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More than just a "Container": Centrality and Versatility of Biobanks in the Era of Scientific Challenges

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Abstract

Biobanks are structures used for the preservation of biological samples. These repositories store biospecimens for short or long period of time, depending on the aim for which they are employed. The collections stored inside consist of different types and for each material there's a specific protocol to be followed, in order to keep sample in the best condition as possible. So, a good state is a primary hallmark and its basic to have a well-protected specimen to obtain reliable results fit for clinical purposes and research. In the last years, medical sciences are developing together with the progress of knowledge and skills: the need for new answer to questions about rare and common diseases has greatly contributed to the creation of a network of biobanks which cooperate in Europe and internationally to discover new findings. Therefore, the importance of biobanks is currently considerable. In this article, the topic of biobanks is argued by reviewing the most relevant aspects of these centers. Due to the strategic role of biobanks, the debate on their management and policy is focused on a variety of issues with the aim of reaching a shared agreement and obtaining a universal concordance. Only so, it will possible to achieve and maintain unity and create homogeneous system of biobanking.

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Introduction

During these years, biobanks are improving themselves thanks to new knowledge; as consequence, cooperation with other countries is growing up and, for the next time, it will be possible to create a network in Europe and in the world which should let the exchange of scientific data about clinic and research through an homogeneous system. Currently, there are several aspects different from country to country: this fact is a limit for many activities, because local laws are often quite dissimilar each other. This diversity involves more fields: those which refer to procedures and protocols, but also about legal, ethical and management issues. So, in this review, the most important features of biobanks will be examined, considering that there are various points of view and the goal for the future will be the realization of single way of governance.

How Define Biobank?

Nowadays, the scientific world is marked by revolution in medical area, following the new discoveries. So, the clinical field is strictly dependent on advanced research and laboratory play a strategic role in the relationship between patients and clinicians. In particular, as a result of technological progress and with the acquisition of specific knowledge, many targets are reached, but we'll still have a lot to do. With the human genome sequence, the era of "personal genomes" is started, and the possibility to prevent disease through personalized medicine is real [1]. In the last years a new opportunity is establishing: the institution of biobank. The term "biobank" is referred to a collection of biological specimens like dna, rna, tissues and cells, also with data and information about donor's health [2]. The storage of samples is used for research studies in general or disease-specific. Infact bio-materials are kept from healthy volunteers or people hit by cancers or other disease, so biobank contains both normal specimens and pathological too. Thanks to these materials, a relationship with risk factor, like environmental or genetic, is investigated and the way of target therapy is easier than in the past [3]. In practice, biobank is a network of information's which are cross-linked each other about biological, clinical and epidemiological features of sample. By the analysis of large amounts of biomaterials and with advanced technologies, a new way of research grows up. It will be reasonable exploitable in personalized medicine, through genetic studies about genotypic features and their variants, also with focus on role of environmental factors [2]. Biobank is central in the managing of biomedical activities: it connects multidisciplinary team of experts and improves the acquisition of knowledge. It allows comprehending a lot of pathological and normal pathways of diseases by the support of high-quality technologies; that's ensured with an appropriate storage of samples and systematic revision too. Certainly biobank is synonymous of innovation and revolution, not only in Europe, but all over the world: just to say, in 2009 it has numbered among the top ten of great ideas. In the beginning, it wasn't easy to say what biobank was. In fact the term appears for the first time in 1996, when PubMed used it to refers a collection of human tissues and data important for genetic research [4]. But there's no evidence of consensus about single mean of word. Infact different authorities and local governments adopted definition according to their national law. So there's no limit around type and amount of materials, or period of storage, or related in formations. It can be thought that biobank even contains samples different from human one, like these of animal species, plants, or microbes [5]. Biobank is a complex and dynamic entity, a system marked by variety and heterogeneity. It works in different ways, such as central place of specimen's storage (in which samples and informations are taken and kept centrally for future use) or like a virtual bank (materials are collected and not used if there isn't a specific purpose) [6]. These two kinds of strategies allow different biobanks to communicate each other and to create a national orinternational collaboration between central database and peripheral collection sites [3]. According to these distinct aspects, selection of biomaterials and related data is linked to a general research process in which biobanks represent a central system of control and monitoring.

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So, biobank organizes and manages collection, analysis and specific studies.

