Biobank Graz

Leader in Biobanking

BioBank GRAZ

Smart Biobanking

Senior Research Analyst for Frost & Sullivan Divyaa Ravishankar discusses the growing need for innovative products in the realm of bio-storage applications...

The concept of biobanking has triggered massive interest in the area of long-term sample storage conditions but with a key challenge of maintaining sample integrity. In order to combat this, biobanks are adopting new storage methodologies and solutions that will guarantee better sample quality to the research community.

Globally, sample storage is an outsourced activity by many large pharmaceutical companies. Commercialisation of biobanking activity has forced the providers to adopt tools that are more sophisticated and facilitate sample tracking. Laboratory information management systems (LIMS) prove to be an essential component in facilitating various biorepository models and it is important to understand the workflow involved in each biobank set up; this will aid the adoption of automation at certain levels.

Market Insights

Researchers handling small quantities of samples are at the risk of getting contaminated. Further, maintaining consistency becomes a huge factor when large quantities of samples are processed. Therefore, automated protocols are replacing manual ones.

Interest in dry-state storing and eliminating freeze-thaw cycles causing unwanted intervention of sample quality has brought many patented automated biobanking storage platforms for -20°C and -80°C with a facility to store samples in both microplates and micro-tube format. Continuous monitoring of samples is ensured even during picking.

The cornerstone of every biorepository lies in the efficiency of its freezer inventory software or the LIMS employed. The key objective is to enable researchers to locate and use biospecimens. Besides tracking the location of the vial of a specific sample, it is important to retrieve the associated additional data such as consent information, demographic information and related regulatory data.

Challenges Associated with Clinical Sample Storage

Primitive methods of storing samples in cryotanks have reported instances of loss of samples, with them either being discarded, owing to the fact that they become unidentifiable, or due to 'handling errors'. The sample retrieval process would be laborious if performed by humans, with the loss of an ID label leading to sample mix-up.

Given the fact that no two biobanks function in a similar way, it is tough to generalise a technology platform that is common for them. A lot of custom work is required to suit the workflow processes of a biobank, and at the same time, funding and financial maintenance of the biobanking infrastructure becomes tougher in the long run.

With time, samples demand more sophisticated methods of storage with clinical samples requiring a highly integrated set up that involves continuous monitoring of temperatures, along with the associated sample information.

An exponential increase in the volume of samples is leading to issues with store capacity and duration, with space to accommodate new samples in the given temperature and conditions posing a huge problem.

Today, the lack of high-quality and clinically annotated samples is seen as a major drawback. There is a need for standardising sample handling and storage protocols globally. Owing to very few standardised quality checking protocols for the pre-analytical phase, there arises a difficulty to compare and share samples, especially when specimen volumes are likely to be high. These issues need to be addressed, as they prove to be a barrier for the development of new treatments.

Many issues associated with the scientific use of biobanking samples are ethical in nature, such as consent, personal integrity, privacy protection, safety of samples and access to data and stored samples. The laws and regulations pertaining to ownership, intellectual property rights and commercialisation discourage the use of resource material. There are also issues pertaining to cross-border shipping of samples, which requires consent from donors. With the sole aim of safeguarding the donor information, biobanking acts in Norway and Sweden allow the analysis of samples but discourage their long-term storage.

Technology Innovations for Clinical Sample Storage

Biobanks seek solutions that are easy, efficient and are able to provide cost-effective sample management. Traditional methods of storage include storing samples in laboratory freezers at -20°C, -80°C and liquid nitrogen, and this process is being largely automated with the help of RFID and the MEMS technology.

On the other hand, the recent trend shows an increasing preference towards room temperature storage. There are firms developing reagents to stabilise the DNA and RNA in order to be able to last long under ambient temperature; this concept has allowed whole blood samples to be shipped and preserved under room temperature for about three months. Adapting to room temperature storage can yield benefits such as eliminating the need for freezer units and extra storage space.

