist.

Background

Heart failure, with a prevalence of up to 10% in those over the age of 65, is a leading cause of hospitalization and death.[9] The physical and economic costs are staggering; it is the one notable heart disease that is increasing in incidence, morbidity and mortality without effective means for preventing or reversing end-stage deterioration of cardiac function. The only options for patients with end-stage heart failure who are no longer responsive to the disease-mitigating effects of medical therapies are orthotopic heart transplantation or implantation of a ventricular assist device (VAD). As alluded to above, we now know more about cardiac physiology at the cellular and molecular levels in the mouse, rat, rabbit and dog than we do in humans. Furthermore, our understanding of the pathophysiology of heart failure in humans is incomplete. Therefore, we and others have come to realize that progress in understanding human heart failure to improve diagnosis, risk stratification and therapeutic strategies demands direct investigation of the molecular underpinnings of adverse structural, electrophysiological and mechanical remodeling during the progression of heart failure in human hearts. For this reason, we established the TCBR for procurement and storage of cardiac tissue for subsequent molecular, biochemical and electrophysiological analyses as a means for facilitating translational research in end-stage cardiac disease.

Getting Started (Technical Logistics)

Recruiting and Retaining the Team

The potential of cardiac tissue banking has long been recognized. Indeed, cardiac tissue banking efforts at Washington University School of Medicine and Barnes-Jewish Hospital were pioneered by Dr. Joseph Rogers and colleagues in 1993.[10,11] Subsequently and independently, Dr. Igor Efimov in the Department of Biomedical Engineering in the School of Engineering and Applied Science and Dr. Nader Moazami in the Division of Cardiothoracic Surgery at the School of Medicine began, in 2008, to collect both explanted hearts at the time of transplantation and nonfailing donor hearts (declined for use in transplantation). Importantly, Drs. Efimov and Moazami studied the electrophysiological properties of viable human tissues, within minutes of explantation, characterizing differences in the properties of non-failing and failing human hearts directly.[12–21]

Despite these individual efforts, establishment of the type of resource that researchers need for current, state-of-the-art investigations into subtle disease phenotypes, expression, progression and treatment requires much more. Perhaps most importantly, standard

operating procedures need to be established, tissues collected need to be archived with detailed clinical histories, treatments and diagnostic test results, and collected tissues need to be integrated with acquired experimental data in accessible, readily queryable databases for interrogation by investigators. In developing the TCBR, we have prioritized cardiac biobanking efforts to include rigorous patient consenting that allows for inclusion of extensive clinical data in the tissue repository and the sharing as well as analysis of genetic material in addition to the establishment of standardized sample handling procedures to ensure that the maximum potential of this biorepository will be realized.

Setting up the Infrastructure

Elements of the infrastructure that are required for integrated cardiac tissue banking are listed in Table 1. The literature and web contain excellent documentation detailing several aspects of biobanking infrastructure.[6–8,22] In our experience, the single most critical and challenging factor requisite for the ongoing success of live cardiac tissue procurement (for both immediate study and consistent biobanking) is the recruitment and retention of trained, reliable and willing tissue collectors. The surgical cases often take place after hours, in the middle of the night and on weekends and holidays. If teams of trained staff members are not available 24/7 to collect tissue, too many cases will be missed, and busy transplant coordinators will lose interest in calling and/or paging people who do not respond in a timely manner or are not properly prepared. The one other element that is challenging and requires a great deal of time, thought and advanced planning is archiving and annotation of samples (see below).

IRB Approval Issues

Each institution has its own Institutional Review Board (IRB) with staff members who can guide investigators through the procedures for obtaining protocol approval. As a general practice, we have chosen to limit the number of team members with full access to Protected Health Information (PHI) to minimize the risk of breaches in patient confidentiality. Aside from the physicians and nurse coordinators with patient contact, only three (out of ~20) team members who are responsible for annotation of the clinical databases have access to PHI. Thus, notification and communications sent to tissue collectors does not contain PHI.

