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Quality Matters: 2016 Annual Conference of the National Infrastructures for Biobanking

Marika Doucet,[1] Karl Friedrich Becker,[2] Jens Björkman,[3] Jacques Bonnet,[4] Bruno Clément,[1,5] Maria-Grazia Daidone,[6] Charles Duyckaerts,[7] Gilles Erb,[8] Helmuth Haslacher,[9] Paul Hofman,[1,10] Berthold Huppertz,[11] Christophe Junot,[12] Joakim Lundeberg,[13] Andres Metspalu,[14] Marialuisa Lavitrano,[15] Jan-Eric Litton,[16] Helen M. Moore,[17] Manuel Morente,[18] Ben-Youssef Naimi,[19] Uwe Oelmueller,[20] Bill Ollier,[21] Barbara Parodi,[22] Liangliang Ruan,[23] Giorgio Stanta,[24] Paola Turano,[25] Jim Vaught,[26] Peter Watson,[27] H.-Erich Wichmann,[28] Martin Yuille,[21] Myriam Zaomi,[1] Kurt Zatloukal,[11] and Georges Dagher[1]

Introduction

On May 17–19, 2016, the Austrian, Italian, and French infrastructures for biobanking (BBMRI.at, BBMRI.it, and BIOBANQUES, respectively) organized a scientific conference in Nice, France, on the quality of biological resources. BBMRI.at, BBMRI.it, and BIOBANQUES are members of the Biobanking and BioMolecular Resources Research Infrastructure (BBMRI), which was established to increase efficacy and excellence of European biomedical research by facilitating access to quality-defined human biological resources.

The goal of the ''Quality matters: improving the quality of biological resources'' meeting was to identify specific gaps in methodology and preanalytical variables that can affect the quality of samples, disseminate evidence-based practices, and promote best practices for the use of biological resources in both basic and clinical research programs.

The meeting brought together researchers and all parties interested in biobanking from Europe, North America, and Asia. The range of quality control issues considered was broad, and included those arising from use of tissue and liquid samples, nucleic acids, and proteins extracted from cell cultures.

Details from each presentation are summarized in the context of the focus given to specific areas of quality in biobanking that served as session tittles. Additional information about individual presentations (including slides and videos) is available at: www.biobanques.eu and http://unspod.unice.fr/search/?q=biobanking.

[1]BIOBANQUES Infrastructure, Inserm US13, Hôpital de la Pitié Salpêtrière, Paris, France.
[2]Technical University of Munich, Munich, Germany.
[3]TATAA Biocenter, Göteborg, Sweden.
[4]Inserm U916, Institut Bergonié, Université de Bordeaux, Bordeaux, France.
[5]Inserm UMR991, Rennes, France.
[6]Fondazione IRCCS Instituto Nazionale dei Tumori, Milan, Italy.
[7]Inserm, Paris, France.
[8]Roche diagnostics, Strasbourg, France.
[9]Medical University of Vienna, Vienna, Austria.
[10]Hospital-Integrated Biobank (BB-0033-00025), FHU OncoAge, University of Nice Sophia Antipolis, Nice, France.
[11]Medical University of Graz, Graz, Austria.
[12]CEA, Paris, France.
[13]Science for Life Laboratory, KTH Royal Institute of Technology, Stockholm, Sweden.
[14]Estonian Genome Center, University of Tartu, Tartu, Estonia.
[15]University of Milano-Bicocca, Milan, Italy.
[16]Karolinska Institute, Solna, Sweden.
[17]National Cancer Institute Biorepositories and Biospecimen Research Branch (BBRB), Bethesda, Maryland.
[18]Biobank Unit of the Spanish national cancer center (CNIO), Madrid, Spain.
[19]AnyGenes, Paris, France.
[20]QIAGEN, Hilden, Germany.
[21]University of Manchester, Manchester, United Kingdom.
[22]Biological Resource Center of the National Institute for Cancer Research (IRCCS AOU San Martino–IST), Genoa, Italy.
[23]Shanghai Clinical Research Center, Shanghai, China.
[24]University of Trieste, Trieste, Italy.
[25]University of Florence, Florence, Italy.
[26]International Society for Biological and Environmental Repositories (ISBER), Bethesda, Maryland.
[27]British Columbia Cancer Agency's Vancouver Island Cancer Center, Victoria, Canada.
[28]Helmholtz Zentrum München, Institute of Epidemiology II, Munich, Germany.

