

Public Payor Lab Chooses Panorama NIPT

LifeLabs, the largest community medical laboratory in Canada, has been providing medical laboratory services to Canadians for over 50 years. In April 2015, LifeLabs received funding from the Ontario Ministry of Health to provide non-invasive prenatal testing (NIPT) in British Columbia and Ontario. LifeLabs, which had been offering the Panorama non-invasive prenatal screen since 2013, elected to license the use of Natera's technology for its own laboratory, making it the first Canadian laboratory to do so. The following is LifeLabs' NIPT journey as told by Dr. Ronald Carter, LifeLab's laboratory director.

In the summer of 2015, LifeLabs opened its genetic testing laboratory in Toronto, equipped to support the implementation of Natera's NIPT technology. By October 2015, the platform was in operation, providing NIPT to Canadian women in Canada for the first time. LifeLabs is the first Canadian laboratory to offer Panorama NIPT testing as part of a public payor health care system.

LifeLabs and the Panorama Test

LifeLabs processes over 130 million laboratory tests for over 19 million patient visits per year across British Columbia and Ontario. In 2013, LifeLabs acquired BC Biomedical in British Columbia and CML HealthCare in Ontario, which made it the largest community laboratory in Canada. Panorama NIPT was the first test that was funded by the Ontario Ministry of Health, and the first major contract for a funded test service.

Funding was received to provide NIPT to high-risk women, including those with positive maternal serum screening, women age 40 and over, fetal nuchal translucency measurements of 3.5mm or more, and/or those with previous pregnancies that were affected with aneuploidy.

The decision to offer Panorama

LifeLabs chose to offer Natera's Panorama test because of the quality of the product. The Panorama test, a leader in the market, produces highly accurate results, even with low fetal fractions (down to 2.8%). In addition, compared

to other NIPT tests on the market, LifeLabs found the unique technology behind Natera's Panorama test to be most appealing: Panorama is the only NGS NIPT test on the market that utilizes single-nucleotide polymorphism (SNP) technology, which can differentiate between maternal and fetal cell-free DNA. Beginning in 2013, LifeLabs offered the Panorama test to Canadian women; samples were sent to Natera's lab in San Carlos, California for processing and its data analyzed on Natera's Constellation platform. The results were returned several weeks later.

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The decision to move to Constellation

LifeLabs' decision to license Natera's NIPT technology to offer Panorama in its own lab was a natural progression, as the relationship built between Natera and LifeLabs up to that point was collaborative and effective. Funding from the Ontario Ministry of Health allowed for LifeLabs to provide Natera's Panorama test from within its own laboratory, an opportunity that was long sought as a way to provide excellent local care to the community: for Canadians, by Canadians.

Natera, which welcomed the opportunity, was able to provide the support to allow for the implementation of its technology at LifeLabs. By licensing Natera's NIPT directly, LifeLabs could run the Panorama test in its own laboratory, and test data analysis could be done in the cloud using Constellation, Natera's bioinformatics platform. With Constellation, next-generation sequence (NGS) data is uploaded directly to a server where Natera's bioinformatics algorithms can be accessed to analyze the information and produce results.

Patient information is kept private, as no names or other identifying information is uploaded, and all data are encrypted. Having the data analysis occur on a central

server precludes the need for specialized hardware and software applications to be held in LifeLabs' local laboratory. Information technology specialists from Natera ensure the proper application of the programming to meet the needs of the users on both ends of the data transfer.

Constellation licensee labs are provided with proprietary reagents and protocols equivalent to those used in Natera's CLIA-certified lab in San Carlos. Technological support was, and continues to be, complimentary.

Technology transfer process

Upon receipt of funding for NIPT, the process of implementation of Panorama began immediately. A team of application scientists was deployed from Natera to work with LifeLabs to train on the protocols and workflows. LifeLabs quickly began the process of equipment acquisition, test validation, and negotiation of supply contracts. Software engineers helped to develop the IT integration between LifeLabs's laboratory information system and Constellation. It took approximately five months from the time funding was granted until the test was operational. The protocol at LifeLabs was set up from the outset using NextSeq instrumentation, which was done in collaboration with Natera as this was the first licensee to be using NextSeq. As the NextSeq platform was simultaneously being revalidated for use at Natera, the applications team worked alongside LifeLabs to ensure the proper implementation of the NextSeq platform.

Equipment (machines and tech)

Upon receiving funding, LifeLabs quickly swung into action to ensure equipment validations and installations. LifeLabs purchased the materials to perform DNA extraction, as well as the reagent kits needed. To complete library preparation, a kit from Natera was used, and specific thermocyclers were ordered that are validated for use for Panorama. The reagents were provided to amplify Panorama's 13,392 SNP loci, and samples were bar-coded to allow multiple samples to be run simultaneously. At the same time that LifeLabs was establishing

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its ability to perform the Panorama test in its own lab, Natera was moving from Illumina's HiSeq to the NextSeq system. As such, the process of validation for the use of NextSeq applications at LifeLabs was done simultaneously and with cooperating efforts. Natera's software engineers worked to ensure sequence data streams directly into Natera's cloud-based servers through



Constellation's application program interface (API). LifeLabs chose GeneLogics' Clarity laboratory information management system (LIMS) and Natera provided direct integration to its LIMS workflows with the necessary modifications to LifeLabs' LIMS. Natera also provided LifeLabs with reporting templates that it was able to use with little modification.

Verification and validation

Verification and Validation (V&V) is important to ensure the proper implementation of a clinical test. Natera's application team worked with LifeLabs to ensure that the process and procedures around V&V were appropriately carried out, and helped to troubleshoot along the way.

After verifying that each step of the workflow was performed properly and reproducibly, LifeLabs procured samples to validate the end-to-end workflow. Like any new test being implemented, there were challenges and technical difficulties, but weekly calls and email, as well as site visits from the Natera applications team, ensured that challenges were addressed and issues were resolved.

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Training

The team of field applications scientists worked closely with LifeLabs to implement the processes for sample collection, preparation, sequencing, and data analysis and interpretation. Laboratory technicians from LifeLabs visited Natera's facilities in California, and field application scientists visited LifeLabs facilities at various points throughout the process of setup.

The marketing and sales teams at LifeLabs were educated about the switch to Constellation: the same test would be provided out of a new laboratory, but collection procedures remain the same and the formatting would comply with Canadian requirements. The same bioinformatics protocol is used to generate reports as well.



Conclusions

In the case of LifeLabs, the Constellation model is proving to be collaborative, beneficial, and effective. With the support of government funding, LifeLabs is able to take the lead in providing NIPT to high-risk women in Canada using Natera's proprietary algorithms and bioinformatics. The cooperation between LifeLabs and Natera allows for the implementation of a well-validated test to be offered from within a Canadian lab to its Canadian customers. Natera provided support to LifeLabs to implement protocols quickly, making efficient use of funding to maximize the utility of the test, and has provided ongoing support.

The ability to offer Panorama from within its own laboratory allows LifeLabs to tailor the delivery of test results to its customers and physicians. As Ron Carter of LifeLabs commented, "There is no generic one-size-fits-all service, even for such a test like this where, biologically, pregnancies are the same all over the world... Marketing that test, the uptake of the test, the way results are delivered, the way the scope of the test is configured and the way you work with patients to deliver those results... is markedly different from jurisdiction to jurisdiction." Natera recognizes those differences, and its Constellation platform enables Panorama to be offered to customers in the most fitting way.

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