In addition to the TCBR having an approved IRB protocol, each investigator interested in accessing TCBR tissue and data resources must have an approved IRB protocol. Individual investigator IRB protocols are “linked” to the TCBR protocol so that users can apply for a Waiver of Consent asserting that the TCBR is responsible for patient consenting; these protocols can then be submitted for expedited review. Tissue specimens are disbursed by the TCBR to end users either coded or fully anonymized, dictated by each user’s specific IRB-approved protocol. This procedure required advanced planning to establish protocols, for example, for (1) “parent” and “derivative” tube labeling, (2) coding and maintenance of code keys, (3) aliquoting to avoid freeze/thaw cycles, and (4) tube labeling of disbursed tissues. Importantly, expedited review and usage of coded or anonymized tissue does not preclude access to important clinical information. We routinely disburse tissue with relevant clinical information that has been fully “scrubbed” of all PHI.

Provisions for usage of tissue for genetic testing and research should be written explicitly into the IRB protocol. At present, DNA is not included as one of the 18 PHI identifiers. However, public understanding and perceptions,[23–25] conventional wisdom, scientific breakthroughs, scholarly ethical considerations,[26] requirements of funding organizations and federal regulations each exhibit flux in ever changing social and regulatory environments. Therefore, working committees that include scientists, ethicists and lay people charged with incorporating scientific advances, public sentiments, and thoughtful evaluation of medical/

legal/ethical issues should meet regularly to address and update policies pertaining to usage (and sharing of information obtained therefrom) of participants' DNA, particularly as codified governance of biobanks does not currently exist. In addition, the issue of data sharing by other investigators or third parties should be covered explicitly in each investigator's IRB protocol. Finally, potentially thorny issues related to large aggregated databases, international collaborative research and interoperability of sample and data management should also be considered during IRB protocol development and explicitly addressed if applicable.[27–30]

Obtaining Informed Consent

Obtaining informed consent from patients is a time-consuming process (our 10-page Informed Consent Form takes ~45 min to review with each patient and their family) that is best done by highly trained nurse coordinators who meet regularly with the physicians involved in surgical decision making. It is also best done by nurses with whom the patients are familiar (e.g. from outpatient clinic visits) and have developed a relationship of trust. Our IRB-approved protocol contains provisions for assessing the capacity of participants to give informed consent, such as in the case of a mentally and/or physically impaired adult patient; consent in such cases is obtained from a Legally Authorized Representative (LAR), and may allow for collection of tissue from patients who are too sick before cardiac surgery to provide the assent that they otherwise would have given. The NIH has useful information pertaining to individuals with questionable capacity to consent (http://grants.nih.gov/grants/policy/questionablecapacity.htm). Children are a special cohort of participants from whom assent should be obtained whenever possible, even when a parent or legal guardian has given consent.

Several studies have addressed public understanding, perceptions and concerns regarding tissue donation and biobanking.[23,24] Some individuals may not immediately grasp or appreciate the ramifications of participation in large biobanks and repositories. Consent from participants whose data will be included in the formation of aggregated databases and/or used by other investigators not involved in the original study must be obtained.

Tissue Procurement

Considerations for optimal tissue procurement and handling have been delineated in several publications.[5–8] Timely harvesting, accurate documentation of the regional and structural origins of the tissue and uniform processing are critical. Failure to standardize these practices may preclude use by investigators as well as reliability of the scientific results obtained. These issues are both relevant and challenging during acquisition of viable cardiac tissue samples. Appendix 2 contains one of the TCBR protocols for sample acquisition that includes tissue dissection and processing and illustrates our approach. Over the past two years, we have collected 220 cardiac samples including tissue from 110 VAD cores, 63 explanted hearts (18 from which we had collected a VAD core previously) at the time of transplant, and 47 donor hearts deemed unsuitable for transplant. The latter samples have been obtained in collaboration with Mid-America Transplant Services (MTS), a private, not-for-profit organ and tissue procurement organization. MTS is located 2.2 miles from Washington University Medical Center. Our tissue collectors procure cardiac tissue in the MTS operating room (OR), adhering strictly to TCBR protocols that are identical to those used in the Barnes-Jewish and St. Louis Children's Hospitals ORs at Washington University Medical Center. Tissue is obtained as soon after excision as possible from the scrub nurse (at Barnes-Jewish or St. Louis Children's Hospitals) or surgeon (at MTS), processed (carefully dissected mindful of anatomy, frozen, preserved, or fixed) immediately, generally within 5 minutes, in the OR, then transported back to the TCBR for immediate use in physiology experiments, further processing, archiving and storage. Although other sources