Controlling Preanalytical Factors

The scientific community widely acknowledges that even the best analytical tools cannot yield reliable results when the quality of samples analyzed is not appropriate. In the rapidly developing field of biobanking, collection and processing of biological samples constitute a complex process with a number of variables that, if not controlled, could alter the quality of samples, leading to invalid data, unreliable diagnosis, and potential harm for patients.

The aim of this session was to discuss the current efforts to standardize protocols and, more particularly, preanalytical workflows involving biospecimens. The ISO 15189 standard defines the preanalytical phase as the processes that start, in chronological order, from the clinician's request and include the examination request, preparation and identification of the patient, collection of the primary sample(s), and transportation to and within the laboratory, and end when the analytical examination begins.

Paul Hofman of Inserm and Pasteur Hospital (Nice, France) described the importance of controlling the preanalytical phase in biobanking activities. In personalized medicine and more particularly in the case of cancer treatment, the choice of a drug is now often determined by the presence or the absence of a molecular target (called a ''predictive biomarker'') detected in a tumor. The management of sample quality, which includes the control of preanalytical parameters, is, therefore, mandatory to obtain samples that are reliable for strong biomarker analysis. He illustrated this issue by providing several examples, including the PD-L1 expression assessment in lung tumors, whose staining pattern can be dependent on the time spent in formalin fixative.[1]

Gilles Erb of Roche diagnostics (France) addressed the issue of quality and standardization of preanalytics by focusing on breast cancer management in countries from the Sub-Saharian region. All patients who may benefit from targeted therapies require diagnosis with optimal tests to avoid any false negatives and false positives. For example, false human epidermal growth factor receptor-2 (HER2) positives could lead to the administration of potentially toxic, costly, and ineffective adjuvant HER2-targeted therapy, whereas false negatives could lead to HER2-targeted therapy being denied to a patient who could benefit from it. Local practices, therefore, need to have quality controls in place, to perform reliable immunohistochemistry, silver *in situ* hybridization (SISH), and fluorescent *in situ* hybridization (FISH) tests that will ultimately inform diagnosis and treatment of patients with breast cancer. In this regard, Roche provides regional coordination and support to participating countries that include partnerships and collaborations, education, and development of local projects.

Uwe Oelmueller of QIAGEN (Germany) further emphasized the need for standardized and improved preanalytical workflows to obtain reliable analytical test results. As coordinator of the EU FP7 SPIDIA (standardization and improvement of generic preanalytical tools and procedures for *in vitro* diagnostics) consortium, he underlined the importance of using clinical samples with preserved bioanalytes profiles, that is, not degraded or changed during sample collection, transport, storage, archiving, and processing. He provided an overview of some of the findings obtained by SPIDIA and presented the current road to standardization with the release of nine technical specification documents addressing preanalytical workflows by the European Committee CEN/TC140 (*in vitro* diagnostic medical devices) the previous year. These standards will apply to medical laboratories performing diagnosis based on genomics or other omics techniques. They are currently processed as an international standard within the ISO Technical Committee: clinical laboratory testing and *in vitro* diagnostic test systems (ISO/TC212).

Paola Turano of the University of Florence (Italy) followed with a presentation on the development of evidence-based preanalytical procedures in metabolomics. In recent years, metabolomics fingerprinting has been increasingly used to investigate the existence of disease signatures and alterations in metabolites caused by physio-pathological states. This approach, however, requires that the measured metabolic profile reflect the original individual metabolome as closely as possible. As a partner of the EU FP7 SPIDIA project, she evaluated the effect of preanalytical procedures on the metabolomic analysis of biofluids (urine, serum, plasma, and saliva) by using nuclear magnetic resonance (NMR). The fact that sample degradation can significantly alter the results derived from NMR analysis has encouraged the development of evidence-based standard operating procedures (SOPs) for sample collection and handling.[2]

Karl Friedrich Becker of the Technical University of Munich (Germany) is a partner of the EU FP7 SPIDIA project and a project leader of the technical committee at CEN and ISO (CEN/TC140, ISO/TC212). He proposed some critical considerations on the use of tissue samples for quantitative protein and phospho-protein analysis. After reiterating the need for standardization of the entire workflow (from test ordering to report of the results of proteomic assays), he demonstrated the crucial role of the preanalytical phase for successful integration of proteomic studies in clinical practice, since sample processing may affect protein and phosphoprotein profiles[3,4] before performing any analytical test.

