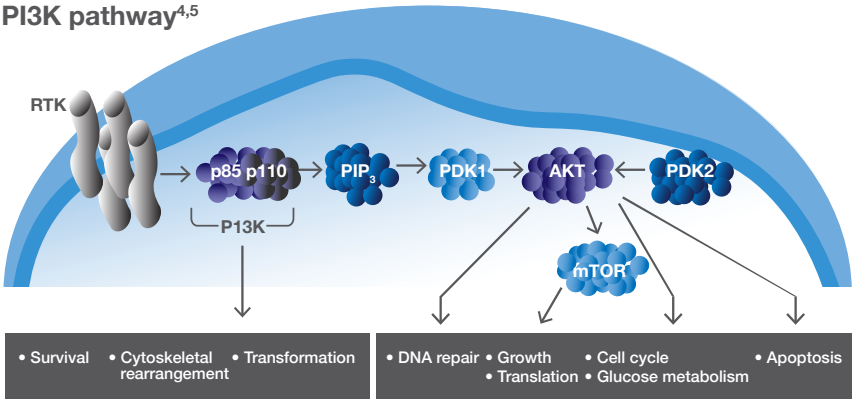
Everything you need to know about *PIK3CA* mutation testing in 2 minutes

Why should you test for *PIK3CA*?

The *PIK3CA* pathway is one of the most frequently altered pathways in human cancers, especially in breast cancer. Many mutations in the *PIK3CA* gene have been shown to be oncogenic, representing an important event in the initiation and progression of this tumor type.

Approximately 40% of *HR+/HER2–* advanced breast cancer exhibit mutations in the *PIK3CA* gene. While the mutations can occur across the entire gene, the most common are observed in specific codons: p.E542X and p.E545X in exon 10 (corresponding to the helical domain), and p.H1047R in exon 21 (corresponding to the kinase domain).[1]

PI3K pathway[4,5]



Adapted with permission from Vivanco & Sawyers, 2002.

PIK3CA gene role in tumor pathogenesis

The *PIK3CA* gene encodes for the p110 alpha (p110α) protein, which is the catalytic sub-unit of the enzyme named phosphatidylinositol 3-kinase (PI3K). PI3K is a major regulator of cell growth and proliferation, metabolism, and migration via the PI3K/AKT/mTOR pathway. Abnormal PI3K signaling events are common in many cancers, with multiple studies showing this pathway to be dysregulated in up to 70% of human tumors.[2]

The role of *PIK3CA* in cancer has been extensively analyzed in both translational studies and clinical trials, with several investigational targeted therapies being developed against its mutated forms.

ThermoFisher SCIENTIFIC

Testing for *PIK3CA*

PIK3CA mutations can be identified using the following techniques:

- Reverse transcription polymerase chain reaction (RT-PCR) or Sanger sequencing–based assays—allow for testing of one gene and are often limited in the number of variants detected
- Next-generation sequencing (NGS)—allow for testing of multiple relevant biomarkers and large numbers of variants

Advantages of NGS

PIK3CA mutation hotspots have been identified in a large study of 24,592 clinical tumor samples at 48 different codons, with the majority having more than one specific variant.[3] A review of *PIK3CA* data in ClinVar shows 75 different potentially pathogenic variants at 44 different codons. Most non–NGS-based assays can detect only a limited number of the most common mutations, and they cannot cover the full spectrum of potentially relevant variants.

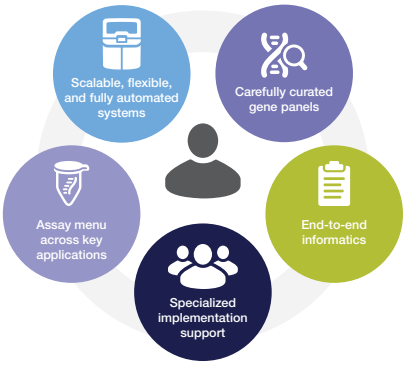
- Detection of *PIK3CA* alterations with full coverage of all exonic regions, which enables analysis of more variants beyond the common few; in this way, all potential candidates for clinical research studies can be identified
- Detection of other co-occurring genomic tumor alterations at the same time, from the same sample, enabling fast assessment of comprehensive relevant tumor profile