of non-diseased cardiac tissue, such as the National Disease Research Interchange (NDRI) and the Cooperative Human Tissue Network (CHTN), exist, the collection and processing of non-diseased tissues using the same protocols as those used for the diseased samples allows one to control collection protocols (for future comparisons with diseased samples) and to minimize variability that might adversely, or inconclusively, affect tissue quality (discussed further below). In addition, local tissue acquisition from a private, not-for-profit organ and tissue procurement organization, such as MTS, also makes it possible to obtain clinical (e.g., echocardiographic, catheterization, electrocardiographic, etc.) information about the function of the donor heart, information that may be important and useful in analyzing and interpreting acquired data.

Establishing Standardized Tissue Handling Protocols

Detailed procedures for tissue procurement, processing, storage and archiving have been developed in the TCBR in consultation with the Washington University Siteman Cancer Center Tissue Procurement Core Facility. One of the most important considerations driving tissue handling protocol development is determination of how banked tissue will ultimately be used. This will inform the most often requested tissue samples and processing methods to be adopted for most efficient biobank operations. Generally, most biobanking includes fresh freezing, fresh preservation (e.g. in RNAlater) and fixation (e.g. with formalin); however, more recent assays (e.g. for epigenetic marks) may require development of specific freezing or preservation buffer protocols. For example, freezing may entail freeze-clamping in liquid nitrogen-cooled spatulas or clamps or timed freezing in 2-methylbutane cooled to −50°C in a controlled freezing unit depending on assay requirements (e.g. for protein, metabolomics, DNase1 hypersensitivity, etc.). After determining end-user requirements, it is also recommended that each biobank perform validation studies to maintain quality assurance.[5,6,29,31,32] Another consideration pertains to blood collection. Depending on what the end user will assay (e.g. DNA, labile proteins, small molecules, specific biomarkers, etc.), different types of blood collection tubes (e.g. containing EDTA or citrate, serum separator, etc.) and blood processing protocols (within 30 min, after at least 30 min, no longer than 4 hr, etc.) may apply. It should be noted here that variations in protocols pertaining to blood (and possibly tissue) acquisition may be required, for example, for pediatric donors due to limited allowable blood draw volumes.

To insure sample integrity, all tissue specimens in the TCBR are kept in locked freezers/refrigerators to prevent tampering, and are monitored with an Accsense on-line temperature and power monitoring system. Finally, we in the TCBR never lose track of the paramount importance of patient care before, during and after each surgical procedure. Our collection protocol includes provisions for submission of tissue to surgical pathology for every explanted heart acquired in the Barnes-Jewish and St. Louis Children's Hospital ORs.

Archiving and Annotation

Archiving and annotation require substantial thought and effort in order to accomplish effective integration of the tissue stores and their accompanying clinical information. Obviously, an accurate record of all samples, derivatives, and associated clinical information, including PHI, must be kept and safeguarded. Various electronic record systems are available. In the TCBR, we utilize two fully integrated web-based applications, ClinPortal and caTissue, developed by the Center for Biomedical Informatics at Washington University. ClinPortal is a Linux-based clinical studies data management system utilizing a secure Oracle database on the back-end. Its graphical web-based application front-end ensures that all required staff members can easily view and/or enter each patient's clinical data given specified permissions. caTissue is part of the NCI's Cancer Biomedical Informatics Grid (caBIG), a biospecimen informatics system that contains a virtual

repository that mirrors the TCBR physical repository and allows us to track the collection, storage, quality assurance, queries, and distribution of our specimens.

