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THE ROLE OF BIOREPOSITORIES AND SPECIMEN MANAGEMENT IN SUPPORTING PRECISION MEDICINE RESEARCH AND CLINICAL TRIALS

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Abstract

Biobanks play a crucial role in enhancing population health. We are now experiencing a new age in the field of medicine, when patients, health professionals, and researchers are increasingly working together to acquire fresh insights and investigate novel approaches to diagnose and cure diseases. Numerous extensive biobanking initiatives are now taking place globally, including institutions, nations, and even multinational collaborations. Biobanks are useful tools in translational research when combined with subject data from surveys and medical records. A biobank must possess samples of superior quality that satisfy the requirements of researchers. Biobank laboratory operations need extensive support, including lab and storage space, skills in information technology, a laboratory management information system, logistics for sample transfer, quality management systems, and suitable facilities. An essential measure of success for a biobank is the principle that each biospecimen deposited in the repository is associated with a participant who has valuable contributions to make towards research for a healthier future. This essay will examine the significance of biorepository activities, particularly in relation to the acquisition and preservation of participants' materials. Emphasis will be placed on preserving the quality of samples, as well as providing the necessary assistance to biorepositories in order to meet their objectives and maintain the integrity of each specimen.

Keywords: Biobanks, biorepository activities, precision medicine research, review, laboratory research, specimen.

1. Introduction

Over the last several decades, advancements in technology and informatics have led to a shift in scientific research. Instead of focusing only on laboratory-based discoveries, researchers now engage in translational research. This kind of study aims to uncover the biological origins of diseases and provide individualized treatment options for patients. Obtaining a significant amount of samples from study groups that can be tracked over time has become crucial for

translational research. In the twenty-first century, biobanks have emerged worldwide to fulfill this need. Currently, there exist various biobanks that cater to different populations. These include large population-based biobanks such as the Kadoorie Biobank in China (1), LifeGene in Sweden (2), CONOR and MoBa in Norway (3, 4), Auria in Finland (5), UK Biobank (6), Estonian Biobank (7), BioBank Japan (8), Korean Biobank (9, 10), Taiwan Biobank (11), and Million Veteran Program (12) and All of Us Biobank (13) in the United States. Biobanks are required to gather, handle, preserve, and distribute biological substances with accurate and comprehensive documentation in order to fulfill the requirements of future translational researchers.

An effective translational research program relies on the presence of biobanks with robust infrastructure that can ensure consistent specimen collection, tracking, quality control management, sample storage, as well as disaster recovery plans and long-term financial stability. These fundamental components serve as the foundation for the success of any biobank and the flourishing of translational research. Both the National Cancer Institute (NCI) and the International Society for Biological and Environmental Repositories (ISBER) have developed guidelines to outline the most effective methods for biobanking and the formation of biospecimen resources. In this article, we provide a comprehensive analysis of key factors to be taken into account while managing biorepository operations (Figure 1). For the sake of this discussion, biorepository operations refer to the many teams responsible for the collecting and storage of biological specimens in several biobanks.

