

KIT Mutation Status (Exon 9 and 11)

TEST DESCRIPTION

Gastrointestinal Stromal Tumor (GIST) is a mesenchymal neoplasm that arises primarily in the gut wall and is typically characterized by the expression of the receptor tyrosine kinase *KIT* (CD117)¹. Activating *KIT* gene mutations including deletions, substitutions, insertions, and duplications have been identified to in 80–85% of newly diagnosed GIST patients². These mutations have been found to influence the clinical response of *KIT*/PDGFR targeted therapies such as imatinib (Gleevec®)^{3,4,5}. In addition, a portion of imatinib treated GIST patients relapse with secondary *KIT* mutations resistant to imatinib suppression of *KIT* tyrosine kinase activation⁶.

MolecularMD offers three validated assays for assessment of *KIT* mutational status to support GIST patient treatment with targeted tyrosine kinase inhibitor therapy. The MolecularMD CLIA/CAP certified reference laboratory is currently active in providing *KIT* mutational testing for international Phase III clinical trials.

DISEASE RELEVANCE:

Gastrointestinal Stromal Tumor (GIST)

DRUG RELEVANCE:

KIT and PDGFR Tyrosine Kinase Inhibitors (TKI's)

KIT Exon 9 Mutation Ala502_Tyr503dup by Q-PCR

Ala502_Tyr503dup is the most common mutation found in *KIT* exon 9. The mutation has been implicated in dose escalation requirements of imatinib for treatment of GIST. MolecularMD offers a rapid, sensitive Q-PCR assay to specifically identify *KIT* exon 9 Ala502_Tyr503dup in solid tumor formalin fixed paraffin embedded (FFPE) samples.

KIT EXON 9 MUTATION Ala502_Tyr503dup by Q-PCR

Method	Q-PCR
Sensitivity	1 to 5%
Turn-around time	Less than 10 business days
Specimen Type	Formalin Fixed Paraffin Embedded (FFPE) or fresh tissue
Specificity	Greater than 95%

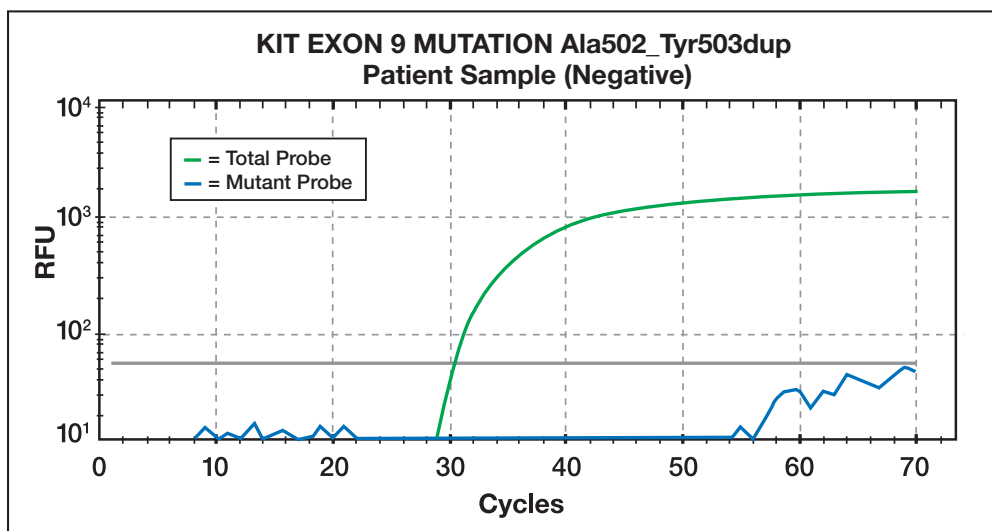


Figure 1: The Q-PCR graph depicts specificity between total and mutant probe. The total probe recognizes exon 9 that is present in the wild type plasmid, the wild type human lymphocyte DNA, and the mutant plasmid while the mutant probe recognizes only the *KIT* exon 9 Ala502_Tyr503dup mutation present in the mutant plasmid construct.

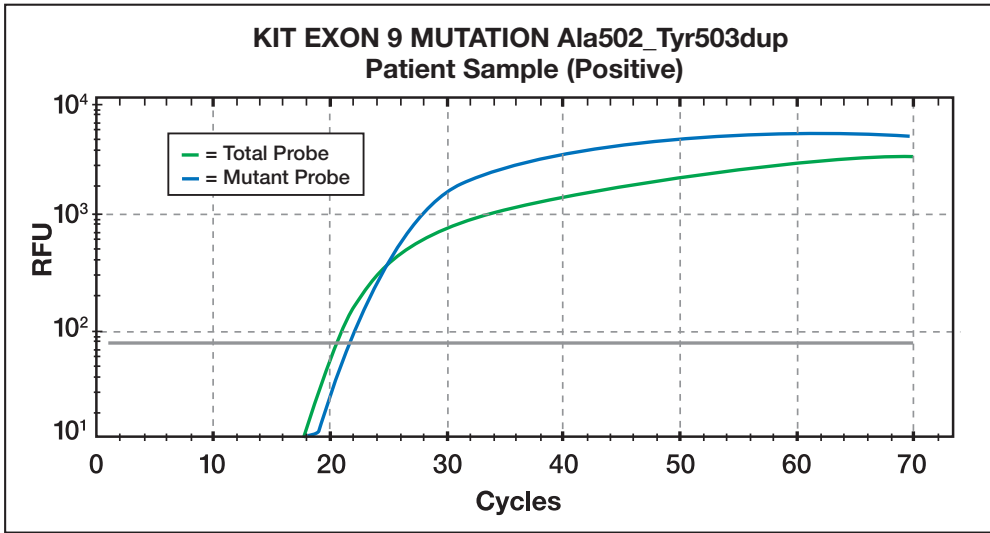


Figure 2: GIST patient sample heterozygous for *KIT* Exon 9 Ala502_Tyr503dup using 200 ng of FFPE derived genomic DNA material. Exon 9 Total probe Ct=20.74. Exon 9 mutant probe Ct=21.80. The one cycle shift reflects a heterozygous sample.

KIT Exon 9 and 11 Direct Sequencing

A wide variety of clinically relevant *KIT* exon 9 and 11 mutations including deletions, substitutions, insertions, and duplications occur in newly diagnosed and imatinib resistant GIST patients. MolecularMD offers direct sequencing assays for *KIT* exon 9 and 11 to identify both common and rare aberrations.

KIT Exon 9 and 11 Direct Sequencing

Method	Direct DNA sequencing
Sensitivity	10-20% mutant allele
Turn-around time	10-15 business days
Specimen Type	Formalin Fixed Paraffin Embedded (FFPE) or fresh tissue

Additional Information

Contact a MolecularMD business development representative for further information on *KIT* Mutational Testing performance and validation (sales@molecularmd.com).