LSUHSC Biospecimen Core

Historical:

Traditionally, research involving human blood and tissues in medical institutions involved collaborative efforts among physicians/surgeons and researchers. Often specimens were collected "on demand" and involved immediate processing and utilization. Except pathological samples which were preserved and archived, there has not been a concerted efforts to collect, identify, and preserve samples for immediate or future use. Countless potentially useful samples were never collected and collected samples were often discarded when there was no demand for research use. Surgeons and physicians often saw no incentive for collection of precious samples and those who were motivated to collect biomedical specimens were often discouraged from doing so by inadequate facilities for storage and processing of samples. Procedural, bureaucratic, legal, and Governmental regulations also stood in the way of procuring and use of biospecimens. During the past 10 years, there have been monumental changes in the regulatory environment as well as in the perception of the use of human tissues and blood samples. Currently the notion that "any sample that is uncollected and unused is a waste of resources" is gaining grounds. As a result, most, if not all Universities and Medical Institutions have established some form of tissue bank to identify, collect, and utilize human samples for research purposes.

1. Current Status at LSUHSC-Where we are?

LSUHSC is growing and is expected to grow rapidly in the future. Almost every department is recruiting basic and clinical scientists. There is a long list of faculty scientists who are currently engaged in research involving human biospecimens and this list is expected to grow. In addition, there is an expected return on the use of human tissues and samples in biomedical research as more and more studies stress the need to expand our research findings on cell and animal based research to studies on humans and human biospecimens.

Currently, there are several identified and unidentified "tissue banks" at LSUHSC. These include the Cancer Tissue Bank, The Brain Bank, PDAY Pathology archives, and other collections. Of these, the Cancer Center Tissue Bank has identified the needs, resources, and has an implementation plan which also includes the collection of normal tissues. This bank specializes in the collection of tumor tissues but also has plans to expand its operation to collecting non-cancerous samples and specimens. The Brain Tissue Bank appears to be inactive currently. Other collections have archived samples and are restricted to specific types of pathological tissues.

It can be reasonably assumed that at LSUHSC, most of the research involving human subjects is conducted on an informal basis purely relying on a willing surgeon/physician and basic/clinical scientists who are eager to extend their research to human tissues and samples. There is also a void of information regarding the efforts of the cancer center core facility in procuring and maintaining tumor as well as normal tissues. In fact, the committee feels that many investigators shy away from embarking on research involving human tissues, not because of procedural difficulties, but because of the lack of suitable mechanism(s) to obtain such tissues. On the other hand, there certainly appears to be a need.

Methodology:

1. Interview with selected researchers.
2. Questionnaire to identify current users of human biospecimens
3. Questionnaire to identify current generators of human biospecimens
4. Search of literature on biospecimens and tissue banks
5. Meeting with Cancer Tissue Bank committee
6. NIH Roadmap guidelines

These resources identified potential problems, legal and ethical issues, financial and spatial constraints, needed human resources, and other issues associated with tissue banking.

Specific problems associated with LSUHSC:

Despite the poor response to the questionnaire (only about 40 faculty responded and several Departments failed to respond), the following "problems and issues" were repeatedly encountered during our "fact finding" mission.

1. It is difficult to find out about available tissues.
2. Specific tissues are unavailable.
3. Normal control tissues are unavailable
4. Fresh tissues are unavailable
5. There is no mechanism to collect tissues from different hospitals and clinics
6. There is no mechanism to store tissues properly.
7. There is no expertise/resource available for the procurement/processing of specific tissues.
8. Blood samples (RBC, white cells, and plasma/serum) need to be separated.
9. There is no mechanism for cataloging samples
10. It is difficult to identify physicians/surgeons who would procure samples.
11. There is no incentive for the collection of samples.
12. Financial resources are unavailable for storage/processing of samples.
13. Fear that a centralized banking system would create an unwanted level of bureaucracy
14. Fear that it would replace the existing banks.
15. There aren't enough investigators who would be interested in human tissues.
16. General apathy from health care providers who see research involving human tissues as violations of patients' privacy and hence are hesitant about collecting specimens.