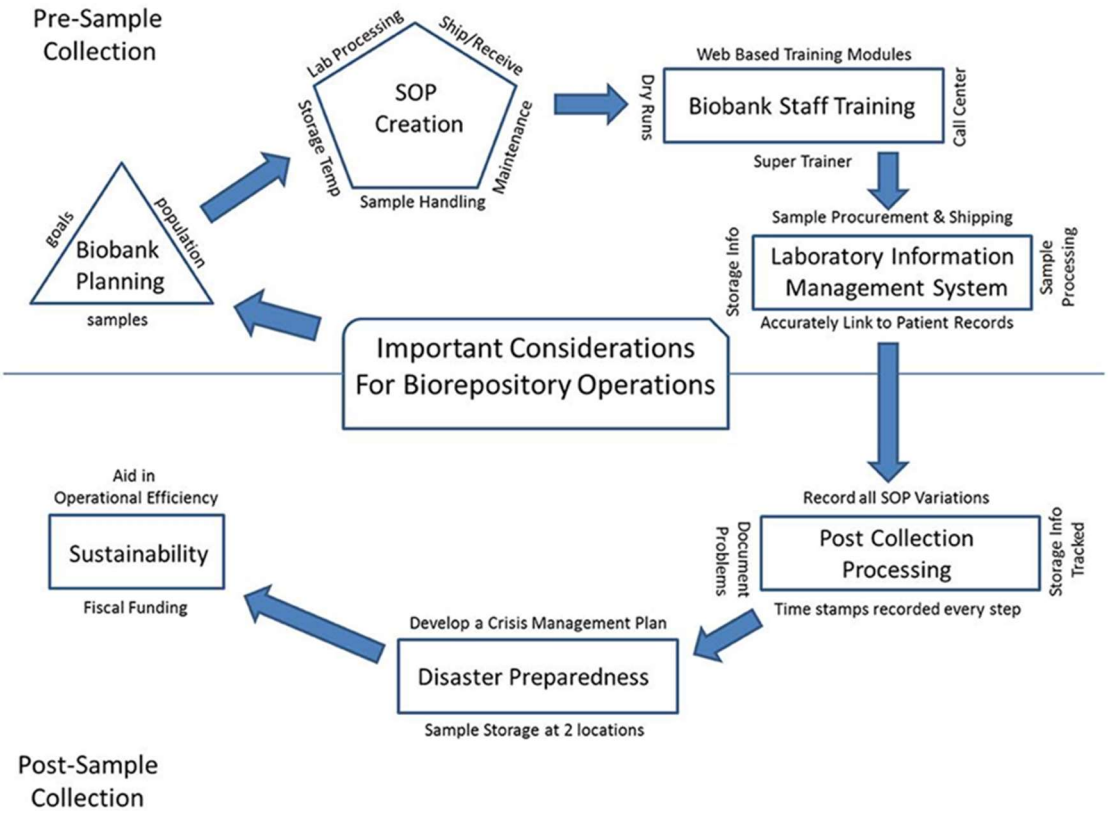

Figure 1. An overview of important considerations for biorepository operations.

2. Biobank Strategic Planning

Before starting a new biobank collection, the operational team of the biorepository must get a clear grasp of the aims of the new biobank, the population(s) of subjects involved, the methods for collecting and processing samples, the storage needs, the necessity for pre-analytical data gathering, and the long-term monitoring requirements. The biobank must have a well-defined strategy to effectively achieve its collecting objectives and address the expected requirements of both present and future translational researchers.

The function of the biorepository operating team starts at the protocol design stage, even before the first participant volunteers to join the biobank. It is necessary to create and evaluate operational protocols to ensure that every sample is collected and processed correctly and promptly, in order to maintain the integrity of the samples. Sample integrity refers to the reliable and consistent handling of a specimen to guarantee that all collected materials remain undamaged and suitable for their intended use. The integrity of the data is monitored by the acquisition of information at every stage of the collecting and storage process. The feature enables the recording of the sample's history to assure the collection of data by researchers, leading to relevant and consistent findings. Ensure that no factors during sample processing or storage have occurred that might potentially modify these findings. Both the staff of the biorepository and biobank (study) share the duty for conducting the collection site feasibility assessment, establishing standard operating procedures (SOP), and training workers participating in sample procurement.

SOP Creation Standard Operating Procedures (SOPs) should be created in order to guarantee the collection of high-quality specimens and maintain consistent handling of samples. This is done to minimize pre-analytical variables, such as the time taken for pre-processing, the temperature at which samples are sent, the speed and temperature of centrifugation, the processing time, and the storage temperature. The responsibility for implementing several SOPs, such as biospecimen handling, laboratory processing, shipping and receiving technique, documentation within a record management system, equipment maintenance assistance, and facility security, lies with the biorepository personnel. However, other SOPs are assigned to the biobank collecting team (16). In 2011, Moore et al. stated that several parameters related to the management of biospecimens might have an impact on subsequent applications (17). Handling effects may have an impact on the outcomes of translational research. Therefore, Moore et al. suggested that every published experimental findings should include a report on the handling of samples during collection, which is referred to as BRISQ (Biospecimen Reporting for Improved Study Quality).

