Domande estratte n. 3 e n. 5

AVVISO PUBBLICO, PER TITOLI E COLLOQUIO, PER L'ASSUNZIONE A TEMPO DETERMINATO DI N. 1 RISORSA NEL PROFILO DI COLLABORATORE PROFESSIONALE DI RICERCA SANITARIA – CATEGORIA D, CON LAUREA TRIENNALE IN BIOTECNOLOGIE(L-2), LAUREA TRIENNALE SCIENZE E TECNOLOGIE INFORMATICHE (L-31), LAUREA TRIENNALE IN INGEGNERIA INFORMATICA (L-8), LAUREA TRIENNALE IN INGEGNERIA BIOMEDICA(L-8) O TITOLO EQUIPOLLENTE O EQUIPARATO AI SENSI DI LEGGE DA ASSEGNARE ALLA UOC ANATOMIA PATOLOGICA DELL'ISTITUTO REGINA ELENA; NELL'AMBITO DEL PROGETTO DAL TITOLO "*DEVELOPING A BIOBANK NETWORK AMONG MAJOR SARCOMA TREATMENT CENTERS TO IMPROVE BIOMEDICAL RESEARCH*,", FINANZIATO DAL MINISTERO DELLA SALUTE, CUP H83C24000390006, P.I. DR.SSA SIMONA DI MARTINO

Prova Colloquio
5 FEBBRAIO 2025 ore 11:30

Prova tecnica

1. Quali sono i dati e i metadati fondamentali per il biobancaggio? Fai degli esempi pratici anche prendendo dei riferimenti dagli standard europei
2. Quali sono gli step fondamentali per le analisi di Patologia Digitale?
3. Questo progetto riguarda una patologia rara, ovvero i sarcomi. Quali sono i biomarcatori molecolari più importanti per i sarcomi?
4. Cosa significa data FAIRness? Puoi fare degli esempi?
5. Quali sono i formati con cui vengono salvati i dati molecolari?

Domande estratte n. 3 e n. 5

AVVISO PUBBLICO, PER TITOLI E COLLOQUIO, PER L'ASSUNZIONE A TEMPO DETERMINATO DI N. 1 RISORSA NEL PROFILO DI COLLABORATORE PROFESSIONALE DI RICERCA SANITARIA – CATEGORIA D, CON LAUREA TRIENNALE IN BIOTECNOLOGIE(L-2), LAUREA TRIENNALE SCIENZE E TECNOLOGIE INFORMATICHE (L-31), LAUREA TRIENNALE IN INGEGNERIA INFORMATICA (L-8), LAUREA TRIENNALE IN INGEGNERIA BIOMEDICA(L-8) O TITOLO EQUIPOLLENTE O EQUIPARATO AI SENSI DI LEGGE DA ASSEGNARE ALLA UOC ANATOMIA PATOLOGICA DELL'ISTITUTO REGINA ELENA; NELL'AMBITO DEL PROGETTO DAL TITOLO "*DEVELOPING A BIOBANK NETWORK AMONG MAJOR SARCOMA TREATMENT CENTERS TO IMPROVE BIOMEDICAL RESEARCH*,", FINANZIATO DAL MINISTERO DELLA SALUTE, CUP H83C24000390006, P.I. DR.SSA SIMONA DI MARTINO

Prova Colloquio
5 FEBBRAIO 2025 ore 11:30

Domande di informatica

1. Cos'è Word?
2. Cos'è Power Point?
3. Cos'è Excel?
4. Cos'è un Database?
5. Cos'è il backup?

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REVIEW AND PERSPECTIVES

Basic principles of biobanking: from biological samples to precision medicine for patients

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Abstract
The term "biobanking" is often misapplied to any collection of human biological materials (biospecimens) regardless of requirements related to ethical and legal issues or the standardization of different processes involved in tissue collection. A proper definition of biobanks is large collections of biospecimens linked to relevant personal and health information (health records, family history, lifestyle, genetic information) that are held predominantly for use in health and medical research. In addition, the International Organization for Standardization, in illustrating the requirements for biobanking (ISO 20387:2018), stresses the concept of biobanks being legal entities driving the process of acquisition and storage together with some or all of the activities related to collection, preparation, preservation, testing, analysing and distributing defined biological material as well as related information and data. In this review article, we aim to discuss the basic principles of biobanking, spanning from definitions to classification systems, standardization processes and documents, sustainability and ethical and legal requirements. We also deal with emerging specimens that are currently being generated and shaping the so-called next-generation biobanking, and we provide pragmatic examples of cancer-associated biobanking by discussing the process behind the construction of a biobank and the infrastructures supporting the implementation of biobanking in scientific research.

