BBMRI.it
Biobanking and BioMolecular resources Research Infrastructure Italy

BBMRI-ERIC
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Interview with Barbara Parodi, Quality Manager of BBMRI.it

Barbara Parodi is a medical doctor and the Executive Manager of the Biological Resource Centre of the National Institute for Cancer Research (IRCCS AOU San Martino – IST) of Genoa, Italy.

Dr. Parodi has been deeply involved in biobanking for many years, dealing with scientific, organizational, technical and ethical issues. Her expertise is mainly in management of Biobanks, Good Laboratory Practices and Good Manufacturing Practices.

She participated in the Organization for Economic Co-operation and Development (OECD) Task Force on Biological Resource Centres (BRCs) and has contributed to the compilation of the OECD Best Practice Guidelines for BRCs (2007).

Dr. Parodi's contribution to the Biobanking and Bio-molecular Resources Research Infrastructure (BBMRI) started with the Preparatory Phase, and continues both at the European and at the National level, where she participates in the Governing Board of the Italian national node of BBMRI (BBMRI.it) with the role of Project Manager and responsiblility for the CS Quality. Dr. Parodi also participates in the Microbial Resource Research Infrastructure (MIRRI) and in the Global BRC Network (GBRCN).

Dr. Parodi is involved in several international working groups, i.e. the "BioResource Impact Factor" initiative and the working group on sustainability of biobanks. She is part of the Board of the European, Middle Eastern & African Society for Biopreservation & Biobanking (ESBB) with the role of Treasurer and she is involved in the ESBBperanto working group, dedicated to harmonizing definitions and languages in biobank databases to enable comparability of biomaterials and data across different biobanks and countries.

Dr. Parodi sees biobanking as a scientific discipline that affects health, social, environmental and global welfare, and she strongly believes that it is of paramount importance for the development of research in the life sciences.

Interviewed by Andrea Wutte

Biobanking – Best practice at the National Node BBMRI.it

A: You are the BBMRI.it National Node Quality Manager with a broad spectrum of biobanks in your network. Please tell us about your collaborations.

Barbara: The Italian node of BBMRI, established with a joint effort by the Ministry of Health and the Ministry of University & Research, includes 90 biobanks located all over Italy and belonging to the National Institute of Health, the National Research Council, 18 universities, 40 hospitals and 23 IRCCS institutes of health care and research.

BBMRI.it includes both population biobanks and pathology, genetic or disease-oriented biobanks, which collect biological samples, such as blood, tissues and DNA, plus associated epidemiological, clinical, and research data. In addition, biobank specimen archives have large collections of well-documented, up-to-

date clinical and biological information samples, supplied with the molecular genomic resources and with links to epidemiological and health care information, which can support retrospective studies and accelerate research progress.

Since 2011, institutions have set up a task force on biobank management and monitoring at national and regional level. In Italy, biobanks are mostly part of the national health system and are therefore supported at a regional level. Regions are also responsible for the identification and certification of biobanks; several regions have already put in place specific resolutions and laws in this direction.

A: You built up the BBMRI.it QMS from scratch. How did you proceed?

Barbara: We set up a 3-step path to identify, evaluate and enrol biobanks in BBMRI.it The first step was a survey of the Italian biobanks and bio resources performed in 2013, with the aim of assessing and selecting well-established Italian biobanks in terms of quality and quantity of samples and data, and to identify biobanks available to provide services to the BBMRI network. And to provide support, advice and documents to those willing to set up new biobanks. The results show that most of the Italian biobanks are disease oriented (about half are devoted to cancer and/or genetic diseases); 16% were already operational before 1990, while 56% were set up after 2001. Almost half of them (43%) have more than 10,000 cases collected, and most of them (66%) collect at least 3 different types of samples per subject (e.g. frozen samples, FFPE, blood derivatives, nucleic acids, cell lines). A large majority (77%) participate in regional, national and/or international networks. The vast majority are ready to offer services to the network (samples, data, molecular analysis, expertise, support in handling, preservation, transfer).

Following the survey, as the second step, we established a procedure for biobank evaluation and monitoring: each applicant was asked to make a self-assessment through an on-line questionnaire. A team of evaluators analyses the results and audits the biobank, based on an agreed checklist of features.

The self-assessment questionnaire was designed

- to verify ELSI compliance and quality system implementation with the aim of identifying Italian biobanks who give assurance of:
  - Service to the scientific community
  - Interoperability
  - Compliance with ethical and legal standards
  - Compliance with national and international best practice
- to provide support to those willing to improve the quality of their collections of biological samples
- to create a network of biobanks that could sign the Partner Charter of BBMRI Europe.

The applicant biobank is then included in the catalogue of BBMRI.it biobanks/collections, based on compliance with the BBMRI-ERIC Partner Charter.