The biorepository operations team should collaborate with the biobank team to assess collection tube alternatives and conduct any required testing to establish the most suitable collection process that will provide the intended final product for the biobank's objective.

Standard operating procedures (SOPs) should explicitly describe the processing instructions and the acceptable time period after collection. These instructions should be based on information from scientific literature and the recommendations provided by the manufacturer. To ensure molecular stability, it is crucial to stabilize or treat materials promptly after collection (18). Nevertheless, various gathered biospecimens will naturally possess distinct processing prerequisites. Elliott et al., for instance, delineates the testing conducted before the commencement of the UK Biobank sample collection (6). A study was conducted to determine the duration for which samples could be maintained at a temperature of 4°C before noticeable variations in significant analytes occurred. The results indicated that there were no changes within a 24-hour time frame, but differences were apparent around the 36-hour period. Therefore, the conclusive Standard Operating Procedure (SOP) was produced to accurately represent those discoveries, affirming that the recommended timeframe for cryopreservation of aliquots should not exceed 24 hours following collection (6). After being created, it is necessary to conduct an annual assessment of all Standard Operating Procedures (SOPs) and make any necessary updates.

3. Training for Biobank Staff

Adhering to established Standard Operating Procedures (SOPs) and providing sufficient training to personnel are effective ways to enhance sample integrity. Ensuring that staff are trained and regularly reviewing the whole process is particularly crucial for biobanks that depend on numerous accrual sites for initial patient contact, specimen procurement, and pre-shipment processing. This is because variances in protocols may occur due to differences in site infrastructure. The training of biobank accrual site personnel should include a highly skilled trainer who would be responsible for training new staff members, in preparation for the expected turnover of workers throughout the project. Web-based training courses might be beneficial to biobank accrual sites by offering ongoing assistance and information on standard operating procedure (SOP) modifications. Remote continuing assistance may be provided via a contact center, where queries are assessed and sent to the relevant staff for prompt responses. Ultimately, dry runs may be conducted throughout the onboarding phase of new collection locations to guarantee a seamless flow of the process from shipping to collection. This strategy has led to very effective accumulation of high-quality samples in various biobanks.

4. Laboratory Information Management Systems (LIMS)

The everyday operations of a biorepository rely on a dependable sample tracking system known as a laboratory information management system (LIMS). It is crucial to have a well-established information technology (IT) LIMS in place to guarantee the integrity of sample data, much like the quality of the samples themselves. The whole life cycle of a biobank collection is managed inside a Laboratory Information Management System (LIMS), where each sample in the collection is associated with the appropriate patient information. This linkage is maintained

throughout the entire process, starting with procurement, through shipping, processing, and ultimately to long-term storage (18).

Large biobanks need the use of an IT LIMS to track specimens. The methodology and use of an integrated IT LIMS, in addition to the method of inputting information, may be achieved via many approaches. As an instance, the Estonian Biobank states that they have a recruiter complete the questionnaire with the participant at the moment of donation, so generating a record (7). Upon encountering improperly completed mandatory fields, the recruiter was promptly notified in real time, enabling fast rectification. One method to guarantee that every information is both comprehensive and precise is by following this approach.

The UK Biobank employs a distinct approach by assigning a singular bar code to each sample and thereafter scanning it at the assessment center to integrate it with the participant's exclusive ID, which was given at recruitment. In this methodology, the bar-coded tubes are not initially allocated to a specific individual in order to eliminate mistakes in participant identification and to avoid the logging of empty blood collection tubes. Bar codes are scanned during collection to activate a timer in the UK biobank's IT system. This allows for automated time linking instead of human linking. Biobank Japan employs autonomous medical coordinators who gather data and then de-identify the samples on-site (8). Therefore, IT systems and their use might vary across biobanks, but they are always vital in guaranteeing precise record-keeping throughout sample acquisition.

