Need for a national oral cancer biobank for cutting-edge translational research in developing countries

INTRODUCTION

Despite making significant progress in our understanding of cancer and its treatment over the past few decades, it remains the leading cause of morbidity and mortality.[1] The introduction of newer sequencing technology has largely validated the discovery of cancer-specific genetic changes, as well as provided justification for the development and deployment of targeted therapies. The most daunting task, however, is the translation of suitable drug molecules from the bench to the bedside.[2] To address this, the current approach to cancer and patient care has shifted dramatically, with a focus on personalised medicine or precision medicine. The cornerstones of personalised medicine, which is based on *-omics* approaches to cancer research, are biobanks.

A biobank is defined as 'a non-profit service unit, aimed at collecting, processing, storing and distributing human biological samples and data related to them, for research and diagnosis. It is officially recognized by the competent health authorities, applies a quality system and guarantees the rights of those involved'.[3] Although blood and DNA are the most frequently collected specimens, other clinical materials collected in biobanks include saliva, urine and tears; blood corpuscles and tissues. In addition to the pathological specimens stored typically in the biorepository, biobanks store biospecimens and data from healthy volunteers.[4]

India has the most cases of oral cancer, accounting for one-third of the global burden.[5] A major source of concern is the lack of established biorepositories in developing countries, which account for more than half of all cancers worldwide. To obtain information on the morphological, genetic, proteomic and epigenetic interplay for cutting-edge research and diagnosis, high-quality biosamples must be collected and analysed. Biobanking uses bioinformatics, genomics, proteomics, metabolomics, pharmacogenomics and transcriptomics to analyse and understand cancer.

GUIDELINES FOR THE ESTABLISHMENT OF BIOBANKS

Various recommendations for the creation and growth of biobanks have been made public by several professional organisations. All biobank operators who are conserving biological resources should refer to ISO 20387:2018, 'Biotechnology - Biobanking - General requirements for biobanking.' It emphasises the role of an advisory board; the profile and purpose of a biobank with reference to the types of specimens included; how relevant data following approved protocols are obtained, and authorisation from the Institutional Review Board (IRB) and Institutional Ethics Committee (IEC). Another crucial obligation for biobanks is to manage volunteers' informed consent in compliance with General Data Protection Regulations (GDRP) before any medical procedures are carried out. Finally, all biological samples collected must be replaced by pseudonyms to protect donors' privacy.[4,6]

Most biobanks are part of national government-funded population-health-based studies. *Biobank Graz* https://www.biobanking.com/biobank-graz/, the Medical University of Graz's non-profit core research centre is one of the world's largest biobanks, with 20 million tissue, blood and DNA samples from over 1.2 million patients.

The *International Agency for Research on Cancer BioBank* (IBB) https://ibb.iarc.fr/has one of the most diverse cancer biorepositories in the world including samples related to oral cancer. IARC recently set up the Biobank learning

platform https://ibb.iarc.fr/links/, a freely available tool that offers training and educational resources for practitioners engaged in biobank-based work in low- and middle-income countries.

RIKEN https://web.brc.riken.jp/en/BioResource Research Centre (BRC) is a comprehensive research institution with a state-of-the-art research infrastructure. BRC is committed to the advancement of basic and applied research by securing and sourcing biological samples.

The *Malaysian Oral Cancer Database and Tissue Bank System* (MOCDTBS) https://drmc.um.edu.my/research-teams/ocrcc/[3] collects, processes and stores samples including buccal cells, blood, saliva and oral tissues. Patients with malignant and pre-malignant oral lesions, as well as healthy subjects, provide data and samples for analysis. The MOCDTBS has aided research into the role of genetic susceptibility in oral cancer, as well as the role of etiological factors influencing the disease outcomes.

The *ACTREC Biorepository*https://actrec.gov.in/cri-research-support-facility-detail/is the custodian of biological samples that have been saved and can be accessed, under a rigorously controlled and supervised method, with researchers having approved projects that aim to investigate the biology of cancer, uncover biomarkers for a more accurate molecular categorisation, or targeted therapy. As part of the *International Cancer Genome Consortium* (ICGC) research, blood and gingivobuccal mucosa tumour samples were obtained from 30 patients, and their genomic DNA was then isolated and transferred to the *National Institute of Biomedical Genomics* (NIBMG), Kalyani for whole-genome scan and sequence capture-based flow cell sequencing. The DBT-funded NIBMG has developed the world's first database of genetic variants in oral cancer. A free resource, dbGENVOC is a searchable online database of GENomic Variants of Oral Cancer.[7] It will be updated yearly with new oral cancer patient variance data from different parts of India and Southeast Asia.