Keywords Biobanking · Biospecimens · Tissue specimens · Cell lines · Standardization · Preanalytical phase

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Introduction

Time magazine featured biobanks among "10 Ideas Changing the World Right Now" back in 2009 [1], highlighting biobanks as an opportunity for scientists and scientists alike to derive knowledge from thousands of samples. Starting from cancer, biobanks were linked to the ambitious chance of screening and treating any disease [1]. During the last decade, the field of biobanking has rapidly grown in parallel with the advent of precision medicine. The crucial role of biobanking research in personalized medicine has also been discussed by *Forbes* [2] in an article referring to the current evolution of biobanks from the usual collection of tissues and blood, nucleic acid, microbiome samples and stem cells to virtual biobanks, which raises the question of whether there is adequate infrastructural and economic support to foster the continuous rapid advance of biobanking. The International Agency for Research on Cancer (IARC) states that biobanks currently represent the foundation of three rapidly expanding domains of biomedical science: (i) molecular and genetic epidemiology (aimed at assessing the genetic and environmental basis of cancer causation in the general population as well as in families), (ii) molecular pathology (aimed at developing molecular-based classification and diagnostic procedures for cancers) and (iii) pharmacogenomics/pharmacoproteomics (aimed at understanding the correlation between an individual patient's genotype or phenotype and response to drug treatment) [3].

Biobanks: definition(s) and key features

Although the term "biobank" first appeared in scientific publications in 1996 [4, 5], there is still no agreement on a precise definition. The term "biobank" has been gradually adopted to describe any collections of biospecimens or human genetic data suitable for research purposes [6]. One of the first definitions, i.e. "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", was introduced by the Organization for Economic Cooperation and Development (OECD) [5, 7]. This description was later updated to depict biobanks as "structured resources that can be used for the purpose of genetic research and which include (a) human biological materials and/or information generated from the analysis of the same and (b) extensive associated information" [8].

One unavoidable feature of biobanking is *the coexistence of biological specimens and associated data*. Biobanks are large collections of human biological materials linked to relevant personal and health information, which may include health records, family history, lifestyle and genetic information that are held predominantly for use in health and medical research [6, 9] (Fig. 1). Interestingly, the document produced by the International Organization for Standardization (ISO) illustrating the general requirements for biobanking (ISO 20387:2018) defines biobanks as legal entities or parts of a legal entity that perform biobanking and states that biobanking is the process of acquisitioning and storing, together with some or all of the activities related to collection, preparation and preservation and testing, analysing and distributing defined biological material as well as related information and data [10].

To accommodate advances in biotechnology and life science, the concept of biological resource centres (BRCs), infrastructures consisting of service providers and repositories of living cells, genomes of organisms and information relating to heredity and the functions of biological systems, was introduced by OECD [11]. Based on these definitions, boundaries between biobanks and other research collections cannot be considered clear-cut [6]. However, the European Commission highlights that biobanks are devoted to collecting biological samples and associated data for medical scientific research and diagnostic purposes and to organizing these in a systematic way [12]. In addition, the key factor that distinguishes a biobank from any other type of research collection is that *established governance mechanisms are in place* to allow outsiders access to resources in a systematic way [12–14].

Both biorepositories (ISBER 2001) and BRCs (OECD 2007) can include tissues from humans and animals as well as cell and bacterial cultures and even environmental samples. In contrast, a biobank typically handles human biospecimens and information about donors, such as demographic and lifestyle information, history of illness, treatment and clinical outcomes.

Since biobanks may have different backgrounds and aims, it is difficult to precisely list the *distinctive features of a given biobank*. Nevertheless, following the description provided by the European Commission biobanks:

(i) Typically collect and store biological materials that are annotated not only with medical but also often with epidemiological data (e.g. environmental exposures, lifestyle/occupational information)
(ii) Are not static "projects", since biological materials and data are usually collected on a continuous or long-term basis
(iii) Are associated with current (defined) and/or future (not yet specified) research projects at the time of biospecimen collection

key in being able to provide feedback to the owners of the samples, to recollect precious information and to reconnect them with the specimens.

