Agilent Case Study

Agilent Automated NGS Solutions Advance Rare Disease Research at Robert Debré Hospital

Exploring rare diseases at Robert Debré Hospital

Characterizing rare diseases offers invaluable insights into their underlying mechanisms, helps identify disease trends, and can drive the discovery and enhancement of investigative technologies. One university hospital group focused on this area of research is the Assistance Publique Hôpitaux de Paris (AP-HP) Nord – Université Paris Cité. Located in northern Paris, this group consolidates several university hospitals, making it one of the largest hospital complexes within the AP-HP network.

The Robert-Debré Hospital for Woman and Children, a leading center for pediatric medicine, offers various programs dedicated to rare diseases affecting children, adolescents, and expectant mothers. These programs, which address both chronic and acute conditions, are supported by highly specialized hospital teams, enabling expertise for technological innovations in rare disease research.[1]

Robert-Debré Hospital, Paris

Adopting a single-workflow strategy

The molecular genetics laboratory within the Robert-Debré genetics department provides a continuum of research, balancing its efforts between hospital services—notably clinical genetics and onco-hematology—and external projects at both national and international levels. It serves as a reference laboratory for specific pathologies and focuses on three main areas of rare disease: somatic, constitutional, and prenatal.

Séverine Drunat, PharmD, PhD, a clinical biologist in the molecular genetics laboratory, highlighted how the lab has integrated next-generation sequencing (NGS) into its workflow to enable deeper genomic analysis.

Given the broad range of complex pathologies and diverse samples they study, a single effective workflow approach to NGS was developed that's effective regardless of the pathology or sample type. This workflow includes the design of the pathology-universal panel, library preparation and target enrichment, capture, and sample quality control using Agilent solutions. Subsequently, extraction, sequencing, data analysis, and reporting is performed using various vendors.

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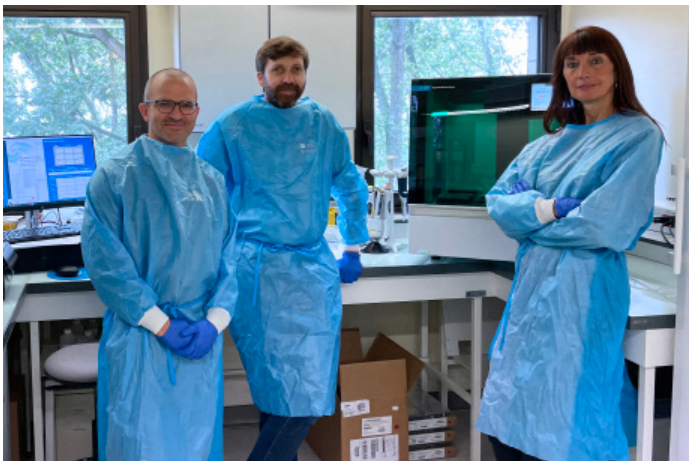

From left to right: Cédric Vignal, medical biology engineer, Dr. Yoann Vial, clinical biologist, and Dr. Séverine Drunat, clinical biologist. Molecular Genetics Laboratory, Robert-Debré Hospital, Paris.

The lab decided to collaborate with Agilent as a one-vendor solution, stemming from a long history of applying Agilent solutions in other departments. For the molecular genetics lab, various Agilent products support its single-workflow approach, including:

- Two Bravo NGS workstations for automating high-throughput NGS library preparation and target enrichment
- One Magnis NGS prep system for automated, walkaway NGS library preparation
- One 4200 TapeStation system for DNA and RNA sample quality control
- Two 2100 Bioanalyzer systems for RNA and protein sample quality control
- SureDesign for creation of custom NGS panels
- SureSelect XT HS2 NGS library prep and target enrichment
- All associated product consumables

The team uses DNA extracted from blood, also DNA of fetal origin (amniocytes or chorionic villi) and circulating DNA from plasma. At this time, sequences of interest are selected and interpreted. The gene panels are reviewed and updated every two years to include new targets, ensuring ongoing validation and accreditation.

Managing high sample volumes with advanced automation

The team processes 96 constitutional samples every three to four weeks and 48 somatic samples per week. All samples are prepared for NGS using the two Bravo NGS workstations for library preparation and target enrichment. Additionally, extra samples are processed on the Magnis NGS prep system, with one to two runs completed per week. When deciding which system to use, the level of urgency is considered. For urgent samples, the Magnis system is preferred due to its ability to prepare eight samples at a time, and small targeted RNA sequencing and exome runs are included. Sequencing is conducted by a technician in the lab, and results are analyzed by the clinical biologists.

Cédric Vignal, MS, medical biology engineer, explained the benefits of using automated systems to manage this large volume of samples. He noted that the lab can now process over 5,000 samples per year, including approximately 3,000 constitutional and 2,500 somatic samples. Since implementing the Magnis system into the workflow, the system's speed and ease-of-use support the sample volume and complexity required the varied laboratory work undertaken.