One of the most important and time-consuming activities of biobank quality control is the entering and validation of clinical information associated with each tissue sample. The ClinPortal application contains a series of “forms” or web pages to which TCBR data entry specialists with clinical proficiency add relevant information obtained from each patient’s electronic medical record. The forms were developed (by AYP, GAE, DLM and KAY) after months of surveying users regarding what information would best enhance (for publication) experimental and translational studies generated from TCBR tissue usage, deliberating over consistent and unambiguous wording, and accessing real medical records to gain experience with data extraction. We found that it is surprisingly challenging to come up with forms that can be populated by the data entry specialists quickly and consistently. For example, it is difficult to extract duration of heart failure without searching through many physicians’ notes, and if found, it may still be difficult to determine when heart failure was first diagnosed and further, if it is of ischemic, nonischemic or mixed origin. A second example is that it is difficult to extract systematic information on medications due to variable and sometimes indeterminate initiation and duration of medical therapies, particularly those that are frequently changed and (doses) fine-tuned in sick patients. Even objective measures obtained from echocardiography or cardiac catheterization reports are sometimes incomplete and are taken at widely variable times before tissue acquisition. Thus, the best annotation would be possible if one were to design forms for data input and then review those forms with the practicing physicians to request that the specified data be obtained consistently and prospectively. Appendix 3 contains a list of input variables presently extracted from patient records by the TCBR. This list does not contain the full contingent of clinical parameters collected from our patients (e.g. in the INTERMACS Database for Durable Devices for Circulatory Support), rather the minimum we have deemed important to document and be appended to each tissue sample acquired.

Maintenance of the Repository

Financial Support for Operations

We initially obtained pilot funding from the Washington University Institute of Clinical and Translational Sciences, supported by a Clinical and Translational Sciences Award from the National Institutes of Health, and the Cardiovascular Division of the Department of Internal Medicine at Washington University School of Medicine. Additional funding was subsequently obtained from the Children’s Discovery Institute, a partnership between St. Louis Children’s Hospital and Washington University School of Medicine, to make it possible to expand our efforts to include the acquisition of tissue samples from pediatric patients. In addition, we are continually seeking additional outside sources of funding for this resource, particularly from the National Institutes of Health which has developed funding opportunities (for example, the R24 and U42 funding mechanisms) for the development and operation of research infrastructure and resources.

TCBR users are charged nominal fees at the time of tissue disbursement. However, this fee is trivial in relation to the real costs involved in the acquisition, processing, storage and distribution of tissue samples and accompanying clinical data. Cost-recovery models of biobanks require substantial leveraging and volume (building scale as well as a variety of functions/services) for sustainability.[33] We have begun to build scale in the TCBR in terms of data expansion efforts, and will charge fees for access to the data repository as well. Nevertheless, large-scale leveraging and volume are more difficult for smaller institutional (as opposed to national, multi-organizational public-private partnership) biobanks to attain.[33] As is the case with the TCBR, billable services alone cannot support ongoing

biobanking efforts, and the general consensus is that some level of institutional commitment is required for long-term sustainability.[3,8]

Protection of Patient Confidentiality

The protection of confidentiality of every participant in every research protocol is of the utmost importance. Typically this is accomplished through one of two methods: coding or anonymization. While the latter is absolute in the sense of severing tissues from their source and accompanying clinical identifiers and thus is safer for protecting participant confidentiality, it is far more restrictive and does not allow users to later retrieve sample information or associated clinical data. In addition, due to the ever expanding capabilities of DNA and RNA sequencing and the resulting sequencing data sets that can be mined with sophisticated bioinformatics tools, it will be increasingly difficult to ensure enduring anonymity.[27,34,35] It seems clear, therefore, as suggested above, that, although DNA is currently not classified as PHI, it should be protected as such. Furthermore, the very premise of an integrated biobank assumes that tissue disbursement and data sharing will occur, thus compounding the risk of breach of confidentiality, and rigorous safeguards must be adopted to minimize such risk. In the TCBR, we minimize the number of individuals who have access to coding identifiers which are kept on a secure password-protected university-networked server behind firewall protection. Any hard copies of TCBR specimen files are kept in one of two offices behind double lock-and-key.

Follow-up/Web Presence

Every participant retains the right, at any time, to withdraw from the biobank/study. Upon such a request, any remaining tissue would be destroyed and disposed of. Per the TCBR IRB-approved protocol and Informed Consent Forms, participants will not be given individual feedback on any results of experimentation or testing done on tissue samples provided. However, ongoing communication with study participants in the form of updates and advances posted on biobank websites or reported in biobank newsletters is an excellent means for maintaining public interest and enthusiasm for tissue donation and study participation[25] as well as reminding participants of their right to withdraw from the biobank/study. This has become an ethical and logistical issue pertaining to the involvement of minors, whose parents gave permission for enrollment in a study, but who may no longer wish to participate.

