



# From biobanking to precision medicine

A group of experts from ISBER shed light on the science of biobanking and its role in delivering modern and precision medicine

**T**wenty years ago, an internet search for the word “biobank” would have returned almost nothing; today, there are millions of results. The term biobank commonly refers to a large collection of tissue samples (with associated biological and medical data), such as surgical biopsies (fresh frozen or in paraffin sections), blood and serum samples, different cell types, DNA, RNA; all carefully collected for research purposes.<sup>1</sup> The science of biobanking is very broad and covers collections of plant, animal, or human specimens. For the purposes of this discussion, we will focus on human biobanks.

Two decades is a very short period of time, for a concept that has become vital to delivering modern, precision medicine – both in terms of research and the clinic itself. One of the first biobanking initiatives came from the Organization for Economic Cooperation and

Development (OECD), which advocated the importance of biobanks, but also insisted on the need to have an accreditation system.<sup>2</sup>

In the years following this OECD proposal, various countries began establishing biobanks as research infrastructure. Thus, many national biobanks and biobank networks were created in Canada, the UK, USA, China, Estonia, South Korea, Finland, Denmark, Sweden, France and many other countries. In our opinion, biobanks crucially underpin and facilitate the national and international medical research efforts, by providing high-quality, research-ready samples. In addition, biobanks are linked to clinical data for investigators, according to a set of best practices and standards.

In 1999, the International Society of Biological and Environmental Repositories (ISBER) was formed



tion and Biobanking, is a well-established, international peer-reviewed journal, that highlights vital research in the field.<sup>4</sup>

### **The road to precision medicine**

Medical research in the era of precision medicine is based on the analysis of samples with clinical data – and, because the associations are often weak, we need these samples in large quantities. The implication is clear: if more, well-characterised, high-quality samples are available through biobanks, the faster research will advance and impact upon the faster delivery of health-care today. However, to fulfil the aim of precision medicine, challenges remain on the road ahead.

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### **Standards and harmonisation**

The most important aspects of a biobank are consistency and quality. The validity of the data generated by biobanked samples, depend on their quality, which is in turn dependent on the use of stringent standards in collecting the biospecimens and delineating patient characteristics. Variations associated with collecting, processing and storing different samples and the accompanying clinical data, make it extremely difficult to extrapolate or to merge data from different studies. Without that information, it’s easy to introduce invisible bias into the work, leading to irreproducible work! Therefore, the standardisation and harmonisation of biobanking practices are of paramount importance.

### **Data and ethics**

As medical researchers “think bigger” than ever before, their need for data grows ever stronger. It demands the gathering and administration of large collections of samples and related data, often from multiple sources. This is not an endeavour for individuals, single projects, or small research groups, because of the high costs in time, sample access, technological resources and the funding involved.

Hence, ‘virtual biobanks’ started forming with institutional collaboration and geographically distributed forms of endeavour. One such major collaborative

([www.isber.org](http://www.isber.org)). Since then, academics, biobankers, NIH Institute representatives, patient advocates, industry representatives, lawyers and others with an interest in biobanking meet annually at the ISBER Annual General Meeting, to share their expert knowledge in the field.

In 2005, ISBER developed and published the Best Practices for Repositories, which was revised at regular intervals and translated into many languages. We are currently anticipating the fourth edition should be published late in 2017.<sup>3</sup>

This is the premier ‘handbook’ for biobankers to achieve quality products in their laboratories. Topics such as cost recovery, facilities, equipment, safety, quality assurance and quality control, ethical issues, specimen collection, processing, and retrieval, training, specimen culling, and many more are discussed. ISBER’s journal, *Biopreserva-*

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# Clinical and hospital-based biobanking for next generation patient care

Professor Berthold Huppertz from Biobank Graz, highlights the importance of maintaining high sample quality in biobanking

The emerging new ISO standards for pre-analytical handling of samples in biobanking give hope that sample quality can be much better maintained and documented. This of course should lead to improvement of patient care. However, where do you find the link between improving the pre-analytical pathway of sample handling in biobanks and improved patient care?

## Overview on the pre-analytical pathway

For any analysis of a human sample, independent of whether this analysis is performed in a research setting or in a clinical routine setting, the sample needs to be taken from the body, transported, processed, maybe stored and used for analysis.

Let's take a blood sample as example. Blood drawing normally takes place in a clinical setting using standard equipment resulting in the receipt of some millilitres of blood in a primary blood tube. In a clinical setting, this primary blood tube is then standing in the clinical ward for a while, transported to a (central) laboratory where processing and analysis takes place.

In a research and biobanking setting, this primary blood will again be taken in a clinical setting, standing in the ward and then is transported to a lab or biobank. Here, the blood is processed, then divided into smaller aliquots, stored (short-term, mid-term or long-



term) and subsequently distributed to be used for a research analysis.

This seems to be an easy path and the question is why there is the need to develop ISO standards for this. To give an answer here, we need to go into detail into this pathway.

## The pre-analytical pathway in detail

### 1. Blood drawing procedure

The person performing the venepuncture needs to have a specialisation and respective training not to harm the donor. Hence, it needs to be documented who has performed the venepuncture and what instruments have been used.

### 2. Labelling of primary blood tube

Not only the person performing the

venepuncture, also the donor needs to be identified. Of course, there is no need to have names and direct person-related data. Codes and identification numbers are sufficient. Therefore, the primary blood tube containing blood of the donor must be specifically and uniquely labelled to provide a clear link between donor, primary blood tube and blood sample.

### 3. Time of blood drawing

As soon as the blood sample has left the body of the donor, the sample is present in a different environment: There is no longer flow of blood, temperature has changed, light is present and the surrounding changed from living cells communicating with the blood cells to a plastic tube. Hence, it is important to document the time of blood drawing to know when the change of environment started.

