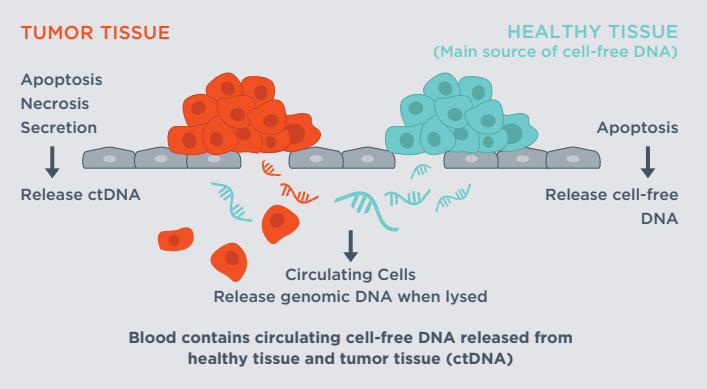
Technical Specifications

FOUNDATIONACT®

FoundationACT is a liquid biopsy assay for solid tumors that analyzes circulating tumor DNA (ctDNA) in blood.

Clinical Background

Cell-free DNA (cfDNA) is DNA that circulates freely in the bloodstream. In a cancer patient, tumor cells that undergo apoptosis or necrosis also shed cell-free DNA. The tumor derived cell-free DNA is called circulating tumor DNA (ctDNA). By analyzing cell-free DNA isolated from a patient's blood, we can identify clinically relevant genomic alterations in ctDNA and match these alterations to targeted therapies and clinical trials.



Blood contains circulating cell-free DNA released from healthy tissue and tumor tissue (ctDNA)

Methods

FoundationACT liquid biopsy:

- Analyzes blood samples from patients with solid tumors including lung, breast, colon, etc.
- Uses a hybrid-capture, next-generation sequencing test method combined with proprietary computational algorithms that enable accurate variant calls by discriminating sequencing artifacts from bona fide mutations.
- Identifies four classes of genomic alterations (base substitutions, insertions and deletions, copy number alterations, and rearrangements).
- Sequences select clinically relevant genomic alterations in 62 commonly altered oncogenes.
- Features an optimized laboratory process to achieve high sensitivity and specificity, with enhanced extraction methodology to generate high quantity and quality ctDNA.
- Utilizes proprietary FragTag™ technology to accurately identify unique ctDNA fragments from plasma, further increasing sensitivity.

PERFORMANCE SPECIFICATIONS			
Performance at 5,000x Unique Coverage	Mutant Allelle Frequency (MAF) / Tumor Fraction[1]	Sensitivity[2]	Positive Predictive Value (PPV)[2]
Base substitutions	≥ 0.5%	>98.9% (CI 98.4%-99.4%)	>99.9% (CI 99.6%-100%)
	0.1% - 0.49%	67.3% (CI 61.7%-72.5%)	93.6% (CI 89.2%-96.3%)
Insertions/Deletions (1-40 bp)	≥ 1%	>99.9% (CI 97.2%-100%)	98.8% (CI 95.3%-99.8%)
	0.1%-0.99%	86.2% (CI 71.1%-95.1%)	100.0% (CI 93.9%-100%)
Rearrangements[3]	≥ 1%	>99.9% (CI 90.8%-100%)	98.0% (CI 87.8%-99.9%)
	<1%	86.8% (CI 71.1%-95.1%)	>99.9% (CI 87.0%-100%)
Copy Number Amplifications[4]	≥ 20%	95.3% (CI 82.9%-99.2%)	97.6% (CI 85.9%-99.9%)
Reproducibility (average concordance between replicates)		96.8% inter-batch precision 100% intra-batch precision	
Specimen Type		Peripheral whole blood (See Specimen Instructions for details)	
Turnaround Time		<2 Weeks[5]	

CI = Confidence Interval

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Reporting

- Test results are provided in an interpretive report, curated by biomedical informatics scientists, and approved by on-site board-certified and licensed pathologists.
- Genomic findings are listed with clinically relevant targeted therapies and clinical trials.
- Reported alterations may indicate response or lack of response to validated targets for therapy (approved or in clinical trials), or may be unambiguous drivers of oncogenesis based on reported scientific knowledge.
- Test results are available via our online portal at www.foundationmedicine.com* or by fax.

*Visit *foundationmedicine.com* to create an online account.

Additional Features

Mutant Allele Fraction (MAF)

The MAF listed denotes the frequency of the mutant allele identified in the sample. It is reported for base substitutions and insertions and deletions (indels).

Connectivity with Prior Tissue-Based Testing

When additional genomic testing with Foundation Medicine precedes FoundationACT, the report will include a comparison of the current FoundationACT results and prior results in a single report.

Current Gene List†

Entire coding sequence (base substitutions, indels, copy number alterations).

BRCA1	*BRCA2*	*CCND1*	*CD274* (*PD-L1*)	*CDH1*	*CDK4*	*CDK6*	*CDKN2A*	*CRKL*
EGFR	*ERBB2*	*ERRFI1*	*FGFR1*	*FGFR2*	*FOXL2*	*KRAS*	*MDM2*	*MET*
MYC	*MYCN*	*NF1*	*PDCD1LG2* (*PD-L2*)	*PTEN*	*PTPN11*	*SMO*	*TP53*	*VEGFA*

Select Exons‡

ABL1	*AKT1*	*ALK*	*ARAF*	*BRAF*	*BTK*	*CTNNB1*	*DDR2*	*ESR1*
EZH2	*FGFR3*	*FLT3*	*GNA11*	*GNAQ*	*GNAS*	*HRAS*	*IDH1*	*IDH2*
JAK2	*JAK3*	*KIT*	*MAP2K1* (*MEK1*)	*MAP2K2* (*MEK2*)	*MPL*	*MTOR*	*MYD88*	*NPM1*
NRAS	*PDGFRA*	*PDGFRB*	*PIK3CA*	*RAF1*	*RET*	*TERT*		

Select Rearrangements

ALK	*EGFR*	*FGFR3*	*PDGFRA*	*RET*	*ROS1*

Notes

1 Copy Number Amplifications were calculated using Tumor Fraction.
2 95% Confidence Interval.
3 Performance for gene fusions within targeted introns only. Sensitivity for gene fusions occurring outside targeted introns or in highly repetitive intronic sequence contexts is reduced.
4 Copy-number ≥8 in genes with at least four targets.
5 Based on typical turnaround time from receipt of sample.
† Current as of September 2017. Please visit foundationmedicine.com for the most up-to-date gene list.
‡ Detailed list available upon request.

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