



Clinical Research & Diagnostics

Establishment of a Sustainable Biobank

Case Study: Building the Infrastructure for a Large-capacity, Sample-management Service

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A biobank was recently established through a partnership between Genome Quebec and the Chicoutimi Hospital in Saguenay, affiliated with the Université de Montréal, to provide high-throughput biological and nonbiological sample-management services.

The premiere customer for the Genome Quebec–Centre hospitalier affilié universitaire régional de Chicoutimi Biobank is CARTaGENE, a public resource dedicated to population genomic and population health research specifically with the aim of improving the health of the Quebec population.

Further, CARTaGENE is one of the founders of an international consortium, the Public Population Project in Genomics (P3G), dedicated to promoting international collaborations in popu-

lation genetics and harmonization of standards for knowledge and material transfer and sharing. Achieving these goals required the founders of the Biobank to take a unique approach in building their infrastructure.

To become a truly world-class opera-

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tion, the Genome Quebec Biobank had to ensure parallel implementation at several sites for redundancy and disaster

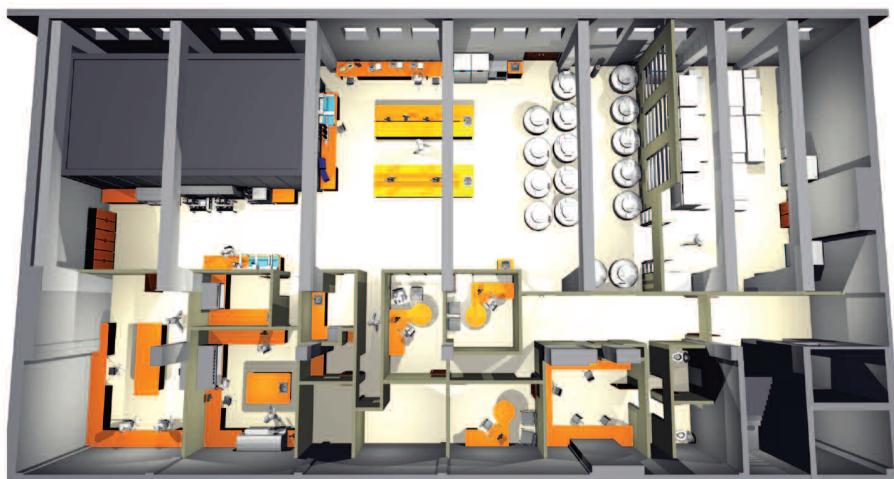


Figure 1. The Genome Quebec and Chicoutimi Hospital Biobank Primary Facility: Each area is defined, including shipping and receiving, freezer storage, cryo storage, and room-temperature storage, as well as lab areas for methods development. Total biosample aliquot capacity at this site is 82,000,000 with flexibility to accommodate different types of storage conditions and different levels of throughput.

recovery. The biobank had to have the ability to store tens of millions of unique samples in different formats. Ongoing operations would have to meet the highest security and quality standards to protect patient privacy as well as this valuable resource as a research tool.

Finally, this infrastructure had to be implemented in a cost-effective way to optimize taxpayer dollars yet remain flexible for modular expansion over time. The group at Saguenay and Genome Quebec determined that a combination of technologies all linked together with a single sample-management software package would best meet their needs.

Storage Platforms

The biobank is made up of three different storage platforms that will ultimately yield enough capacity to store 82 million aliquots in their primary facility (*Figure 1*), which is located within the Chicoutimi Hospital and encompasses about 7,500 square feet. The sample-storage systems include a fully automated, room-temperature DNA storage solution from **GenVault** (www.genvault.com); liquid nitrogen cryo-containers from **Cryo Bio System** (www.cryobiosystem-imv.com) for plasma and serum samples; and -80°C freezers for RNA and legacy samples.

All sample information is logged into GenConnect, a sample-management package developed by GenVault. This software allows users to track biosamples from acquisition to analysis, to store and mine annotations associated with those samples, and to network and monitor the use of the archive.

By utilizing a central database with a rich client interface, the archive can be accessed remotely, and offsite physical storage locations can be monitored from anywhere. Secure communications between the client and database are

managed through web services and access is granted based on user roles and a project-based permission system. Finally, GenConnect's infrastructure enables integration with existing LIMS or other information systems.

