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Clinical biobanks in Italy and Liguria: Ethical and social issues, initiatives at the national, regional and local level

Barbara Parodi
IRCCS San Martino University Hospital – IST National Institute for Cancer Research, Genoa, Italy

Abstract
This article aims to revise the ethical and social implications for clinical biobanks and their application in Italy, in the Liguria Region and in a comprehensive cancer centre in Genoa. The policies already in place in the regional network and in the IST National Institute for Cancer Research in terms of involvement of the community of patients and citizens are described, as well as the future development of initiatives aimed at improving the active participation of the community. The author is a biobank manager and not a professional bioethicist. The world of biobanks in Italy includes large numbers of small initiatives, and 'biobankers' are aware that public engagement is essential to ensure public trust and to give legitimacy to the research. The governance of these research infrastructures requires new tools in order to improve involvement of participants. The October 2011 Conference, 'New Patient-Centric Perspectives in Medical Research: Ethical and Governance Challenges' has been an important occasion for bringing together different experiences and expertise and for learning about new forms of participant-centric approaches and tools.

Keywords
biological resource centres, clinical biobanks, informed consent, trust

Corresponding author:
Barbara Parodi, Biobank and Cell Factory, IRCCS San Martino University Hospital – ISTNational Institute for Cancer Research, Largo Rosanna Benzi, 10, 16132 Genoa, Italy.
Email: barbara.parodi@istge.it

The biological resource centre concept

Biological resource centres (BRCs) are now widely considered to be one of the key elements for sustainable international scientific infrastructure. A definition of BRC has been provided by the Organization for Economic Co-operation and Development (OECD) Task Force on BRCs in 2001 in the OECD publication, *Biological Resource Centres: Underpinning the Future of Life Sciences and Biotechnology* (OECD, 2001). The definition is broad, including collections of microorganisms, animal and plant cells and human tissue samples:

> Biological resource centres are an essential part of the infrastructure underpinning biotechnology. They consist of service providers and repositories of the living cells, genomes of organisms, and information relating to heredity and the functions of biological systems. BRCs contain collections of culturable organisms (e.g. micro-organisms, plant, animal and human cells), replicable parts of these (e.g. genomes, plasmids, viruses, cDNAs), viable but not yet culturable organisms cells and tissues, as well as data bases containing molecular, physiological and structural information relevant to these collections and related bioinformatics. BRC must meet the high standards of quality and expertise demanded by the international community of scientists and industry for the delivery of biological information and materials. They must provide access to biological resources on which R&D in the life sciences and the advancement of biotechnology depends.

The OECD Task Force concluded its work in December 2006, with a mandate from the Ministers of Scientific Research from member states to produce a reference standard for BRCs, and to form the basis for setting up a Global BRC network. The end result, *Best Practice Guidelines for Biological Resource Centres*, was published in 2007 (OECD, 2007).

Biobanks in Europe: The European biobanking and biomolecular resources research infrastructure

The concept of BRC was adapted immediately to the world of biobanks (Parodi and Truini, 2008). In the *European Roadmap on Research Infrastructures (Report 2006)* (ESFRI, 2006), biobanks were included by the European Strategy Forum on Research Infrastructures (ESFRI) among the six core infrastructures for the development of European research in the field of life sciences. The project for the construction of a European Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) (Yuille et al., 2008) was funded by the European Commission in 2007. BBMRI has grown into a 53-member consortium with more than 280 associated organizations (largely biobanks) from over 30 countries, making it one of the largest research infrastructure projects in Europe. The preparatory phase of BBMRI ended in January 2011 and the infrastructure will be implemented under the ERIC (European Research Infrastructure Consortium) legal entity. The headquarters (central coordination) will

be in Graz, Austria, responsible for coordination of the activities of National Nodes established in participating countries. By December 2011, 13 countries (Austria, Bulgaria, Czech Republic, Estonia, Finland, Greece, Italy, Latvia, Malta, the Netherlands, Norway, Spain and Sweden) have signed the Memorandum of Understanding where they express their aim to establish BBMRI as a European Research Infrastructure Consortium (ERIC) and become Members of BBMRI-ERIC. The application to the European Commission is in its final stages of completion. The expected start date of BBMRI-ERIC operations is the second half of 2012. BBMRI aims to act as an interface between biological specimens and data (from patients and European populations) and top-level biological and medical research. BBMRI takes care of the two main models of biobank: disease-oriented (clinical) biobanks and large epidemiological sample collections and population cohorts.

