The future of biobanking

January 4, 2013 Martin Frey, Annette Summers, Mary Napier Clinical 0

The biobanking market is poised for explosive growth if it can overcome the challenges of an adolescent industry. According to an August 2012 Infiniti Research report titled "Global Biobanking Market 2011-2015," the biobanking market will increase 30 per cent from 2011 to 2015 to nearly $183 billion.[1] Growth is being driven by an increase in population genetics studies, personalized medicine, and the use of genetic information in food safety, forensics, and disease surveillance.

Biobanking throughout the decades

Biobanks are typically cryogenic storage facilities maintained by institutions that manage a collection of biological materials, such as human tissue, serum, plasma, urine, and blood, along with the donors' data. The majority of biobanks store tissue that will be used in medical research. A small collection of blood samples kept in a freezer can technically be classified as a biobank, but the term is often associated with larger facilities maintaining hundreds of thousands of samples.[2]

Sample collections must be maintained reliably with minimal deterioration over time, and they must be protected from any physical damage.[3] Quality sample management is a well-known challenge facing life science investigators, and the need for biobanks is growing as the pharmaceutical industry shifts toward personalized medicine, which requires more usable, well-maintained biospecimen collections.

Biobanks have been around for at least 50 years. First-generation biobanks stored and retrieved samples manually from liquid nitrogen tanks or -20/-80°C freezers. Sample management and information system standards varied between institutions.

"In existing conventional biological storage, warming events can have significant impact on

the integrity of samples," explains Matt Hamilton, vice president at Hamilton Storage Technologies. "The opening and closing of a manual freezer door creates the opportunity for extreme and continuous temperature fluctuations inside the entire storage compartment which can adversely affect each sample in the freezer. The thermostability of each sample, and therefore the potential for damage, is dependent upon the type of tube the sample is stored in, the storage buffer pH and the volume in the storage tube. It is important to evaluate the storage conditions very closely since multiple factors can impact sample integrity during storage."[4]

A door held open on a manual freezer for even a short period can result in a significant temperature increase. Data gathered by Hamilton Storage Technologies shows that the temperature of samples taken from -80°C storage to ambient conditions increases by an average of up to 21.5°C per minute (Figure 1). Holding a manual freezer door open for more than one minute can expose some samples to temperatures inside the freezer that are above -60°C depending upon the freezer configuration and sample storage conditions. This can happen countless times over the lifetime of a sample stored and retrieved manually. Accumulated temperature elevations above this level are believed to damage the integrity of many biospecimen types.[5]

Since the late 1990s, biobanks have become a key resource for a growing number of genomics, personalized medicine, and other types of studies. Since the early 2000s and the completion of the Human Genome Project, second-generation biobanks have emerged to meet the needs of modern researchers. One-third of all biobanks have been installed since the early 2000s, after the draft of the human genome was completed. The growing presence of biobanks reflects their growing importance in advancing genetic research and testing.[6] Second-generation biobanks offered improved operational design through standardized protocols for sample storage and annotation, and began to use automated liquid handling for some tasks.

The gap between second-generation biobank infrastructure and researchers' needs became

