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Original Research Paper

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FUTURE OF BIO BANKING AND PARADIGM SHIFT IN BIO-ANALYSIS AND CLINICAL RESEARCH

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ABSTRACT Biobanks are comprehensive storage and library management services.Biobanks are an organized collection of human biological material and associated information stored for one or more research purposes.Biobanks have focused on protecting donors' welfare and privacy.The collection, processing and storage of biological samples occur in the larger context of organizations known as biological resource centres . Biological resource centres are service providers and repositories of living cells, as well as genomes of organisms, archived cells and tissues, and information relating to these materials. Biorepositories are facilities that collect, process, store, and distribute biological samples to aid scientific research. The most obvious subcategory is biobanks which specialize in the collection of human biological material. Their importance has continued to grow over the past several years and now represents a vital tool in advancing the study of disease and research targeted at developing personalized medicine. Biomarker studies require processing and storage of numerous biological samples with the goals of obtaining a large amount of information and minimizing future research costs.

KEYWORDS : Biobank, Cell line biobanking, DNA testing assays, National Centre for Advanced Research and Excellence in HF (CARE-HF)

INTRODUCTION

In many countries biobanks are defined as a collection of human biological samples stored and regulated for use in scientific study by connecting the samples to the phenotypic and demographic data of the donor.(1)

The main purpose for creating the biobanks is to have this genotype-to-phenotype-relationship database accessible for various research projects aimed at improving the understanding of medical conditions including their diagnosis, prevention and treatment (2,3)

Samples such as serum (plasma) and solid tissue specimens are commonly being stored. Nevertheless, other biobanks also maintain peripheral blood cells or bone marrow, cord blood derivatives, pathological body fluid, cell lines, saliva, urine, stools, hair and toenails (4)

Prior to the collection of samples and data, the donors would undergo a baseline interview that includes a few questions regarding their lifestyle, medical history and demographic information(5)

Other physical assessments such as height, weight, waist and hip circumference, body fat percentage, bone density, fitness, grip strength, lung function, heart rate, blood pressure, vision and hearing are also being recorded (6)

By linking biospecimens and related health data, biobanks enable researchers to study the multifactorial nature of disease. It is hoped that this will ultimately lead to improved health care outcomes (7)

However, complex ethical, legal, and social issues accompany the scientific promise of biobanks and most of the ethical concerns have primarily focused on the risk of harm related to the privacy interests of donors (8)

Yet little discussion has been devoted to consent issues surrounding *future* uses of biobanked samples. Some suggest that the blanket consent acquired at the initial time of donation is sufficient for all possible future studies or that additional consent should be collected by investigators whenever possible (9)

Individuals willing to donate to biobank that allow research studies to be performed on banked tissues concerned with risks to their welfare and privacy.(10)

Biobanks are a remarkable and rapidly expanding resource that creates new research platforms while also preserving human dignity, necessitating legal, ethical, and regulatory considerations, as well as the incorporation of biobanks into existing regulations. (11)

The effective utilisation of these biological resources is dependent on an effective governance structure and processes that increase the legitimacy and social licence to

operate.(12)

The fundamental prerequisites for effective governance include transparency, accountability, and the adoption of oversight systems.(13)

Transparency permeating all aspects of a system allows for the storage of samples and data, their use and exchange, and accountability to stakeholders.(14)

When the handling of research subjects, personal data, and biological samples increases, oversight systems put in place by the organisation to oversee its activities in the best interests of impacted parties become increasingly important(15)

Expansion of research paradigms such as precision and personalised medicine necessitates large collections of samples (16)

Furthermore, the quest for extracting relevant patient records from big data has seen the emergence of artificial intelligence: a transformative technology with regulatory challenges that must still be addressed.(17,18)

The standardisation of sampling, storage, and quality control protocols is critical to the establishment, reliability, and long-term viability of a biobank.(19)

This would allow researchers to learn more about sample processing, identify collections that would be a good fit for their investigations, and understand the specifics of the treatment in order to compare results with samples from different biobanks (20)

Biobank History

The last several decades have seen tremendous improvements in the collection and storage of human samples, allowing the worldwide scientific community to obtain very important results in the field of medical research.

The first biorepositories have existed in various forms for over 150 years, from early small collections to modern automated facilities with millions of samples. The term "Biobank" was coined in 1996.

Operations of Biobank

a. Collection of Biospecimen
b. Processing
c. Storage
d. Distribution
e. Data Management

Biospecimen

A biological specimen (also called a biospecimen) is a biological laboratory specimen held by a biorepository for research. Such a specimen would be taken by sampling so as to be representative of any other specimen taken from the source of the specimen. When biological specimens are stored, ideally they remain equivalent to freshly-collected specimens for the purposes of research.Human biological specimens are stored in a type of biorepository called a biobank, and the science of preserving biological specimens is most active in the field of biobanking.