At present, 70 biobanks have demonstrated that they have have a quality system compatible with the requirements of the Partner Charter, have joined BBMRI.it and actively participate in the national infrastructure, and of these, 35 biobanks have already signed the BBMRI-ERIC Partner Charter.

A: How do you define an "adequate QMS" for the Biobanks of BBMRI.it? What are your required standards?

Barbara: The list of features to be evaluated in order to define an "adequate QMS" for the BBMRI.it Biobanks has been built by the evaluation team based upon the expertise of the evaluators in several initiatives, including the OECD Task Force on BRCs, the BBMRI Preparatory Phase, the BRIF initiative, the EORTC policy, the Telethon Network of Genetic Biobanks (TNGB), the ESBB Biobank of the Year competition and taking in consideration all relevant ISO standards.

The check list used to audit the biobanks includes 8 items on quality (QMS, Certification/Accreditation, quality control, approved SOPs, improvement plans, dedicated staff and training, audits, disaster plans), 5 items on transparency (website, annual report, access policy, information and consent, public involvement), 4 items on catalogue (means of dissemination, variety of samples, number of samples, clinical / genetic/lifestyle data), 5 items on use (evidence of use – in/out activity, distribution procedure , number of requests, MTA, distributed/preserved samples rate), 3 items on interoperability (participation in national thematic networks, participation in regional networks, participation in international networks), 3 items on scientific productivity (authorship/acknowledgements in publications, traceability of publications, data recovery policy), 5 items on sustainability (institutional recognition, short-medium-long term funding, projects, dedicated personnel, cost recovery policy).

BBMRI.it reference standards are those mentioned in the 'Quality Management' chapter of the BBMRI-ERIC Partner Charter: OECD Best Practice Guidelines for Global BRC Networks and WHO/IARC guidelines for BRCs for cancer research whenever feasible. Other internationally and nationally available guidelines are taken into account, such as the ISBER Best Practices For Repositories, the National Cancer Institute Best Practices for Biospecimen Resources and the Guidelines for Genetic Biobanks produced by the Italian Society of Human Genetics and Telethon Foundation.

A: Why do you believe that Biobanks should have controlled processes and how is your approach to convince the Biobanks to control these processes?

Barbara: Biobanking is a complex process and it includes a range of different activities that affect quality: quality of samples, quality of data, and quality of services offered. As such, the issue of quality is intrinsic to all processes and procedures within biobanks and biological resources.

The OECD definition of BRCs highlights the need for BRCs to "… meet the high standards of quality and expertise…" and "… provide access to biological resources on which R&D in the life sciences and the advancement of biotechnology depends." This cannot be achieved by biobanks and BRCs without a quality management system in place. The objective of establishing a quality management system is to ensure operational consistency and control, thus guaranteeing the reliability of the biobank/BRC and its content. The concepts more specifically related to the quality management system and its components that apply to biobanks are quality assurance, quality control, standard operating procedures, best practices, traceability, authentication, qualification, and validation.

Indeed, Italian bio bankers are perfectly aware that quality is an integral part of all operations and includes all processes and procedures within the biobank, all methods of processing, storage and measurement, all data registered. Quality extends to all personnel and their operations, and as such must include personnel training. The process must always be monitored to identify areas for improvement.

The issue is not convincing the biobanks that they should have a QMS in place and that they should work

on the basis of controlled processes. The issue is to convince the Institutions hosting the biobanks that biobanks are important, and that they need to invest in quality and personnel.

A: QA & QC are the main targets for providing high quality controlled samples to research. You have developed and implemented a validated QC method for cell lines. Please tell us more!

Barbara: Human and animal cell lines are widely used in basic and translational biomedical research, because they are a simple and representative model system for functional studies and identification of diagnostic tools and therapeutic targets. Each cell line has unique features and can be used for specific studies.

Recent results, obtained using high-throughput genomic analyses, confirm that cross-contamination of human and animal cell lines is a repeated and frequent cause of scientific misrepresentation, and the assumption that the results obtained with the same cell lines by different researchers in different laboratories are fully comparable is often not true.

Molecular methods for cell line authentication, such as fingerprinting, short tandem repeat (STR) profiles and single nucleotide polymorphisms (SNPs) analysis, have been proposed in order to overcome this problem. In particular, an STR profile international reference standard for human cell lines was proposed by the leading cell banks from the United States, Europe, Asia and five large research institutes worldwide, who tested 253 human cell lines.

The Biobank of Genoa, Italy, provides an authentication service for human cell lines and has produced a database, the Cell Line Integrated Molecular Authentication (CLIMA) database that allows authentication data to be linked to actual cell lines. The CLIMA database is one of the tools developed during the Preparatory Phase of BBMRI.

A human cell line can be considered as misidentified if it no longer corresponds to the individual from whom it was first established. Many cases of misidentification are caused by cross-contamination where a different, faster-growing cell line is introduced into the culture. Authentication testing is an effective way to combat cell line misidentification. The International Cell Line Authentication Committee (ICLAC) makes available a Database of Cross-Contaminated or Misidentified Cell Lines, which is updated regularly to include new instances of false cell lines.

