

Massachusetts General Hospital Adopts Advanced Analytical Technology in Fight Against Cancer

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The Massachusetts General Hospital (MGH) Center for Integrated Diagnostics in Boston has been applying molecular pathology in the ongoing battle against cancer. Patients at MGH are routinely tested with advanced, specialized clinical assays to profile their tumors at the molecular level. Identification of cancer driver mutations would enable oncologists to customize treatments for their patients in a more personalized manner or to better define the patient's disease with respect to diagnosis and/or prognosis. This type of genotyping and personalized medicine for cancer is being practiced in academic medical centers across the country.

For the last two years MGH Center for Integrated Diagnostics has been using an instrument called the Fragment Analyzer™ as part of its routine clinical diagnostic workflow. Designed and manufactured in Ames, Iowa, by Advanced Analytical Technologies, Inc., the Fragment Analyzer is an automated capillary electrophoresis instrument for evaluating DNA and RNA size and quantity. The Fragment Analyzer provides excellent data quality, automation, and speed, which are important particularly for clinical laboratories that need to process samples, generate data, analyze the results, and report the findings back to the clinicians in an efficient manner.

Dr. Long Phi Le, a pathologist at MGH, said, "We had been looking for an alternative to agarose gel electrophoresis for a number of our clinical assays and also for next-generation sequencing applications. Our goal has always been to provide clinicians and staff with timely, safe and accurate results to ensure the best patient care possible." In particular, the laboratory now performs clinical MGMT and MLH1 promoter methylation analysis with the instrument which is faster and safer than using agarose gel electrophoresis with ethidium bromide staining. The data output from the ProSize software also eliminates the need to visualize and capture images of the agarose gel while yielding better resolution and sensitivity than gel electrophoresis.

In addition to routine clinical applications, the Fragment Analyzer has also been instrumental in assay development for the laboratory. The MGH Center for Integrated Diagnostics recently launched a novel targeted RNA-seq next-generation sequencing assay for clinical detection of gene fusions for ALK, RET, and ROS1. These targets are particularly important for patients with lung adenocarcinoma for which there is the FDA-approved crizotinib inhibitor that has been demonstrated to be effective. This test is based on a method called anchored multiplex PCR (AMP), which was developed at MGH. The Fragment Analyzer was a critical tool used in the development of the assay particularly for qualitative analysis of the targeted libraries



that were generated during the optimization of the protocol.

Finally Dr. Le's group has further plans to launch two targeted next-generation sequencing cancer panels in 2014. One panel highly focused on hotspots and also a few key tumor suppressor genes is designed for rapid turnaround and low input DNA. The second will be a larger gene panel covering all exons of many cancer genes. Both clinical assays will be used for formalin-fixed paraffin-embedded tumor tissues which is a challenging substrate to handle given the poor quality of DNA in these samples resulting from fixation. The Fragment Analyzer will be used during the development of these assays and also in clinical production to analyze the quality of input samples and their libraries prior to sequencing. Dr. Le states, "It is important in a diagnostic laboratory to have quality metrics to ensure that the work we perform and the results we report meet clinical standards, particularly for specimens of poor integrity like FFPE."

"It gives all of our employees great satisfaction to know that an outstanding organization like Massachusetts General Hospital is using our product for such a worthy cause," said Dr. Steven J. Lasky, CEO of Advanced Analytical Technologies. "We also take great pride in the technical support we provide to ALL of our customers. We recognize that it's not enough to design and build great products – we also need to stand behind them with great technical support."

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