Blood---------- Cell Lines

Plasma----------Urine

Serum----------CSF

RBC White Cells----------Bone marrow

DNA----------StemCells

RNA----------Tissue

Collection and storage

These are the banks that collect & store biological material that is set aside for research. Samples can be collected from:

Vacutainers for blood sample collection

Five Main Operations of BIOBANKS
a. Collection of Biospecimen b. Processing c. Storage d. Distribution e. Data Management
a. COLLECTION of BIO SPECIMENS

Blood----45 ml of blood with vacutainer system

Plasma--------Blood centrifuged with anticoagulants

Blood and Serum collection tubes

Serum----------Blood centrifuged with anticoagulants

Collection of specimens---

Tissue homogenates 40-500ml PVC container with Teflon lid

Hair follicles

Hair Follicles Wide mouth container or foil (usually in testing drug abuse)

a. COLLECTION of BIOSPECIMEN

Biological specimens (or biospecimens), such as blood, urine, saliva, and many other types, are collected for a variety of reasons, for normal patient monitoring and care as well as for basic,clinical and epidemiologic research studies.

Urine

Minimum 9ml of urine for processing

Feces

Aluminium foil container (usually for DNA extraction from feces

Gastric Matrix

Large stainless steel container with formaldehyde & water

COLLECTION of BIOSPECIMEN

Saliva

sterile Salivette Tubes are used.(usually for hormonal biomarkers)

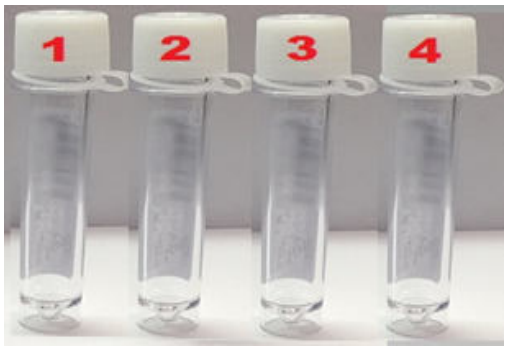
CSF

Sterile PVC vacutainer system

Saliva Collection Tube

CSF

Sterile PVC vacutainer system



CSF collection Tubes

COLLECTION of BIOSPECIMEN

Seminal Fluid

Sterile Capped containers convenient for Harvesting

Cumulus cells & Oocyte

oocyte retrieval with a Steiner-TAN needle

Sputum

Sterile PVC container

COLLECTION of BIOSPECIMEN

Biological Matrix

(Non cytoplasmic) Connective Tissue Extracellular Matrix Jelly-like structure 1.Finger Nails 2. Toe Nails

BIOBANKS

Five Main Operations :

b)Processing

1. Pretreatment

DNA extraction from whole blood and saliva RNA extraction from whole blood Plasma/serum isolation Sample plating Sample retrieval Tissue extraction

2. Stabilization

DNA in salt buffer to stabilize for long-term storage. 3. Aliquoting Larger sample into smaller parts.

BIOBANKS -

Five Main Operations :

c) Storage

Stored accordingly based on the required temperature and environment. Some samples are stored in freezers while some can be stored at room temperature. Blood, plasma, serum, and DNA are stored in -80°C freezers. Tissues and cell lines are preserved in liquid nitrogen freezers at -1960 C

Different types of storage containers Liquid Nitrogen Tanks4 (-190°C)

Liquid Nitrogen Containers

BIOBANKS

- Five Main Operations :

d. Distribution

Occurs when the biobank receives an order or request from a research team. Identification of biomarkers Request for sample marker Scrutiny of the request Supply of specimen in proper container

BIOBANKS -

Five Main Operations :

e. Data Management Manage

Data in disposition & distribution of specimen Research data archives Database on gene function & structure Cellular and chromosomal localization Clinical effects & Disease pattern Epidemiological data & forecast Pathological features of worked out pathogens Endemic & Pandemic progression etc,,.

