PGD | MET*DETECT*-R™

MET*DETECT*-R™ APPROACH

Throughout tumorigenesis, the selection and expansion of tumor cells with acquired genetic alterations in specific genes has been described as a mechanism of resistance to targeted therapy. Unfortunately, due to a lack of available tissue biopsies, it is often not possible to examine the multiple lesions present in an individual to determine the presence and mechanism of acquired resistance during therapy. Circulating tumor DNA can be used to analyze the genomic landscape of tumors in a non-invasive manner.

The MET*Detect*-R™ assay evaluates the *MET* tyrosine kinase receptor locus and surrounding regions using next-generation sequencing at extremely high coverage to identify mutant alleles for prediction of therapeutic response. The MET*Detect*-R™ assay can be applied to both plasma and tumor tissue samples to identify *MET* amplification that occurs in small percentage of DNA molecules (0.10%).

MET*DETECT*-R™ HIGHLIGHTS

- Digital detection of focal *MET* amplfication
- Non-invasive, real-time, multi-lesion
- PARE (Personalized Analysis of Rearranged Ends) technology to identify structural changes in tumor-specific DNA, including amplification-associated rearrangements
- Proprietary capture design and patented Digital Karyotyping analysis for high resolution annotation of copy number alterations with high sensitivity and specificity
- CLIA-certified, GCLP and FDA 21 CFR Part 11 compliant

MET*DETECT*-R™ CIRCULATING TUMOR DNA ANALYSIS DELIVERABLES

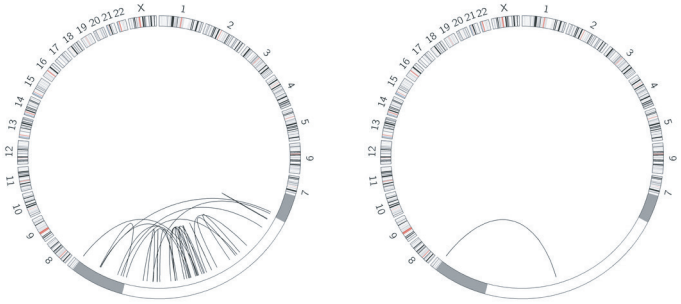
- Identification and schematic representation of tumor-specific *MET* amplification
- Annotation of predicted rearrangement consequences
- Data summary statistics (read data and depth distribution across target regions)
- Integrated Analysis Report (incidences and frequencies of mutations identified)

Related References
Diaz et al. Oncotarget. 2013 Oct;4(10):1856-7.
Leary et al. Oncotarget. 2013 Aug;4(8):1119-20.
Leary et al. Sci Transl Med. 2012 Nov 28;4(162):162ra154.
Leary et al. Sci Transl Med. 2010 Feb 24;2(20):20ra14.

MET*DETECT*-R™ SEQUENCING KEY METRICS	
Regions Analyzed	Focal amplification of *MET*
Sequencing Method	Illumina HiSeq next generation sequencing
Bioinformatics	Patented PARE and Digital Karyotyping methods
Assay Sensitivity	100% (95% CI, 48%-100%): detection capability 0.10%
Assay Specificity	100% (95% CI, 85%-100%)
Sequencing Coverage	2,000x
Turn-around Time	3 weeks
Sample Requirements	Blood or tumor tissue
Sample Types	Plasma or frozen tumor, FFPE, cell lines, and xenografts
Plasma Sample Input Required	3 ml (minimum 1 ml)
Tumor Sample Input Required	1 µg (minimum 50 ng)

FIGURE 1. IDENTIFICATION OF *MET* GENE AMPLIFICATION THROUGH ANALYSES OF PLASMA DNA
Somatic rearrangements associated with amplification of *MET* were detectable in patients with *MET*-amplified tumors (top panel), while no somatic rearrangements were detected in patients with *MET* unamplified tumors (bottom panel). Note: chromosome 7 positions 114 Mb-118 Mb (hg18) are enhanced by 375-fold to visualize genomic rearrangements in the *MET* genomic region.

EXAMPLES FROM PATIENTS WITH *MET* AMPLIFICATION



EXAMPLES FROM PATIENTS WITHOUT *MET* AMPLIFICATION