Tissue Use and Disbursement

Application for Services/Advisory Committee

Archived human tissue samples housed in a biobank are a finite resource and some (e.g. paired VAD and explant) tissue samples are expected to be more sought after than others. We have established an independent Advisory Committee consisting of four faculty members from four different Departments on the Washington University Medical and Danforth (Arts & Sciences) campuses which receives every application for request for tissue samples. This committee, which includes a statistician, is responsible not only for approving applications based on scientific merit of the proposed study and tissue usage but also for adjudicating any conflicts that may arise in the course of distributing a finite, limited resource.

Experimental Considerations

One unique aspect of the TCBR is that our top priority for tissue acquisition is immediacy (in addition to consistency and standardization) of collection. Every heart (both failing hearts collected in the Barnes-Jewish or St. Louis Children's Hospital ORs and nonfailing hearts collected in the MTS OR) are cold-cardioplegically arrested via direct perfusion

through the coronary arteries for preservation during subsequent processing and transport. This allows for high quality physiological studies to be performed,[12–21] including isolation and investigation into the cellular physiology of human cardiac myocytes.

Another unique aspect of the TCBR is our ability to collect and store tissue from nonfailing hearts to be used as "control" samples in experimental studies. As stated above, these donors hearts are procured after they have been declined for use in transplants (for a variety of reasons including age, poor systolic function, evidence of coronary artery disease, etc.) and MTS has obtained consent for each heart to be donated for research purposes. Interestingly, after rigorous examination of ECGs, echocardiography reports and/or catheterization data, we have determined that there is a substantial amount of cardiac disease in many donors who have died of non-cardiac causes. Documentation and awareness of moderate to severe heart disease or dysfunction in donors whose tissue might otherwise be used as nonfailing "controls" may avoid inclusion of tissue samples, in experimental studies, that are likely to confound interpretation of results obtained. Certainly hearts and samples acquired from donor sources without detailed patient histories and clinical data should not be assumed to be normal tissue.

Data Repository

As is true with many biorepositories, only a fraction of the total collection of tissues will ever be utilized; some sources cite <5%.[22] We have come to the realization that perhaps even more important and far-reaching than preserving precious tissue samples will be the collection and availability through a data repository of experimental results that have been obtained by various investigators using TCBR tissue samples. Recent RNAseq analyses of RNA remodeling in failing hearts pre- and post-VAD treatment, compared to nonfailing controls,[36] illustrates this point, as the gold mine of data produced by these analyses will become available through the TCBR to investigators who might not otherwise have access to these types of samples or sample analyses. Similarly, future unique and powerful datasets derived from TCBR-enabled studies will also be deposited in the TCBR data repository. We see the legacy of the TCBR as contributing rigorously obtained experimental results that will facilitate further translational studies that were unimaginable at the time the tissues in our biobank were collected.

Conclusions

Cardiac tissue biobanking has the potential to have a considerable, widespread impact on translational research in the area of heart disease. Although numerous resources are now available to guide those wishing to establish or utilize an integrated cardiac biobank, several critical elements of the requisite infrastructure cannot be overemphasized. These include: recruitment and retention of trained, dedicated personnel to collect, process and archive collected specimens; organization, foresight and patience to negotiate the regulatory and compliance jungles, to set the priorities for optimal operational efficiency and to acquire financial support; and commitment to a vision that focuses on the lasting contributions of/from the biorepository to the cardiovascular research community.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Financial support: NIH/NCRR CTSA Grant UL1 RR024992, the Children's Discovery Institute, the Barnes-Jewish Hospital Foundation, and the Richard J. Wilkinson Trust

