Biobanking Expands into Research Services

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phenotypes, treatment journeys, and even lifestyles.

So, while biobanking has been slow to fly biospecimens around via drones, it is rapidly expanding into bioinformatics and medical analytics. It is also bringing patients into the process, encouraging donations, soliciting input on individual healthcare experiences, and updating donors about the status of their specimens—as well as telling donors how their specimens are contributing to medical research.

In general, biobanking is less about hoarding and more about sharing. This shift's implications were discussed at Biobanking 2018: Visions for Innovation, the first conference organized by the Swiss Biobanking Platform, a national organization that "aims to respond to the increasing requests from biomedical researchers regarding quality and the interconnectedness of biobanks for research purposes." At this conference, which was held recently in Lausanne, Switzerland, international biobanking experts discussed how they might harmonize procedures; promote sustainability; and meet ethical, legal, and social obligations.

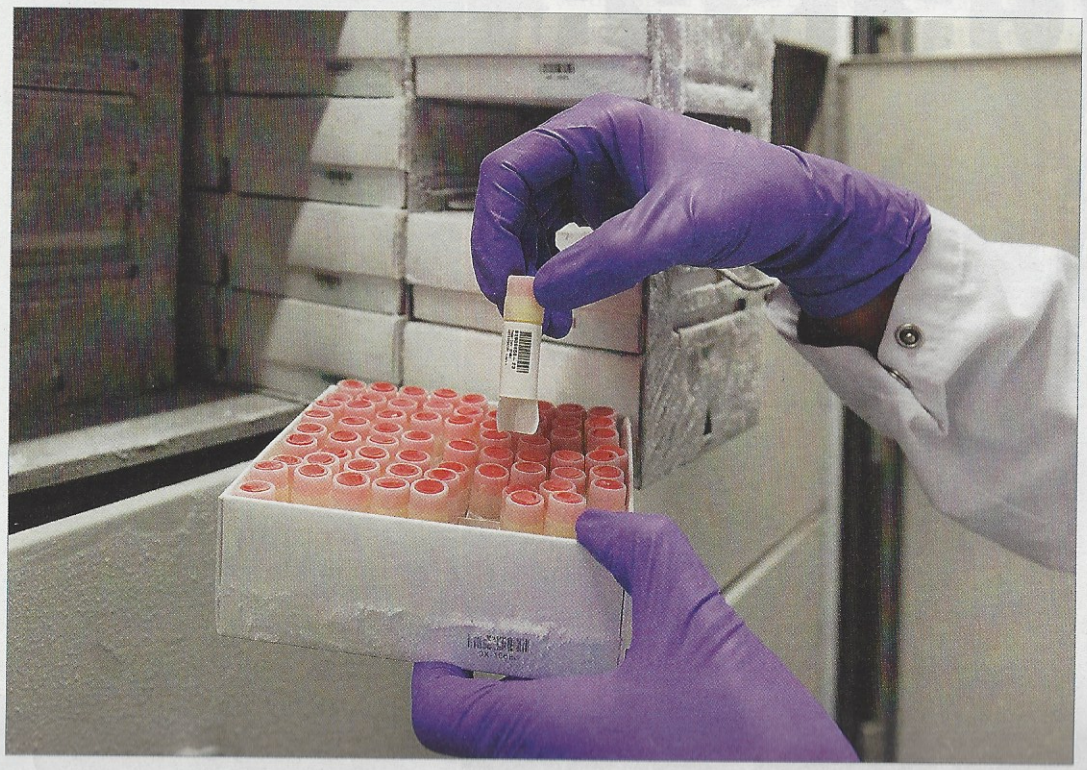
Reaching Out to Researchers

"We have two billion samples stored in biobanks globally, but—according to some market research reports—less than 5%, even less than 3%, are being used. That number needs to go up," said Erik Steinfelder, director general of the BBMRI-ERIC (*Bio*banking and *BioM*olecular resources *R*esearch *I*nfrastructure—*E*uropean *R*esearch *I*nfrastructure Consortium), an organization that is trying to centralize at a European level information about different biobanks.