5. Processing after collection

Once biospecimens are collected, some techniques may need minimum processing to preserve specimen stability. Alternatively, other biospecimens may be held at a designated temperature prior to being transported to a processing facility or the main biobank site. All processing activities conducted at collecting locations must be recorded in the IT system, which should include the exact time of processing as well as any issues or deviations from the standard operating procedure (SOP) that have been published. The transportation methods and time from accrual sites to the biobanks differ depending on the stability of the sample type. It is essential to trace samples via the IT system and record the arrival time and temperature of each specimen upon delivery. As an example, specimens in the Kadoorie Biobank are first kept at a temperature of 4°C for a short period of time before processing. They are then maintained at a temperature of -40°C for a duration of 3-4 months. Subsequently, they are transported to a central blood repository using dry ice and stored at a temperature of -80°C for long-term preservation (1). The Million Veteran Program transports entire blood to a processing site where DNA extraction takes place on the same day. The samples collected for the UK Biobank undergo minimum processing at the collecting locations and are then stabilized at the proper temperatures. They are then transmitted on the same day of collection to high throughput centers for further processing.

Biobanks often use a commercial courier service to transport specimens overnight. Commercial couriers are the preferred mode of transportation for specimens due to their

specialized training in temperature management and efficient delivery of specimens. Upon reaching the Biobank, every sample package must undergo a quality inspection to ensure temperature consistency and packaging integrity. The received samples must be matched with the accompanying request form. Any detected discrepancies should be documented in the Laboratory Information Management System (LIMS) in relation to the respective samples.

The assessment of biorepository operations should include an evaluation of the laboratory infrastructure to determine its quality. Large biobanks must allocate resources to acquire instruments in order to reduce human mistakes and streamline the processes of sample processing and storage (12, 19). Robotics, when suitable, may provide diverse benefits such as cost reduction, enhanced repeatability, and improved overall quality assurance. Robotics may be advantageous for sample annotation and tracking in LIMS. Utilizing robotics to retrieve samples can guarantee temperature stability.

The objective of biorepository operations management is to maintain the utmost quality of specimens for translational research. Protocol violations might cause variations in the preanalytical stage, which can affect the subsequent utilization of samples (20). In 2000, Narayanan conducted an extensive analysis of three aspects of pre-analytic variability: physiological parameters, specimen collecting methods, and the impact of interfering elements that must be taken into account during specimen collection (21). It is evident that the responsibility of reducing pre-analytic factors will be placed on the biorepository. A multitude of publications and reviews have been published, examining and discussing the most effective methods for biobanks, particularly in the areas of sample collection and processing, tracking, and storage (18, 21–23).

These materials serve as valuable guidance for biobanks. Quality management may be maintained by implementing regular testing and using quality control measures for the processed specimens, along with the usage of laboratory robots. All deviations from standard operating procedures (SOPs), as well as routine quality control (QC) and maintenance records, must be properly recorded. Ultimately, the biorepository personnel should regularly examine the biobanking literature to guarantee that standard operating procedures (SOPs) are updated with the most recent progressions, as indicated by recently published studies and newly accessible technology.

6. Conclusion

Biobanks play a crucial role in enhancing population health. We are now experiencing a new age in the field of medicine, when patients, healthcare providers, and researchers are working together more and more to acquire fresh insights and investigate novel approaches to detecting and treating illnesses. Numerous extensive biobanking initiatives are now under progress globally, including institutions, nations, and even multinational collaborations. Biobanks are useful tools in translational research when combined with subject data from surveys and medical records. A biobank must possess samples of exceptional quality that

precisely fulfill the requirements of researchers. Biorepository operations need substantial assistance in several areas, including laboratory and storage infrastructure, skills in information technology, a laboratory management information system, logistics for sample transportation, quality management systems, and suitable buildings. An essential measure of success for a biobank is the principle that each biospecimen deposited in the repository is associated with a participant who has valuable contributions to make towards research for a healthier future.

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