

Biobanking shifts to “precision medicine”

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Abstract: The shape of the global health care system is changing rapidly to an approach that is much more patient-centered and focused on “precision medicine.” This is especially due to the development of large-scale “omics” biology results that rely on using and sharing sample collections and databases contained within bioresource facilities. “Personalized medicine” or “precision medicine” is the premise to help individuals to get the “right medicine for the right problem at the right time.” For several decades, tissues, body fluids, and cells obtained from patients with selected diseases have been cryopreserved in hospital-based biobanks, but samples were not accessible worldwide. Instead, the value of biobanks relies on the availability, at a necessary scale, of high-quality biospecimens and related data in order to respond to specific biological questions. However, the next generation of biobanks needs to face a major challenge – the costs related to the collection and processing of a large number of samples. Here, we describe the shift of biobanks from conventional repositories to functional infrastructures able to respond to specific medical demands.

Keywords: next-generation biobanking, personalized medicine, tumor biotypes

Introduction

In the last decade, by virtue of global health care changes and epidemiological population and disease stratification, in addition to the contribution from the “omics” platforms, biomedical science has engaged in developing new biorepository or biobanking infrastructures.¹

Thirty years ago, biobanks resided in one or few freezers, predominantly in university-based hospitals and were mainly used to respond to specific, in-house research projects, and the relative data were confined to laboratory handbooks.²

Institutions and, in some cases, government-supported biorepositories have evolved only recently in response to the changing needs of investigators and types of projects. These changes derive from the development of genomics and proteomics techniques. Indeed, data associated with stored biospecimens have increased in complexity, accuracy, and reliability over the last decade.³

The science of cryopreservation or cryobanking, by preserving tissues and body fluids, has become mainstream to business development. According to the British Broadcasting Corporation, the global biobanking market in 2010 was over US\$140 billion, with a projected 30% increase by the year 2015 towards fostering biobanking initiatives.^{4,5}

In 2009, *Time* magazine reported that biobanking is one of the ten ideas that is changing the world and is becoming the basis for the development of future drugs, which will be directed toward more precise diagnoses.⁶

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The core principle of biobanks is to collect and store tissues, body fluids, and cells derived from controls and/or patients with selected diseases and make them available to the scientific community for: biomarker discovery, drug monitoring, population screening, and disease prognosis.⁷ Overall, the flow of information in today's research is more complex, outpacing the traditional hypothesis-driven fundamental structure.⁸

The value of a biobank rests on the availability of a large number of high quality biological samples obtained from carefully characterized individuals (control and diseased) and detailed medical records. The biospecimens have to be made available to all researchers with proven scientific and ethical credentials, in order to contribute to scientific improvement. Thus, the peer-reviewing process for the application requests and their acceptance by the governance board must be an integral part of the biobank sample management system.⁹ By providing tissues, cells, fluids, and raw data, biobanks have become the drivers of the translational research cycle, since they are the custodians of the biospecimens and related anonymized data (genetics, genomics, proteomics, imaging, physiology, biophysics, biochemistry, nanotechnology, informatics, sociology, epidemiology, and statistics) and processes (pathophysiological and sociobiological), offering biomarker or target validation (multi-population assessment, high-throughput screening, and clinical trials). With next-generation sequencing platforms, introduced in 2005, and the rapid improvements in bioinformatics and analytical laboratory technologies, "the era of clinical diagnostic genome sequencing" has arrived.¹⁰ Today, this is referred to as "precision medicine," and more and more published papers show how genomic technology can positively affect patient care.

As the diagnostic power of biomarkers and genomic tests improves, physicians move away from "empirical medicine" to turn, progressively, toward "personalized medicine" or "precision medicine."^{11–18} In the context of "precision medicine," an individual's genetic background is associated with his own phenotypic and environmental factors, yielding a realistic health care program that fits the person. Instead of a "one size fits all medicine," the right treatment to the right patient at the right time is given, which is based on improved knowledge of the patient's biology.¹⁹ Coupling DNA variant data from each patient to the electronic medical records will enable point-of-care decision support when drugs, with pharmacogenomic variants, are prescribed.²⁰ However, the implementation of "personalized medicine" or "precision medicine" requires that biobanks become more precise;

in this context, "precise" refers to the type of biological fluids and tissues that are collected, as well as the type and number of quality controls performed on the samples in order to guarantee the actual applicability of the results.²¹

Besides tissues and body fluid collections, today we are experiencing a remarkable increase in the demand of human and animal stem cells for research purposes. This necessitates the development of stem cell-dedicated biobanks that can meet the demands at a transnational and even global scale.²² Human pluripotent stem cells hold great translational potential and applicability and biobanks play a crucial role in the stem cell research field, as they provide integrated processes in the expansion, characterization, and cryopreservation of the cell lines. Moreover, the main activity of the biobanks is to ensure the broad availability of stored biospecimens to all qualified users.²³ To achieve this goal, governance and scientific practices should be connected by establishing global standards and minimal sets of criteria for stem cell research. This approach will ensure the generation of high-quality pluripotent stem cells that can fulfill the future scientific requirements. In Europe, a consortium of 26 partners has been formed to establish the European Bank for Induced Pluripotent Stem Cells, which is supported by the Innovative Medicines Initiative. This cell bank will act as a central storage and distribution facility for human induced pluripotent stem (iPS) cells, which will be used in academia and industry-based studies. It is a public-private partnership project of US\$47 million, which aims to become the European human high-quality iPS-cell provider.²⁴