Mr. Steinfelder took up his post August 1, 2017. During the selection process, he suggested that the BBMRI-ERIC should become more service oriented. He also outlined a three-year plan describing how the BBMRI-ERIC could promote the use of its biobank samples.

"The BBMRI-ERIC," Mr. Steinfelder noted, "was a very scientific organization." It supported the investigations of universities, national laboratories, and large research consortia. Yet the BBMRI-ERIC also saw a need to broaden its activities, to "have a better understanding of our customer base—not just biobanks, but clinicians and the general public."

According to Mr. Steinfelder, biobanking is a key part of basic research and drug development. But, biobanking underperforms in these activities if it fails to speak to a wider audience. "There are biobanks that are still very protective of their collections and refuse to share," Dr. Steinfelder complained. "Researchers can spend months looking for samples that others have."



The Novartis Institutes for Biomedical Research (NIBR) maintains a distributed biorepository instead of a centralized storage facility. Specimens are kept at different NIBR sites and managed locally. In this image, a barcoded sample is being retrieved from a freezer that keeps samples at –80 °C.

Patients, especially those with rare diseases, are among the groups with whom biobanks should be collaborating. This observation was offered by Olivier Menzel, Ph.D., chairman and founder of the Blackswan Foundation. "The experts are really the patients," he declared, "especially with rare diseases."

Dr. Menzel maintained that a patient with a rare disease, or their parent or caregiver, can sometimes be more knowledgeable than a professor. He recommended that biobanks shouldn't be afraid to ask patients for advice or admit when a specimen doesn't produce a diagnosis.

"A biobank can't exist without patients donating biological

samples," Dr. Menzel insisted. "They have a right to their samples and hope to get something back from them [in the form of new treatments]—they're important stakeholders."

Also important is using patient data to find new treatments (a major reason why patients with rare diseases are especially proactive in donating to biobanks). "If biobanks say: 'Thank you for donating your data, but we never use it,' then, at some point, patient organizations will say, 'What's the point of filling in the paperwork?'" warned Mr. Steinfelder. "It sounds a bit black and white, but we've got to position it that way."

Speaking the Same Language

The need to share samples as a way to facilitate collaborative research is also appreciated by pharmaceutical companies, asserted Georges Imbert, Ph.D., biobanking project leader, **Novartis Pharma.** In his presentation, Dr. Imbert reflected on his experience with the Human Tissue Network (HTN), a distributed network of human tissue experts and users.

Established in 2011, the HTN supports Novartis' research activities, including those carried out by the Novartis Institutes for BioMedical Research (NIBR). The HTN is designed to ensure specimen quality, consistent processing, and compliance with regulations across six research sites on three different continents.

Unlike a conventional biobank, the HTN has no centralized storage facility or management organization. "We prefer to use the word biorepository," Dr. Imbert explained. "A biobank, in the classic sense, is an organization that prospectively collects samples and makes them available at a later stage for many different projects and for researchers who are often working in a different institution." He added that the specimens are kept at different NIBR sites and managed locally.

"The underlying idea is to give a lot of flexibility to our researchers," Dr. Imbert asserted. "We also want to help them meet the same high standards of quality, compliance, and ethics, so that we always speak the same language."

The HTN offers online tools for NIBR scientists to find and source biological samples, as well as training for scientists on applicable regulations, such as ensuring patient consent.

"When patients are donors and make a gift of biological samples," said Dr. Imbert, "this comes with responsibilities on our end."

Guaranteeing Sample Quality

Improving the quality of samples is crucial to the future of biobanking, proclaimed Berthold Huppertz, Ph.D., formerly the director and CEO of Biobank Graz, the largest clinical biobank in Europe, and currently professor of cell biology at the Medical University of Graz. Dr. Huppertz added that "the handling of samples, from taking them from the body to analyzing them, and everything that lies between, has a major effect on analysis results—and these activities need to be harmonized and documented."

Once a biological sample leaves the body, its quality deteriorates over time. "If you go for a coffee and leave your sample on the bench, the sample is no longer fit for purpose," he pointed out. Every second between collection and freezing must be documented—both to preserve sample quality and to inform later research.