Kurt Zatloukal of the Medical University of Graz (Austria) and director of the Austrian national node of BBMRI-European Research Infrastructure Consortium (BBMRI-ERIC) (BBMRI.at) further explained the importance of sample quality in the rapidly developing field of biobanking. He detailed some outputs of the previously mentioned SPIDIA consortium, which include several European standards (CEN technical specifications CEN/TCs), addressing preanalytical quality requirements for human blood, tissue samples, and other most relevant analytes (DNA, RNA, proteins, metabolites). These technical specifications provide a series of useful definitions and a comprehensive list of documentation requirements of quality-relevant parameters. In the context of the upcoming European regulatory framework for *in vitro* diagnostic (EU IVD Regulation), which requests validation of several key preanalytical parameters in the development of molecular diagnostics, CEN/TCs will become even more relevant.

Finally, *Helen M. Moore*, Chief of the National Cancer Institute (NCI) Biorepositories and Biospecimen Research Branch (BBRB) in Bethesda, MD, provided the audience with a U.S. perspective on developing biospecimen evidence-based practices (BEBPs). First, she presented the NCI best practices for biospecimen resources, which were updated earlier this year to reflect the most recent developments in biobanking activities. To increase the reproducibility of basic

and clinical research, several other resources are available, including the NCI Biospecimen Research Database (https://brd.nci.nih.gov/brd/) housing biospecimen science literature and SOPs, NCI-sponsored biospecimen science research programs, and the reporting recommendations known as BRISQ (Biospecimen Reporting for Improved Study Quality).[5] Best practices are being incorporated into the new biorepository accreditation program of the College of American Pathologists. The NCI BEBP is a series of procedural guidelines developed and annotated with published findings from the field of human biospecimen science. To date, one BEBP is available and three are in preparation. One current challenge is to translate the requirement for ''ideal'' specimens described in BEBPs into the ''real world'' of clinical practice, where fit-for-purpose quality metrics will help to increase research reproducibility.

Present and Future of Biobanking

This section provides an overview of the current development of the Pan-European infrastructure BBMRI-ERIC as well as that of national infrastructures for biobanks in Austria, France, Italy, and Spain. Furthermore, different experts presented their vision of what could be the biobanking of the upcoming decade.

Biobanking infrastructures

Jan-Eric Litton of the Karolinska Institute in Sweden described the Pan-European BBMRI-ERIC of which he is the director general. After presenting the infrastructure, he detailed some of the 2016 work programs involving quality and international standard developments, which involve 5 expert groups representing 71 experts in 16 member states. By being an observer liaison for ISO, BBMRI-ERIC keeps track and contributes to the biobank relevant international standard developments (ISO/TC276 biotechnology and ISO/TC212 clinical laboratory testing and *in vitro* diagnostic test systems). It also acts as an information hub by communicating expert knowledge of the ISO working group to the BBMRI-ERIC community and vice versa.

Several biobanking national infrastructures belonging to BBMRI-ERIC then updated the audience on their activities. *Kurt Zatloukal* of BBMRI.at described the Austrian national infrastructure (created in 2013), which supports local biobanks with its healthcare thematic focus (integrated biobanking for cancer, metabolic diseases, rheumatic diseases, rare diseases, and infectious diseases), biobanking of animal diseases with human disease relevance, biobanking for translational research, and the advancement of precision medicine. BBMRI.at also contributes to the national digital pathology infrastructure, the European Fund for Strategic Investment (EFSI), with the infrastructure for the management of medical and patient-related research data, and it is involved in the development of a secure and sustainable medical data storage program.

Georges Dagher of Inserm (Paris, France) reported on BIOBANQUES, the French node of BBMRI-ERIC, which entered its operational phase in 2014 and now comprises a network of 85 biobanks. In addition to providing expert services and facilitating access to biological samples and associated data to its users, BIOBANQUES fosters and supports national and international research consortia, encourages innovative technologies, contributes to the development of public-private partnerships, and improves academic and industry access to biological resources at national and European levels. In relation to ensuring quality of biological resources, BIOBANQUES has implemented the French standard for biobanks (NFS 96900) and contributed to the certification of 52 biobanks since 2012.

