Cancer oriented biobanks: A comprehensive review

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Abstract

Biobanks provide a platform for innovative biomedical research and has improvised translational and personalized medicine to a great extent. Time 2009 published *10 ideas changing the world right now* with biobanks on the list emphasizing its role in discovery and development of new therapeutic drugs. They form the cornerstone, providing resources for future investigations and biomarker discovery to understand the effects of genetic, environmental and lifestyle factors on human morbidity, mortality and health. The aim of this review paper is to understand the role of biobanking in cancer research, the challenges faced and strategies to overcome these, for long term and sustainable research in the field of oncology.

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Introduction

Though the field of oncology has progressed immensely in the last decade, cancer still remains as one of the main causes of mortality and morbidity worldwide.[1] Personalized medicine has evolved greatly in the current era and is characterized as *4P*, personalized, preventive, predictive, and participatory. This has changed the approach to patient care immensely.[2] Biobanks forms a main component of personalized medicine that depends on proteomics, metabolomics and epigenomics (omics) that form the three main pillars for cancer research. Mutual relationship between biobanks and omics has evolved over the years and has played a decisive role in understanding the pathogenesis of cancer.[3] The diagnosis, prognosis and treatment aspects have benefitted with intense development in cancer research. Biobanks have helped in biomarker discovery and future drug therapy.[2]

Biobank and its role in cancer research

Biobank is defined by the Organisation for Economic Co-Operation and Development (OECD), *as a collection of biological material and the associated data and information stored in an organized system, for a population or a large subset of a population*.[2] There is a systematic process of data collection, processing and functioning of a biobank (Figure 1). They involve bioinformatics, cytomics, genomics, proteomics, metabolomics, peptidomics, pharmacogenomics, tissomics and transcriptomics to analyse and understand cancer, its prognosis and improvise treatment modalities.[4] A multidisciplinary approach is employed with all aspects of disease prevention, prediction, therapy monitoring, optimalization, drug discoveries and drug development.[2]

In the last decade, the importance of biobanks in the field of cancer research has increased with the emergence of *big data* collection.[2] There are many repositories around the world where samples are segregated based on race, population, type, stage and grade of different cancers from diverse patient profiles.[5] The patient's information on specific symptoms, epidemiological data, environmental-occupational factors, lifestyle, societal data and histological cancer characteristics are registered.[3]

Most cancer tissue banks and biorepositories collect blood, swabs from lesional sites, biopsy tissues, body fluids. These are maintained in living tissue banks/intravital biobanks.[3,6] They provide a platform for research related studies as they replicate the complex structural heterogenecity of human cancers.[3] Here, the

cancer tissues and cells retain the normal tumor microenvironment, intact tissue architecture with functional hormones and inter-cellular and intra-cellular signalling properties. This helps cancer-related analysis to be monitored on a real-time basis.[3]

DNA barcoding and molecular/integrative nomenclature have helped large genome sequencing projects, testing on multitude of different species, adding new barcoding markers and reaching *next-generation barcoding*.[7,8] They support various genetic and molecular studies that include genotype-phenotype correlations, cross-sectional, case control and cohort studies.[2] This data can help co-relate the cancer initiation, progression/regression pattern with genetic variations across the globe. They play an essential role in acheiving effective patient-tailored therapies.[9] Since, biobanks and cancer research are still in budding stage, scientific discoveries and advances in oral/head and neck cancer has still not been established.

Traditional approach of practice to personalized medicine

Traditional approach of practice consists of *One size fits all* method, where all patients receive the same treatment for a particular disease. Here, the treatment outcome varies, where some patients recover completely, where as others return with recurrence and metastasis which puzzle the oncologists.[2,10] The human genome sequencing in 2001, paved a new path in cancer research with improved molecular profiling, genomic and proteomic studies.[9] This enabled understanding the cancer mechanisms from cellular to sub-cellular and molecular levels. This is helping in designing personalized medicine and the patients in trials have shown improvement in health post cancer detection.[11]

An ideal cancer treatment strategy should specifically target and confine only to the tumor site, with predetermined sensitivity to anticancer agents, potential for concurrently acting

through different anticancer mechanisms that can be adaptively replaced based on the situation. The biobank ideally requires international advice and collaboration, funding agencies, ethical clearance with a good governing body[12] (Figure 2).

