Cancer Bio-Repository

Shima Fakher[1], *Mozhdeh Zamani[2], Leila Ghahramani[2], Seyed Vahid Hosseini[2*], Pooneh Mokarram[1,3]***

[1]*Department of Biochemistry, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran*
[2]*Colorectal Research Center, Shiraz University of Medical Sciences, Shiraz, Iran*
[3]*Autophagy Research Center, Shiraz University of Medical Sciences, Shiraz, Iran*

Co-Corresponding authors:
Pooneh Mokarram, Autophagy Research Center, Shiraz University of Medical Sciences, Shiraz, Iran. **Tel:** +98 9177160754; **Email:** mokaram2@gmail.com
Seyed Vahid Hosseini, Colorectal Research Center, Shiraz University of Medical Sciences, Shiraz, Iran. **Tel:** +98 9171175582; **Email:** hoseiniv@sums.ac.ir

◄ **Abstract** ►

Background: Cancer research is highly dependent on the availability of a vast amount of data and high quality samples, which can both be provided by networks to enable large-scale multi-center research projects. Biologic materials, such as blood, tissue samples, DNA, body fluids and the related data obtained in cohorts and clinical trials are valuable sources for research that should be managed by policies and standard operating procedures as biorepositories or biobanks.
Methods and Evidence Acquisition: The authors investigated and summarized the Pubmed database articles related to studies in which biobanks had been used, and described the related policies.
Conclusion: Biobanking as a young discipline in different countries needs new technologies, standards and harmonization. In this review article, we have provided an overview on biorepositories, cancer biobanking and the emerging registry in Iran.

Keywords: Biobank, Biorepository, Biobank network, Colorectal cancer

Biobanking

The term biobank means a collection of human biological specimen and associated information stored for one or more research purposes (1) which may also be utilized for non human material. Researchers collect tissue or fluid samples and related clinical data as biobanks to improve their research progress and reveal the role of genes in health, disease, and interactions with the environment (2).

Human-based biobanks comprise three types:

1. Population banks. They contain biomarkers of susceptibility and population identity obtained from germinal-line DNA from a huge number of healthy donors.

2. Disease-oriented banks for epidemiology. The focus is on biomarkers of exposure, using a huge number of samples, studying germinal-line DNA or serum markers and the related data.

3. Disease-oriented general biobanks (i.e. tumour banks). The goal is the biomarkers of disease through collections of tumour and no-tumour samples and

the related DNA, RNA or proteins, based on clinical data or clinical trials. (3).

Blood, urine and tumor tissue are the most frequent biological samples in biobanks that are donated after the approval by the consent forms, however other biospecimen including hair, nail clippings, saliva, faeces and breast milk might also be collected and processed according to guidelines (4). Biobanks of human samples include various classifications such as disease oriented biobanks concerning hospital materials and population-based biobanks based on normal specimen (5, 6). All biobanks must adopt policies and standard operating procedures (SOPs) which are well established by various organizations and lead to the international collaboration in research (7).

Technology can be helpful to ensure biospecimen quality including reliable freezers with monitoring and alarm systems and ambient temperature storage solutions. Laboratory information management systems (LIMS) are also due to technology and automation for sample tracking and helping to ensure that SOPs are fully performed (8).

The most comprehensive option to improve quality control of the biomaterial includes the collection of serum, plasma, whole blood, live cells, purified DNA/RNA and would support genomics, transcriptomics, proteomics, metabolomics, epigenomics, and immunomics. Whole blood can be frozen directly with no further processing which would be suitable for metabolomics since metabolic activity is banned immediately with freezing (9).

Cancer Biobanks

Cancer biobanks are disease-oriented biobanks which are often hospital-based and include tumour banks as well as samples collected from normal control individuals (10, 11)

Initially the participants sign and approve the consent and the next step is tissue acquisition from the hospital pathology laboratory where the patient had the cancer surgery. In most countries these tissue samples are kept for 10 years but some hospitals will store the materials for a much longer time, but most will discard the specimens to free some storage space (12).

Colorectal Cancer Biobanks

Colorectal cancer (CRC) is one of the most common cancer affecting 1.23 million individuals (9.7% of overall cancers) annually and is the fourth common cause of cancer deaths (8% of overall cancer deaths) worldwide (13).