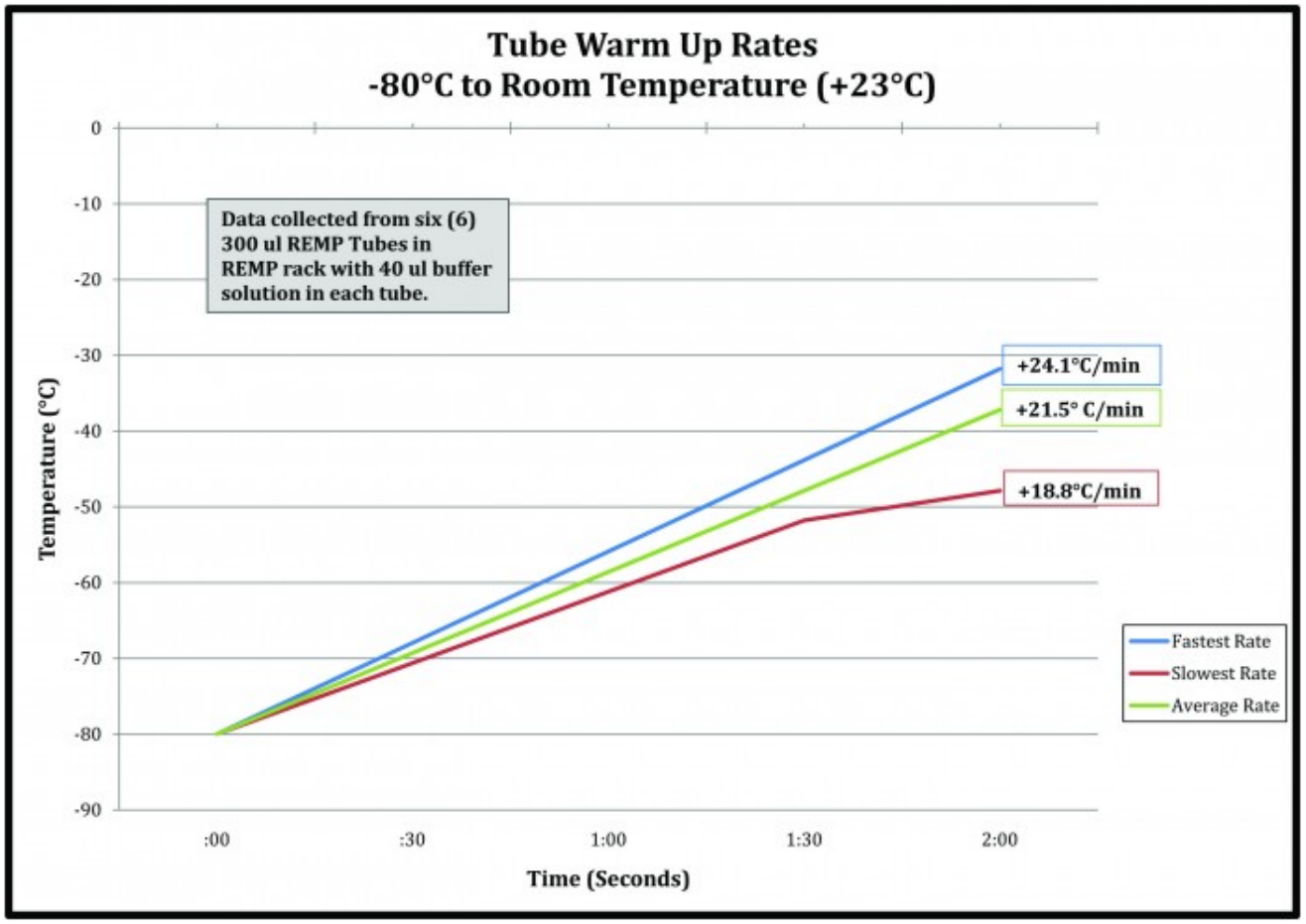

Figure 1

apparent in large genetic studies such as The Cancer Genome Atlas (TCGA) program.[7]

TCGA began as a three-year pilot in 2006 with an investment of $50 million from the National Cancer Institute (NCI) and the National Human Genome Research Institute (NHGRI). The project's goal was to create an atlas of genetic changes that manifested as a cell became cancerous.[8]

TGCA characterized more than 20 tumor types, which required the careful collection of

thousands of cancer samples.[9] Dozens of bio-repositories in the US assured the institute that at least 500 samples of each required cancer type could be easily provided. Early in the project, it became clear that many specimens were unfit for analysis due to the lack of sample storage standards. The rate of unacceptable shipments from some institutions ran as high as 99 per cent.[10,11]

To achieve their mission of mapping the genetic changes in cancer, the investigators had to elevate the challenges of fixing, storing, and annotating samples. Because of this need, the Office of Biorepositories and Biospecimen Research (OBBR) published its first guidelines for the industry in 2006. During 2007, forums were held to distribute and educate professionals on the guidelines, which increased standards for reliability and sample handling.[12]

The rise of third-generation biobanking technology

Reliability of third-generation biobanks is measured by "uptime."[13] Third-generation systems typically include four main building blocks: automated tube storage and retrieval, tube processing assisted by robotic liquid handlers, a plate storage and retrieval system, and a database infrastructure that stores clinical information about the sample.

In a third-generation system, researchers do not open freezer doors; they simply place sample tubes in a temperature-controlled hatch and a robotic arm retrieves the tube and stores it in a unique interior cell. Tubes are barcoded so researchers can use laboratory information management systems (LIMS) to search for appropriate samples. This information system enables the researcher to store and retrieve the sample securely. When a researcher wants to retrieve a sample for a particular study, they transmit their request to the automated biobank's LIMS and the robotic arm retrieves the sample. The arm deposits the sample in a delivery hatch and an email is sent when the sample is ready to be picked up. The -80°C freezer also records how many times each sample is removed from frozen storage and for how long. The automated system reduces sample retrieval time, preserves the chain of custody, and minimizes the sample's time outside its optimal storage temperature.

“Removing the uncertainty about storage conditions ensures that data derived from sample testing will be accurate and reliable,” explains Hamilton.[14]

Users and technology

The most common laboratories or organizations utilizing this type of automated storage system are those collecting biological samples that need to be stored in large quantities at ultra-low temperatures for a long period. Typically, biobanks support researchers who are performing population- or disease-based studies, or forensic institutions storing samples from crime scenes. Biobanks storing tissue also need to track chain of custody, and virtually all laboratories need to maintain temperature stability and thus the value of their samples.

Hamilton Storage Technologies, a leader in laboratory automation, recently introduced its third-generation BiOS™ automated storage system to meet the demands of today’s labs and clinics.[15] This ultra-low-temperature storage system is designed to store more than 10 million sensitive biological samples in multiple types of labware such as tubes and microplates. All samples within the BiOS system are stored in -85°C freezer compartments to maintain temperature stability even while sample picking. One- and two-dimensional barcode reading and sample tracking provide chain-of-custody documentation, with software tools to support compliance with the FDA’s 21 CFR Part 11 regulations. Multiple redundant backup systems ensure that samples stay at -85°C, even in emergencies.

