

Editorial

Biobank as an Important Tool for Biomarker Discovery and Validation

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EDITORIAL

Biomarker is a measurable indicator, such as protein, genetic alteration, or metabolite that found in tissue, blood, or other body fluids. Identification of biomarkers that specifically associated with the particular medical conditions such as cancer, cardiovascular disease and neurological disorder is useful for early detection, prevent, and therapy of the diseases. Availability of biomarkers for disease diagnosis, prognosis and prediction of response to therapy can advance personalized medicine and significantly improve clinical outcomes and enhance patient care. The biomarker pipeline consists of a series of phases: biomarker discovery, verification, and clinical validation, which require availability of high quality and well characterized patient samples [1,2]. Therefore, it is critical to have a large collection of patient samples with patient clinical, pathologic and outcome data for biomarker discovery and validation.

Biobank is an entity that collect, process, store and distribute biospecimens and associate patient information for use in future research. The principle of biospecimen collection and storage is relative straightforward, but the practicalities of biobank are quite complicated and require significant collaborative efforts. Expertise in standardization, quality control, clinical and pathological practices, and information technology are generally required for a biobank operation and management. Biospecimens include blood, tissue, bone marrow, urine and other body fluids, etc. Blood is one of the most easily accessible biospecimens and has been a most used biomarker discovery matrix to date. Biomarker investigators have been discovered and assessed biomarkers in the blood for variety disease including cancer and non-cancer diseases such as Alzheimer's disease, and cardiovascular disease [3-5]. Collected blood samples should be divided into its fractions such as plasma, serum, white blood cells, and red blood cells, and stored separately to maximize its value in biomarker studies. Plasma and buffy coat are collected in a tube with anticoagulant such as Ethylenediamine Tetra-Acetate (EDTA), citrate, or heparin. EDTA coated collection tubes are suitable for a wide range of DNA and protein based arrays [6], while plasma from heparin-stabilized blood is often used for metabolomics studies [6,7]. Citrate produces a higher yield of lymphocytes, therefore citrate dextrose coated tubes are used for harvest of peripheral

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blood lymphocytes [6,8]. Serum is collected in a tube contains a clot accelerator such as silica and thrombin and is useful for certain assays in clinical biochemistry and metabolomics studies [6]. Serum samples are generally collected in 30-60 minutes at room temperature for a clot to form, longer than 60 minutes are likely to experience lysis of cells in the clot and releasing cellular components in serum [9]. Buffy coat can be used as a long term biobank specimen for DNA and RNA in lieu of immediately isolating those biomolecules at the time of blood collection. Buffy coat is one of the best DNA source for methylation assay in cancer risk biomarker studies [10]. Urine is another most easily obtained biospecimen and has been widely used for biomarker research [11]. Urine can be aliquoted and freeze intact or enrich the cellular content by centrifuging the urine and store the cell pellet separately from the clear supernatant. Other body fluids such as Cerebrospinal Fluid (CSF) demonstrated a high value for biomarker studies in neurological diseases [12]. CSF must be processed with 30-60 minutes of collection and stored at -80°C for biobanking.

In addition to body fluids, tissue is another key requirement for biomarker identification and validation. Fresh frozen tissue collected for biobanking should be aliquoted and stored at -80°C to avoid freeze thaw cycle. Because of the heterogeneous nature of solid tissue, subsequent morphological analysis by a pathologist is required to determine the percentage of tumor and normal adjacent tissue, and presence of inflammatory and necrotic cells. To reduce microheterogeneity within tissues, manual macrodissection or laser capture microdissection are often required to select specific cells to enrich purity of cells of interest (e.g. tumor cells) prior to RNA/DNA/protein extraction for downstream biomarker analysis [13]. In parallel, tissue microarray combine with immunohistochemistry or in situ hybridization offer a high throughput screening tool for biomarkers studies.

The most important aspect of a successful biobank for biomarker discovery and validation is the quality of biospecimens. Investigators studied using low quality biospecimen will likely generate erroneous and misleading data. Proper biospecimen handling is crucial for high quality biobank development.

Biospecimen should be processed, and banked ideally within 30 minutes of collection to reduce the ischemic time. Patient

information associated with the biospecimens should be centrally stored on a computer-based database with a secure method and should be backed up frequently. A section should be routinely generated from tissue sample for quality control purpose. The morphological details of the tissue section need to be documented by a pathologist [14]. Quality of DNA, RNA and protein that are extracted from banked tissue samples can be assessed by Agilent TapeStation system and spectrophotometry such as Nanodrop. DNA and RNA isolated from FFPE tissue samples often require PCR analysis to determine the quality [14]. DNA and RNA extracted from non-tissue biospecimens such as blood and blood fractions can be measured in the same way to determine the quality. The quality assurance of bodily fluids primarily involves selecting the parameter of collection, processing and storage, and investigator feedbacks. It is important to process and freeze the bodily fluids as soon as possible within one hour of collection. The College of American Pathologists has recently set up detailed biorepository accreditation requirements to insure that quality assurance and quality control procedures are implemented in biobanks [15].

The infrastructure and accessibility of biobank has a direct impact on biomarker research. Long-term institutional support and chargeback mechanisms should be in place in order to make long term sustainability of biobank. Identification and validation of candidate biomarkers for disease diagnosis, prognosis and prediction of response to therapy promises personalized medicine. Biobanks have been proved as an invaluable scientific resource for developments of novel personalized medicine that significantly improve clinical outcomes and enhance patient care.

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