The authors would like to express gratitude to Dr. Susan Joseph, and Lynelle Jolliff, Janice Amsler, Jean Flanagan and Anne Platts for obtaining consent from the patients participating in the TCBR; to Drs. I-wen Wang, Sunil Prasad, Ari Cedars, Nicholas Foeger, Scott Marrus, Wei Wang and Kai-Chien Yang, and Amy Huntley, Evelyn Kanter, Noel Bernabe and Joe Futhey for tirelessly and enthusiastically collecting tissue; to Drs. Charles Canter, Pirooz Eghtesady, Umar Boston and Patrick Jay, and Traci Boschert and Teresa Roberson for collaborating with us in extending our TCBR experience to include tissues obtained from pediatric patients/participants; to Dave Mulvihill, Nitin Jain, Mary Ulmansiek and Chris Champion of the Center for Biomedical Informatics for helping us develop our ClinPortal and caTissue archiving and annotation applications; to Dr. Mark Watson, and Vicky Holtschlag and Amy Brink of the Siteman Cancer Center Tissue Procurement Core Facility and Lora Staloch for thoughtful input and assistance in protocol development; to Drs. Sandra McDonald, James Miller, Kenneth Schechtman and George Van Hare for their service on the TCBR Advisory Committee; to Dean Kappel, Diane Brockmeier, Jason Coleman and their colleagues at Mid-America Transplant Services for their enthusiastic and helpful collaboration in the acquisition of nonfailing cardiac tissue; and to each of the patients, participants, organ donors and their families for allowing their tissue to be used for biobanking and research. This effort is supported by the National Institutes of Health National Center for Research Resources CTSA Grant UL1 RR024992, the Children's Discovery Institute, a partner of St. Louis Children's Hospital and Washington University School of Medicine, the Barnes-Jewish Hospital Foundation, and the Richard J. Wilkinson Trust.

References

1. Haas J, Katus HA, Meder B. Next-generation sequencing entering the clinical arena. Mol Cell Probes. 2011; 25:206–211. [PubMed: 21914469]
2. Nelson TJ, Martinez-Fernandez A, Terzic A. Induced pluripotent stem cells: Developmental biology to regenerative medicine. Nat Rev Cardiol. 2010; 7:700–710. [PubMed: 20956984]
3. Hewitt RE. Biobanking: The foundation of personalized medicine. Curr Opin Oncol. 2011; 23:112–119. [PubMed: 21076300]
4. Moore HM, Compton CC, Alper J, Vaught JB. International approaches to advancing biospecimen science. Cancer Epidemiol Biomarkers Prev. 2011; 20:729–732. [PubMed: 21430299]
5. International Society for Biological and Environmental Repositories. 2012 Best practices for repositories: Collection, storage, retrieval, and distribution of biological materials for research. Biopreserv Biobank. 2012; 10(2):81–161.
6. Office of Biorepositories and Biospecimen Research, National Cancer Institute, National Institutes of Health, U.S. Department of Health and Human Services. [Accessed August 16, 2012] NCI Best Practices for Biospecimen Resources. 2011. p. 1-85.http://biospecimens.cancer.gov/bestpractices/2011-NCIBestPractices.pdf
7. Vaught J, Rogers J, Myers K, Lim MD, Lockhart N, Moore H, Sawyer S, Furman JL, Compton C. An NCI perspective on creating sustainable biospecimen resources. J Natl Cancer Inst Monogr. 2011; 2011(42):1–7. [PubMed: 21672889]
8. Brisson AR, Matsui D, Rieder MJ, Fraser DD. Translational research in pediatrics: Tissue sampling and biobanking. Pediatrics. 2012; 129:153–162. [PubMed: 22144705]
9. Hunt SA, Abraham WT, Chin MH, Feldman AM, Francis GS, Ganiats TG, Jessup M, Konstam MA, Mancini DM, Michl K, Oates JA, Rahko PS, Silver MA, Stevenson LW, Yancy CW. 2009 Focused update incorporated into the ACC/AHA 2005 guidelines for the diagnosis and management of heart failure in adults: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2009; 119:e391–e479. [PubMed: 19324966]
10. Sack MN, Rader TA, Park S, Bastin J, McCune SA, Kelly DP. Fatty acid oxidation enzyme gene expression is downregulated in the failing heart. Circulation. 1996; 94:2837–2842. [PubMed: 8941110]
11. Yamada KA, Rogers JG, Sundset R, Steinberg TH, Saffitz JE. Upregulation of connexin45 in heart failure. J Cardiovasc Electrophysiol. 2003; 14:1205–1212. [PubMed: 14678136]
12. Hucker WJ, Fedorov VV, Foyil KV, Moazami N, Efimov IR. Images in cardiovascular medicine: Optical mapping of the human atrioventricular junction. Circulation. 2008; 117:1474–1477. [PubMed: 18347223]
13. Hucker WJ, McCain ML, Laughner JI, Iaizzo PA, Efimov IR. Connexin 43 expression delineates two discrete pathways in the human atrioventricular junction. Anat Rec. 2008; 291:204–215.