Over time, it becomes tough for biobanks and biorepositories to track and retrieve samples when stored at ultra-low temperatures. Traditional methods of storage involve microplates with barcode readers. Retrieval of a single sample from a microplate meant thawing the entire plate, which affects the freeze-thaw cycles of other samples simultaneously. For this purpose, sample storage is being carried out in microtubes and individual vials. Earlier, equipment and robotic arms were designed to handle microplates; now, systems are flexible to cherry pick individual microtubes. Most of the storage systems today provide robotic interfaces inside a chilled atmosphere in order to prevent the disturbance of unused samples.

Conclusions

A totally integrated system of hardware, software and consumable tools would be the way to “smart biobanking”. With many new technologies, biobanks oriented towards the future can retain sample quality/integrity by employing smart and smooth sample handling systems available in the market today.

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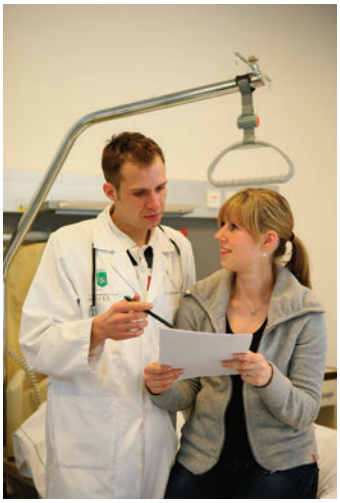
About biobanks and Biobank Graz in particular

Biobanks are collections of biological specimens and their associated data, organised in a structured, readily analysable format. In Austria the history of biobanking is based on a royal decree published in 1813 that remitted medical doctors to collect pathological specimens. Biobank Graz, a publicly-owned non-profit organisation, became a central research infrastructure of the Medical University of Graz in 2007. Today, Biobank Graz is the largest academic biobank in Europe housing more than 6 million human specimens including blood, serum, plasma, buffy coat, fresh frozen tissues, formalin fixed, paraffin embedded (FFPE) tissues as well as their associated clinical data. This collection of samples and data represents the perfect basis to support national and international research in an optimal way.



Clarification of the informed consent at the Medical University of Graz

Biobank Graz focuses on legal and ethical aspects

The use of clinical data and specimens from Biobank Graz is restricted to ethically and scientifically approved research projects. Therefore, many criteria have to be met before a participant may donate specimens and even more before a research-project can use specimens from Biobank Graz. The public image of a biobank depends on a variety of facets including public relations, especially for adequate transparency in preparation and allocation of biobank specimens for medical research. At Biobank Graz the contact between patients and medical researchers plays an important role to carefully explain this sophisticated system and its benefit for the public health care.

For this reason, Biobank Graz has put a special focus on their donor relations shown in a detailed informed briefing and consenting, as well as in extensive public communication such as information meetings for the general public, specific panels with guest specialists (e.g. on ethics) and guided Biobank Graz tours. Transparency of biobanking processes and information transfer to the potential donors within the population promotes public trust, reflected by an increased number of participants for biobanking in Graz.

Signing the informed consent of Biobank Graz

The detailed briefing of donors and the informed consent (IC) of Biobank Graz focus on the following key aspects:

- What is a biobank all about?
- How can participants provide samples to a biobank?
- What happens with the specimens and where are they used?
- How can a biobank help in fostering medical progress?
- Who has access to private data of participants?
- What are the criteria for participation as well as for its cancellation?

The warranty of maximal data protection is yielded by pseudonymisation of all participants' data and samples and the limited access to clinical data to single authorised users who are bound to professional discretion. Biobank Graz keeps the anonymity of participants by storing samples identified by numerical codes only. Their associated clinical and personal data are kept in the clinical IT-system and thus, sample information and associated data are stored separately in different IT-systems without any direct connection.

An ethical study about understanding the informed consent of Biobank Graz, has shown that participants have kept in mind crucial information like the possibly unlimited time of storage or criteria for cancellation, which is feasible anytime without justification.

Moreover, the informed consent and the corresponding folder as well as every project which asks for biological specimens with associated data from Biobank Graz, are evaluated by the local ethics committee of the Medical University of Graz. In addition, the approval committee of Biobank Graz evaluates the relevance and scientific value of each project request before Biobank Graz releases any specimen.