One Word, Many Kinds

A unique biobank not exists itself, because as we said, this entity is various and comprehends many different types. There isn't a real classification, because the aspects concerning the establishment of biobank are several. It means that when we talk about biobanks, we refer to a lot of variants. So, in order to classificate biobanks, we consider several features such as size, type of specimens, way of storage, target of research, donor's selection and related data. If we collect samples from population, we have a biobank population-based, which contains specimens for large studies and it has great size; it is really important, for example, for the analysis of biomarkers and for detection of disease. In order to look for particular features of illness, otherwise, specific biobanks exist for collection of pathological samples which derive from people affected by disease. Sample's collection and their related data, in this case, are functional for the investigation of multifactorial, common diseases and rare too [1]. The choose of biological sample is connect with the type of research and includes high-quality material: dna, rna, tissues, cells,whole blood, plasma, serum, saliva, urine, and cerebrospinal fluid [7]. And that's not all: infact more possibilities of human materials are available, like buccal swab, marrow, amniotic fluid and solid tumoral tissue specific of each cancer form [8]. Evaluating the key role of sample, like a starting point of research process, the integrity of biospecimens is unquestionable. So, good practices carried out in order to have the best material to manipulate. Several factors can influence specimen's stability and its maintenance, till damage vitality and restrict or loss the possibility of studies. It's important to pay close attention to procedures of biosample management: collection, preparation, analysis, storage and transport and, if necessary, it occurs to deliver some protection systems for ensuring maximum sample quality [9]. Moreover, it must be evaluated to store information and sample data in electronic way in order to preserve from loss and look for them easily. Barcode system and database are useful to reach this purpose: infact they allow to have a unique encoding of sample [10]. The planning of research project can be different and it's variable in relation to the clinical context: in general, we can group studies in: cross-sectional, case–control and cohort studies [2]. A nodal point refers to specimen's selection and sample taking from donor. There isn't an ideal donor, and it doesn't exist an ideal sample, because each specimen derives from people who leaves it in hospitals, clinical laboratories, and pathology or public health departments. In addition, samples are given directly to the biobank from individuals. Specimens aren't related only to adult persons: it occurs that biological materials derive from pediatric people, or even newborn, and also samples can be referred to post mortem era [11]. A large amount of volunteers take part in building of biobanks with their samples. In general biobanks are divided into three fields, according to biomaterial: dna/rna biobank, biobank of body fluids and tissue one. Donor's specimens can be defined by healthy or unhealthy status [12]. Since the study about "Human Genome Project" started, several news about human life and pathological pathways are discovered, and thanks to innovative technologies, sequencing of dna is now a reality. This approach had allowed studying whole genome and exome sequence in order to obtain strategic information about genetic features of people. So, a challenge for the future research is to obtain genetic data from analyzing samples to study relationship between clinical features and evidence of health or disease, in the context of personalized medicine. Infact the health care consists in a way to investigate risk factors for multiple diseases and thanks to genetic profile we have complete personal information useful for understanding specific disorders by integration of test results with clinic history [13]. DNA is strategic for genetic studies, so its quality must be tested through different methods and this also for rna [14]. Infact, over time, the requirement of genetic biobanks which collect samples (dna and/or rna) for biomedical research, referred to different fields like rare diseases or specific conditions, was great [15]. Not only these specimens are stored in biobank: infact tissues represent another way of doing biobank. Nowadays, human tissues are strategic for transplantation, in order to nurse clinical features and so, the taking of sample and next steps of process, storage and preservation are the main practice enterprise of tissues biobank [16]. Besides, we can obtain another kind of biosamples from individual patients that are body fluids. The clinical meaning of this collection is related to the use of biomarkers in medicine, because of their helpfulness in diagnostic, prognostic and therapeutic area. So, we can collect serum, plasma, urine, saliva, cerebrospinal fluid and several ones for using as protein biomarkers in order to underline the presence of abnormal biological process [17]. The reality of different biobank types, such those cited previously, is symbolic of application of new way doing medicine. An example of schematic classification is shown in the table 1.

Sample Stored	Source of Sample	Finality of Biobank
→Cells	→Diagnostic procedures	→Research (basic or applied): study purposes
→Tissues	→Therapeutic procedures	→Clinical and Therapeutic: for purposes of treatment
→Organs	→Donation for research project and storage for future use	→Public Safety: criminal investigation
→Blood	→Donation for transplantation	
→Body Fluids	→Dead person/ Autopsy	
→Dna		
→Rna		

Table 1: Features of Biobanks.
In this table a schematic view of biobanks is shown. The classification of biorepositories concerns the type of samples, their origins and the purpose of biobanks.