Components of a cancer biobank

The biobanks are designed to develop proficiency in tissue and data collection procedures, adequate storage and processing of the information to bring out the best results. The designing is based on the incidence of cancer in that area, heterogenecity of patients, the collection mode, transport media and storage requirements for the tumour, financial support or funding agencies for the functioning of the biobank and labour charges.[13,14]

The data/samples in the biobank are not static projects, as they are collected continuously for a long period of time. As they form the backbone of all research and future innovations, it is important to understand the various components of a biobank[4,15] (Figure 3).

Biological human material and data storage

Patient case history records with his ethnicity, demographic data, occupational details, with note on his adverse oral habits, association with carcinogens, clinical data, exfoliative cytology samples, radiographs with CT, MRI, PET scans, lesional and sentinel node biopsy specimen is essential. All these data should be collected, systematically arranged and stored.[16,17]

Ethics, informed consent, legal and social aspects

Biobanks should protect the patient's identity, rights by applying codes or anonymization to ensure privacy. It should be seen that the patient can be re-identified to provide relevant information back to them.

The three main factors of informed consent are adequate information, voluntariness, and competence. The participant should be informed of the objectives of the study, importance of their

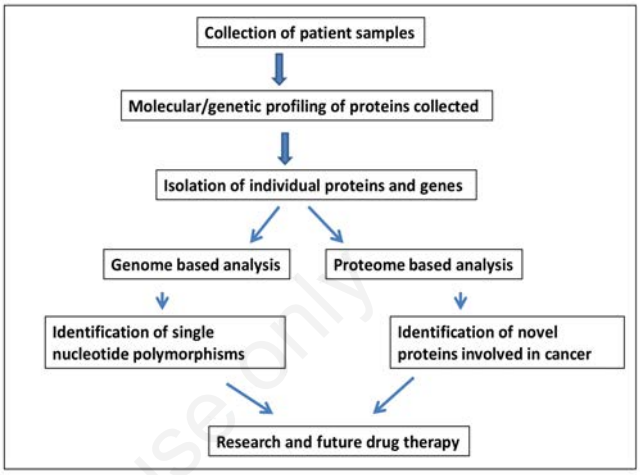

Figure 1. Functioning and purpose of a biobank.

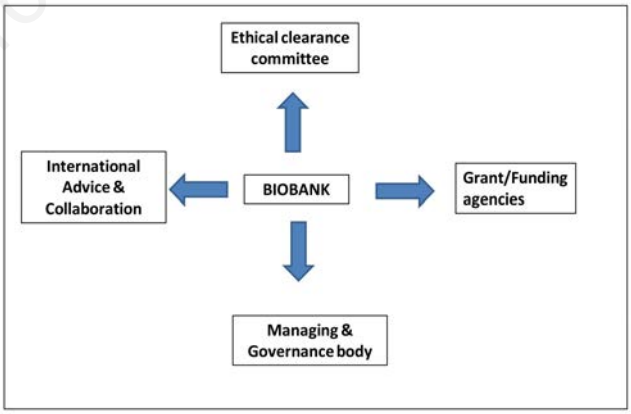

Figure 2. Requisites of an ideal biobank.

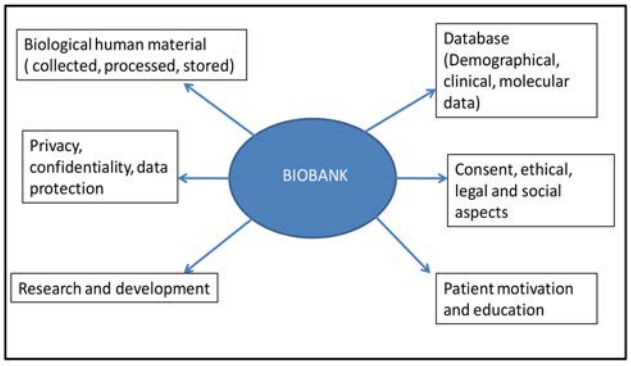

Figure 3. Components of a biobank.

involvement to cancer research, potential risks involved and the chances of withdrawal at any time in the future. The patients are encouraged to participate in the study and their autonomy and vulnerability are respected.[18,19]

Confidentiality, privacy, and data protection

Protection and conservation of personal data, maintaining privacy and confidentiality are the fundamental duties of a biobank. Participants have control and right over their personal information and require assurance that all their information are safe from malicious use.