Marialuisa Lavitrano of Milano-Bicocca University (Italy) and coordinator of BBMRI.it described the Italian node of BBMRI-ERIC, which started in 2013 with the support of the ministry of health and the ministry of university and research. Some of the specific strengths of BBMRI.it are the number of its biobanks, the link between biomedical research and clinical care in the IRCCS (institute of healthcare and research) network, the close collaboration with patient associations, scientific community and bio-industries, as well as a number of thematic clusters of excellence such as the Telethon network of genetic biobanks. Similar to other national nodes, BBMRI.it has developed common services (IT, ELSI, quality) and actively contributes to the ISO/TC276 and CEN working groups with BBMRI-ERIC.

Manuel Morente of the biobank unit of the Spanish national cancer center (CNIO) presented the Spanish national biobank network (SNBN), a nationwide initiative of which he is the coordinator. The Spanish national infrastructure in biobanking was created in 2009 and is funded by the Spanish Institute of Health Charles III (ISCIII), with the aim of promoting biomedical research of excellence and adding value to the Spanish biobank system in a coordinated manner. SNBN is currently in its second period of funding (2014–2017), integrating 52 institutions. These biobanks are mainly hospital based and disease oriented, following the Spanish legislative framework that came into force in 2011.

Next-generation biobanking

After presentations of national infrastructures for biobanking, some interesting perspectives on the present and future of biobanking were provided. *Bill Ollier* and *Martin Yuille* of the University of Manchester (United Kingdom) and the Center for Integrated Genomic Medical Research (Manchester, United Kingdom) provided some information on precision public health (PPH). PPH aims at prevention by using individual risk profiles developed for all members of the population. Precision medicine typically refers to the development of more precisely targeted medicines, whereas PPH refers to the development of public health policy and practice to achieve universal prevention by including new tools such as biomarkers to specify individualized health improvement interventions. PPH is driven by public policy, and, therefore, it has a good prospect of achieving improved population health regardless of socioeconomic and educational status. Bill Ollier presented a bottom-up approach of PPH and its role as an ''engine'' for health improvement, whereas Martin Yuille focused on a top-down approach from theory into practice. They are currently developing a PPH pathfinder project on risk of chronic disease, including obesity-related disease for Greater Manchester, where the essential infrastructure for PPH already exists.

Joakim Lundeberg of the Science for Life Laboratory (SciLifeLab) and KTH Royal Institute of Technology (Stockholm, Sweden) updated the audience on next-generation histology by using next-generation sequencing. The common and widely

used histological techniques based on staining protocols are characterized by low throughput, being restricted to the analysis of a single or a few markers in individual tissue sections. With the development of next-generation sequencing, more global and quantitative measurements can be achieved. In this regard, he presented Spatial Transcriptomics, a new approach that combines histology and RNA sequencing. This novel technology allows both visualization and quantitative analysis of the transcriptome with spatial resolution in individual tissue sections.

Paul Hofman of Inserm and Pasteur Hospital (Nice, France) then gave a presentation on next-generation biobanking for a better management of human biological samples. Biobanking 1.0 (1990–2005) and biobanking 2.0 (2005–2014), respectively, focused on the quantity and quality of biospecimens, whereas next-generation biobanking (or biobanking 3.0) should be centered on external stakeholders.[6] The main objectives are to respond to the requirements of stakeholders, maintain a sustainable economic model, participate in the constitution of national and international networks of excellence, define innovative measures in the field of biobanking, and integrate more individual-related sensitive data (biological, genetic, and associated clinical data) to the collected samples.

Finally, *Bruno Clément* of Inserm (Rennes, France) addressed the issue of sustainability of biobanks in further detail. He defined biobank sustainability as a framework made of three dimensions: operational, financial, and societal.[7] In relation to the financial dimension, he provided some information on the assessment of costs, using the BBMRI calculation grid,[8] and offered some thoughts on cost-recovery models.[9,10]

To ensure sustainability, some key challenges were identified by both Paul Hofman and Bruno Clément and included the need to establish methods of evaluation with pivotal indicators, develop peer-reviewed evaluations of biobanks (e.g., for productivity, quality, accreditation), and implement robust business plans.

Quality Control in Genomics

The development of biomarkers and precision medicine rely, to a large extent, on genomics. This section deals with requirements that are aimed at guaranteeing the appropriate quality of nucleic acids.

Jens Björkman of TATAA biocenter (Göteborg, Sweden) gave an account of quality control for the quantification of gene expression biomarkers. He described measures to test for RNA degradation with a new molecular method called ΔAmp,[11] inhibition in quantitative real-time polymerase chain reaction (qPCR), and genomic DNA background and provided means to compensate for inter-plate variation.

