CLAIMS

1. A method for detecting cMET alterations, the assay comprising

contacting a portion of a nucleic acid sample with a set of primers which detect alterations in cMET gene copy number variation;

in which the set of primers comprises subsets of primer pairs that amplify at least one gDNA-specific sequence of cMET, the primers having sequences selected from SEQ ID NOs: 10, 11, 12, 28, 29 and 30, and

at least one gDNA-specific reference gene sequence of each of:

i) KDELR-2 which is located on chromosome 7; and

ii) SOD1 or SPG21, which are not located on chromosome 7;

to detect cMET gene copy number variation, the primers have sequences selected from SEQ ID NOs: 16, 17, 18, 34, 35, 36, 95, 96, 97, 113, 114, and 115;

performing a PCR amplification regimen comprising cycles of strand separation, primer annealing, and primer extension on a reaction mixture comprising the portion of the sample and the set of primers;

detecting the level of the cMET amplicons relative to the reference gene amplicons, thereby detecting the presence or absence of:

a) a chromosome 7 amplification comprising a cMET alteration; and

b) cMET gene amplification alteration.

2. A method according to Claim 1, in which the set of primers further comprises a subset of primer pairs that amplify at least one gDNA-specific sequence of EGFR; and

the assay further comprises comparing the normalized level of EGFR amplicons to a gDNA EGFR reference level; in which a higher level of a gDNA-specific EGFR amplicon as compared to the gDNA EGFR reference level indicates the presence of a gene amplification alteration of EGFR in the sample.

3. A method according to Claim 1 or 2, in which the method further comprises comparing the normalized level of KDELR-2 amplicons to a gDNA KDELR-2 reference level;

in which a higher level of a gDNA-specific KDELR-2 amplicon as compared to the gDNA KDELR-2 reference level indicates the presence of a gene amplification alteration of KDELR-2 in the sample.

4. A method according to Claim 2 or 3, in which the presence of a gene amplification alteration of cMET, EGFR and KDELR-2 indicates the presence of chromosome 7 amplification.

5. A method according to Claim 2, 3 or 4, in which the primer set comprises subsets of primer pairs that amplify one gDNA-specific sequence of KDELR-2 and three gDNA-specific sequences of each of cMET and EGFR.

6. A method according to any preceding claim, in which the primer set comprises subsets of primer pairs that amplify at least one gDNA-specific sequence of SOD1 and SPG21.

7. A method according to any preceding claim, further comprising contacting the portion of a nucleic acid sample with a second set of primers, in which the second set of primers detects changes in cMET gene expression level;

in which the second set of primers comprises subsets of primer pairs that amplify mRNA-specific sequences of cMET and at least mRNA specific sequences of at least two reference genes; and

in which an altered level of a mRNA-specific cMET amplicon as compared to a mRNA cMET reference level indicates the presence of a gene expression level alteration of cMET in the sample.

8. A method according to Claim 7, in which a primer set comprises primer pair subsets that amplify at least one amplicon of each gene.

9. A method according to Claim 7, in which the at least two reference genes amplified by the subsets of primers that amplify mRNA-specific sequences are SOD1 and SGP21.

10. A method according to Claim 7, in which the primer sets comprise primer pair subsets that amplify at least two gDNA-specific amplicons of each of cMET, EGFR, and KDELR-2 and at least two mRNA-specific amplicons of each of cMET, SOD1 and SGP21.

11. A method according to any preceding claim, further comprising:

contacting a second portion of the sample with a third set of primer pairs in which the third set of primers comprises subsets of primer pairs that amplify cMET sequences comprising sequence variations;

performing a PCR amplification regimen comprising cycles of strand separation, primer annealing, and primer extension on a reaction mixture comprising the second portion of the sample and the third set of primers;

detecting the level of the amplicon for each primer pair, in which the presence of an amplicon indicates the presence of the sequence variation for which that primer pair is specific.

12. A method according to Claim 11, in which one or more sequence variations of cMET are SNPs.

13. A method according to Claim 12, in which the cMET SNP is selected from the group consisting of:

S1058P; V1101I; H1112Y; H1124D; G1137V; M1149T; V1206L; L1213V; K1262R; M1268T; V1238I; Y1248C; and D1246N (SEQ ID NO: 131).

14. A method according to Claim 11, 12 or 13, in which the same PCR thermocycling regimens are used for both reactions.

15. A method according to any preceding claim, in which the nucleic acid sample is prepared from a FFPE tumor sample.

16. A method according to any preceding claim, in which the sample comprises tumor cells from a subject diagnosed with a condition selected from the group consisting of:

gastric cancer; renal cancer; cholanigoma; lung cancer; brain cancer; cervical cancer; colon cancer; head and neck cancer; hepatoma; non-small cell lung cancer; melanoma; mesothelioma; multiple myeloma; ovarian cancer; sarcoma; and thyroid cancer.

17. A method according to any preceding claim, in which one or more primers are dual domain primers.

18. A method according to any preceding claim, in which the amplified products from two or more primer pairs of a primer subset can be distinguished.

19. A method according to any preceding claim, in which the amplified products from two or more primer pairs of a primer subset are distinguished by being of distinct sizes or by being labeled with different detectable labels.

20. A method according to any preceding claim, in which the amplified products from the first set of primers and the second set of primers are distinguished by being labeled with different detectable labels.

21. A method according to any preceding claim, in which one or more primers are selected from the group consisting of SEQ ID NOs: 1-83 and 89-124.

22. A method according to any preceding claim, in which the primers are present in the reaction mixture at the concentrations of Table 2.