APML Clinical Laboratory Director Melissa Kelly, PhD. Photo courtesy of Melissa Kelly

The Jackson Laboratory advances precision medicine with an end-to-end workflow

How a world-renowned lab is using bioinformatics as a driving force for genetic discovery and molecular profiling services

NEARLY A CENTURY AGO, The Jackson Laboratory[1] was founded in Maine as a nonprofit biomedical research institution. Today it has 11 locations around the world, with a mission to discover precise genomic solutions for disease and empower the global biomedical community in the shared quest to improve human health.

The Jackson Laboratory's Advanced Precision Medicine Laboratory (APML) is a CLIA-certified, CAP-accredited lab established in 2014. It focuses on clinical genomics, leveraging multiple technologies to provide critical diagnostic and therapeutic information to clinicians for both oncology and rare disease. APML also uses cutting-edge technologies, including SNP and methylation arrays, next-generation sequencing, and long-read sequencing, to answer complex research questions. Unsurprisingly, the lab has complex data needs.

Based in Farmington, Connecticut, APML's primary business is providing actionable information, through methylation profiling and next-generation sequencing, on glioblastomas and other brain tumors for health centers at the University of Connecticut, Vanderbilt University, the University of Texas, MaineHealth, and elsewhere. The lab also provides germline whole-genome sequencing for the diagnosis of rare disease.

"As part of APML's commitment to improving human health, our scientists and staff provide tools, curate critical data, and deliver diagnostic services that help the achievement of goals held by research and clinical communities around the world," says APML Clinical Laboratory Director Melissa Kelly, PhD.

In all of its cases, fast turnarounds are crucial.

APML's recent upgrades to its data analysis pipeline have significantly improved accuracy and efficiency. Previously, the pipeline's automation and filtering settings meant that common but important variants were sometimes missed.

For example, the APOE4 variant, associated with Alzheimer disease risk and found in nearly 15% of the population, and the H63D variant in *HFE*, linked to hemochromatosis with a frequency of 13.2%, would likely have been filtered out under the old system.

"If the tertiary analysis platform filters out alleles that are above 10% frequency in the population, we're

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potentially going to miss crucial information," Kelly says. "They're tailoring it for fast analysis, but that's at the cost of not seeing variants that could be really important."

Now, with enhanced tools and more flexible filtering, APML is equipped to identify a broader range of relevant variants—faster and more accurately than ever before, which is critical for unlocking clinical research insights.

Upgrading the workflow

APML's new Illumina data analysis pipeline has simplified and accelerated their work, improving their ability to quickly understand large, complex datasets for genomes and exomes. With Illumina's tools, it takes APML two days or less to create a final report for a complex genetic disease case. But just as important as turnaround time is the need for high-quality, reproducible analysis.

APML is equipped with an Illumina NextSeq 2000 System and a NovaSeq X Plus System. The lab recently added a suite of Illumina tools to manage and interpret its data, including Clarity LIMS,[2] Illumina Connected Analytics,[3] DRAGEN,[4] and, for variant interpretation, Illumina Connected Insights[5] for oncology and Emedgene[6] for genetic diseases. APML's new next-generation sequencing workflow combines the tracking of samples, high-quality secondary analysis, and variant interpretation all in a single environment, automating their flow of data from sequencer to draft research report.

APML received support throughout the process of adopting a full end-to-end solution. Illumina's Customer Success & Implementation team[7] guided them through planning, onboarding, optimization, and ensuring they were getting the best results.

"Having the full end-to-end data analysis pipeline has been so helpful to our work," Kelly says. "We load the sequencer and the data shows up. It's automated, it's fast, and we don't have to perform any manual interventions."

APML's work requires systems that automatically produce accessible data. "With both Connected Insights and Emedgene, the user interface is fantastic," Kelly says. "The information is displayed in a way that's easy to digest, and we can classify variants quickly." Connected Analytics allows her to easily queue high-quality, consistent analysis with DRAGEN, providing readouts that are automatically fed into Connected Insights (for somatic variants) or Emedgene (for germline variants) and make perfect sense out of the box.

These new tools help the team return analyses quickly. APML is also teaming up with local hospitals in hopes of incorporating whole-genome sequencing into newborn screening. Their new pipeline, which enables rapid interpretation and report generation, puts them in a great position to integrate this service among others.

"Current newborn screening covers 30 to 60 diseases using a combination of biochemical and genetic testing," Kelly says. "Our approach would be much broader—targeting over 200 diseases associated with more than 400 genes, each of which can be treated and/or better managed with early detection. We're excited, because children will have better outcomes than if we just waited for the disease to develop." ◆

To learn more about Illumina's Customer Success & Implementation services, go to: illumina.com/services/bioinformatics.html

2. illumina.com/products/by-type/informatics-products/lab-management-software/clarity-lims.html
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