14. Efimov IR, Fedorov VV, Glukhov AV, Lou Q, Ambrosi C, Janks D, Hucker WJ, Kurian T, Schuessler RB, Moazami N. Multiscale imaging of the human heart: Building the foundation for human systems physiology and translational medicine. Conf Proc IEEE Eng Med Biol Soc. 2010; 2010:5170–5180.
15. Fedorov VV, Glukhov AV, Chang R, Kostecki G, Aferol H, Hucker WJ, Wuskell JP, Loew LM, Schuessler RB, Moazami N, Efimov IR. Optical mapping of the isolated coronary-perfused human sinus node. J Am Coll Cardiol. 2010; 56:1386–94. [PubMed: 20946995]
16. Glukhov AV, Fedorov VV, Lou Q, Ravikumar VK, Kalish PW, Schuessler RB, Moazami N, Efimov IR. Transmural dispersion of repolarization in failing and nonfailing human ventricle. Circ Res. 2010; 106:981–991. [PubMed: 20093630]
17. Kurian T, Ambrosi C, Hucker W, Fedorov VV, Efimov IR. Anatomy and electrophysiology of the human AV node. Pacing Clin Electrophysiol. 2010; 33:754–762. [PubMed: 20180918]
18. Fedorov VV, Glukhov AV, Ambrosi CM, Kostecki G, Chang R, Janks D, Schuessler RB, Moazami N, Nichols CG, Efimov IR. Effects of KATP channel openers diazoxide and pinacidil in coronary-perfused atria and ventricles from failing and non-failing human hearts. J Mol Cell Cardiol. 2011; 51:215–225. [PubMed: 21586291]
19. Lou Q, Fedorov VV, Glukhov AV, Moazami N, Fast VG, Efimov IR. Transmural heterogeneity and remodeling of ventricular excitation-contraction coupling in human heart failure. Circulation. 2011; 123:1881–1890. [PubMed: 21502574]
20. Glukhov AV, Fedorov VV, Kalish PW, Ravikumar VK, Lou Q, Janks D, Schuessler RB, Moazami N, Efimov IR. Conduction remodeling in human end-stage nonischemic left ventricular cardiomyopathy. Circulation. 2012; 125:1835–1847. [PubMed: 22412072]
21. Lou Q, Janardhan A, Efimov IR. Remodeling of calcium handling in human heart failure. Adv Exp Med Biol. 2012; 740:1145–1174. [PubMed: 22453987]
22. Eiseman, E.; Bloom, G.; Brower, J.; Clancy, N.; Olmsted, SS. “Best Practices” for a Biospecimen Resource for the Genomic and Proteomic Era. Santa Monica, CA: RAND; 2003. Case Studies of Existing Human Tissue Repositories.
23. Pullman D, Etchegary H, Gallagher K, Hodgkinson K, Keough M, Morgan D, Street C. Personal privacy, public benefits, and biobanks: A conjoint analysis of policy priorities and public perceptions. Genet Med. 2012; 14:229–235. [PubMed: 22261752]
24. Luque JS, Quinn GP, Montel-Ishino FA, Arevalo M, Bynum SA, Noel-Thomas S, Wells KJ, Gwede CK, Meade CD. Tampa Bay Community Cancer Network Partners . Formative research on perceptions of biobanking: What community members think. J Cancer Educ. 2012; 27:91–99. [PubMed: 21927867]
25. Saha K, Hurlbut JB. Research ethics: Treat donors as partners in biobank research. Nature. 2011; 478:312–313. [PubMed: 22012372]
26. Cambon-Thomsen A, Rial-Sebbag E, Knoppers BM. Trends in ethical and legal frameworks for the use of human biobanks. Eur Respir J. 2007; 30:373–382. [PubMed: 17666560]
27. Karp DR, Carlin S, Cook-Deegan R, Ford DE, Geller G, Glass DN, Greely H, Guthridge J, Kahn J, Kaslow R, Kraft C, Macqueen K, Malin B, Scheuerman RH, Sugarman J. Ethical and practical issues associated with aggregating databases. PLoS Med. 2008; 5:e190. [PubMed: 18816162]
28. Hewitt R, Hainaut P. Biobanking in a fast moving world: An international perspective. J Natl Cancer Inst Monogr. 2011; 2011(42):50–51. [PubMed: 21672898]
29. Kiehntopf M, Krawczak M. Biobanking and international interoperability: Samples. Hum Genet. 2011; 130:369–376. [PubMed: 21761135]
30. Eder J, Gottweis H, Zatloukal K. IT Solutions for Privacy Protection in Biobanking. Public Health Genomics. 2012; 15:254–262. [PubMed: 22722689]
31. Grizzle WE, Sexton KC, Bell WC. Quality assurance in tissue resources supporting biomedical research. Cell Preserv Technol. 2008; 6:113–118. [PubMed: 21572596]
32. Ahsman MJ, Tibboel D, Mathot RA, de Wildt SN. Sample collection, biobanking, and analysis. Handb Exp Pharmacol. 2011; 205:203–217. [PubMed: 21882113]
33. Vaught J, Rogers J, Carolin T, Compton C. Biobankonomics: Developing a sustainable business model approach for the formation of a human tissue biobank. J Natl Cancer Inst Monogr. 2011; 42:24–31. [PubMed: 21672892]