Biobank's World between Clinic and Research

In research and diagnostic the modern medicine is going through a period of changes in order to develop a strict integration of two activities. Thanks to technological advance is now easier to realize a synergistic way of collaboration and molecular pathology's aim helps this challenge [18]. So, it is necessary to have a storage place in which collect specimens for clinical and research studies. And, to achieve this purpose, biobanking is a useful biorepository. Biobanking is a newborn activity, and shows complexity and heterogeneity because, according to different targets, biobanks have independent features [19]. So, we can identify biobanks focused on diseases, for epidemiology or general purpose, and population biobanks for storage of human samples from healthy donor. In particular, while population and epidemiologic banks collect biospecimens for specific studies, instead, biobanks oriented on a particular disease, like these inside the hospitals, are set towards diagnostic and therapeutic purposes [20]. Biobanks generally are suitable for development of medical science,

especially for most recent improvement of "omics" medicine, about patient care. Thanks to the relationship between biobanks and databases, there's an interaction with basic medicine and research and this aspect influences the progress of personalized medicine [21]. Since biobanks collect human samples and scientific studies concerned donor's materials, people must be informed on enormous advantages derived from their willingness to participate in a project research. Infact, the role of people's donation is important for progression and development of different medical fields. People who is available for research, usually, is well informed and sensitive about necessity of scientific research and the tendency of participation in biobank is influenced by personal education and cultural path [22].

Legal Issues: Biobank's Rule

The presence of biobank network around the Europe and the world helps the exchange of data samples among states and supports the cooperation for comprehension and study of diseases. It exists a different law, in every nation, which regulates biobanking operations [23]. Until a few years ago, there was no homogeneous management of biobanks, but now it's necessary to achieve the creation of biobanks network. These structures are referred to biomedical research and health care, so it must be created an appropriate way of governance. According to the recommendation of European Commission, a mechanism of reciprocity would be created between European society and biobanks and these structures would have a regulatory system based on specific legal aspects which guaranteed protection about people and their privacy. There's a real complexity around biobanks legislation: infact there are different regulatory bodies at various levels and this is also for guidelines and practices. The existence of disegual legislation has consequential effects on development of biobanks, such as for collection data and samples. So, in order to obtain a real advance of biomedical research across the Europe, cooperation from country to country is to consider the new challenge. And it will be possible only with a single way of governance [24]. With advance of knowledge, new questions about patient's privacy grew up and require an improvement of current law in order to obtain a general regulation above states within Europe. Thus, it's advantageous to have a specific legal document for control of biobanking activity. Infact, this is helpful especially when samples come from other countries. Nowadays, collaboration together with research centers in Europe is difficult, because available papers aren't uniform. As key role of biobanks is storage of donor samples, and since they are related with data, protection of information is required. So, with informed consent, it's possible to permit others to manipulate samples [25]. But, also in this case, there's a great difference among European biobanks and so, the achievement of standardization of legal aspects, is a key concept to ensure the establishment of biobanks network [26]. Regarding Italian biobanking, first of all, there is not a legal definition of biobank and then, there's a difference between therapeutic and research biobanks. So, every single biobank decides what type of sample must be stored according to different aim of study. Because of the lack of regulatory system, when there's no national legislative reference, recommendation of Council of Europe should be adopted. In order to solve this problem anyway, both in national and international level, it's necessary to establish a certain and distinct regulation. Only after the acquisition of standard system of laws and guidelines, research carried out in collaboration with other European countries will be implemented in a better way [27].