IC-folder to simply explain biobanking

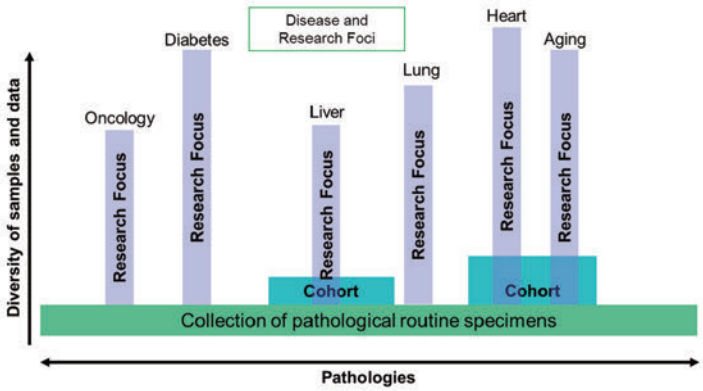
Biobank Graz: The hub for biomedical research

Besides gaining public trust biobanks need to convince scientists and medical staff to participate in the field of biobanking by sample recruitment as well as by using already existing repositories and associated data. The trust of research partners is reflected by a large number of interdisciplinary cooperations with departments, clinics and institutes of the University Hospital Graz, assuring the collection of large numbers of scientifically relevant samples and associated clinical data at a high quality level.

Biobank Graz, considering itself as a research partner and not a simple sample provider, represents two collection strategies. This combination provides the ideal basis for epidemiological studies as well as allowing scientists to validate biomarkers for the identification of specific diseases and determining response to treatment:

- A cross sectional collection of unselected pathological samples and clinical data, representing all detected diseases at their natural frequency of occurrence in Styria, collected since 30 years;

- A disease focused approach for selected diseases (such as different types of cancers as well as metabolic diseases) through the collection of a range of different samples of highest quality and detailed even longitudinal clinical follow-up data.



Collection strategy of Biobank Graz

Biomedical research is progressing rapidly, reflected by increasingly sophisticated methods, putting pressure on scientists to have access to samples of highest quality. Due to this rapid progress in different research areas, the structural collection of high quality human biological samples and corresponding data gained more and more attention in the last decade. The guarantee and improvement of sample quality is achieved at Biobank Graz by operating a certified quality management system according to ISO 9001:2008.

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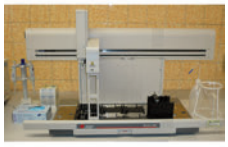
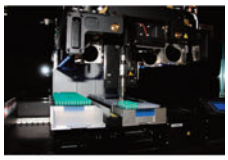
Manual liquid handling process



Semi-automated liquid handling



Fully automated liquid handling process

Semi-automated cryo storage system

Manual handling of incoming and outgoing FFPE slides and blocks

Semi-automated FFPE (blocks and slides) storage

New technologies at Biobank Graz to improve sample quality

To further optimise sample management and sample quality, Biobank Graz has implemented stepwise automation in different working processes.

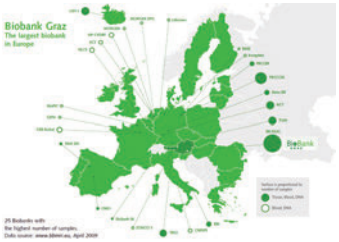
An excellent example is handling of liquid samples, which has dramatically changed to highly improve sample quality. In the past, sample processing was performed manually with all the pitfalls of timing and errors. A new fully automated robot for processing liquid samples has been custom designed for Biobank Graz and is a unique robot worldwide. To facilitate collection of body fluids like serum, plasma or urine, Biobank Graz defined an interface for data transfer in cooperation with two companies, one for the pipetting robot and one for the Lab-Information-System (LIS). The robot scans barcodes of primary tubes, transmits these to LIS and gets back the pipetting information. The robot is equipped with four pipetting channels and special tools for opening, closing and transporting 2D Data Matrix coded target tubes without any interaction of an operator. An integrated camera creates images of the primary tubes. An image processing software recognises the buffy coat and generates scripts to automatically separate fractions into target tubes. Afterwards, the samples are frozen at minus 20°C immediately after pipetting by an integrated freezing system on a single tube level. For final storage of liquid samples Biobank Graz now uses a fully automated storage system at minus 80°C with single tube picking of single aliquots at minus 20°C, thus preventing loss of sample quality due to (even partial) thawing and freezing.