Ethical and social implications of clinical biobanks

In outlining ethical, legal and social issues raised by clinical biobanks, at least four distinct areas can be identified (Solbakk et al., 2009): access of biological material and information to the biobank (What type of consent? Under what conditions can biobanks established for diagnostic or therapeutic purposes be converted to biobank for research? Which rights does the donor 'transfer' to the biobank by donating his/her biological material and information?); biobanks as institutions (What is their role? Are they allowed to do research or should they behave as 'custodians' of samples?); access to the material by the researchers (How are priorities established among competing projects? How are intellectual property rights and a benefit sharing mode defined?); access to results (How can confidentiality and protection of personal data be ensured? How may the results be made public and under what conditions?).

To ensure the protection of the community, the biobank needs to address all these issues, which are not limited to the institution of informed consent. Informed consent was originally developed in the context of the patient–physician relationship (Convention, 1997) and later extended to the relationship between researcher and participant in the clinical trial. In these two situations, it is certainly possible to inform the potential research participant on the exact nature and possible risks of the operations covered and regulated by the consent (surgery or invasive diagnostic, testing of a drug). In the context of a biobank, comprehensive and exhaustive information is rarely possible: as research on the material collected is by its nature not defined, we cannot describe the future possible uses of the material because we have not a clear idea of the new perspectives that will open up thanks to new discoveries and technologies.

The recent literature on consent in relationship with biobanks is abundant, and increasingly many authors do not agree with the role that consent has assumed in the biobank context (Hoeyer et al., 2005; Laurie, 2008; Simon et al., 2011), as it emphasizes individual rights of citizens and patients (autonomy, self-determination, privacy) (Pullman et al., 2012), while other values are neglected (Knoppers and Chadwick, 2005), such as reciprocity, collective identity, solidarity, citizenship and universality. Patients and donors have an interest in protecting their individual integrity, but also to encourage the development of new drugs and diagnostic methods for themselves, their families and the community (Hoeyer, 2008).

Several surveys (Hansson, 2005, 2009) show that, among the concerns of donors, being constantly and precisely informed on the purpose and the development of research project is never in the first place. More important to donors are the value of the study for the community, project evaluation by independent auditors, the absence of corporate economic interests, and the protection of personal data. Moreover, the consent is often even seen as a protection of the institution and researchers, rather than of the patient.

In fact, the confidence and trust of both patients and public is essential to the success of a biobank (Cambon-Thomsen, 2004), and this trust should be improved through different forms of protection for participants. An important element is trust in the institution. The biobank of a research institute (e.g. a comprehensive cancer centre) should enable patients, through publications and brochures, to understand that the mission of the institute is not only to cure the disease, but also to study the cellular and molecular basis for developing new therapies and identifying new forms of prevention. At their first access to the institution, the patients should be informed that the organization is engaged in research, that a biobank is available because biological samples that patients can donate are an essential tool for research, and that this initiative can only succeed with the support and cooperation of patients and citizens.

The biobank shall make available to the donor community its Code of Ethics, which sets out the principles and forms of protection of the integrity of the patient, in accordance with national laws and international conventions. In the statute the public function of the biobank should be emphasized, aimed at improving health care in the interests of the community. 'Biobankers' should be seen as guardians of the patient samples, each project should be submitted for review and approval by an independent ethics committee, and the protection of personal data should be guaranteed through appropriate standard operating procedures. The biobank should have clear procedures for the distribution of samples to academic and industrial partners (material transfer agreement) and follow strict rules to respect the privacy of donors (Confidentiality Disclosure Agreement).

Organizations representing the patients should have the opportunity to participate in the activities of the biobank, research results should be disclosed in aggregated form in a language appropriate to the public, and a policy should be put in place with regard to disclosure to patients of any results that may have a direct impact on their treatment.

The perception and understanding by the population of the concepts and issues related to biobanks is of great importance as biobanks depend not only on donors but also on social and political support. The knowledge and acceptance of biobanks is very heterogeneous, and in the preparatory phase of BBMRI, investigations have been launched in several European countries to assess the degree of acceptance of biobanks. However, little information is available yet on the attitudes of the Italian population with respect to these issues.