In 2015 in the Netherlands surgically resected tissue was obtained from colorectal cancer patients who were not previously untreated and 3D organoid cultures derived from healthy and tumor tissue from colorectal cancer patients were collected as a bio-bank to identify gene drug associations in order

to achieve personalized therapy (14). In a study of colorectal cancer etiology and prognosis in 2014 blood samples and buccal cell samples were collected from cohort members and archived colorectal tissue blocks were collected from hospitals to build a colorectal tissue repository (12). In 2019 based on UK Biobank as a prospective questionnaire-based study on half a million men and women from 2006 to 2010 the effect of diet compositions on colorectal cancer was investigated in (15) and the association between cardiorespiratory fitness and colorectal cancer was also examined using the biobank data (16).

In a 2019 published study of CRC tumor model in Germany, patients operated on at the University Medical Center Rostock from 2006 to 2017 participated in the comprehensive biobanking and tumor-modelling approach (HROC collection) and serum, lymphocytes, tumor tissues and the adjacent normal epithelium were collected using strict SOP. Patient and tumor data collected included classification, clinical course and outcome, molecular subtype, and results of model establishment. Finally patient-derived xenografts with primary and secondary cell lines were successfully established (17).

As reported in a 2019 research, Parelsnoer institute Biobank for Hereditary CRC in Netherlands was established in 2009 to help researchers investigate the genetic factors leading to the development of CRC, and the disease. Participants were either diagnosed with a genetic mutation resulting in CRC and/ ultimately, prevent or Polyposis or unaffected individuals with an increased risk of hereditary CRC and/or Polyposis. Biomaterial collection, handling, pre-analysis, registration, processing, shipping, storage and long term preservation were based on SOPs. A minimal dataset was defined for the Biobank including patient information, details on medical and family history plus endoscopy and surgery, results of microsatellite instability and molecular genetic tests which was stored on a national level after approval. The biomaterial and the associated clinical data were stored by unique codes to guarantee the privacy of the participants (18). Ethically it is critical to develop a secure system for irreversible de-identification of the research participants' samples while entered the repository (19).

Biobanks of Iran

In Iran Cancer is the third cause of death after coronary heart disease and accidents. Cancer Registry is the systematic collection, storage and analysis of data on cancer cases usually performed in a specific population. It was established and started its activity in Mazandaran province since 1969 till now that a population-based cancer registry has been founded in 5 provinces (Table 1). These five provinces (Golestan, Ardebil, Kordestan, Kerman, and Khozestan) have a total population about 8% of Iran population. All of these registries are now run by the local universities of medical sciences (13).

Table 1: The activities for cancer registry in Iran (13)

Year	Activities
1969	Establishing the first population based cancer registry by University of Tehran and the International Agency for Research on Cancer (IARC)
1984	A bill was passed by the Parliament mandating the report of all tissues "diagnosed or suspected as cancer tissue" to the Ministry of Health
1992	Digestive Disease Research Center (DDRC) was established in Tehran University of Medical Sciences
1998	Tehran Population-Based Cancer Registry (TPBCR) started to collect data from cancer cases of Tehran metropolis

CRC in Iran is the fourth cause of cancer after stomach, bladder, and prostate in men and second cause after breast in women with about 7200 new cancer cases (7.4% of overall cancers) and 4300 deaths (8% of overall cancer death). Among the cancers in Iran stomach, bladder, prostate, and colorectal cancers account for about one-half of all cases in men, while the most commonly diagnosed cancers in women are breast, colorectal, stomach, and esophagus (13).

The Tabari cohort study (TCS), part of the Prospective Epidemiological Research Studies in IRAN (PERSIAN) from 2015 to 2017, was a large longitudinal prospective cohort for the better understanding of risk factors associated with major non-communicable diseases (NCDs) in two urban and mountainous regions in Mazandaran province. The biological samples were collected in as fast as possible. A portion of collected blood was used for biochemistry tests and a complete cell blood count, while the rest was grouped into whole blood, plasma, serum and buffy coat and stored at -70°C. Urine samples were stored at -30°C while hair and nail samples were wrapped in aluminum foil and placed in plastic bags to keep at room temperature. All freezers were equipped with sensors for temperature fluctuations and electricity loss. Biobank rooms were also equipped with air conditioners, fire alarm and electric generator in case of power outage. Backup software was designed to keep the data safe. To respect confidentiality, all participants received a unique cohort ID, which issued for any data analysis. The principal investigator was the only one who could access the dataset. Data was collected and recorded using an online software, designed by the PERSIAN cohort and data was analyzed by STATA 14 (20).

In a 2019 study the distribution of CRC was investigated in all registered cancer cases in the Iranian military community biobank during the period 2007–2016 which was a data bank including registered CRC cases (21).

Since the personalized diagnosis and treatment in medicine is based on "omics" it has gained much attention in Shiraz University of Medical Sciences, Shiraz, Iran and the related software is programmed to reach this goal.

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