He also highlighted that the Bravo system adds value to their workflow due to its programmability and large sample capacity. Although the Bravo system is slightly more intricate to use than the Magnis system, the lab has established an in-house training program to enable new users to quickly and efficiently operate the system. Additionally, the lab has developed a detailed Standard Operating Procedure (SOP) to guide users in performing their tasks.

With the current setup, the lab can easily expand to process more samples.

Simplifying operations with a unified workflow

Reflecting on the overall lab performance, Dr. Drunat emphasized the advantages having a one-vendor NGS workflow, with Agilent as its partner. She noted that this setup simplifies lab operations by eliminating the need for extensive discussions with multiple suppliers. The comprehensive global support provided by the Agilent team, including field service engineers and field application scientists specializing in automation and genomics, is a pivotal factor in the successful collaboration between the two entities.

Dr. Drunat added that choosing SureSelect XT HS2 reagents was a natural progression when introducing NGS testing into the lab, given their familiarity with Agilent microarrays and scanners in the cytogenetics laboratory. This continuity in using Agilent products has further streamlined their processes and elevated their research capabilities.

Advancing innovation through collaboration

Integrating Agilent NGS solutions into the Robert-Debré hospital's molecular genetics laboratory has enhanced its research outcomes and operational efficiency. Using a single-workflow approach with advanced automation systems enables the team to process complex samples quickly and accurately, underscoring the vital role of innovative technologies in advancing rare disease research.

References

1. Robert-Debré Hospital. https://robertdebre.aphp.fr/

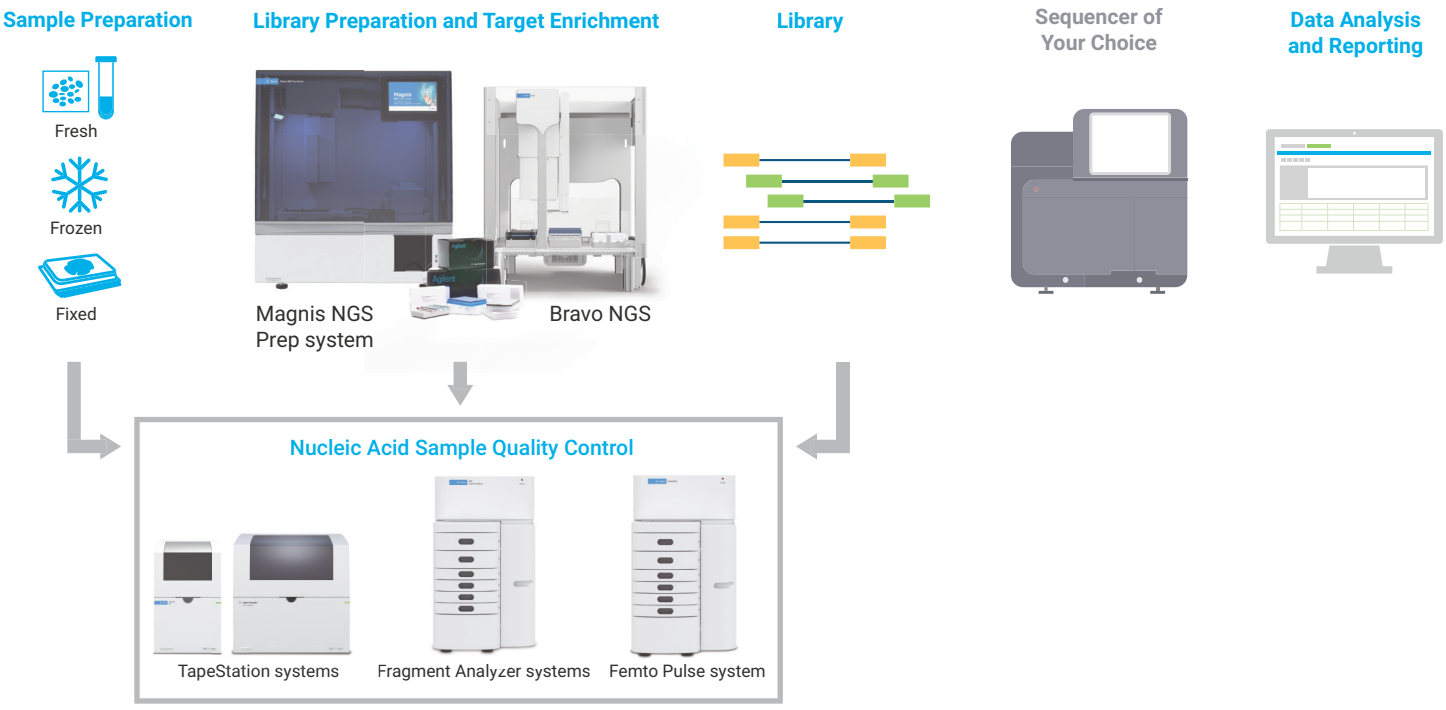

Figure 1. The Agilent NGS workflow includes nucleic acid quality control (QC) instruments, Agilent SureSelect library preparation kits, Agilent SureSelect target enrichment catalog and custom panels, and automation with the Agilent Bravo NGS workstation and Agilent Magnis NGS prep systems.

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