Since 2010, STR profiling has become a widely accepted standard for human cell line authentication, and the most qualified scientific journals now accept papers involving the use of human cell lines only with certification that the cell line in question has been profiled and its identity has been confirmed by a recognised biobank.

STR profiling should become a sound standard for confirmation of authenticity (defined as originated from a specific individual) of biological materials stored in a wide range of biobanks, such as population biobanks, rare disease biobanks, or oncological biobanks.

A: Are there other specific QC methods at BBMRI.it biobanks?

Barbara: QC methods obviously depend on the characteristics of the material collected. For issues related to pre-analytical conditions, the Italian biobanks refer to the Biospecimen Reporting for Improved Study Quality (BRISQ) (doi: 10.1002/cncy.20147) and to the Standard Pre-analytical Coding for Biospecimens (SPREC) (doi: 10.1158/1055-9965.EPI-09-1268). The Italian oncological biobanks follow the

WHO/IARC guidelines for BRCs for cancer research, the TNGB has agreed a common technical SOP Manual, which is published in the TNGB web site. The working group of Section I of the *Consiglio Superiore di Sanità* has recently published the "Guidelines on traceability, collection, transportation, storage of cells and tissues for diagnostic pathology", endorsed by the Italian Health Ministry. Furthermore, BBMRI.it biobanks are working together in the identification of molecular signatures to validate pre-analytical procedures, and are testing temporary storage under vacuum of biological samples to be used for genomics, transcriptomics, proteomics and metabolomics multicenter studies.

A: Within the National Node, the cooperation between the biobanks and the researchers from academia as well as from the industry is supported by BBMRI.it. Would you share with us your experience?

Barbara: BBMRI.it involves the main research institutions in Italy i.e. the National Institute of Health, the National Research Council, Universities, Hospitals and IRCCS – institutes of health care and research, and in addition, a network of stakeholders which includes industries and 8 patients associations supports and works together with the node. Scientists provide expertise, scientific societies collaborate with BBMRI.it in the definition of aims, organization, structural and technological requirements, access, informed consent and privacy. In 2013, in cooperation with the scientific societies AIOM (medical oncologists) and SIAPEC-IAP (pathologists), BBMRI.it has produced the guidelines for oncological biobanks: 'Oncological Research Biobanks. Definition, purposes, organization, structural and technological requirements, informed consent, privacy and access policy'. Patient associations (i.e: FAVO, UNIAMO) work in strong synergy with infrastructure initiatives.

The access to biological samples is provided by BBMRI.it biobanks through agreed SOPs and material transfer agreements, and most of the biobanks have a dedicated committee for the evaluation of projects. The national catalogue of BBMRI.it is under construction, while national thematic networks such as the Telethon Network of Genetic Biobanks already have a common policy on access in place. The public-private partnership has been already experienced through the first BBMRI Expert Centre on Metabolomics, which is located in Florence Italy.

A: Please tell us your thoughts about 'cross-border biobanking' in Europe.

Barbara: Cross-border biobanking is essential for the future of biomedical research, and it is one of the main reasons for building a European infrastructure. Rare disease biobank networks, such as the Telethon Network of Genetic Biobanks in Italy, know this very well, because sharing of samples and data is particularly relevant for rare diseases – and they have integrated their catalogues in order to provide the users with homogeneous sets of samples.

Many issues are involved in cross-border biobanking, including ELSI and the need to harmonize the rules for biological material transport across Europe. Our cell bank in Genoa has long experience in cross border transport, as it has been distributing established cell lines all over the world for more than 20 years.

BBMRI-ERIC National Nodes should work together with the aim to complete the construction of a European infrastructure able to provide standardized biological material and data to the scientific community.

A: Dear Barbara, thank you for this interview! Congratulations to this impressive number of 70 Italian Biobanks, already certified to international Standards! We are looking forward to your talk at HandsOn Biobanks 29-31 July 2015 in Milan, Italy.

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FACTS of BBMRI.it

National Node		**BBMRI.it**
National Node Director		**Prof. Dr. Marialuisa Lavitrano**
QM Coordinator, BBMRI.it		**Dr. Barbara Parodi**
QM Coordinator, local	**70**	http://www.bbmri.it/organigramma
Number of biobanks	**90**	http://www.bbmri.it/network-board
Partners	90	**Universities, Hospitals, IRCCS, CNR, ISS**
Type of biobanks		**disease-oriented biobanks** **population biobanks** **archive tissue biobanks**
Catalogue		http://www.bbmri.it/network-board
Number of certifications	**70**	**ISO 9000** **ISO 15189** **ISO 17025** **SIGUCERT (Italian Human Genetics Society)** **JACIE**
Number of certification in progress	**16**	