Classification systems

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At present, no fully recognized guidelines for biobank classification are on record; nevertheless, a universal biobank classification system would be helpful to facilitate users in searching for biospecimens. Undoubtedly, biobanks are very heterogeneous, as they can differ in size, research topic, health status of the participants, specimens collected, procedures for sample collection and processing and storage systems [6, 12] (Fig. 1).

In the attempt to devise a classification, a first level of categorization acknowledges that biobanks can be "population-based" or "disease-oriented" (Fig. 1):

- *Population-based biobanks* provide specimens from individuals of a general population with the aim of studying the role of individual genetic susceptibility and exposure to external factors in the development of specific disorders by linking molecular data with other associated information [15].
- *Disease-oriented biobanks* collect disease-specific biospecimens. They may be focused on a single type of tissue or include biospecimens from different sources that are relevant to a disease such as cancer [15, 16].

Malsagova and colleagues reported that large-scale epidemiological research or collections from clinical trials of new medical interventions can represent a biobank [17]. Therefore, biobanks can be labelled *according to the type of research* they intend to support:

(i) Population study biobank
(ii) Basic research biobank
(iii) Translational study biobank
(iv) Clinical trial biobank
(v) Pathology archive biobank [18].

In addition, some have illustrated biobank categories based on the associated opportunities of biomarker discovery [19]:

(i) Population biobanks (biomarkers of individual genetic susceptibility and identity)
(ii) Disease-oriented and epidemiology-driven biobanks (biomarkers of exposure and biological effect)
(iii) Disease-specific biobanks, such as tumour banks [19].

A second method of classification considers *the type of samples collected*, such as biobanks collecting frozen tissues, formalin-fixed paraffin-embedded (FFPE) tissues, cells, whole blood and derivatives, urine, buccal cells and saliva, bone marrow aspirate, semen, hair, nails and nucleic acids (DNA, RNA, cDNA/mRNA, microRNA) [3, 15].

Watson and Barnes proposed a schema for classifying human research biobanks that was adopted by the Canadian Tumour Repository Network (CTRNet) [18, 20]. This system enables the categorization of biobanks following four functional elements: the type of donor/participant, the collection methods and design (e.g. retrospective or prospective accrual, size and scope), the features of the biospecimens (e.g. the predominant type of biospecimen preservation, such as fixed or frozen) and the nature of the brand and intended users (e.g. single group, institution or multiple users) [18, 20].

Finally, we should acknowledge a further category represented by virtual biobanks, i.e. electronic repositories of biological samples and other related data, regardless of where the real specimens are stored (Fig. 1) [16, 17, 21].

To have a practical idea of the biobanks available across the European area and of the type of samples they have at disposal, it may be useful to refer to the directory of the Biobanking and BioMolecular resources Research Infrastructure - European Research Infrastructure Consortium (BBMRI-ERIC) [22, 23]. In 2011, the catalogue included 63 population-based and 219 clinical biobanks, which in a few years has grown to 515 biobanks, representing more than 60 million biological samples [22, 24].

Biobanks can exist within hospitals, research centres, pharmaceutical companies and patient advocacy organizations. Biobanks located in an academic setting or as a part of a company reflect different cultures, aims and work practices characterized by a significant gap between them [25]. Academic biobanks are research-driven and usually supported by institutional funding and grants. In contrast, industry biobanks are more focused on end products and more business-oriented [25]. Despite these differences, there is a need for a reciprocal understanding of industry and academic backgrounds and to establish collaborations. For this to happen, it is necessary for industries to understand that human specimens and data cannot be treated as a commercial product and that biobanking is a scientific activity involving humans [25]. From the perspective of precision and personalized medicine, it is necessary that even biobanks start to move towards a patient-centred approach [26]. The Patient-Centered Outcomes Research Institute (PCORI) has established pathways for funding practical research by considering the patients' interests [27, 28]. Patient-centred biobanking should look for ways to support investigators in conducting patient-centred research to make results more useful in healthcare decision-making [26, 28].