A major issue, which the next-generation biobanks need to face, is the costs associated with the sample handling and storing.²⁵ This may partially be overcome if the next-generation sample collection is designed to meet the type of therapy applied. This approach is particularly important in cancer studies. Although personalized medicine is an exciting approach to cancer treatment, it still remains unclear exactly what the sequential and temporal model of cancer development is. Enhancing high-quality genetic and genomic information in the clinical setting will allow the era of "precision cancer medicine" to rapidly evolve. The term "precision" refers to prospects for enhanced molecular resolution, mechanistic clarity, and therapeutic cogency that can facilitate rational treatment choices tailored to individual patients.^{26,27} Cancer is a genome disease that comprises several biological capabilities acquired during the multi-step development of the tumor. These capabilities include; sustaining proliferative signaling, evading growth suppressors, resisting cell death, enabling replicative immortality,

angiogenesis, and activating invasion and metastasis.²⁸ The instability of the genome underlies these hallmarks, generates genetic diversity, expedites alteration acquisition, and remarkably increases the complexity of the next-generation trademarks of cancer. In addition to cancer cells, the tumor mass contains a repertoire of recruited, ostensibly normal cells that contribute to the acquisition of hallmark traits by creating the "tumor microenvironment".²⁹ The advent of "personalized medicine" reflects the growing body of evidence that cancer cells mutate in various and unpredictable ways in their struggle to survive the therapies deployed to kill them. As this occurs, drugs gradually lose their effectiveness and patients eventually succumb.

As current studies on cancer are increasingly focusing on specific stages and cellular subtypes, biobanks should also reorganize the sample collection methods in order to achieve the goals of personalized medicine. Today biobanks store primary tumor specimens, but the next-generation of biobanks should collect and store cellular components of the cancer mass and what is considered to be morphologically normal. Future medical treatments will be based on individual disease expression. Since cancer is a complex disease which affects whole or parts of multiple biochemical and biophysical pathways, it is important to collect specific and multiple biospecimens from the same individual over time, and/or related family members, and process them with the most advanced technology. The importance of sample collection relies on disease progression, metastasization, tumor relapse, and isolation of specific cellular subtypes.³⁰ A new method of sample collection is based on acquiring a biospecimen from the primary tumor and serially from the tumor mass that will enable researchers to accurately study the evolution of the disease during therapy and understand how the genetic composition of the cancer cells evolves toward drug resistance. This will provide better understanding of tumor biology, highlight intratumoral heterogeneity, and decipher tumor–host crosstalk. Moreover, this approach will assist physicians in prescribing a course of treatment that targets the molecular foundation of a patient's cancer and accordingly adjust those treatments based on changes that occur in the make-up of the disease.³¹ Thus, it is of outstanding importance to set new criteria for sample collection. First of all, a crosstalk between the biobank and the partners is essential to pursue a valuable method for sample acquisition. Unfortunately, this method cannot be easily applicable to archival samples, as their quality and collection methods were not standardized and so they do not meet the basic criteria to fulfill the next-generation biobank requirements.³²

The next generation of biobanks should distribute standard operating clinical protocols to; minimize variability inherent to multicenter trials, assure the quantity and quality of the collected biospecimens, and improve data integration.³³ Next-generation "omics" technologies based on single-cell analysis will deepen the investigation of tumors and lead to "individualized therapeutics."³⁴

The collection of next-generation biospecimens, tumors, and blood samples at defined time points during the disease trajectory represents the future of cancer research and treatment. Unfortunately, the majority of hospital-based biobanks have leftover surgical sections from primary tumors and not from metastases, casting doubt on the quality of the stored specimens, as well as on the; epidemiological, clinical, biological, and molecular information collected from a large number of patients. Next-generation biospecimens must be compatible with multiple discovery platforms (array comparative genomic hybridization, whole genome expression analysis, and methylation/microRNA/long non-coding-RNA profiling) in addition to proteomics- and metabolomics-based platforms.³⁵

Considering the growing number of clinical and molecular data associated with each sample, the possibility of erroneous entries should be examined. Therefore, a further level of quality control should be implemented in the biobank, using internal and external auditing-based processes.³⁶

Next-generation biobanks face big challenges, as networks within networks are generated. Indeed, the possibility of sharing the data worldwide, while maintaining the public's and law makers' interests of each country and guaranteeing individuals' privacy, still remains a major concern.

It is clear that next-generation biospecimens represent the future of research and treatment over the coming decade in "precision medicine." A detailed workflow across a variety of disciplines has become an acquired need, in order to ensure valuable quality and usability of patient specimens. With the contribution of next-generation biobanks, many common and complex diseases (including cancer) can be redefined by their general responses to drug therapy. In this way, pharmacogenomics holds the potential of repurposing existing drugs for whole defined patient subsets, as well as for identifying new drug targets. The development of networks between biobanks with different types of expertise and purposes is necessary to achieve this goal. By protecting participants' privacy and data confidentiality, newest generation biobanks will be the key drivers for health care changes and patient care.

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Author contributions

Ida Biunno and Aikaterini Ntai contributed to the conception, design, and critical revision of the manuscript for important intellectual content. Simona Baronchelli and Tatiana Pellegrino contributed to the acquisition of data and drafting of the manuscript. Pasquale De Blasio contributed to the conception and review of the manuscript. All authors approved the final version to be published and agreed to be accountable for all aspects of the work ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Disclosure

The authors report no conflicts of interest in this work.

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