2. Human Tissue Procurement and Banking Services-Where we would like to be?

The establishment of a centralized Human Biospecimen Procurement, Processing, and Banking Services facility has allowed many Universities, a more organized and coherent operation of tissue procurement. Such facilities also assure compliance with the HHS Privacy Rule regulations (http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.pdf.). Centralization facilitates the collection of fresh or immediately needed tissue requests of investigators. It also helps to coordinate tissue acquisition, processing and distribution of other "satellite" tissue banks. A great advantage is seen in "translational research" when more investigators and clinicians would participate and use human biospecimens that are efficiently procured, accessed, and utilized.

When properly implemented, it would provide a system-wide documentation of needs and resources and would allow matching of investigators with potential sources of target specimens. More importantly, it would make it would permit easy and streamlined coordination of efforts and help us to meet legal and ethical guidelines set by Federal and State agencies. One of the advantages in a centralized system would be the uniform identification, documentation, and archival of biospecimens so that cross reference across the "satellite" banks could be achieved.

Types of biospecimens:

1. Surgical and autopsy tissues that are not used for diagnostic purposes.
2. Fresh, frozen, formalin and alcohol-fixed paraffin embedded blocks.
3. Fresh unfixed tissues and specimens.
4. Cryofreezed biospecimens.
5. Isolated cells and fluids.
6. Whole blood.
7. Buffy coat or white cells.
8. Plasma or serum.

3. **What do we need**? **Implementation**:

We need a clear definition of what is human biospecimens and what is the intended purpose of the Biospecimen core. Simply stated, the definition would include *all* constituent parts of the human body, including urine, feces, menstrum and other secreted fluids, collected for the purpose of conducting biomedical research. It may not include tissues procured for human transplant or diagnostic purposes.

Second, all mandated compliance regulations must be met. This includes approval of protocols by the institutional human investigations committee, approval by other committees that might be required under special circumstances, completion of the investigators' approval test for conducting studies on human tissues, patients' informed consent, and a clear understanding of the role of the investigator and the physician/surgeon. Too many valuable tissues, time, and collaborations are lost when the expectations of the investigators and physicians/surgeons are different.

Third, all research, involving human tissue and biospecimen research must go through the central or the satellite cores. In other words, an investigator may only obtain human biospecimens for research even if the tissue is generated within his/her own practice.

Please refer to the following documents and web sites for additional guidelines and details:

1. http://nihroadmap.nih.gov
2. http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.pdf
3. C.M. Dunn and G. Chadwick. Protecting Study Volunteers in Research. A manual for Investigative Sites. Center Watch, Inc. 1999.

Resources:

The following resources need to be identified and budgeted:

1. **Space**: It is recommended that at least 500 sq.ft of refrigerator/freezer/equipment space, 500 sq.ft. of adjacent laboratory space, and 500 sq.ft of office/business space is provided for the core. In addition to refrigerators/freezers, the facility will house, liquid nitrogen tanks, centrifuges for blood sample processing, dry ice chests, microscopes, and a sterile hood. A dedicated high volume server and access terminals around the campus are essential.
2. **Personnel**:
   Director: A part time researcher-M.D./Ph.D in pathology-biomedical sciences would be essential for the operation of the core facility. The director should have active ongoing research program to utilize the technician to the fullest extent.
   Tissue "Corrarian" (Curator-Core Librarian) is recommended. A trained librarian familiar with cataloging/medical terminology would be a great asset and would bring novelty to the core. Traditionally samples are archived by bar codes and description of the samples. A biospecimen librarian would be able to offer professional cataloging of samples according to the nature/source which would make both archiving and retrieval easy. An added advantage would be the ability of the librarian to provide technical details and medical literature pertaining to the samples. This person also will be the liaison between the central unit and the "satellite" units. Besides, this would set a role model and precedent for other core units around the country and expand the traditional role of medical librarian to new frontiers.
   Research coordinators/technicians: For day to day operations, archiving and retrieval of samples. A technician with B.S. in Biology would be preferred. The technician will process blood samples in the laboratory. Dissection of tissue samples, further processing etc. will be performed by the end user.
   In addition, support personnel from IT department, periodic quality control measures, and other needed items might be required.
   Tissue procuring assistants: At least two staff members are needed for physically transporting samples and specimens from hospitals and clinics to the central location.
3. **Equipments and supplies**: As identified earlier, freezers/refrigerators/centrifuges/sterile hood, liquid nitrogen tanks, computers and accessories, cold storage units, biological waste disposal, and other routine laboratory and tissue banking supplies are needed.
4. **Budget**: An adequate budget that is reviewed periodically on a yearly basis is needed to maintain staff, equipment, and others.

