

KIT (D816V) Mutation by PCR

FOR DIAGNOSIS OF SYSTEMIC MASTOCYTOSIS AND SEMINOMA

Clinical Background

- Human systemic mast cell disease (SMCD) is a clonal disorder of the mast cell and its precursor cells that results in the infiltration and accumulation of clonally-derived mast cells in one or more organs. The most commonly affected organ is the bone marrow, but the liver, spleen, or gastrointestinal tract may also be affected.
- KIT is a type III receptor tyrosine kinase expressed on mast cells (MCs) and others that acts as a ligand for stem cell factor (SCF). Upon binding of SCF, the KIT undergoes dimerization and autophosphorylation, leading to activation of signaling pathways including PI3 kinase and v-src sarcoma (Schmidt-Ruppin A-2) viral oncogene homolog (Src), which lead to cell proliferation and inhibition of apoptosis.
- The D816V heterozygous activating mutation of *KIT* results in a single base pair substitution of A in wild-type to T in mutant at nucleotide position 2447. This substitution changes the amino acid at codon 816 from aspartic acid (D) to valine (V), leading to constitutive activation of the tyrosine kinase II domain (TK2), resulting in cell proliferation and inhibition of apoptosis. Moreover, patients who express D816V show imatinib resistance.
- The D816V mutation identifies a group of SMCD that does not respond to imatinib. Rapid and accurate diagnosis is essential for guiding the choice of therapy. Histology is not specific for D816V.

Indication for Ordering

The principal use for this test is to detect the presence of the D816V mutation in patients with SM. This test is not intended to detect minimal residual disease.

Methodology

Genomic DNA extracted from archived paraffin-embedded tissue, fresh/frozen tissue, or whole blood/bone marrow samples is subjected to PCR amplification of a fragment of the *KIT* gene as a control and allele-specific amplification of D816V. PCR products are detected by electrophoresis and UV-illumination of ethidium bromide-stained gels.

Interpretation

- Not Detected: D816V mutation is not detected.
- Positive: D816V mutation is detected.

Limitation

Results of this test must always be interpreted in the context of morphologic and other relevant data and should not be used alone for a diagnosis of malignancy. A negative result does not preclude the presence of the D816V mutation below the limit of detection.

Reference

1. Aiken C. Molecular diagnosis of mast cell disorders: a paper from the 2005 William Beaumont Hospital Symposium on Molecular Pathology. *J Mol Diagn* 2006;8(4):412-9.

Test Information

0040132	KIT (D816V) Mutation by PCR, Tissue
0040136	KIT (D816V) Mutation by PCR, Paraffin
0040137	KIT (D816V) Mutation by PCR, Fluid

For specific collection, transport, and testing information, refer to the ARUP website at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.