Stakeholders in a biobank include the patients whose tissues and data are taken, grant agencies, biobanks/institutions maintaining the biosamples, researchers and ethical clearance committee.[20,21]

Management of the biobank

The biobank committee has representatives from scientific advisory committee, ethical committee, funding agencies and host institution. The management committee of the host institution takes decisions regarding the facilities, equipments and implementation of guidelines on best practices. Generally a manager is appointed who links all these representatives, governing bodies and people employed for the functioning of the biobank. These personnels employed involve in locating specimen, collection, transport, designing and maintaining the integrated information.[22]

The cancer biobanks around the world

The cancer biobanks support data of biospecimens with emphasis on good quality management, logistics, histopathological and molecular data analysis. There is a stringent regulatory framework that works on ethical and legal grounds that works on certain standard operating procedures. The operating procedures are standarised among various biobanks and they follow international guidelines, such as the National Cancer Institute Guidelines in the US, the Confederation of Cancer Biobanks Guidelines in the UK and the International Society for Biological and Environmental Repositories Guidelines in Europe.[23] Biobanks worldwide and their collaborative projects are discussed in Table 1.[24-33]

i) The NCRI's Confederation of Cancer Biobanks (CCB) consist of over 30 member biobanks and is based in United Kingdom (UK). This is a consortium of biosample collection and they encourage harmony amongst biobanks. They collaborate with researchers and raise awareness of best practices, providing advice and mutual support that will eventually enrich all biobanks.[24]

ii) The Texas Cancer Research Biobank (TCRB) bridges the gap between researchers and surgeons to improvise the preventive, diagnostic and therapeutic modalities.[25]

iii) The Victorian Cancer Biobank is a non profit consortium of biobanks, that is supported by the Victorian Cancer Agency (Victorian Government). They aim at providing high quality research inputs to support research to improve cancer diagnostics and treatment.[26]

Table 1. Worldwide biobanks and their collaborative projects.[22,24]

Sr. No	Biobank	Place	Establishment year	Collaborations
1	NCRI Confederation of Cancer Biobanks (CCB)	UK	2006	CCB collaborates with the NCRI CM-Path initiative to improve access to histopathology samples Collaborates with BBMRI-ERIC to promote quality standards Collaborates with the UKCRC Tissue Directory and Coordination Centre to help them to develop a web-based sample portal as a national resource
2	The Texas Cancer Research Biobank (TCRB)	Texas, USA	2010	Collaborative projects between Texas Tech University Health Sciences Center School of Medicine Cancer Center the University of Texas were undertaken They developed biobanks of cell lines, mouse xenografts from tumor specimens for future in vitro therapeutic studies
3	The Victorian k Cancer Bioban	Melbourne, Australia	2006	Collaboration with this biobank allows researchers to access clinically annotated data associated with tissue and blood samples across multiple sites via a simple platform
4	The Wales Cancer Bank (WCB)	Wales, UK	2004	Collaborations targeting at personalized medicine Target to collect samples from longitudinal studies and metastatic disease for further research
5	Manchester Cancer Research Centre	Manchester, UK	2006	Collaboration between the University of Manchester, Cancer Research UK and the Christie NHS Foundation Trust It brings together the expertise, vision and resources of its partner organizations to work together in the field of cancer research
6	The University of Massachusetts Cancer Center Tissue and Tumor Bank	Central New England	2006	UMass Cancer Center in collaboration with its affiliated clinical departments has a number of early cancer detection programs in otherwise healthy, asymptomatic individuals. Collaboration of faculty of different disciplines who treat specific disease-based groups to select, provide and evaluate treatments for particular cancer types
7	The Cancer Research UK Leicester Centre and University Cancer Theme	Leicester, UK	2006	Collaborates with the public, cancer patients, scientists, the National Health Service, universities and Cancer Research to translate new discoveries to accelerate translational research
8	The Australasian Biospecimen Network (ABN)	Australia and New Zealand	2001	Collaboration by establishing an Australia-wide network of tissue biorepositories that collect cancer related tissue using established and accepted guidelines and protocols
9	National Cancer Tissue Biobank (NCTB)	Chennai, India	2015	NCBT works in collaboration with Cancer Research and Relief Trust (CRRT) to provide researchers with high quality cancer tissues and patient data in order to facilitate cancer research

