

PIK3CA Mutation Detection by Pyrosequencing

FOR HELPING PREDICT PATIENT PROGNOSIS AND THERAPEUTIC RESPONSE IN MANY CANCERS, INCLUDING THOSE OF THE COLON, OVARY, BREAST, BRAIN, LIVER, AND LEUKEMIA

Test Highlights

- The majority (~80 percent) of somatic mutations in *PIK3CA* are located in three hotspots: two in exon 9 in the helical domain of codons 542 and 545 and one in codon 1047 in the exon 20 kinase domain.¹
- *PIK3CA* mutational status may indicate a tumor that will respond to drugs targeted at genes downstream of *PIK3CA* in the AKT/mTOR-signaling cascade²
- Mutations in exon 20 of this gene can also inhibit therapeutic response to EGFR-targeted therapies in patients with metastatic colorectal cancer.³
- This test excludes interference from a pseudogene on chromosome 22 with >95 percent homology to *PIK3CA*.

Disease Overview

- In the United States, colorectal cancer is the third most common form of cancer; individuals have a 6 percent lifetime risk of developing this disease.
- Most cancer is caused by somatic mutations and is not hereditary.
- Somatic mutations in *PIK3CA* occur in up to 30 percent of common epithelial cancer, which includes breast, colon, prostate, and endometrial cancers.⁴

Indications for Ordering

- *PIK3CA* exon 20 mutations may indicate a tumor that will not respond to anti-EGFR therapies (as in colon cancer).
- *PIK3CA* mutations may indicate a tumor that will respond to drugs targeted at genes downstream of *PIK3CA* in the AKT/mTOR-signaling cascade.
- *PIK3CA* mutations are associated with a significant increase in colon cancer-specific mortality and shorter breast cancer-specific and disease-free survival.^{5,6}

Interpretation

- The presence of an oncogenic mutation in codons 542, 545, and 1047 of *PIK3CA* is indicative of a tumor that may respond to drugs targeted at genes downstream of *PIK3CA* in the AKT/mTOR-signaling cascade.
- Mutations in exon 20 of this gene may also indicate tumors (e.g., metastatic colorectal cancer) that will not respond to EGFR-targeted therapies.

Methodology

- Tumor tissue is microdissected and DNA extracted from five micron sections of formalin-fixed, paraffin-embedded tissue blocks.
- Regions covering codons 542, 545, and 1047 of the *PIK3CA* gene

are amplified using polymerase chain reaction (PCR), followed by pyrosequencing.

- All potentially oncogenic mutations in codons 542, 545, and 1047 are detected.
- Limit of detection for this assay is 10 percent mutant alleles.

Limitations

- Mutations in other locations within the *PIK3CA* gene or in any other gene will not be detected.
- Absence of *PIK3CA* mutations does not guarantee a positive response to anti-EGFR therapies in metastatic colorectal cancer.
- Presence of mutations in codons 542, 545, and 1047 does not guarantee a positive response to therapies targeted to the AKT/mTOR-signaling cascade.

References

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2. Di Nicolantonio F, et al. Deregulation of the PI3K and KRAS signaling pathways in human cancer cells determines their response to everolimus. *J Clin Invest* 2010;120(8):2858–66.
3. De Roock W, et al. Effects of KRAS, BRAF, NRAS, and PIK3CA mutations on the efficacy of cetuximab plus chemotherapy in chemotherapy-refractory metastatic colorectal cancer: a retrospective consortium analysis. *Lancet Oncol* 2010;11(8):753–62.
4. Engelman JA. Targeting PI3K signalling in cancer: opportunities, challenges and limitations. *Nat Rev Cancer* 2009;9(8):550–62.
5. Aleskandarany MA, et al. PIK3CA expression in invasive breast cancer: a biomarker of poor prognosis. *Breast Cancer Res Treat* 2010;122(1):45–53.
6. Ogino S, et al. PIK3CA mutation is associated with poor prognosis among patients with curatively resected colon cancer. *J Clin Oncol* 2009;27(9):1477–84.

Test Information

2004510 *PIK3CA* Mutation Detection

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.