Ben-Youssef Naimi of AnyGenes (Paris, France) followed and reported on a molecular platform for biomarker profiling (SignArrays). This platform can be used for identification and validation of disease biomarkers, as well as for drug development. It includes high-throughput analysis of signaling pathways and specifically designed software for data mining and analysis.

Jacques Bonnet of Inserm (Bordeaux, France) followed with a presentation on quality control of nucleic acids. These controls are particularly important for the estimation of quantity, purity, and integrity of DNA and RNA. After a brief summary of existing techniques for nucleic acid quality control tests, he highlighted their limitations and possible measures to overcome them.

Giorgio Stanta of the University of Trieste (Italy) concluded this session by examining the causes of RNA degradation in archive tissues and provided some precautions for RNA extraction.[12] Of interest, he mentioned that cold ischemia can be prevented by preservation of large tissue specimens at 4°C under vacuum conditions. With this method, RNA integrity can be maintained for up to 3 days and the collected tissue can then be banked at −80°C, fixed, or even used for cell culture.

Quality Control in Biobanks

This section deals with the implementation of evidence-based quality control in biobanks.

Jim Vaught of the International Society for Biological and Environmental Repositories (ISBER) (USA) gave an overview of evidence-based biobanking practices with his perspective as editor-in-chief of Biopreservation and Biobanking, the official journal of ISBER. After reiterating the central importance of controlling preanalytical variables and the need for harmonization and standardization of protocols to obtain biospecimens of high quality, he described a number of reporting standards that were relevant to biobanking activities that were developed in the past 10–15 years. They include CONSORT (consolidated standards of reporting trials),[13] REMARK (reporting recommendations for tumor marker prognostic studies),[14] STARD (standards for reporting of diagnostic accuracy),[15] STROBE (strengthening the reporting of observational studies in epidemiology),[16] BRISQ (biospecimen reporting for improved study quality),[5] and SPREC (standard preanalytical code).[17] SPREC and BRISQ are closely related and were developed to encourage control of preanalytical factors impacting biospecimen integrity. He also mentioned that although editors of scientific journals support these guidelines, there is currently no information on how widely these recommendations have been followed by authors and reviewers.

Charles Duyckaerts of Inserm (Paris, France) then introduced the GIE NeuroCEB brain bank and presented some valuable insights on quality control in a brain bank. Assessment of the quality of brain tissue is carried out by using pH examination of the cerebrospinal fluid and cell morphology, which allows identification of pathological inclusions. Other quality controls include RNA integrity number and Western blots on tissue homogenates to evaluate the quality of RNA and proteins. Both, however, lead to loss of sample topography. Since precise distribution of lesions is crucial to diagnose neurodegenerative diseases, techniques such as laser micro-dissection coupled to mass spectrometry (MS), time-of-flight secondary ion MS,[18] or, more recently, CLARITY[19–21] may be of particular interest for analyzing the lipid or protein contents of lesions in specifically delimited brain regions.

Andres Metspalu of the Estonian Genome Center (Estonia) gave an overview of the Estonian biobank. The Estonian biobank is a longitudinal, prospective, and population-based biobank that was established in 2000. To date, 52,000 donors have been recruited, which represents 5% of the adult population of the country. Since a wide range of recruitment personnel is involved, all protocols were

standardized from the start and a computer-assisted questionnaire was used to guarantee the high quality of the collected samples and associated data. The biobank also set up a specific monitoring unit to oversee the incoming questionnaires. Diagnoses were validated by using the different existing health databases and national registries. Finally, laboratory information management systems (LIMS), the certified service provider (CSPro) program, and the ISO 9001: 2008 standard are in place and further ensure quality control and quality management systems.

Liangliang Ruan of Shanghai Clinical Research Center (SCRC) (China) described a molecular biology-based quality control program to ensure high-quality biobanking in China. The SCRC was founded in 2008 and has a quality management system that covers all activities of the biobank. He more specifically focused on validation of DNA quantitation by spectrophotometry, a basic bio-analytical method in molecular biology. This simple validation model for DNA quantitation is part of the sampling program for biospecimen quality control in the China biobanking network.[22]

Finally, *Manuel Morente* of the Spanish national cancer center (CNIO) (Spain) concluded this session by examining the broader meaning of quality in biobanking. Biobanks are at the crossroad of individuals (donors), users (scientific community), and society. In this context, he explained how the quality of samples managed by biobanks is more than a technical issue and acquires an ethical dimension to respond to the altruist donation from subjects, the compromise with researchers, and the perspective of the social value of biobanking activities.