#### 4. Duration and conditions of sample transport

After blood drawing, the sample is normally placed in a rack together with other samples and waits to be transported to the laboratory. At that time, the sample is still alive and will adapt to the changes of its environment (temperature, light etc.). To give an example: The cells sense lower temperature and stop of blood flow and will react with increasing their level of stress proteins as in the body both conditions are extremely harmful. The longer the samples are staying in the rack the more changes within the sample will occur. This is true for the time the sample is staying in the clinical ward as well as for the time the sample is transported to the laboratory. Hence, documentation of times and temperatures are essential.

#### 5. Biobank

Documentation of the arrival time at the biobank is needed to calculate the duration of sample transport. The sample will be processed according to the protocols of the biobank and divided into smaller aliquots. These aliquots will be taken from a single sample and thus allow multiple different analyses of the same sample without freeze-thawing the sample multiple time. The aliquots are then frozen and stored at minus 80°C or lower until use. Documentation of each step during processing and storage is mandatory for a biobank.

#### 6. Analysis

Finally, the primary blood sample will be distributed and send to a laboratory, where the analysis will take place. Within the laboratory, the sample will be further processed depending on the needs of the analysis, the analysis will be performed and the respective results will be used to increase knowledge.

#### The pre-analytical pathway today

Today, there is quite some variability between biobanks and hospitals in the documentation details of the pathway described above. In some hospitals all or nearly all the steps are documented as described, while in other hospitals only some or few of the steps are documented. Hence, depending on the hospital setting, sometimes only little data on the pre-analytical pathway can be retrieved for subsequent analysis.

This discrepancy has a major negative impact on research results – and hence on patient care. If biobanked samples are used for analysis, they should be comparable in terms of handling, timing, temperatures, processing etc. If some samples are used only the day after blood drawing standing in a room or in the sun in summer or in the cold in winter, this will of course dramatically influence the content of the samples. Hence, there is massive variability in the analytical test results that is simply due to differences in pre-analytical handling of the samples rather than due to differences between healthy and diseased donors.

#### The pre-analytical pathway tomorrow

The emerging ISO standards for biobanking will set the stage for improved documentation of the pre-analytical pathway. Hence, any variation not linked to the health status of the donor can be linked to variations in pre-analytical handling of the samples.

This, of course, is not enough! What is needed is a much better understanding of the major impact, handling of samples has on the quality of results

obtained with these samples. Hence, it is not only documentation that makes the difference, but rather proper handling of the sample at each step of the pathway to optimally maintain its quality.

Only then, results from the clinical setting in combination with the results from the research setting can – without doubt – be directly linked to the health status of the donor.

This will have a direct and major positive impact on:

- Patient care in the clinical setting: no longer false positive or false negative results!
- Research on e.g. identification of new biomarkers for prediction: no longer massive variations in a cohort due to differences in sample handling!
- Development of new treatments and medication: no longer very time consuming pre-clinical testing due to missing comparability of samples!



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effort, is the Biobanking and Biomolecular Resources Research Infrastructure (BBMRI-ERIC).<sup>5</sup> The pan-European BBMRI vision emerged from the recognition that keeping up with policies and developments elsewhere, most notably in the USA, necessitates integrated European research.

These “big data” approaches in precision medicine require access to personal and often identifiable information and are coupled with ethical challenges. For example, the ‘big data’ complexity may impact informed consent; or the need/ability to return the outcomes of test to the patients who originally donated their samples. Considered together, a constructive and transparent inclusion of ethical questioning in this rapidly evolving field is necessary to support the societal acceptance and responsible development of the technological advancement.

### Costs and sustainability

The aspect of biobank sustainability is critical for precision medicine research. Recent advances in health research (including social and public health research, and advances in technology) have increased demands on the types of samples and processing provided by biobanks.

Specifically, researchers require increasing sample numbers and associated clinical data, biobanks increasingly implement standardised processes to attain higher quality standards, while funders seek performance metrics and assurances for their investments. Research funding agencies, institutions and philanthropic organisations, often assume that beyond the initial start-up operational and infrastructure costs that biobanks at some point should be become “self-sustaining.”

This is rarely achievable in the context of planning a large national infrastructure with a 15- to 20-year life cycle even with governmental or institutional funding, and it does not represent most biobanks attached to integrated academic/health institutions or disease focused biobanks, such as those assisting with rare genetic conditions research.<sup>6</sup> Thus, new or more flexible operating and funding models are needed to support the growth of biobanking in the medium and long-term. ■

### References

- 1 Parodi B. (2015) Biobanks: A definition. In Ethics, Law and Governance of Biobanking, Mascalonzi D. (ed.), The International Library of Ethics, Law and Technology 14, Springer Science and Business Media Dordrecht 2015. DOI 10.1007/978-94-017-9573-9.
- 2 Organization for Economic Co-operation and Development (OECD). (2006) Creation and Governance of Human Genetic Research Databases. OECD Publishing: Paris.
- 3 ISBER Best practices for repositories: Collection, storage, retrieval, and distribution of biological materials for research. (2012) Biopreserv Biobank; 10:79-161.
- 4 [www.liebertpub.com/overview/biopreservation-and-biobanking/110/](http://www.liebertpub.com/overview/biopreservation-and-biobanking/110/)
- 5 [www.bbmri-eric.eu/](http://www.bbmri-eric.eu/)
- 6 Watson PH, Nussbeck SY, Carter C, et al. (2014) A framework for biobank sustainability. Biopreserv Biobank; 12:60–68.



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