The journey of Biospecimens: Mortuaries to Biorepositories

Our obsession for a sneak preview inside the causation and progression of cancer revolves around the study of tumours, normal tissues and body fluids and in current parlance all these are termed as 'Biospecimens'. In the 19th century these biospecimens comprising of human parts and organs were provided by the mortuaries and museums; in the 20th century the biospecimens were paraffin embedded tissues and were provided by the pathology departments; and in the 21st century the ultimate provider of all biospecimens will be the organised world of 'Biorepositories'. Diligent biospecimen providers kept pace with how the clinicians, pathologists and scientists of their era could best utilise these biospecimens, which to some extent depended on the technologies available to them. The naked eye examination of the cancer affliction of various organs during autopsy studies laid foundation to principles of cancer surgery and also resulted in the famous 'Seed and Soil' hypothesis on cancer metastasis by Paget in 1889. Substantial progress was then made with the power of microscopy that allowed detailed study of cellular and nuclear morphology by pathologists and resulted in the all important histological types and subtypes of cancer that we presently recognize. The biospecimen par excellence of the microscopy era were tumour and normal tissues chemically fixed and paraffin embedded and stored for decades. The merger of molecular and cell biology and the emerging '…omics' technologies are now demanding a large number of biospecimens in the form of fresh or frozen tumour and normal tissues and body fluids. It is believed that as the microscope led to great knowledge of histological types and subtypes, the present technologies will utilise these biospecimens to understand and define molecular types and subtypes of cancer, validate new biomarkers and lay the foundation for pathway specific or targeted therapy.

If we were to believe all that is promised by the modern techno biologists and give them a fair chance, it becomes imperative to collect, store and distribute biospecimens in an appropriate manner. As the custodian of biospecimens, modern biorepositories could be a gold mine, providing biospecimens suitable for all kinds of technology platforms. The real value addition comes when biospecimens are linked with the clinical, histopathology, treatment response and disease outcome data. Biorepositories with demography, exposure and longitudinal health outcome data will be an invaluable resource not only for cancer research but the normal tissues stored may be very useful in genomic research in other common chronic diseases which share some risk factors with cancers such as tobacco, diet, physical activity, obesity etc. It is unlikely that such a well annotated biorepository of normal tissues and blood with baseline and longitudinal health, exposure and genetic data will be available for the common life style related chronic diseases.

The major ethical concern is that only tissues that are left over after satisfactory pathological examination are collected for this research study and it should not affect the patient’s medical care in any way. Other issues revolve around the ownership of these biospecimens, commercial interests and distribution rules. The major scientific concern is how various collection and storage procedures may alter the biological environment of the biospecimen and cause it to react adaptively which may sometimes be misinterpreted as disease-related change.

There are thousands of project driven mini biorepositories of frozen tissues all over the world. However, the investigators often treat these biospecimens as private properties and there is no assurance of the biospecimen quality. With increasing demand for larger number of quality assured biospecimens, there is an urgent need for biorepositories as organised facilities for systematic collection, storage and distribution of biospecimens. This would mean additional space, human resources and investment in to facilities for long term storage of well annotated
biospecimens and linking them with disease outcome data. No one can guarantee the quantum of returns but at the moment it does seem a wise investment. In the United States, the National Cancer Institute invests over 50 million US Dollars annually in direct biorepository programmes in addition to the biorepositories supported through the investigator initiated RO1 grants. Despite such funding, the NCI report shows that in the absence of a common SOP, database and defined mechanism for biospecimen access, some of the NCI supported biorepositories were not optimized or coordinated to optimize resource value. The Biorepository Coordinating Committee set up by the NCI in 2005 is advising the NCI’s Office of Biorepositories and Biospecimen Research for optimizing the quality and accessibility of biospecimens for the broad cancer research community. The American initiative and plans for biorepository have been recently summarized in the ‘First Generation Guidelines for NCI supported Biorepositories’. (http://biospecimens.cancer.gov/biorepositories/guidelines). Such biorepositories will be crucial for the success of the recently launched Cancer Genome Atlas project.

Outside North America, some European countries and a handful of Asian countries, biorepositories are still an individual project or hospital driven effort rather than national coordinated programmes. Over the next decade, acquiring new technology and hiring trained personnel may become more affordable for several Asian countries but their cancer research efforts may be seriously thwarted if immediate attention is not given to national biorepository programmes. Some recent leading publications describing discovery and validation of novel biomarkers and targets using well banked biospecimens makes a strong prima facie case for providing the research community these resources. While the users will be research scientists, the potential beneficiary may be industry and patients but the onus of creating and maintaining this lifeline for future research is on the clinicians, pathologists and apex research advisory and funding agencies. As the biospecimens in any biorepository may not always be used for local projects but also in national and international collaborative projects it is important that there should be international consensus on common minimum guidelines for patient consent and material distribution. All nations hoping to conduct serious basic or translational research in cancer need to take this issue very seriously. For international harmonization, it would be prudent to debate and if possible retain the essential elements of the NCI model consent form and the Group Banking Committee Access Principles and incorporate additional points if deemed necessary under the National regulations and ethical guidelines of each country.