Along with the BiOS system, Hamilton Robotics provides a fully integrated, automated liquid handling workstation, the Microlab® STAR , which utilizes the Rack Runner™ robot for true hands-free operation, further ensuring integrity of the sample transfer from the BiOS system to finished preparation for analysis.[16] This robot is configurable for almost any sample preparation requirement and supports the speed requirements of high-throughput labs using next-generation sequencing for gene expression and genotyping applications.

The Netherlands Forensic Institute (NFI) and the LifeLines Biobank at the University Medical

Hamilton Storage Technologies' SAM and Rack Runner systems at the Netherlands Forensic Institute in The Hague. Photo Credit: Netherlands Forensic Institute.

Center Groningen (UMCG) in the Netherlands have purchased the new Hamilton BiOS system to store their sample collections.[17]

LifeLines is a major, three-generation population-based study of 165,000 residents of the Netherlands' northern provinces. The study is based on UMCG's healthy aging program and seeks to identify universal risk factors, and their modifiers, for multifactorial diseases such as cardiovascular disease, diabetes, asthma/COPD, and depression. By 2017, LifeLines expects to collect and store more than 8 million samples in the BiOS system, including urine, plasma, serum, and buffy coat extracts. The BiOS system ensures long-term sample viability and

provides redundant cooling along with sample picking at ultra-low temperatures.[18]

“Sample safety was our foremost goal when we started the tender process,” explains Marcel Bruinenberg, research laboratory manager at LifeLines. “The technology in the Hamilton BiOS system guarantees that the samples will never go above -65˚C, significantly lowering the risk of degradation. Our goal is to keep samples viable for 30 years or longer.”[19]

NFI performs the vast majority of forensic DNA casework in the Netherlands, including providing second opinions and analyses for cold cases. NFI will utilize the BiOS system for long-term storage of DNA extracts from crime scenes. Ultimately, one million crime scene samples will be stored in the system for 80 years, as required by government regulations. NFI will also use a +4°C SAM™ system to store active case samples, providing access without freeze-thaw cycles.[20]

NFI was impressed with the degree of innovation Hamilton’s biobanking automation solutions offered. Specifically, AutoLys tubes and FlipTubes™ which enable sample lysis to be automated.[21] Hamilton had identified sample lysis as a major bottleneck in DNA forensics analysis and invested in developing a completely new solution. NFI had been hand-processing the lysis step on critical crime samples to meet quality and yield demands. When validating their new biobanking system, they tested an automated sample lysis and DNA extraction solution. AutoLys tubes are test tubes designed explicitly for automated DNA sample lysis and DNA extraction for forensic studies, and are used with Hamilton Microlab® AutoLys STAR liquid handling instruments. Initial validation work with the AutoLys STAR system produced results at quality levels comparable to the lab’s manual process standards. Automating this process also reduces the possibility of manual errors, lowers contamination risk, and offers the ability to run assays overnight. NFI expects this system to improve overall lab throughput.[22]

Expanding markets

More laboratories are adopting third-generation systems, like the Hamilton BiOS system, to keep up with industry standards, increased workloads, tighter regulatory requirements, and data analysis needs. Biobanks are becoming larger, more sophisticated, and more centralized, which improves sample storage economics and concentrates the workload to a few highly skilled workers. The trend toward larger and larger biobanks will continue as genetic testing expands beyond the medical field.

As genetic information becomes more affordable to obtain and analyze, this information can be used to make our environment and our neighborhoods safer. For example, genetic testing has taken off in forensics. Crime statistics indicate that arrests, identifications, and

prosecutions double when genetic information is used to solve a crime. All 50 states now mandate the collection of DNA samples from offenders of certain crimes. This policy has had an unintended consequence of creating processing delays. A report from the National Institute of Justice in 2011 indicated that the number of backlogged samples in the US has exceeded 100,000 for several years.[23]

Agricultural industries also now employ genetic testing to track outbreaks. Using simple environmental testing methods, FDA field stations use genomic assays to quickly identify the pathogens causing the outbreak. Genomic information can now be used to improve response time to an outbreak and resolve a challenging business problem between food producers and distributors.[24]

Conclusion

In the future, the biobanking industry will likely include more globally centralized centers for studying specific genetic diseases and monitoring the health of our environment. This shift toward consolidation for the large and mid-sized centers will reduce the number of biobanking facilities that do not meet newer standards and will lower overall storage costs.[25] These larger facilities will need to adopt technologies that include complete sample processing, both up- and downstream, using robotic liquid handling systems. Centers will have advanced LIMS that track samples and maintain chain of custody from collection to storage to extraction. By improving the quality of biobanking facilities, precious samples will be protected and more useful to researchers, which will lead to a better understanding of disease biology and improving methods to safeguard our environment.

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