Biobank Graz has also improved the storage of tissue samples. Cryo samples have been stored in common liquid nitrogen tanks where handling is complicated and shows an increased risk for the operator. Nowadays, semi-automated cryo-storage systems without interruption of the cold chain represent the new standard to increase sample quality.

A similarly innovative development took place for tissue samples stored at room temperature. A semi-automated storage system for FFPE samples has replaced the time-consuming work processes of manually handling incoming and outgoing FFPE tissue blocks in daily routine. To store large sets of samples, an optimised use of space is required. One central item of the new storage system is a specifically designed storage box developed in cooperation with the Technical University of Graz. Each sample (FFPE and the corresponding slides) is labelled with a 2D Data Matrix code, scanned during the storage process, and linked to clinical data. Each incoming and outgoing sample is documented in specific databases. The scientific value of the existing tissue collection is based on its size, technical homogeneity, and its population based character. These features provide ideal opportunities for epidemiological studies and allow the validation of biomarkers. Improvements of different processes are essential for answering research questions, which are becoming more complex and represents the importance of Biobank Graz as a competent research partner.

Biobank Graz as part of the national and international biobanking community

Besides the local cooperations, Biobank Graz is an active leading player in (inter-)national projects and activities aiming to improve interactions between, and cooperation amongst, biobanks and scientists. Coordination, consolidation and networking of existing European biobanks for the further development of biomedical sciences are central issues for Biobank Graz. The development of biobanking is increasingly essential for enhancing the knowledge about health and disease and will have a major impact on health care planning, implementation strategies and further biomedical research.



Biobanks involved in setting up BBMRI in 2009

The importance of networking of biobanks has been emphasised repeatedly and there are several major biobank network initiatives worldwide, including the European Biobanking and Biomolecular Resource Research Infrastructure (BBMRI-ERIC) and its national Austrian counterpart BBMRI.AT.

Biobank Graz emphasises sustainability

Transparency, public trust, high quality, improvement of working processes, as well as networking, contribute to the sustainability of Biobank Graz.

Steady increase of project requests at Biobank Graz

The sustainability of Biobank Graz becomes obvious in many facets of biobanking such as the widespread spectrum of sample types and storage systems. This diversity of biological specimens and their various conditions of storage lead to nearly unlimited possibilities of applications for researchers. This is further boosted by the in-house storage of FFPE samples from the last 30 years connected to the respective clinical data.

It is not only the quantity of samples that is important, since today, quality of samples comes into focus more and more. All the new -omics technologies can only provide an in-depth analysis of a given sample based on its respective quality. Hence, innovative technologies to increase and maintain sample quality are essential to maintain the sustainability of a biobank.

At the same time, the sustainable use of specimens from biobanks asks for optimal use options. The most important criteria for increasing the efficient use of specimens are interaction, networking and harmonisation of biobanks. Only in this way can the development of sufficiently large cohorts can be realised, which is of course relevant for investigations of rare diseases as well as for genetic association studies in need of several thousands of samples.

Certainly, sustainability of biobanks is essential to foster medical research to finally improve health care for the general population. This can only be achieved by taking commercial partners on board and to find ways to communicate and cooperate in joint projects. The integration of industrial research and partners into biobank research (PPP), presents an important aspect to yield an innovative and sustainable benefit for biobanks and finally for society. Furthermore, sustainability can only be reached with secured financial support. Biobank Graz is funded by the Medical University of Graz, as well as the federal government of Austria (Konjunkturpaket II) and the local government of Styria (Zukunftsfond Steiermark).

BMWF

ZUKUNFTSFONDS STEIERMARK

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