Likewise, Dr. Huppertz explained, manually searching a freezer for a single specimen often exposes other tubes on the same well plate to room temperature for a couple of minutes. This allows the surface of the specimen to thaw and changes its molecular composition.

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New Challenges Facing Biobanking

The underlying mission of any biobank is to store high-quality samples for future use. As front-end strategies and technologies (solutions, containers, protocols) for preserving cells and tissues continue to improve, a new challenge has emerged: What can be done to improve the quality

to-sample variability."

To overcome this, "automated" thawing devices, replacing the water bath, are under development to streamline the thawing process and reduce end-user variability, continues Dr. Baust, who is also an editorial board member of *Biobanking and*

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Part of the solution is carefully documenting the processing and handling procedures for each specimen. This includes avoiding handwritten or ambiguous labeling, which can lead to misdiagnoses—which account for most preventable medical errors. Referring to a famous report issued in 1999 by the U.S. Institute of Medicine, Dr. Huppertz informed Biobanking 2018's attendees that misdiagnoses are responsible for 98,000 deaths in hospitals each year in the United States alone.

Turning to Automation

Another way to improve sample quality is through automation, especially as biobanks get bigger and more sophisticated. "Our clinical biobank, the largest in Europe, has 20 million samples," said Dr. Huppertz. "If people had to run around, looking for samples labeled with handwritten codes, it would be a nightmare."

A fully automated system can select a single tube from a 96-well plate while maintaining a temperature of –80 °C—removing the risk of sample degradation due to heating, explained Dr. Huppertz. Samples can also be processed using a highly automated procedure to reduce the time between sample collection and freezing.

Liquid samples can be stored at temperatures as low as –150 °C within an hour of collection, noted Carlo R. Largiadèr, Ph.D., vice director of the University Institute of Clinical Chemistry at the University Hospital of Bern, and academic head of the Liquid Biobank Bern (LBB). At LBB, which started operating in 2017, blood samples are delivered by courier to the hospital's Centre for Laboratory Medicine, where they are placed into a laboratory automation system.

The system reads the barcode of the sample and directs it to a centrifuge for separation into plasma and other components. A pipetting robot then dispenses the components into cryotubes before they are moved manually to cryobenches for automated controlled freezing. The biobank management system tracks every step and alerts hospital staff whenever manual intervention is required.

According to Dr. Huppertz, such systems can help biobanks meet the challenge of complying with recent International Organization for Standardization (ISO) standards covering preanalytical procedures for *in vitro* diagnostics in laboratories and biobanks (CEN/TC 16826-1/2, 16817-1/2/3, 16835-1/2/3, 16945—published in 2015/2016), as well as the standards due to be developed by the European SPIDIA4P (Standardization and improvement of generic *P*re-analytical tools and procedures for *I*n vitro *DIA*gnostics *for* Personalized medicine) project over the next couple of years.

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Automation also enables the biobank to collect thousands of samples with only five full-time-equivalent staff, indicated Dr. Largiadèr, and the biobank is "ramping up rapidly" with about 30,000 cryotubes stored to date. Some hospital wards are active in sampling a cross-section of their patients who are asked to donate an extra specimen for the biobank and agree to the use of their medical history for research purposes.

This high degree of automation also holds the potential for longitudinal sampling of patients with complex conditions, such as lung cancer, who can be monitored with continuous sampling during their treatment, Dr. Largiadèr explained. For example, the automated system can initiate sample collection at specified time points at scheduled follow-up visits. "I think this degree of automation and integration into the routine informatics in a hospital setting is unique," he stated. GEN

Lentiviral Systems for Gene Delivery

OriGene Sees its Mission as Providing Genome-wide Research Tools and Technology Platforms

OriGene Technologies was founded as a research tool company focused on the creation of a large commercial collection of full-length human cDNAs in a standard expression vector. Company officials say the firm's mission is to prepare comprehensive, genome-wide research tools and technology platforms to allow scientists to better study

Dr. Liu: Lentivirus is an efficient gene-delivery tool. It is modified from HIV-1. The lentiviral vector was engineered not to contain any viral-coding genes so the gene of interest can be cloned into the vector. The other necessary viral genes for replication and viral packaging are provided separately.