Key biomarkers in breast cancer clinical research

Breast cancer subtype	Biomarker	Possible testing method
Any	*HER2*	Single-gene testing methods (IHC or FISH) or **NGS**
Any	*BRCA1* mutations/CNV (full CDS) *BRCA2* mutations/CNV (full CDS)	Sanger sequencing or **NGS**
HR+/HER2–	*PIK3CA* mutations (hotspots)	PCR or **NGS**
HR-/HER2–	PD-L1 expression (≥1% on tumor-infiltrating immune cells)	IHC
Any	*NTRK* fusions	Single-gene testing methods (IHC, PCR, or FISH) or **NGS**
Any	MSI-H/dMMR	IHC, PCR, or **NGS**
Any	*BRCA* 1/2	Sanger sequencing or **NGS**

Oncomine Solutions for *PIK3CA* mutation testing

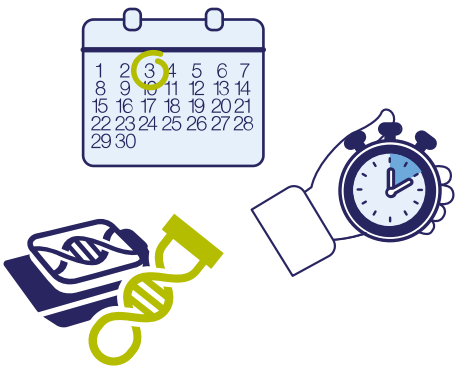
Oncomine™ Solutions are integrated end-to-end, sample-to-answer NGS workflows for precision oncology research testing. They have been carefully designed for oncology research labs and are easy to implement and simple to use.



- Relevant biomarker coverage and detection of all key *PIK3CA* variants including C420R, E542K, E545K, E545G, E545D, E545A, Q546E, Q546R, Q546K, H1047R, H1047L, and H1047Y
- A complete end-to-end workflow, including bioinformatics
- Fast, 1–3 day turnaround time from sample to report
- Low sample input requirements, enabling testing of very small samples

Featured solution

Empower your lab to deliver NGS genomic profiles with the speed and simplicity of immunohistochemistry. The Ion Torrent™ Oncomine™ Precision Assay, combined with the Ion Torrent™ Genexus™ System, will let you experience a whole new world of easy NGS.



- **One-day hands-off workflow** with only two user touchpoints and 10 minutes of hands-on time*
- Compatible with **formalin-fixed, paraffin-embedded (FFPE) tissue as well as liquid biopsy samples** and small batch sizes

Ion Torrent™ Oncomine™ assays for *PIK3CA* testing

PIK3CA variants	FFPE			Liquid biopsy		Dual use (FFPE + Liquid)
	Oncomine Comprehensive Assay V3 and Plus	Oncomine Focus Assay	Ion AmpliSeq Cancer Hot Spot Panel V2	Oncomine cfDNA Breast Assay	Oncomine cfTNA Pan Cancer Assay	Oncomine Precision Assay
p. C420R	x	x	x	x	x	x
p. E542K	x	x	x	x	x	x
p. E545K	x	x	x	x	x	x
p. E545A	x	x	x	Covered	x	x
p. E545G	x	x	x	x	x	x
p. E545D	x	x	x	Covered	x	x
p. Q546E	x	x	x	Covered	x	x
p. Q546K	x	x	x	x	x	x
p. Q546R	x	x	x	x	x	x
p. H1047Y	x	x	x	x	x	x
p. H1047R	x	x	x	x	x	x
p. H1047L	x	x	x	x	x	x

x — Called by hotspot file

Covered — Not in hotspot file, but designed on the panel and can be called informatically

Make your testing workflow time- and cost-effective: simply add breast cancer specimens to your analysis and sequence them along with other tumors.

References

1. Cerami E, Gao J, Dogrusoz U, et al. The cBio cancer genomics portal: an open platform for exploring multidimensional cancer genomics data. *Cancer Discov.* 012;2(5):401-404.
2. Cerami E, Gao J, Dogrusoz U, et al. The cBio cancer genomics portal: an open platform for exploring multidimensional cancer genomics data. *Cancer Discov.* 012;2(5):401-404.
3. Chang MT, Asthana S, Gao SP, Lee BH, et al. Identifying recurrent mutations in cancer reveals widespread lineage diversity and mutational specificity. *Nat Biotechnol.* 2016 Feb;34(2):155-632017;41(11):1547-1551.

* Specimen-to-report workflow will be available after the Ion Torrent™ Genexus™ Purification System and integrated reporting capabilities are added in 2020. Fully integrated specimen-to-report workflow will be available after the Ion Torrent™ Genexus™ Software 6.4 update.

Learn more at **oncomine.com**

ThermoFisher SCIENTIFIC