ClariFind™ White Paper

INTRODUCTION

The correlation of clinical features with specific drug therapies and clinical trial options, customized to each patient, has become a crucial component of cancer care. For this reason, our experts developed ClariFind to add clarity to molecular testing with personalized treatment options for cancer patients. ClariFind employs next-generation sequencing (NGS) for comprehensive genomic profiling of a patient's tumor sample to identify potential clinically actionable targets and associated therapies, which could have significant positive impacts on patient outcome.

WHAT IS THE CLINICAL UTILITY OF NGS IN CANCER STUDIES?

Multiple papers have reported on alterations that predict positive and negative responses to certain therapies with the potential to improve outcomes including progression free survival. In many cancers, mutations in more than one gene have been identified as predictive targets, as illustrated with the identification of EGFR, ALK, KRAS, ROS1, RET, MET, BRAF and ERBB2 (HER2) genes in lung cancer and KRAS, NRAS, BRAF, PIK3CA and PTEN in colorectal cancer. Other cancers such as breast cancer, exhibit even more heterogeneous variant profiles and the list of targetable genes for a multitude of cancers is ever expanding.

Cancer genes are more diverse than previously thought and tumors from the same organs can exhibit quite different variant profiles. Conversely, the same mutational profiles can be found across multiple cancers and genetic studies should not be limited to genes that are historically characteristic for a single tumor type. Tumor location, which traditionally formed the basis for cancer treatment, is now eclipsed by genetic criteria, which has emerged as a defining prognostic and therapeutic indicator. Furthermore, since heterogeneity exists over the lifetime of a cancer, with differing patterns of genetic changes between primary and metastatic tumors, it is essential in patients with metastatic disease to establish a baseline profile followed by sequential studies to follow the evolution of the tumor over time.

A significant number of cancer patients do not achieve desired response with first-line/standard of care therapy or become resistant to therapy as the disease progresses. Certain patients may better be served with alternate first tier therapies or clinical trial enrollment and, for some cancers, patient participation in a clinical trial is “unanimously endorsed” over first line therapies, particularly in advanced cases. NCCN Guidelines recommend the best management for ANY patient with cancer is in a clinical trial and ASCO strongly encourages the use of NGS to determine eligibility. Leading organizations including the College of American Pathologists (CAP), the Association for Molecular Pathology (AMP), the American Society of Clinical Oncology (ASCO), and the National Comprehensive Cancer Network (NCCN) have published recommendations supporting mutational profiling, which has become standard of care for a growing number of cancers; thus, moving NGS into the forefront of clinical cancer genomics.

The clinical utility of NGS has been well reported, and multiple and high throughput sequencing is now widely considered the gold standard for genetic diagnosis. The benefits of this platform are numerous. Eliminating the need for multiple stepwise studies, NGS provides information beyond targeted mutation analysis and single gene-by-gene Sanger DNA sequencing. Increased efficiency helps preserve specimens and avoid repeat biopsies. This technology reduces costs both in the laboratory and clinically, by limiting the use of expensive therapies in patients that may be more inclined to respond poorly.

HOW IS CLARIFIND DIFFERENT FROM OTHER TESTS?

ClariFind covers all DNA coding regions (+/-5-10bp flanking intronic sequences) of 277 key cancer genes. Single nucleotide changes, insertions, deletions and copy number alterations in 39 genes are detected.
mutational burden is also included in the analysis as a predictive biomarker to immunotherapy. Additionally, our chemistry is designed for improved coverage of GC-rich regions in genes such as CEBPA and CCND1, which have poorer coverage with traditional approaches. While many panels are appropriate for only a subset of tumors, ClariFind is appropriate in individuals with solid tumors and/or hematologic malignancies and can be completed on a variety of sample types. Using a unique molecular barcoding approach, our assay mitigates PCR duplicates and bias, and allows for confident low-level variant detection, from 5% down to 1%. ClariFind requires very little DNA — as low as 40 ng — enabling testing on small biopsies.

Utilizing robust data resources, analysis is performed by a team of in-house, board-certified molecular pathologists, curation scientists, and bioinformatics experts. Our proprietary reporting system includes a detailed interpretive summary that follows published guidelines set forth by AMP, ASCO and CAP. With a focus on clinical significance, we provide patients with available personalized drug therapies and clinical trial options. Each case is thoroughly reviewed by board-certified clinical experts to aid in optimizing patient care and who remain available for further clinical consultation.

EXPERIENCE OF BAYLOR GENETICS

For nearly 40 years, Baylor Genetics has been the leading pioneer in genetic testing. Currently, we offer a full spectrum of cost-effective genetic testing and provide clinically relevant solutions. Our team’s unmatched knowledge and experience deliver a combination of advanced technology and deep patient data sets that lead to more accurate interpretations. The team at Baylor Genetics is well versed in NGS technology and has reported extensively about our experience with this highly complex test.

WHO ARE WE?

Brian Y. Merritt, MD: Dr. Merritt is currently the Medical Director for the Cancer Genetics laboratory. He attended medical school at Baylor College of Medicine, where he also completed his residency and fellowship training in pathology. He obtained his certifications from the American Board of Pathology for Anatomic and Clinical Pathology in 2013, Hematology in 2014, and Molecular Genetic Pathology in 2015.

Pengfei Liu, Ph.D.: Dr. Liu earned his Ph.D. at Baylor College of Medicine, where he also went on to complete his fellowship in clinical molecular genetics. In 2015, Dr. Liu obtained his board certification from the American Board of Medical Genetics for Clinical Molecular Genetics. Currently, he is an Assistant Professor at Baylor College of Medicine for the Department of Molecular and Human Genetics, and a Lab Director for Exome Re-analysis at Baylor Genetics.

Shashikant Kulkarni, MS, Ph.D., FACMG: Dr. Kulkarni is the Chief Scientific Officer at Baylor Genetics and a Professor, Co-Vice Chair of Research, Co-Program Director of the Molecular and Human Genetics Program at Baylor College of Medicine. He earned his PhD. at All India Institute of Medical Sciences and completed fellowship and post graduate fellowships at Hammersmith HospitalImperial College, Harvard Medical School and Washington University School of Medicine.

Christine Eng, MD: Dr. Eng joined Baylor Genetics in 2000 and is Professor of Department of Molecular and Human Genetics at Baylor College of Medicine and Chief Medical Officer and Chief Quality Officer of BaylorGenetics Laboratories. She has been recognized for contributions to the implementation of genomics in clinical practice. She is senior author of articles in the NEJM and JAMA regarding exome sequencing and is principal investigator of the Genomic Sequencing Core for the NIH Undiagnosed Diseases Network.

CITATIONS


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