Need for oral cancer biobank in the era of precision oncology

Human biological specimens are paramount for translational purposes in cancer research, including those of oral and oropharyngeal cancers. A large number of clinical samples of oral squamous cell carcinoma (OSCC) are received in our regular pathology practice and processed for diagnostic purposes. Tissues obtained from tumour surgical resection make up a significant portion of the specimens. These are stored as formalin-fixed paraffin-embedded (FFPE) blocks, which continue to be the gold standard for histological and immunohistochemical analysis. At the same time, they can be assembled into biobanks that can be stored for several years. Cohort identification is made simple by the retrospective analysis of these reliable, easily accessible archives that are linked to clinical and pathological data. This is especially required for the development of tissue microarrays or high-quality nucleic acid libraries for advanced molecular analysis.

Traditional tissue biobanks may, however, be limited in their ability to be used as a tool for the identification and validation of therapeutic targets because not all fixed or frozen tissues are viable. In such cases, a viable living cell biobank of patient-derived cell (PDC) models derived from surgical biopsy samples might be the best option. In comparison to traditional tissue storage, these could provide better pre-clinical cancer models that are amenable to functional assays. PDC models are biologically relevant[8] as they retain patient-specific characteristics making them suitable for *ex vivo* experiments. As a result, they have the potential to functionally complement molecular and pathological tumour assessment and aid advancement in precision oncology.

Ethical and practical issues influencing the functioning of Biobank

There are ethical and legal ramifications to developing and exploiting the resources in a biobank, which calls for the active participation of numerous specialists. Informed consent from a participant is necessary for protecting the rights of individuals, and the study protocols must be in line with the ideals of beneficence, non-maleficence and fairness. Protecting personal information, ensuring biological safety and making collections available for reuse for research purposes with consent are the institution's and researchers' responsibilities in the establishment and maintenance of biobanks.[9] Standardising the tissue collecting procedure and establishing a code of conduct for the exchange of samples are both necessary. In light of this, it is evident that clear scope, specified informed consent for patient participation, and standard operating procedures for sample collection and data administration might contribute to high-quality research through biobanking without undermining public trust.[10]

To fully utilise the potential of the biobank sample, all data, including the pathological status of the collected material, must be provided, and information must be maintained, particularly about patient outcomes. This calls for coordinated work from numerous teams, including those responsible for the creation of information technology, data managers, doctors, and

researchers. Accorded consent, ontologies, data formats and definitions that are strengthened by standard operating procedures for data collection and management can help overcome the issues of integrated databases. Consent forms may ask for alternatives for specifying how the samples may be reused if they could be retained, whether they could be used for genetic testing, as well as whether the information could be shared. A system should be in place with an anonymisation approach, and any necessary transfers should be thoroughly recorded if the need to move data or material arises. Harmonisation of policies, a key role of the IRB and IEC, as well as other concerns such as patient access to information and withdrawals of samples and data, are necessary for the biobanks to operate effectively and for the efficient use of resources.[10]

A biobank explicitly dedicated to oral cancer is vital to enable the collection of a large number of samples from each subsite of the oral cavity that can be analysed extensively to resolve the heterogeneous behaviour of this disease. Accessibility to biological samples of oral cancer and their associated data paves the way for newer developments in this field.[2] Oral cancer biobanks serve as the foundation for three rapidly growing fields: molecular and genetic epidemiology, molecular pathology and pharmacogenomics/pharmacoproteomics. In the future, biobanks shall include patient-derived organoids (PDO) that mimic the characteristics of a primary tumour and bridge the gaps in PDC and patient-derived xenograft (PDX) models.[8]

FUTURE PERSPECTIVES

Establishing biobanks in an Indian setting poses a unique set of challenges. The scarcity of a designated budget, a lack of infrastructure, a dependable power supply, ethical, legal, social and political impediments, as well as a lack of knowledge among the general public and researchers, are some of these challenges. Since cancer research opportunities in developing countries are many and are backed by strong government support, high-quality clinical samples must be made available in large quantities. To ensure high-quality and standardised diagnostic and treatment methods across India, several regional biobanks ought to be connected to a comprehensive national cancer biobank. This may attract global policymakers to pay attention to developing next-generation tumour biorepositories in countries such as India to source specimens from.[11]

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