Types Of Biobanks

1. Population-based Biobanks Large repository of donated human specimens & its information collected from volunteers with and without disease in the interest of the public health
2. Hospital or academic based Biobanks Biobanks in medical colleges & attached hospitals ex.Cardiff Univ. Biobank & Hospital of Whales.
3. Disease-oriented Biobanks Biobanks established as disease-centric. ex.AIDS Specimen Bank, San Francisco.
4. Commercial Biobanks In-house stocks of biosamples sourcing from public sector biobanks & from commercial Research centers

Biorepository

It is a facility that collects, catalogs, and stores samples of biological material for laboratory research. Biorepositories collect and manage specimens from animals, plants, and other living organisms. Biorepositories store many different types of specimens, including samples of blood, urine, tissue, cells, DNA, RNA, and proteins. The purpose of a biorepository is to maintain biological specimens, and associated information, for future use in research. The biorepository maintains the quality of specimens in its collection and ensures that they are accessible for scientific research.

BIOBANK

Collection, Processing, Storage of Human Biospecimens

BOTH TERMS "BIOREPOSITORY" AND "BIOBANK" ARE OFTEN USED INTERCHANGEABLY

Cell line biobanking

The history of cell line biobanking started with generation of the HeLa cell line in 1951 at Johns Hopkins Hospital, where the medical staff obtained the first cancer cell line from a patient named Henrietta Lacks (HeLa). Cancer cells were obtained without her consent after surgery and cultured in the lab using an experimental approach that made the cells immortal, thereby achieving, for the first time, an in vitro cancer model system for research (21)

The HeLa cell line is used worldwide in the research

laboratories because it is easy to grow and offers an optimal and stable model system for in vitro research experiments. Thanks to the epochal HeLa cell line, scientific results have been gained with crucial advantages for global health, including the development of polio vaccines (22)

The success of the HeLa cell line encouraged the stabilization and use of immortalized cell lines for medical research, particularly during the 70 s and 80 s when several continuous cancer cell lines were established.

Tissue BioBanking

Human biological samples include a vast range of tissues, biospecimens, organs, body parts, extracted DNA or RNA, blood, bodily fluids, cell lines, cell suspensions, plasma, and so on. Today, a large number of research projects focus on genome, transcriptome, proteome and metabolome areas conducted on tissue samples of patients with a defined clinical and pathological diagnosis or on cell lines/ suspensions derived from patients' blood. Human tissues are usually obtained from surgeries and autopsies; immediately after surgery tissues undergo histopathological examination by pathologist. In this step, the most accepted clinical practice for preventing tissue degradation and diminishing unwanted enzymatic activity is fixing the tissue usually with neutral-buffered formalin. Before the advent of technologies that allow partial or complete evaluation of the genome, epigenome, transcriptome, metabolome, and proteome components, formalin-fixed paraffin embedded (FFPE) tissue was the specimen usually collected in biobanking databases, and frozen biospecimens were used in research programs.(23)

Blood Biobank

Blood is one of the most common biological materials used in research. It is collected in test tubes containing preservatives and additives, depending on the specific intended use and the required blood fraction (serum, plasma, white blood cells, red blood cells). While serum samples are usually obtained by using tubes containing a coagulation activator, such as thrombin or silicon dioxide, plasma samples are obtained using tubes containing various anticoagulant additives. Most biochemical analyses are performed using serum, while plasma is used for the analysis of DNA and RNA. For example, citrate-stabilized blood contains higher-quality DNA and RNA and a higher number of lymphocytes compared to blood treated with other anticoagulants, while collection tubes coated with ethylenediaminetetraacetic acid (EDTA) are preferred for protein analysis and most DNA testing assays (24,25)

Further, heparin is suitable for metabolic studies but is not indicated for the study of lymphocytes, since it affects the proliferation of T cells (26)

The timing of the pre-analytical phase is also of considerable importance. For example, the integrity of protein molecules is maintained if blood plasma is prepared immediately (27,28)

and the optimal quality of DNA extracted from blood samples will be ensured if sample preparation is carried out within 24 h at 4 °C (29).

Significance and fundamentals of biobanking

Biospecimens (including DNA, RNA, microorganisms, body fluids, cells, tissues, *etc.*, from humans, animals, and plants) are crucial resources and essential elements in the research of life science and biotechnology. A biobank is a repository that collects, processes, preserves, stores, and distributes the biospecimens along with detailed information about each biospecimen. Biobanking is defined as the practice of creating organized and standardized biobanks (30,31)

Over the past 30 years, biobanking of human biospecimens has become indispensable for promoting and developing great advancements and breakthroughs in biomedical research, making a great impact on the gene/cellular therapy to cure acquired diseases and correct genetic defects, regenerative medicine, tissue engineering, personalized medicine, new vaccine or drug development, disease screening and diagnostics, in vitro fertilization, and biotechnology development, *etc.* Although human biospecimens have been collected and stored for over 100 years--(32)

Modern Biobank Activity –

Biobanks play an increasing role in contemporary research projects. These units meet all requirements to regard them as a one of the most innovative and up-to-date in the field of biomedical research. They enable conducting wide-scale research by the professional collection of biological specimens and correlated clinical data. Pathology units may be perceived as the roots of biobanking. (33)

