*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 shared mission of finding genomic solutions for disease and other conditions.

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. In all of its cases, fast turnarounds are crucial.

Unfortunately, the team's previous data analysis pipeline had inconsistent automation and it often failed to provide timely answers. There were also problems with their previous analysis software, which prefiltered results to exclude common variants, leaving out important data.

"If the tertiary analysis platform filters out alleles that are above 10% frequency in the population, we're going to miss really crucial information," says APML Clinical Laboratory Director Melissa Kelly, PhD. "They're tailoring it for fast analysis, but that's at the cost of not seeing variants that could be really important." Kelly cites examples such as the *APOE4* variant associated with Alzheimer disease risk. It has a population frequency of nearly 15%, and the low-penetrant *H63D* variant in *HFE*, associated with hemochromatosis, has a frequency of 13.2%. Both of these would have been missed with APML's prior analysis pipeline.

In addition, their previous tertiary analysis software lacked an intuitive user interface, making it challenging

*1. jax.org*

to understand large, complex datasets for genomes and exomes. As a result, it took a long time to classify variants, delaying critical, time-sensitive insights.

"On the whole-genome side in particular, the data analysis pipeline was running into problems," Kelly says. "The way it was configured, we could only run two samples at a time through our bioinformatics pipeline, and it might take two days to do that. Our tertiary platform was essentially a glorified Excel spreadsheet."

**Upgrading the workflow**

APML's new Illumina data analysis pipeline has simplified and accelerated the work. Prior to the change, it could take the lab as long as two weeks to create a final report for a complex genetic disease case. Now, it takes two days or less. 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.

"We have seven people in our entire lab, so we're a small team," Kelly says. "There's no way we could have pulled all this together on our own. The implementation support was huge."

"Having the full end-to-end data analysis pipeline makes it so much easier," she continues. "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—we're not waiting 12 hours for somebody to wake up and kick off the pipeline."

Because the lab does not have full-time access to a bioinformatician to support its research, they need 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 much faster." 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*

*To register for Melissa Kelly's March 6 live webinar with GenomeWeb, entitled "Scaling the Genomics Lab for the Data Deluge: Streamlined and Efficient Data Analysis Workflows as a Strategic Pillar for Growth," go to: event.on24.com/wcc/r/4842977/3F31FE975903505FCADEC4112C62DFD4*

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