Quality Control in Cell Cultures and Liquid Biopsies

Up to one third of tumor cell lines used in scientific research are affected by inter- and intra-species cross-contamination or have been wrongly identified, thereby rendering many of the conclusions reported by researchers doubtful, if not completely invalid.[23] Since the publication of this worrying statistic, several international guidelines and standards have been developed to ensure the quality and identity of cell lines.

Barbara Parodi of the Biological Resource Center of the National Institute for Cancer Research (IRCCS AOU San Martino–IST) (Genoa, Italy) discussed good cell culture practices with guidelines including the development and acquisition of new cell lines, authentication, preparation of master and working banks, cryopreservation, exchange between laboratories, microbial contamination, and misidentification.[24,25] With short tandem repeat profiling, researchers are now equipped with powerful tools for cell authentication. Multiple resources such as the cell line integrated molecular authentication (CLIMA) database and activities of the international cell line authentication committee (ICLAC) are also available to ensure the identity and quality of cells used in biomedical research.

Erich Wichmann of Helmholtz Zentrum München (Germany) gave an overview of the KORA cohort in Augsburg and the German National Cohort (GNC), two large-scale prospective epidemiological studies with long observation periods. To date, the GNC has recruited 44,000 adults (representing 5 millions of aliquots) in 18 study centers, who will be followed for the next 20–30 years. The high quality of samples is ensured with the implementation of SOPs for specimen collection and sample preparation, staff training and certification, data quality checks, quality reports, and so on. Preanalytic processing of liquid samples is a particularly crucial step with the high number of biospecimens under investigation. The 18 study centers have, therefore, been equipped with liquid-handling robots, allowing plasma and serum to be completely processed within 2 hours of blood draw. Long-term storage facilities at −80°C and −180°C are currently semi-automated and should be fully automated by 2018.

Recent studies have indicated that blood could replace invasive surgical biopsies and represent a ''liquid biopsy,'' which contains circulating tumor cells, cell-free nucleic acids (circulating tumor-associated microRNAs and cancer-specific mutations in circulating DNA) released by primary and metastatic lesions. The development of novel and highly sensitive technologies now enables the detection and characterization of these circulating tumor cells and cell-free nucleic acids, as well as measurement of their dynamic changes. The use of liquid biopsies in precision medicine is, however, not devoid of technical and biological caveats. *Maria-Grazia Daidone* of Fondazione IRCCS Instituto Nazionale dei Tumori (Milan, Italy) reviewed some of these challenges, represented by non-uniform sample choice, handling and processing of samples (e.g., blood cell contamination during sample preparation), and lack of consensus for data normalization in the case of nucleic acids. A pivotal point exposed was that further work is needed to obtain specific and sensitive cancer biomarkers from liquid biopsies that could confer an important advance in the disease management.

Quality Control in Metabolomics

After a presentation on metabolomics of biofluids on the first day of this conference, *Paola Turano* of the University of Florence (Italy) gave an overview of metabolomics carried out on tissues. As previously seen, metabolomics provides a snapshot of what is happening in a tissue at the metabolic level. The old approach of tissue metabolomics involved solution NMR of tissue extracts (lipophilic or hydrophilic extracts). She then described a new method called high-resolution magic angle spinning that enables NMR of intact tissues. Some key issues occurring during the preanalytical phase were highlighted, such as sample heterogeneity (especially in liver) and surgical procedures (warm ischemia, cold ischemia), leading to changes in the concentration of various metabolites.[26] Since warm ischemia is inevitable and cold ischemia can be difficult to reduce, it is, therefore, essential to annotate samples as comprehensively as possible.

Christophe Junot of CEA (Paris, France) reviewed the use of liquid biopsies in metabolomics studies. In contrast to the presentation of Paola Turano focusing on NMR methods (see Controlling Preanalytical Factors section), he provided some insights on the use of MS methods. Both gas chromatography electron impact MS and liquid chromatography atmospheric pressure ionization MS are more sensitive than NMR, but are, however, less reproducible. In the past few years, a number of reference protocols[27–29] and studies documenting the stability of metabolites in different human biological matrices (serum, plasma, urine) have been published in an effort to obtain standardized protocols.