Biobanking in Microbiology

Millions of biological samples, including cells of human, animal or bacterial origin, viruses, serum/plasma or DNA/RNA, are stored every year throughout the world for diagnostics and research. The purpose of this review is to summarize the resources necessary to set up a biobanking facility, the challenges and pitfalls of sample collection, and the most important techniques for separation and storage of samples. Biological samples can be stored for up to 30 years, but specific protocols are required to reduce the damage induced by preservation techniques. Software dedicated to biological banks facilitate sample registration and identification, the cataloguing of sample properties (type of sample/specimen, associated diseases and/or therapeutic protocols, environmental information, etc.), sample tracking, quality assurance and specimen availability (34)

India's first Heart Failure Biobank starts beating at SCTIMST in Kerala

Set up at the National Centre for Advanced Research and Excellence in HF in Thiruvananthapuram, the facility has sophisticated storage facilities for biospecimens

--The first Heart Failure Biobank in the country to study genetic, metabolomics and proteomic markers of health outcomes in heart-failure patients has come up at the National Centre for Advanced Research and Excellence in HF (CARE-HF) at the Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST) here.(35)

ICMR considers biobank of samples for research, test validation While samples are being discarded currently, the task force members overseeing diagnostics and biomarkers said the agency has selected at least nine ICMR laboratories with easy access to COVID hospitals, where they can store positive and negative throat, nasal, and blood samples for research purposes.The task force set up by the Indian Council of Medical Research (ICMR) has recommended launching a biobank or repository of test samples to understand clinical patterns in coronavirus cases, expedite test kit validation, and study the immune response to the virus. **Follow coronavirus pandemic LIVE updates**

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How a small firm came to manage bio-specimens for Oxbridge and other elite institutions

Krishagni's OpenSpecimen software involves the management of bio-banks of human samples, such as tissues, tumours, DNA, RNA, blood, saliva and plasma, among others, which are required by researchers.In January 2021, the Medical Sciences Division of the University of Oxford announced that it had purchased a software called OpenSpecimen Sample Inventory Management System, made by Krishagni Solutions Pvt Ltd, "to support research involving human tissue material collected, processed or stored…".

In Pune, the small team of Krishagni that had created the OpenSpecimen platform realised that they had crossed a milestone — the University of Oxford had joined its client list of more than 70 top institutions in more than 20 countries. Since then, Krishagni has grown to 85 institutions.(37)

Mumbai to get India's first biobank to store, test cancer sample

Countries first biobank started at Tata Memorial Care Hospital,Mumbai.It can store one lack specimens for a duration of 1000 years,engaged in genomic testing for various types of cancers (38)

Biobanks in India

1. BIOBANK LOCATION ,Website,and Disease—

NCTB National Cancer Tissue Biobank; Chennai, Tamil Nadu,https://nctb.iitm.ac.in/about/index. html Cancer

2. BIOBANK LOCATION ,Website,and Disease-

NLDB National Liver Disease Biobank New Delhi www.nldb.in/ Liver diseases

3. BIOBANK LOCATION ,Website,and Disease-

Rajiv Gandhi Cancer Institute and Research Centre New Delhi www.rgcirc.org/res earch/biorepositor y/ Cancer

4. BIOBANK LOCATION ,Website,and Disease-

NIMHANS National Institute of Mental Health and Neurosciences Bangalore, Karnataka http://the nimhansbrainbank.in/ Brain disorders

5. BIOBANK LOCATION ,Website,and Disease–

The Tata Medical Centre Biorepository. Kolkata, West Bengal www.web.tmckolkata .com/biobank/index. html Cancer

6. BIOBANK LOCATION ,Website,and Disease--

National Cancer Institute-All India Institute of Medical Sciences Jhajjar, Haryana http://nciindia.aiims .edu/en/ node/16 Cancer

7. BIOBANK LOCATION ,Website,and Disease–

Sapien Biosciences Hyderabad, Telangana http://sapienbio. co.i n/biobank/

Commercial biobank

8. BIOBANK LOCATION ,Website,and Disease--

NCCS National repositories for cell lines & hybridomas Pune, Maharashtra www.nccs.res.in/ind ex.php/TeamsNCCS/

Repositories Cell lines, microbial resources

9. BIOBANK LOCATION ,Website,and Disease—

ADBS Accelerator Program for Discovery in Brain Disorders Bangalore, Karnataka https://www.ncbs.res.in/adbs/bio repository Brain disorders using pluripotent stem cells

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