Biobank as AaModel Working in Quality

As biobanks represent a place of samples storage and information which require an accurate protection to ensure patient's privacy, it's necessary to adopt a working methodology, safe and effective. We can reach, maintain and improve the quality just working through operations according to standard procedures, guidelines and directions. The quality refers to a manage system which aims to achieve perfection under fixed laws. For implementing the performance, it's essential to apply a set of practices which are useful for the achievement of this objective [28]. Thanks to reliable standards used in the medical field, nowadays it can be ensured protection of people's healthcare and quality of services: the improvement of these aspects represents the challenge of the future. It often occurs that human biospecimens are not validate during the process of collection, storage and analysis, and so it's not found a uniform, certain way of treatment, which is certified. Therefore, a note of explanation referring to the samples is required, regardless of the type of specimens, in order to obtain and certify reliability of studies and research. The action of certification contemplates that each material is provided with a several assays which are necessary for biobanking activities. But this is not enough: in fact additional information is required for a better characterization and as assurance that human samples are suitable for biopreservation and biobanking. The purpose of certification is to demonstrate that biospecimens are endowed with all requirement for their use and for the aim of employment: so, only after this is well established, they may be used for clinical studies, research and short- term or long-term storage [29]. The presence of methods and procedures standardized ensures an optimal management of biobanks and biorepositories, because each specimen has high-quality features and it is fit for a specific use. It could be very useful to adopt best practices, whereas they show the way of working and suggest better operations for the management of biological materials. However, considering the continuous advance of scientific knowledge, together with technological progress, the acquisition and implementation of best practices shouldn't be regarded as a single step, but as a continuous update and growing improvement. Besides, we must consider that, maybe, it's necessary to incorporate these practices with other forms of regulation that are valid and in use at different levels [30]. Following the development and cooperation among biobanks internationally, coordination of activities and assurance that samples are in the best conditions for their scientific use, are essential. Apart from the type of study and biobank's design, staff working inside the structure should be trained and skilled; structures should be suitable for the processing of the samples and specimen's integrity should be assessed. In particular, noting that errors can occur in every moment of operations, it's advisable to pay attention in the managing of human samples. They are typical of a biological state and so they will preserve their features not only at the moment of collection, but also in the future, for clinical and research studies. So, it should be ensured the highest stability and integrity, to avoid changes that may affect their usefulness: for example, at the preanalytical step. Therefore it is desirable to achieve a system that watch over biospecimens and data through implementation of quality. Quality management takes a long time for the organization of activities and provides for the involvement of personnel; often it's very expensive, but the creation of quality program is helpful for tracking and checking materials collected. Usually, quality can be reached having documentation as complete as possible about sample's handling and using standard operating procedures, protocols of actions, audits, evaluation of critical situation and others. Moreover, there are several strategic policies for "production" quality, as assurance programs for certification of be applied generally to biobanks for the fulfillment of quality and constant advance, even if there's no specific norm covering all biobanks activities. So, it's required an integration of guidelines with

other norms for a better management of these structures [32].

Ethics and Biobank

Biobanks put themselves in a context where a large number of factors cooperates for the realization of scientific aims and in clinical field, as in a research one, we must consider that behind a specimen there's a unique, single patient who has the right to see his interests protected. The steps of collection, processing, storage and analysis of human samples follow a set of norms whose aim is to guarantee integrity and stability for the purpose of request. And that's not all: infact everything about donor must be considered when patient decides to donate a little of himself/herself to biobanks, allowing these medical structures to use their own samples to study diseases, make diagnosis, evaluate genetic state and so on. From the Declaration of Helsinki of 1964, ethical questions about human trials and clinical research have been periodically addressed and revisited, in parallel with new issues emerging referred to human tissue samples and relating data. In order to samples stored have a real usefulness, they are combined with several information about patients, like lifestyle, healty conditions, genetic background, and several. As biobanks keep sensitive data, their protection should be guaranteed and their use should be limited to situation of real need, to ensure privacy and not compromise trust of people and institutions. So, informed consent is required when biorepositories take samples; but, in some situations, it can't be avoided the risk of its arbitrary utilization. This is a real ethical trouble, since it can be occurred that particular groups of people may be excluded and emarginated [33]. Another important topic for ethical implications is the returning of results from the research. In fact, sometimes, the conclusions of a study might have positive consequences, but if it doesn't occurr patients involved in research react in different way and this implies stress and indisposition [34]. This aspect is relevant overall when a genetic research is conduct and participants hope that studies could avoid diseases or improve health conditions [35].

Conclusion

It is clear that biobanks represent a place of great importance, for the role they play in medical field and for the versatility of applications in science. Since they have become increasingly specialized in collecting human samples, it was necessary to set the distinctive features to identify the best mode of operation. Also following the progress of scientific knowledge, biobanks are dealing with new challenges and, to reach this purpose, it is required a continuous compare with other countries and institutions. For this reason, many issues need to be negotiate simultaneously, including those not strictly scientific, to establish a profitable and positive cooperation among centers and to facilitate communications and work together with medical institutions. Indeed, the main purpose of biobanks, and the most important from a moral point of view, is to serve the scientific community in the collection of samples: then, to help people to take care of their health and to find solutions to diseases.

Competing Interests

The authors declare that they have no competing interests.

Author Contributions

Nicola Daniele, Fulvia Fraticelli and Silvia Franceschilli, contributed in drafting the manuscript. Francesco Zinno, contributed in drafting and reviewing the manuscript.

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