34. Fullerton SM, Anderson NR, Guzauskas G, Freeman D, Fryer-Edwards K. Meeting the governance challenges of next-generation biorepository research. Sci Transl Med. 2010; 2:15cm3.

35. Homer N, Szelinger S, Redman M, Duggan D, Tembe W, Muehling J, Pearson JV, Stephan DA, Nelson SF, Craig DW. Resolving individuals contributing trace amounts of DNA to highly complex mixtures using high-density SNP genotyping microarrays. PLoS Genetics. 2008; 4:e1000167. [PubMed: 18769715]

36. Yang KC, Yamada KA, Patel AY, Topkara VK, Ewald GA, Mann DL, Nerbonne JM. Deep RNA sequencing reveals dynamic regulation of myocardial noncoding RNA in failing human heart and remodeling with mechanical circulatory support. [abstract]. Circulation. 2012 in press.

Table 1

Infrastructure Elements of an Integrated Cardiac Tissue Biobank

1. IRB approval; Informed Consent Forms
2. Nurse coordinator or other staff for patient consenting (7)
3. Surgeons for tissue excision (5)
4. Teams of tissue collectors with after-hours access to ORs (6)
5. Advisory or Oversight Committee (4)
6. Standard operating procedures and written protocols for notification (Appendix 1)
7. Standard operating procedures and written protocols for tissue handling (Appendix 2)
8. Standard operating procedures and written protocols for pathological specimens
9. Physical space for tissue handling and storage
10. Equipment: dedicated freezers, temperature monitoring system, refrigerators, centrifuges, computers
11. Consumables: personal protective equipment, surgical instruments, tubes and racks, liquid nitrogen, RNAlater, formalin, glutaraldehyde, other
12. Training and compliance requirements: Human Subjects Research (e.g. Collaborative Institutional Training Initiative or CITI); Health Insurance Portability and Accountability Act (HIPAA); OSHA Bloodborne Pathogen Standard; TB testing; hepatitis B vaccination; OSHA Hazard Communication Standard; Hazardous Research Materials/Carcinogens Protocol, Hazardous Waste Disposal; Biohazard Waste Disposal; US DOT Hazardous Materials Regulations (for shipping)
13. Archiving system: databases, labeling, approval/access to Protected Health Information (PHI) for annotation

Numbers in parentheses are number of TCBR staff members currently involved in activity.

IRB, Institutional Review Board

OR, operating room

OSHA, Occupational Safety and Health Administration

SOP, standard operating procedures

TB, tuberculosis

US DOT, United States Department of Transportation