Patient-centric initiatives in Liguria and at the BRC of Genoa

Disease-oriented biobanks are recognized as a key resource for biomarker discovery and are closely related to the health care system. In Italy, the governance of the health care system is devolved to regional authorities. Liguria region is traditionally rich in initiatives in the field of biobanks and recently the region has officially recognized the role of biobanks for diagnosis and research (Deliberation no. 34, January 2010). In the resolution, the region has established the criteria for accreditation of existing resources and further initiatives. To be accredited, the biobank should: (a) be formally established within the hospital/research centre; (b) have dedicated space and equipment; (c) be active for at least three years; (d) use dedicated staff to ensure quality and continuity of services; (e) operate within a certified quality system; (f) document the presence of SOPs for involvement of patients, acceptance, preparation and storage of samples, information management and catalogue, and distribution of biological material; and (g) act as a service unit and document ‘in’ and ‘out’ activities. The Liguria region coordinates the national working group on biobanks set up within the State-Regions Conference. The regional network includes biobanks specializing in rare diseases, and among these is the ‘Cell line and DNA biobank from patients affected by genetic diseases’, which currently coordinates the Telethon Genetic Biobank Network. Oncological biobanks are also represented, and among these is the Biological Resource Centre of the National Institute for Cancer Research of Genoa (CRB-IST).

The CRB-IST, institutional facility of the National Cancer Institute of Genoa, was established in 2008, aimed at co-ordinating already existing biobanking activities, establishing an agreed quality system and participating in the European Infrastructure of Biobanks and Biomolecular Resources. The main aims are to:

facilitate high quality translational research dependent on biological material and data; address ethical issues on biobanking; promote the project at the population level; harmonize technical and management SOPs according to international best practices; help to reduce costs for collection and storage of biological material and favour institutional recognition at a regional, national and international level. CRB-IST participates in the Liguria network of biobanks, in the national networks Rete Italiana BioBanche Oncologiche (RIBBO) and Network of Italian Pathology Biobanks (NIPB) and in the European Infrastructure of Biobanks and Biomolecular Resources (BBMRI). Common SOPs have been developed for collection and preservation of samples as well as a common Material Transfer Agreement for distribution of samples and information. All projects are evaluated by a Scientific Committee and by the Ethical Committee. CRB-IST has produced a website for the patients that keeps the population informed on the ongoing scientific projects. The promoters have always been aware that this initiative could only succeed with the support and cooperation of the community of patients and citizens.

In order to ensure communication, transparency, fairness and accountability to all stakeholders, and particularly to donors and the public, CRB-IST has taken a number of initiatives. The ethical code of conduct has been agreed and it is distributed to the patients, who receive information by trained nurses on the aims of the biobank and on the use of the material. A brochure has been published, both on paper and on the website, to provide answers to common questions facing people who want to participate in the project (how can I participate?, will I face any risks?, what are the benefits?, who will use the samples?, how will confidentiality be guaranteed?). CRB-IST also publishes a quarterly newsletter to update the population about the research projects sponsored by the biobank, acknowledging the fact that the samples donated by the patients have helped contribute to a new medical finding or treatment. All personnel involved have been trained, and the office for public relations of the Institute collaborates in the initiative.

The recent (1 September 2011) integration in a new hospital/research centre (IRCCS University Hospital San Martino − IST National Institute for Research on Cancer) offers the opportunity to greatly expand the activities of the CRB-IST, which may rely on much higher numbers of samples. This is also an occasion for improving the involvement of the local community and for setting up tools aimed at better understanding how patients and citizens feel about the storage and use of biological samples and medical information for research purposes.

Future developments

The integration of the Cancer Centre in a much larger hospital implies the need to agree and standardize the procedures for informing the patient, obtaining consent, and collecting samples and data. The first aim is to promote the participation of

nurses and medical staff of a number of departments (pathology, clinical and surgical oncology, clinical and experimental research). A city-wide initiative will be aimed at raising the awareness of patients and the public about the donation of biological samples.

We are setting up a number of focus groups representing different categories of biobank stakeholders, based on what has been achieved in several European countries in the preparatory phase of the construction of a European BBMRI, work package 6. The groups, composed of 5−7 individuals, relate to cancer patients, citizens, health professionals (nurses), medical doctors and researchers. To conduct focus groups, applicants will use the models already validated in the research cited. At the conclusion, each of the groups will appoint a spokesman for a second level group, in which the different components will meet to compare results and discuss further. The results of this discussion will be used for the preparation of questionnaires to be used for the survey on the perception of biobanks among institutional operators and users.

A survey is being performed, within the hospital and at a community level, about preferences in terms of consent, reconsent, benefit sharing, and return of information to the participants. The survey is conducted in collaboration with the public relations office of the Institute, based on interviews and written questionnaires. A project also exists to introduce an IT resource for a 'dynamic electronic consent', on the basis of the experience with the Chris study, recently developed by the European Academy of Bozen/Bolzano (EURAC) and presented at the 2011 Conference, 'New Patient-Centric Perspectives in Medical Research: Ethical and Governance Challenges'.

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