The Seven Benefits of Clinical Genomics Universal Standardization: A Customer Success Story

We gathered some key first-hand insight from clinical diagnostics veteran Dr. Andrea Ferreira-Gonzalez, who has seen many changes over the 25 years she's been in the trenches. Dale Yuzuki of SeraCare caught up with her recently, and their conversation revealed some important trends driving success in the precision medicine field.

Andrea Ferreira-Gonzalez, PhD has been the director of the Molecular Diagnostics Laboratory at the Virginia Commonwealth University (VCU) Health System in Richmond VA, since 1994 and Chair of the Division of Molecular Diagnostics in the Department of Pathology at the VCU Health System since 2008.

In the VCU Health System Molecular Diagnostics Laboratory, they are using next-generation sequencing (NGS), including whole-exome sequencing and targeted sequencing of fixed gene panels with cancer-associated genes. The fixed gene panels reduce the time and cost associated with studies.

A New Era of Precision Medicine in Clinical Diagnostics

Dr. Ferreira-Gonzalez discussed the dramatic shift in the clinical diagnostics scene with the onset of next-generation sequencing platforms in molecular pathology laboratories.

In particular, for oncology patients, the previous lack of tools to analyze the complexity of cancer had been a hindrance in gaining a comprehensive picture of the status of the patient. "So now with these technologies, including next-generation sequencing, we can get a more in-depth analysis of the genetic profile of these patients. The technology is instrumental in gathering a deep level of information for diagnostic, prognostic, and theranostic applications," says Ferreira-Gonzalez.

Theranostics, and the uptick in the use of companion diagnostic tests in recent years, has been a powerful force in the precision medicine space, allowing diagnostic labs and physicians to identify specific patients who will benefit from a therapy, and to monitor ongoing effectiveness throughout treatment.

The trend in the application of precision medicine is clear, and the statistics paint the picture. Over the last three years, more than 25% of new molecular entities approved by the FDA fell into the personalized medicine category. In 2016, half of the approved personalized medicines were indicated in oncology.[1]

At VCU's Massey Cancer Center, we have the opportunity "to interact and hear stories from patients we've been able to help. Having individuals with very advanced stages of disease where we've done the testing, and now they are alive, many, many years afterwards, has been extremely rewarding. Actually it's what keeps me going every day," says Ferreira-Gonzalez.

An Interlaboratory Evaluation of Standardized Reference Materials for Tumor Profiling

Extensive experience has taught Ferreira-Gonzalez the critical importance of developing standardized technologies and methodologies for the greatest effectiveness of clinical diagnostic tests. The full impact of this advantage was made clear after an interlaboratory test of standardized reference materials for the greatest effectiveness of clinical.

"We have learned after 25 years of clinical molecular diagnostics that as we standardize our technologies and methodologies, we can compare results from different institutions or studies and further evaluate the clinical validity of these tests and advance the clinical utility knowledge of tests," says Ferreira-Gonzalez.

Let's look at some of the benefits that she's seen from using standardized reference materials at VCU for her NGS-based assays.

Benefit #1: Identification of an Array of Variants at a Specific Allele Frequency

In order to measure their assays' performance against that of other laboratory's assays and platforms, the VCU Health System Molecular Diagnostics Lab participated in a much-needed interlaboratory test of standardized reference materials for somatic mutations in cancer, which involved 26 different common and rare cancer mutations. This type of analysis is made possible with the use of reference material such as the Seraseq™ Tumor Mutation DNA Mix v2 (AF10) HC: a multiplexed mixture of 40 variants across 28 genes with a known allelic frequency, blended with a genomic background.

"Using reference materials has been key in helping us gain added confidence in detection of a variety of genetic changes: single-nucleotide variants (including in homopolymer regions) and insertion-deletion mutations (INDELs), says Ferreira-Gonzalez. Structural variants (SVs) can also be detected with the SeraCare reference material.

Benefit #2: Validation of Chemistry

"So all of the careful design that has been included to help us address some of the challenges we see has been paying off. This is because we now have reference materials - some control materials - that we can use for the validation of the assays. With these we can validate the (assay sequencing) chemistry, we can validate the informatic pipeline, to say 'this is what I'm supposed to be detecting," says Ferreira-Gonzalez.

Benefit #3: Tracking Patient Results over Time

Another important benefit of the reference materials is that labs can monitor long-term assay drift while tracking patient results over a period of time to see if there are any changes. "Which is key, because some of the patients will have to be tested again…and we want to make sure the quality of our assay is maintained over time," says Ferreira-Gonzalez. These reference materials can provide a critical check on the quality and performance of assays.

Benefit #4: Alternative Assessment to Proficiency Testing

Furthermore, the VCU lab uses SeraCare reference material as an alternative assessment to supplement proficiency testing material from the College of American Pathologists (CAP). They use the reference material for training personnel and for proficiency assessments.

Benefit #5: Assessment Across Different Laboratories

In terms of the interlaboratory study, they had "extremely exciting results", in which they found that the reference material was "a very robust material that was performing well across laboratories. We had six clinical laboratories, all CLIA-certified either through CAP or state laboratories, that were clinically offering this test," says Ferreira-Gonzalez.

Benefit #6: Assessment Across Different Platforms

The reference material also performed well across platforms: Illumina's MiSeq®, and Thermo Fisher's Ion Torrent® and Ion PGM® System. Each of the laboratories had developed their own Laboratory-Developed Test (LDT).

> ***"Seeing consistent performance of these reference materials across six different laboratories, with all of us working with our own protocols, chemistries, IT pipelines, is outstanding. Because it points to the quality of these materials, as well as how robust this technology is becoming. Developing this standardization is paying off." - Dr. Ferreira-Gonzalez***

Benefit #7: Reproducibility with Repeated Freeze-Thaws

Another key benefit the study revealed is the reproducibility of results with the SeraCare reference material, even with repeated freeze-thaws. "We have the same control material that we can freeze and thaw, using the same lot number that we don't have to QC again, reducing the variability and decreasing the cost for our laboratory. It was really nice to see that we could use the same materials, freeze and thaw eight different times, and have such consistency over the period of testing," says Ferreira-Gonzalez.

This case study illustrates the importance of SeraCare reference material throughout the entire NGS process: from initial validation to full-scale clinical practice. Here we see its prominent role in assay validation, in tracking patients over time, and for proficiency testing of personnel. The importance of reference material as a universal control also becomes clear when it's put to the test in an interlaboratory study, where we see SeraCare reference material perform well across laboratories as well as across NGS platforms.

Visit www.seracare.com/clinicalgenomics to learn more about SeraCare's precision medicine solutions.

References

1. Konski, A. Personalized Medicine Bulletin: More Than 25% of New Molecular Entities Approved in 2016 Are Personalized Medicines 2017; Available from: https://www.personalizedmedicinebulletin.com/2017/02/05/more-than-25-of-new-molecular-entities-approved-in-2016-are-personalized-medicines/.

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