iv) The Wales Cancer Bank (WCB) is licensed by the Human Tissue Authority from Wales Research Ethics Committee to store human tissue for cancer related research. The samples are stored to form a biorepository to which researchers worldwide can apply for biosamples and/or data.[27]

v) The Alberta Cancer Research Biobank is a Canadian tissue repository network that has large collection of tissue samples of several types of cancer. They support the collection of samples, its storage and provides open access to independent research groups to address unanswered questions concerning prevention, prognosis and treatment of cancer.[28]

vi) Manchester Cancer Research Centre of United Kingdom (UK) as a world class cancer research centre, fully licensed by the Human Tissue Authority. It has been set-up to collect large quantities of high quality biological samples from cancer patients in the Greater Manchester area for research purposes.[29]

vii) The University Of Massachusetts Cancer Center Tissue and Tumor Bank is based in Central New England. The biobank facilitates scientific discovery to improve patient care. They work towards early detection, prevention and discovering better treatments and inspiring the next generation of clinical and scientific investigators and caregivers to carry this mission forward.[30]

viii) The Cancer Research UK Leicester Centre and University Cancer Theme oversees the cancer research strategy at Leicester and intends to facilitate high quality research.[31]

ix) The Australasian Biospecimen Network (ABN) aims to assist at locating biospecimens online to researchers. It helps locate multiple biobanks at any given time. It lends a platform to address technical, legal and administrative issues regarding cancer biobanks within Australia and New Zealand.[32]

x) National Cancer Tissue Biobank (NCTB), is a non-profit organization which is a joint initiative of Department of Science and Technology (DST), Government of India and Indian Institute of Technology Madras (IITM) in collaboration with Cancer Research and Relief Trust (CRRT).[33]

The International Agency for Research on Cancer (IARC) in Lyon, France is a specialized cancer agency of the World Health Organization. They promote international collaboration in cancer research. They emphasise on elucidating the role of environmental and lifestyle risk factors and studying their interplay with genetic background in population-based studies and appropriate experimental models. Key publications include the Cancer Incidence in Five Continents series and GLOBOCAN.[34]

Challenges

Biobanks are governed by specific regulatory bodies and in several countries due to stringent regulations, there is restriction to export human cancer tissues. Legal, ethical and social factors challenge numerous promising initiatives. Apart from this, there are certain errors in the discovery and analysis of data for predictive biomarkers caused by variations in preanalytical procedures and specific parameters in biobanking. Lack of coordination, quality, miscommunication in data collection and processing are also seen. Due to these reasons, many scientific institutions, who are in collaboration with biobanks are in a legal *gray zone*.[2,35]

The main challenges of adequate functioning of a biobank as noted by Ardini *et al*. are:

i) *Deficient record maintenance:* The biobanks collect data from various sources. Incomplete data recording, ethical clearance, inconsistent sample identification, collection and information storage can lead to numerous errors.

ii) *Deficient linkage of information:* Sample identity that links patient identity is not available in most cases. It is essential to maintain patient anonymity throughout the procedure. But after the study the patient has the right to know the results and should be informed.

iii) *Data sharing:* Data sharing is essential for research and development. Hence, it is essential that the required information is available for the researchers in a timely manner. Delay in receiving this information hampers the research progress

iv) *Patient Consent:* Standardized patient consent formats are still not developed in many countries.

v) *Sustainability:* For regular functioning of a biobank, labour costs, infrastructure and handling costs require funding agencies that cover all the expenses. Finding the right funding agencies are important for sustenance of biobanks.[36]

Strategies to overcome the challenges

To combat deficient record maintenance, biobanks should develop a flexible international exchange protocol to prevent restrictive regulations, as this affects cancer research opportunities. There is a need for co-ordination and harmonization to regulate the ethical woes.[37]