While some sample types may be best preserved via cryostorage, others can be preserved in a more cost-effective way at room temperature. For DNA-containing samples collected by CARTaGENE, the Genome Quebec Biobank has chosen a



Figure 2. GenVault's GenPlate (left) is optimized for the preservation of DNA at room temperature. Maximum space and operating efficiencies can be achieved when pairing GenPlates with Dynamic Archive (right) for sample storage and retrieval.

fully automated, dry-state, room-temperature system (*Figure 2*) from GenVault. The key drivers for this technological choice were maximum storage space efficiency, as well as low operating costs, fail-proof sample identification and high-quality stabilization of the samples.

System's Core

The core of this system is the GenPlate, a high-density, room-temperature storage container for biological samples preserved in the dry state. The GenPlate is a 384-well plate that contains a 6 mm disc of FTA® paper in each of the 384 wells. FTA paper is a macroporous cellulose matrix that is chemically treated to inactivate bacteria and viruses.

Upon application of 10 μL of blood directly to the paper, cells are lysed and DNA is released. The DNA becomes entwined with the fibrous network of the cellulose matrix and is completely dried at room temperature. When DNA is

required for downstream analysis, high-quality, double-stranded DNA can be reliably recovered with GenVault's GenSolve chemistry. DNA has been stored in this format for more than 18 years making it a proven and reliable technology for DNA storage.

GenPlates are fully automatable and compatible with commonly available liquid handlers for sample application. While several hardware solutions for their storage are available, the Genome Quebec

Biobank has chosen the Dynamic Archive from GenVault. This is a fully automated system for archiving and retrieving GenPlates at room temperature.

The system utilizes a robot to access the shuttles containing trays on which GenPlates are housed. Dynamic Archives are flexible and customizable to meet varying biosample archiving needs. The storage shuttles are scalable both vertically and horizontally and they also are modular allowing users to add shuttles to increase capacity without investing in additional automation. The Dynamic Archive has a small footprint: 75 million aliquots can be stored in 450 square feet, 300 plates/hour can be processed, and 800+ plates/square foot can be held.

With GenPlates and the Dynamic Archive, the Genome Quebec Biobank will have a fully automated system that will utilize proven technology, resulting in a 10-fold increase in storage capacity relative to freezers at one-third the cost

of a comparable -80°C automated freezer room.

Many sample types such as plasma and serum are currently best preserved through liquid nitrogen cryostorage. For these samples collected by CARTaGENE, the Genome Quebec Biobank has chosen a high-security and high-density storage system from Cryo Bio System based on high-security straws, rather than classical cryovials. The decision to choose this system was based on considerations of storage-space savings, preservation, safety, and traceability of the samples.

The straw design allows the biobank to maximize overall storage space efficiency of the LN2 repository by a factor of four. The total capacity for aliquots stored in this format will exceed 6 million.

From a quality and safety standpoint, these straws feature a higher surface-to-volume ratio that enhances the thermal exchange during the freezing process. They are sealed at both ends, making them suitable for long-term storage in the liquid phase of nitrogen (-196°C) and eliminating the risk of cross-contamination among samples.

Aliquot generation and identification are done in an automated laboratory workflow, using dedicated processing equipment provided by Cryo Bio System. Organization and tracking of the specimens at the Saguenay repository are facilitated by the fact that all physical components of the system (straws and storage

elements) are color-coded.

Each straw also bears a tamperproof external jacket on which a “customized” identification is permanently imprinted as part of the workflow. This identification consists of a human-readable alphanumeric ID number next to its corresponding bar code in high-density linear symbology code-128. Samples stored in this format will also be managed with GenConnect software.

Traditional freezers were chosen for a subset of legacy samples, and a dozen freezers already operating at the Chicoutimi Hospital’s research lab were transferred to the biobank. Samples stored in this format are managed with GenConnect software.

By working together with CARTaGENE, P3G, and other national and international partners to implement sample-storage technologies, the Genome Quebec Biobank boasts high-quality operations and high security standards. The biobank provides long-term storage with mirrored sites for redundancy and flexibility for different user types, storage conditions, and sample types. This biobank has the capacity for tens of millions of samples.

By selecting a combination of storage technologies that maximize space and minimize operating costs, the group has created a sustainable infrastructure that will prove to become an important research resource for many future generations to come. **GEN**