Fee recovery:

The high cost of operation of a Biospecimen core would demand a) a sustained support from the University, or b) a mechanism for generating revenue, or c) obtaining additional revenue via contracts and grants.

1. Investigators may include tissue procuring costs in contracts and grants.
2. Clinical trials may add the cost of tissue banking/storage to the contracts.
3. A fee of $50 per sample or a set of samples (e.g. blood) could be levied. For example, it is customary for many cell culture core laboratories and other laboratories to charge a fee for cells.
4. A fee of $100 could be levied for special "on demand" tissues that require additional involvement of physician/surgeon time.
5. A fee up to $250 upon the publication of any article that originated from the use of samples from the Biospecimen core depending on the number of tissues used.

Items 3-5 might be waived by the committee for unusual circumstances such as a student/resident/fellow initiated research activities.

Recommendations:

1. **Of the existing centers at LSUHSC, the Cancer Center Core appears to be well developed and already in place. Despite a few minor deficiencies, the Cancer Center core is better suited to serve the needs of the campus. It is recommended that this core is further developed to utilize the procurement of normal tissues and blood samples. The Cancer Center Core would thus become the centralized and main biospecimen core of the campus.**
2. **It is recommended that a "wet laboratory" is setup to process blood samples to isolate cells, plasma/serum and to dissect out tissues.**
3. **It is recommended that the Cancer Center Core incorporate additional members in their committee who would advise on the procurement of control and normal samples.**
4. **It is recommended that specific people/protocols are identified for investigators to contact the core regarding the need of samples.**

Future directions:

1. The Biospecimen core could be integrated with a “clinical trials” office.
2. Novel cells derived from tissues could be immortalized (Technology Transfer)

Appendix:

1. An example for tissue procurement:

1. NAME OF PRINCIPAL INVESTIGATOR
2. NAMES OF THE PARTICIPATING INVESTIGATORS
3. INSTITUTION AND ADDRESS, PHONE NUMBER OF INVESTIGATOR (Physician/Surgeon)
4. INSTITUTION AND ADDRESS, PHONE NUMBER OF PARTICIPATING INVESTIGATOR (Physician/Surgeon)
5. PROTOCOL TO FROM WHICH TISSUE IS OBTAINED
6. TITLE OF RESEARCH PROJECT
7. RESEARCH OBJECTIVES: List
8. RESEARCH PLAN: Describe briefly how the research objectives will be accomplished, including specifics of methods to be used and endpoints to be evaluated. Be specific on the number of tissue specimens required.
9. WASTE TISSUE GENERATED AND DISPOSAL
10. QUALIFICATIONS OF INVESTIGATOR AND LABORATORY TO PERFORM STUDIES: Describe the specific qualifications of all members of the team
11. SOURCE OF FUNDING FOR THIS STUDY: Be specific and include grant numbers
12. BUDGET FOR STUDY:
13. BIOSKETCH OF PI AND THE PARTICIPATING INVESTIGATORS (NIH FORMAT)
14. COLLABORATORS AND INSTITUTIONS WHO WILL PARTICIPATE IN STUDY
15. DURATION OF STUDY
16. IRB APPROVAL
17. SIGNATURE
18. LETTERS OF COLLABORATION:
    Site Committee representative or protocol PI
    Statistical Unit evaluation and approval
    Tissue Bank (stating number of samples and type of tissue available)
19. PROPOSAL DISPOSITION:
    Completed application, in the above format, should sent to: