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An introduction to starting a biobank

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Summary

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The purpose of a biobank is to process, organize, and maintain various types of biospecimens that are to be utilized for both clinical and research-based services. There are different types of biobanks, so the goals of the biobank should be delineated at the outset of forming a biobank. The startup of a biobank benefits from accreditation and stringent adherence to standards of practice. Fundamental to these practices is the protection of privacy and informed consent. A budget must be developed, and sources of funding should be obtained to properly equip the designated space and personnel. The appropriate space for freezers and for biospecimen processing should be identified. Information technology is also a critical part of the biobank and effort should be expended to ensure that this aspect is effective and secure. Given the ethical concerns surrounding biospecimens, engagement with the public is also highly valuable.

Keywords

Biobank; Biorepository; Biospecimen; Clinical; Research; Accreditation

1. Introduction

Biobanks or biorepositories are specialized pathology laboratories that allow for future clinical or research studies by collecting, processing, and storing biospecimens. Biospecimens, often obtained from surgeries and autopsies, may be used as part of a clinical work-up or in prospective or retrospective studies (1). In recent years, more biobanks have been developed due to increasing tissue requests for translational studies (2). With this demand, there is a need to develop standards of practice and accreditation. Standard operating procedures (SOPs) should be used in all aspects of the biobank process, from procurement to shipment to safety (3). Furthermore, the development of these practices

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should involve engagement with the public to resolve potential ethical, legal, and social issues (4). The public must also understand the funding needs for biobanks, which are increasing together with the growth of biotechnology. Biospecimens are no longer being simply stored in jars of formaldehyde but may now require elaborate procurement processes and stringent storage requirements. As such, there is considerable cost associated with the entire biobanking process. In order to support funding, the public, clinical research organizations, and government agencies will have to be involved more than before (5). Another key element of the biobank is the creation of a protected database to track biospecimens. Within these databases, it is crucial to provide a link to track the specimen; including the source, collection date, clinical information and molecular and genetic information. Furthermore, to maintain privacy, encryption methods should be used along with a secured server. This chapter provides considerations for the formation of a biobank including accreditation, standards of practice, and funding issues.

2. The purpose of biobanks

Biobanks are established to provide a repository of biospecimens that may be used to elucidate the pathophysiology, diagnoses, and ultimately treatments of diseases (6). To achieve this goal, a biobank collects, stores, and processes human biological material in accordance with current protocols supported by available scientific data. Depending on the specimen source and study plans, biobank personnel decide how biospecimens are collected and processed. With this in mind, the creation of multiple aliquots or samples allows for greater leveraging of the biospecimens for both clinical and research purposes (7). Depending on the study goals and the kind of institution that will carry out the research, there are different types of general biobanks, some of which are summarized below:

2.1 Disease-oriented biobanks

Perhaps the most common types of biobanks are those used to collect disease-specific biospecimens. The focus and breadth of disease types and specimens in these biobanks is varied. Disease oriented biobanks may be useful for basic research, case-control studies and clinical trials pertinent to the disease. Some disease-oriented biobanks may focus on a single type of tissue, such as injured human spinal cords. Others may be much broader and include biospecimens from throughout the body that are relevant to a disease process such as cancer (8). Cancer centers often have biorepositories that store biospecimens from a broad range of cancers that, while sharing some similarities, are effectively different disease entities. A cancer biobank may have lung, breast, liver, colon, renal, prostate, and lymphoma biospecimens. Even when a cancer branch focuses on a specific organ like the brain, a variety of very different cancers may be collected. For example, the Brain Tumor Translational Resource (BTTR) at the University of California, Los Angeles stores gliomas, meningiomas, schwannomas and other brain tumors as well as associated blood and cerebrospinal fluids.

2.2. Population-based biobanks

Population-based repositories that provide biospecimens, such as germline DNA from individuals of a general population, have broad uses. Umbilical cord blood or screening

blood spots from newborns have been used in transplantation and stem cell research studies (9). The need to obtain a large number of samples for the study of rare diseases also may require this type of biobank. Screening a large population of patients may elucidate specific alleles that may underlie a unique disease phenotype. Alternatively, studies may attempt to distinguish environmental from genetic effects by studying monozygotic and dizygotic twins. Such a prospective approach can be used for preventive medical programs and epidemiological studies (10).

2.3. Virtual repositories

Virtual repositories represent “clearinghouses” for stored specimens located in other places. A typical model would comprise of a searchable central database that archives the biospecimen and content at multiple existing medical center pathology departments or research biorepositories. The virtual repository is often guided by an oversight committee for the consortium of centers. A virtual repository can expand efficient access to multiple distant sites without the necessity, risk, and cost of moving all the samples to a central location. This type of repository can avoid new collection efforts, time and cost wasting and may be useful for retrospective cohort studies (11). Some virtual repositories will also prospectively collect and index new biospecimens as well. Typically, a set of clinical, pathology, and molecular data is linked to the virtual biospecimens. A researcher will request a cohort of biospecimens with specific characteristics from the virtual repository. Such potential cases will be identified and approved by an oversight committee. The National NeuroAIDS Tissue Consortium (U.S.A) is such an example. A central data coordinating center provides online query tools and a centralized requesting mechanism that, after approval from an oversight committee, can facilitate shipping of specific biospecimens from four biobanks located in California, New York, and Texas.

3. Requirements for biospecimen collection

3.1 Accreditation

Pathology laboratories in most countries must have the appropriate accreditations as determined by law. Accreditation of a biobank ensures that the laboratory controls and optimizes the use of biospecimens in good professional practice, as defined by internationally established standards. Necessary requirements for accreditation include an operational quality management system and a continuous control of the methods used for diagnostic purposes (12). In this way, the biobank is recognized for maintaining high quality processes and these are ultimately reflected in patient care and research. The process of accreditation gives the biobank recognition by ensuring consistency and standardization of practice. For some countries, the accreditations standards may be found in ISO 15189 and ISO 17025. In the United States, biorepository accreditation standards are promulgated by the College of American Pathologists (CAP). These standards are similar in that they require pathology laboratories to implement a system of quality management and to continuously monitor protocols. Accreditation of a laboratory is therefore intended as a strong indicator of quality for the biobank, which should thereby produce reliable results.

3.2 Informed consent, ethical, and legal considerations

As biotechnology continues to grow, biobanks are faced with many new ethical and legal concerns which must be addressed with the public. Therefore, all clinical and research protocols that involve the biobank must be approved by a relevant Institutional Review Board (IRB) and/or Medical Ethics Committee (MEC) (13). The bedrock of human bioethics is informed consent, which requires the patient and/or subject to be given an overview of the study, discussion of protocol specifics, and a disclosure of potential benefits and risks. General information of participants should also be maintained to contact them for future studies. However, since a re-consent approach of large-scale studies has some practical difficulties and adds labor and costs, many biobanks obtain a broad informed consent that participants can accept for current and future studies. In other words, participants may fill out consent forms without any information of future studies, but these consents may not encompass all potential ethical issues (14). Beyond informed consent, additional unresolved ethical issues for biobanks include participant withdrawal and the potential of some protocols to interfere with patient diagnosis or treatment. Furthermore, as there are different kinds of health issues between different population groups, biobanks must also often consider gender and ethnicity. Thus, organizing biobanks while recognizing different racial populations may be useful to progress treatments and disease prevention (15). Given the potential for new and/or unresolved ethical issues, biobanks must maintain transparency and have open engagement with the public.

3.3 Standard operating procedures

There are a variety of standard operating procedures (SOPs) or best practice protocols for biobanks and determining which to use is often dependent on the particular needs of the clinical or study being performed. The International Society for Biological and Environmental Repositories (ISBER) and the National Cancer Institute Biorepositories and Biospecimen Reseach Branch (NCI BBRB) have published best practices that are available online (16). ISBER published a biobank handbook called Best Practices for Repositories that includes topics such as specimen collection, processing, and retrieval, training, ethical issues, and many more (17). IBSER website should be checked periodically to stay up to date with the latest revisions biobanking protocols. The NCI BBRB similarly provides guidelines to promote biospecimen and data quality, and to address ethical and legal issues. The SOPs used by these organizations assist practitioners and help them provide good clinical decision making when developing a biobank (18). Patient privacy and safety of biobank personnel are recurrent themes throughout all SOPs and as such will be discussed in greater detail below.

3.4 Personnel considerations

Depending on the size, multiple types of personnel may be required to properly staff a biobank (19). There are major considerations when hiring personnel. The first is the quality of the person and the second is their knowledge and prior training or certification (if available). With respect to hiring high quality personnel, criteria that should be considered include work ethic, timeliness, intellectual capacity, teamwork, and communication skills. With respect to knowledge and prior training, histopathology, molecular, or other relevant

laboratory or management experience are advantageous. Education materials and programs should be provided to give personnel the necessary certifications (20). Furthermore, to ensure consistency of processes across time, certifications should be renewed on a regular basis. Biobank personnel may have a range of responsibilities such as procurement, processing, storage, and disbursement of specimens along with database maintenance. In order to meet all these needs, core personnel may also include a director, a pathology supervisor, laboratory manager, quality control manager, and full-time laboratory technicians. Such positions may be covered by one or more people, depending on the size and needs of the biobank.

3.5 Biosafety requirements

There are numerous potential biosafety hazards that may be encountered when working with biospecimens. Therefore, it is imperative that all personnel take the appropriate safety precautions. To achieve this, the National Institutes of Health (NIH) provides the required biosafety guidelines. These guidelines provide safety information related to work in laboratory research and should be a part of established good practice SOPs. At a local level, an Institutional Biosafety Committee (IBC) will help establish further guidelines and oversee the biosafety requirements, and all protocols used by a biobank should be submitted to the IBC for approval. In addition, biosafety information documents for all materials used in the biobannk should be reviewed by relevant personnel and be made readily available. These include the Material Safety Data Sheets (MSDS), which contain health hazard information for chemicals and infectious agents, and requirements for when to use chemical fume hoods and biosafety cabinets (21). Occupational Safety & Health Administration (OSHA) also publishes information about blood-borne pathogens and needle stick prevention and offers some required training courses to improve knowledge about safety issues. Basic training should include the use of appropriate protective gear, such as hand/arm protection, lab coats, and closed-toe shoes, as well as knowledge about decontamination procedures to remove and minimize the effect of biohazardous materials. However, it is ultimately the responsibility of all personnel to be properly trained and adhere to safety requirements.

3.6 Equipment and space considerations

The type and quantity of materials that will be collected and processed, will determine the different equipment and space requirements (22). Therefore, the necessary equipment and facilities should be established according to the overall mission of the biobank as well as specific SOPs. The biobank room must meet requirements to provide a safe place for the staff and material stored. In order to design a workflow, Lean Laboratory Design may be used as a reference (23). The room should have enough space for equipment, specimens, biohazard hood, chemical hood for tissue fixation, handling biohazardous materials, workstation, computers, specimen receiving area, chemical storage cabinet, an emergency eyewash and shower station, water bath and utility sink. Storage in freezers or at room temperature may necessitate additional space (24). Furthermore, space may be needed for tissue processing, tissue embedding, molecular workstations, automated slide staining and labeling. When possible, each lab space should have up to two exits (25). The laboratory

also should be built close to operating rooms and autopsy rooms in order to reduce the time of specimen collection, and it should be in close association to office personnel.

3.7 Information technology

3.7.1 Software—Equally important to a biobanks role in the procurement and processing of biospecimens, is the management of relevant clinical and research data for each of those biospecimens. Hence, it is crucial to maintain a software system, which supports data collection, analysis and management while providing strong security and protection of privacy. There are many different types of software on the market, but in general the software should have some important abilities that are recommended in the aforementioned practice guidelines. These include allowing authorized users to operate at various locations and computers, and to have easy access to documents and records. In addition, the software should provide a secure environment that protects data, includes an exclusive and unchangeable ID for all of the biological samples, and an ability to continuously track the sample's location. Encryption, which is the process of encoding data in a software system, is another important way of protecting data from being recovered by non-authorized users. A well-designed software system should have infrastructure that supports the operation 24 hours/7 days a week and also has the ability to cope with disasters and downtimes and recover stored data.

3.7.2 Hardware—Access to information in today's changing world is getting easier by using Information Technology (IT). It is important to access data through suitable computers that can handle the infrastructure required by software systems. Media storage, network share drives, printers, scanners, fax machines and cameras are other examples of hardware, which will be part of the network. Although hardware provides a huge benefit to its users, there are some disadvantages in regard to lifetime, battery life, and possible breaches that may affect the storage of data. Therefore, it is critical to store the hardware in locked rooms, back up all the data, and try to replace them when they are getting close to the end of their life expectancy (26). Computer hard drives, external hard drives, USB sticks and other portable memory should be appropriately encrypted to the latest standards.

4. Funding

Biobanks need funding for both their development and long-term maintenance. Furthermore, as the size and scale of biobanks increases together with biotechnology, so will the demand for funding. Thus, obtaining funding for a biobank is a perpetual task. Various startup costs are associated with the formation of a biobank, including the purchase of equipment and preparation of the space. To maintain the biobank, budgets will include salary for personnel, facilities and material costs. Additionally, consideration must be taken as to what biospecimens are necessary to collect, in order to prevent duplication of efforts and unnecessary costs (27). To meet these costs, there are various funding sources including federal, state, university, and hospital, pharmaceutical, and foundation/private donors. Examples of different types of funding models and steps to obtains funding are listed below:

4.1 Public biobank model

Public biobanks are supported through governmental funding organizations. In the United States, the National Institutes of Health (NIH), part of the US Department of Health and Human Services, acts to support biomedical researches financially (28). Whereas in the United Kingdom, biobanks are funded publicly by the National Health System and by a charity service, the Welcome Trust. State and county governments may see fit to support biobanks as well.

4.2 Biosocial model

Within biosocial models of funding, patient activity groups, grassroots, and private organizations are more intimately involved in the development and maintenance of biobanks (29). For example, the Genetic Alliance biobank in Washington D. C. was created by patient's grassroots activities, and the UCLA AIDS Institute is supported by individual donors and charity events.

4.3 Applying for funding

The application process varies slightly between different organizations and institutions. In the United States, the best place to start is through Grants.gov. In doing this, it is critical to understand the legal aspects for the different types of funding, and carefully read the application instructions that are described by each awarding institute. As a next step, current application forms and documents should be completed and thoroughly reviewed, as these may change from one funding cycle to the next. With these documents, specific budget data should be carefully documented, including room for additional unexpected costs. Some granting agencies may choose to only fund a portion of the budget. Most applications may simply be downloaded from the internet and submitted electronically. Formal evaluation of the grants is typically performed by a committee or study section, which provides scores based on ethical standards and scientific merit. After the application is reviewed, scored, and determined to be eligible for funding, the awards will be issued. Progress reports are then submitted to the granting agency at regular intervals to ensure proper use of the funding and the potential for receiving future awards (30, 31, 32).

5. Conclusion

The development of a biobank has similar requirements to other pathology and research laboratories, with perhaps an emphasis on ethical considerations. However, by obtaining the necessary accreditations, and following stringent SOPs, biobanks have the potential to offer the public unique clinical and research-based services. Biospecimens are the critical fuel needed for human disease-oriented research. It is vital that governmental and private funding agencies continue to recognize the importance of biobanks in advancing our understanding of health and disease.

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