4

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In the context of patient-centred biobanking, it is interesting to highlight the experience of the PATH Biobank (Patients' Tumour Bank of Hope), a non-profit biobank in Germany founded by breast cancer survivors and dedicated to supporting breast cancer research, both in academic and industrial fields [29]. This approach highlights how the role of patients in biobanking is changing: from simple donors to an active part [26]. Interestingly, within PATH Biobank at the end of the diagnostic process, the leftover is divided into two parts, one remaining at the disposal of the patient and the other being dedicated to research. After the death of the patient, the patient's sample becomes a property of PATH and is available for research [29].

What to know when building a biobank

Given the complexity of biospecimen handling and management, setting up a biobank may be challenging (Fig. 1). Harati and colleagues tried to provide indications for the creation of a biobank, including accreditation, standards of practice and funding issues [16]. A guidance document produced by the government of South Australia suggests that a defined purpose or business plan is key, and governance, funding and other financial considerations, data and specimen management and consent must be considered [9]. In addition, the process of accreditation and the observation of the standards of practice allow biobanks to operate professionally and to provide biological specimens of adequate quality [17].

It is necessary to prioritize *ethics*, *privacy*, *informed consent*, *data security* and *standardization* (Fig. 1). According to the IARC, developing biobanks involves ethical, legal and social issues (ELSI) and requires the design of governance systems [3]. IARC's recommendations are based on guidelines that incorporate the knowledge gained from projects such as Standardization and Improvement of Generic Preanalytical Tools and Procedures for In Vitro Diagnostics (SPIDIA), BBMRI – Large Prospective Cohorts (BBMRI-LPC) and the International Genomics Consortium (IGC) as well as the European Committee for Standardization (French, Comité Européen de Normalisation, CEN), Technical Specifications for molecular in vitro diagnostic examinations and International Organization for Standardization (ISO) norm [3].

According to the IARC, the following key features should be considered when creating a biobank:

- Type, number, aliquots, size of biospecimens
- Storage containers
- Storage temperature and conditions
- Frequency of access to biospecimens
- Requirements for identification of biospecimens
- Availability of storage space
- Requirements for temperature monitoring
- Associated data
- Financial and operational sustainability [3].

The IARC document also provides protocols for sample processing and useful templates for a consent form and for a *material/data transfer agreement* (MTA/DTA) (Fig. 1) [3, 30].

An important aspect of the creation, reliability and sustainability of a biobank is the standardization of processes connected with sampling, storage and *quality control* (QC). In recent years, specific projects on the standardization of preanalytical, analytical and postanalytical procedures in scientific laboratories, including biobanks, have been undertaken. For instance, the "SPIDIA" project was launched by the European Union FP7 programme in 2008, with the participation of leading academic institutions, international organizations and life sciences companies. The project specifically addressed the standardization and improvement of preanalytical procedures for in vitro diagnostics. Within CEN/Technical Committee 140 for "In vitro medical devices", the SPIDIA results enabled the development and introduction of the first 9 CEN Technical Specifications (CEN/TS) for preanalytical workflows in Europe. In 2017, the SPIDIA4P project was built on the SPIDIA results to develop and implement a comprehensive portfolio of an additional 14 pan-European preanalytical CEN/TS and ISO/IS documents as well as external quality assessment schemes (EQAs), addressing the important preanalytical workflows for personalized medicine. SPIDIA4P was recently acknowledged as one of three success stories by the European Commission.

Information technology (IT), data systems and record administration are also critical aspects of biobanks, and efforts should be made to guarantee that these elements are effective and secure [16]. For excellent biobank implementation, it is important to have a good system for sample traceability, in particular exploiting a barcoding system and an IT platform integrated with all institutional operating systems to automatically integrate data, thus avoiding potential errors stemming from manual entry.

Biobanks shall *ensure* not only *traceability of biological material and associated data* but also destruction [10]. Indeed, biobanks should be able to *manage the process of destruction of biological material and/or deletion of associated data* beyond any possible reconstruction. A legacy plan should be formulated to guide who, what, when, where, why and how specimens and associated data should be transferred or destroyed following a specific event [31]. From an ethical perspective, destruction of samples after consent for use is not usually included in the informed consent: biobanks traditionally communicate to participants how the