Quality Assurance in Biobanking

Berthold Huppertz of the Medical University of Graz (Austria) described ways to increase sample retrieval rates of paraffin-embedded tissues. In many pathology departments, storage of formalin-fixed paraffin-embedded tissue blocks and slides often follow the model of handwritten code on labels, manual sorting and picking, sorting mostly done chronologically, and users leaving a ''marker'' label when picking samples. This outdated storage organization leads to many issues ranging from returning a sample to the wrong spot with subsequent ''disappearance'' of the sample to very little control of incoming and outgoing samples, and misdiagnosis due to confusion when deciphering handwritten labels. To improve identification of samples, Biobank Graz has successfully implemented 2D dot matrix codes and a semi-automated storage system. To reduce the number of identification errors, one of the key points is to use electronic coding linking the printer system to the clinical LIMS system, and to avoid the manual typing of codes into the printing system.

Peter Watson of the British Columbia Cancer Agency's Vancouver Island Cancer Center (Canada) followed with a presentation of quality assurance programs and tools to disseminate biobanking standards. He more specifically detailed the Canadian Tissue Repository Network (CTRNet) Certification Program, which promotes better standardization of biobanking, provides education, encourages adoption of standards, and fosters public confidence. Key elements of this program include self-assessment (to classify the biobank), exposure to relevant education and SOPs, and commitment to standards, such as the required organizational practices. Of note, the elements of this program are designed to be scalable and applicable to all entities conducting biobanking, and they target many aspects of quality (biospecimen, data, and governance). More information is available on the Biobank Resource Center website.

Myriam Zaomi of Inserm (Paris, France) presented the implementation of quality management in French biobanks and the lessons learned from it in the past 10 years. She detailed the specific development of the NFS 96900 standard for Biological Resources Centers (BRCs), the implementation of this standard in >60 biobanks, as well as a quality department at the French Infrastructure BIOBANQUES. She also highlighted the fact that development of targeted training and cross auditing has helped improving processes related to biological resources and promotion of biobanking activities in France.

Helmuth Haslacher of the Medical University of Vienna (Austria) then presented a comprehensive summary of quality management at BBMRI.at, whose goals are to support consortium partners, harmonize procedures on the basis of CEN/TC preanalytical standards, and establish mutual quality audits within the consortium. On a local basis, all Austrian consortium partners agreed on the ISO 9001 standard as the basis of their quality management systems, since no biobank-specific international standard on quality management systems has yet been published. In a similar manner to BIOBANQUES, BBMRI.at is implementing a national cross-auditing system that should help monitor compliance within biobanks. He ended his presentation by mentioning that cross-audits enable a deep insight into a biobank's management system and require a high degree of trust and cooperativeness.

Conclusions

Biobanking has become a national and international endeavor, with biobanks now commonly organized in networks. One objective of the BBMRI-ERIC Pan-European infrastructure is to increase the efficacy and excellence of biomedical research by facilitating access to quality-defined human biological resources.

This objective can only be attained if human samples are of good quality. However, for many biomedical studies, the greatest source of variation is found at the preanalytical stage (during collection, transport, and initial processing of biospecimens) and preanalytical errors represent the most common error in clinical laboratories. Since preanalytical variability of biospecimens can have significant effects on downstream analyses, controlling such variables is, therefore, fundamental for the future use of biospecimens in precision medicine.[30,31] During this meeting, preanalytical factors encountered in metabolomics, genomics, and other fields relevant to biobanking were clearly identified and multiple ways to control them were proposed. They included the need for standardization and harmonization of protocols and implementation of proper quality programs. The release of SOPs, technical specifications (CEN/TCs) and the development of international standards relevant to biobanks demonstrate the willingness of the scientific community to develop the best practices for biobanking. Dissemination of evidence-based practices, education, and training programs, as well as the development of quality systems, including audits and certification/accreditation of biobanks, will also contribute greatly to the improvement of sample quality. These should, ultimately, lead to a higher quality and reproducibility of research results using biospecimens.

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Address correspondence to:
Georges Dagher, PhD
BIOBANQUES Infrastructure
Inserm US13
Hôpital de la Pitié Salpêtrière
47, bd de l'Hôpital
75651 Paris Cedex 13
France

E-mail: georges.dagher@inserm.fr