PrimBio Cancer Hotspot Gene Mutation Panel - Targeted Mutation Detection by Next Generation Sequencing

Test Information: Cancer is caused by acquired accumulation of genetic changes. These genetic changes result in abnormal cell proliferation and invasive behaviors which can lead to neoplastic growth or cancer. The genetic molecular changes in cancer can be categorized into two major groups: chromosomal genetic changes and nucleotide sequence changes. Most common nucleotide sequence changes in cancer involve single-nucleotide variants (missense and nonsense) and small insertions or deletions (some of which may result in frameshift mutations). This assay tests for individual genetic changes in 50 genes associated with most human cancers.

The genes tested in this panel are common tumor suppressor genes and oncogenes. All of the tested genes are "driver" genes, in that deleterious mutations in these genes are involved in the initiation, progression or metastasis of cancer. This test can be utilized to test solid tumors or hematological cancers. The variants tested in this assay are associated with almost all known cancers including breast, ovarian, lung, colorectal, liver, skin, brain and blood. In addition there are approximately 120 therapy options (FDA approved and in clinical trials) associated with the variants tested.

This panel is used to determine the genetic information (somatic mutations) of a specific cancer or tumor so that a physician, genetic counselor, or other health provider can offer the optimal treatment plan for a cancer patient. The primary cause of treatment failure of most cancers is due to acquired resistance to therapy, which occurs approximately 90% of the time. This test can determine which therapies will be effective for a specific cancer or which cancers will be resistant to a specific therapy. In addition the health provider can determine alternate therapies associated with a specific variant that are FDA approved for a different condition or are in clinical trials.

The ordering physician or genetic counselor will receive a comprehensive clinical report along with the sequencing information that will list all pathogenic variants, as defined by strict regulatory guidelines. In addition the report will contain, but will not be limited to: the clinical significance of the variant, the biological function of the variant, FDA approved therapies for the condition and the variant, therapies that are in clinical trials for the condition, therapies that are in clinical trials for a particular variant in an alternate condition and all available therapies. In addition the report will contain information on which variants will be resistant to specific therapies. Below is an example of the first page of the comprehensive clinical report:

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PrimBio Cancer Hotspot Gene Panel Report

Targeted Mutation Detection by Next Generation Sequencing

Patient Name:	Test Code:	Cancer Hotspot Gene Panel	Staff Initial:	
Date of Birth:	Date Collected:		Physician Tel. #:	
Gender:	Date Received:		Physician Fax #:	
Hospital #:	Date Reported:	10/6/17	Contacted Person:	
Ordering Person:	Date Ordered:		Result Read Back:	Y / N
Accession #:	Unexpected Result Reporting		Date:	10/6/17
Sample Type:			Time:	2:21 PM

Test Summary:

This test was used to determine somatic variants in 50 of the most common tumor suppressors and oncogenes in a patient diagnosed with Non-Small Cell Lung Carcinomas using molecular/pathological/hormonal tests as indicated by the information provided by the ordering physician.

Two variants were reported in ClinVar and COSMIC databases as pathogenic and related to the patient's condition. By using Ion Reporter software, one variant was predicted as pathogenic although there was no evidence in ClinVar.

Markers and FDA Approved Therapies

Gene	Nucleotide Change	Amino Acid Change	Therapies approved for the indication	Therapies approved for alternate conditions	Resistance to therapies	Drug Effect
EGFR	c.2155G>T	p.Gly719Cys	Erlotinib, Afatinib	Erlotinib, Afatinib	Gefitinib	Progression-free survival
EGFR	c.2303G>T	p.Ser768Ile	Erlotinib, Afatinib	Erlotinib, Afatinib	Gefitinib	Progression-free survival
KRAS	c.145G>A	p.Glu49Lys	N/A	N/A	N/A	N/A

Laboratory Director: Dr. Kip Kuttner

PrimBio Research Institute

Selected therapies in clinical trials

Therapy	Markers	Cancer Type	Clinical Trial
Dacomitinib	Pan-ErbB family tyrosine kinase	Non-small cell lung carcinoma (NSCLC)	Phase III NCT01774721, NCT01918761
Icotinib	EGFR	Non-small cell lung carcinoma (NSCLC)	Phase IV NCT02404675, NCT02961270
ASP8273	EGFR	Non-small cell lung carcinoma (NSCLC)	Phase III NCT02588261
Trametinib	MEK1,2	Non-small cell lung carcinoma (NSCLC)	Phase II NCT02642042
Selumetinib	MEK1,2	Non-small cell lung carcinoma (NSCLC)	Phase III NCT02503358
Binimetinib	MEK1,2	Non-small cell lung carcinoma (NSCLC)	Phase II NCT03170206
Ganetespib	Hsp90	Non-small cell lung carcinoma (NSCLC)	Phase II NCT01562015
AT13387	Hsp90	Non-small cell lung carcinoma (NSCLC)	Phase I NCT01712217

Kip Kuttner D.O. _____ Date_____
Laboratory Director

Laboratory Director: Dr. Kip Kuttner
PrimBio Research Institute Clinical Services were developed under guidelines set forth by the Clinical Laboratory Improvement Amendments of 1988 (CLIA) for use by physicians. The content herein is collected from sources believed to be reliable.

Test Details

Special Notes:	This PrimBio Cancer HotSpot Gene Panel performed by next generation sequencing (NGS) uses the Ion Ampliseq Cancer Hotspot Panel v2, which is designed to target 2855 mutations in the following 50 key cancer genes: *ABL1, AKT1, ALK, APC, ATM, BRAF, CDH1, CDKN2A, CSF1R, CTNNB1, EGFR, ERBB2, ERBB4, EZH2, FBXW7, FGFR1, FGFR2, FGFR3, FLT3, GNA11, GNAS, GNAQ, HNF1A, HRAS, IDH1, JAK2, JAK3, IDH2, KDR, KIT, KRAS, MET, MLH1, MPL, NOTCH1, NPM1, NRAS, PDGFRA, PIK3CA, PTEN, PTPN11, RB1, RET, SMAD4, SMARCB1, SMO, SRC, STK11, TP53, and VHL*. This mutation panel is designed to detect targeted mutations only. The 50 genes are not sequenced in their entirety. Mutations outside the targeted regions will not be detected. The limit of detection is 3.5% at 500X coverage and 5% at 200X coverage. This technology cannot reliable detect mutations at coverage below 200X. Confirmation of actionable mutations is performed by Sanger sequencing.

Technical Information

Methodology:	Multiplex PCR followed by Next Generation Sequencing
Test Type:	Sequence Analysis

Sample & Shipping Information

PrimBio currently accepts extracted DNA samples, frozen fresh tissues, blood samples and FFPE slides for gene panel testing.