Sharing of data and best practice procedures in biobanks require cooperation to ensure effective exchange of information and tissue samples. Harmonization is required for synergistic work that includes areas of data collection, pooling, evaluation, sharing with researchers. The results from various biobanks can be compared to check the similarities and differences and thereby understanding the cancer pathogenesis effectively.[2]

There are two main strategies for collecting samples from a network of collection sites known as *centralized model* and *federated model*. The physical transfer of samples from peripheral collection sites to a centralised biobank, where they are stored, processed, and accessed by researchers is known as the *centralized model*. Large scale biobanks and projects such as International Cancer Genome Consortium work on centralized model. In the second method, known as the *federated model* the cancer tissue samples are stored at the peripheral collection sites and not transferred to a biobank but the sample information is transferred to a central database.[38]

Both these models of data collection have varied advantages. The centralized model works in a standardized manner that allows sample processing and storage to be controlled and monitored effectively. The stakeholders and funding agencies prefer the federated model as the material remains at the peripheral collection sites and they closely involve in the decision-making processes. Motivating the stakeholders to take part both at the central and peripheral sites is an important factor.[38]

A biospecimen locator can help researchers to search the required specimen or data online easily. They can also search numerous biobanks at the same time. A meta-model analysis is an on-going project undertaken as a gateway to share data among biobanks that exhibit remarkable heterogeneities to curb the diversities and bring uniformity. An international multidisciplinary cooperation that can aid in development of biobanks, ease its complex functioning and provide quality research material is essential.[39]

Another novel, cost-effective alternative to collection of serum samples is a form of biosampling called Dried Blood Spots (DBS). It is recently been used for collection and storage of samples for drug monitoring, genetic analysis and molecular epidemiological studies. A dried blood spot mass spectrometry metabolomic approach for rapid breast cancer detection was recently carried out

with good results.[40]

Biobanks should target at identifying prognostic and diagnostic biomarkers by collecting tissue samples from individuals without any clinically evident disease. In future, the recognition of subclinical periods of disease development will help prevent cancer formation, regress the growth and also aid in designing new drug targets.[2]

Biobanking methods can be altered by incorporating smart business strategies like advertising and marketing metrics to attract funding agencies. For a long term and sustainable research, assessment of current investment levels and future cost-effective resource requirements is essential. Researchers should get access to range of cancers to compare the potency of a specific biomarker. The administrative process should simplify and data should be easily accessible to all.[12]

Infrastructure/facilities

The requirements for a cancer biobank includes a dedicated personnel/technician, adequate storage facilities, with ethical, legal, and technical requirements fulfilled. The biobank should be located in a convenient place, directly connected with clinical units, such as surgical unit, onco-pathology unit etc. The biospecimen collection, processing, storage, distribution, collection of patient data (sociodemographic, clinicopathological details, their lifestyle, follow-up data), validation documentation, management reporting functions should be with quality assurance and quality control.[41-43]

The Certified Repository Technician Training Program conducted by International Society for Biological and Environmental Repositories (ISBER) is a global certification program to train Repository Technicians.[44] The technical staff should be provided with best-practice guidelines and tools to collect, store and manage the biobank resources. Blood samples, other body fluids, paraffin-embedded tissues, and DNA/RNA material should be stored under ambient conditions, refrigerators, and freezers (–80, –40, and –20°C). Temperature monitoring systems, which will ensure a safe and reliable environment for the stored samples should be provided. A regular and uninterrupted power supply is essential.[45]

Laboratory information management systems that help in cataloguing, documenting and tracking biological samples should be used. In order to facilitate collaboration and inter-operability between the partners, the network should have common data collection programmes and quality management tools, such as Biological Reporting for Improved Study Quality (BRISQ), Standard Preanalytical Code (SPREC) and MIABIS (Minimum Information About Biobank Sharing) for all research purposes. This will increase the visibility and recognition of the facilities internationally.[46]

Conclusions

Cancer biobanks are complex systems where there is systematic and programmed storage of cancer tissues and associated data. It has been established globally for cancer prevention, prediction, diagnosis, treatment and has become an integral part of personalized medicine. Biobanks will definitely redefine research and bring advancement in genetic research and future drug targets.

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