

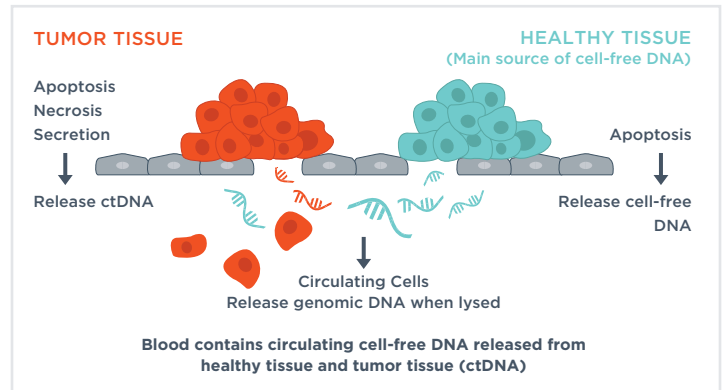
Technical Specifications

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.



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			
	Mutant Allele Frequency (MAF)/ Tumor Fraction ¹	Sensitivity ²	Positive Predictive Value (PPV) ²
Base substitutions	≥ 0.5%	99.3% (CI 99.1% - 99.4%)	100% (CI >99.9% - 100%)
	0.25% - 0.5%	95.7% (CI 94.9% - 96.4%)	100% (CI 99.8% - 100%)
	0.125% - 0.25%	70.0% (CI 68.3% - 71.6%)	99.9% (CI 99.8% - 100%)
Insertions/Deletions (Indels) (1-40bp)	≥ 0.5%	98.5% (CI 97.3% - 99.2%)	100% (CI 99.4% - 100%)
	0.25% - 0.5%	86.6% (CI 81.4% - 90.5%)	100% (CI 97.8% - 100%)
	0.125% - 0.25%	68.5% (CI 62.1% - 74.3%)	100% (CI 97.1% - 100%)
Rearrangements ³	≥0.5%	100% (CI 77.1% - 100%)	100% (CI 77.1% - 100%)
	0.25% - 0.5%	100% (CI 56.1% - 100%)	100% (CI 56.1% - 100%)
	0.125% - 0.25%	80% (CI 29.9% - 99.0%)	100% (CI 39.6% - 100%)
Copy Number Amplifications (CNA) ⁴	≥ 20% ctDNA fraction	95.3% (CI 82.9%-99.2%)	97.6% (CI 85.9%-99.9%)
	< 20% ctDNA fraction	Varies depending on amplitude of CNA and ctDNA fraction	
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	

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. For genes with ≥ 4 targets. 5. Based on typical turnaround time from receipt of sample.



Reporting

- Test results are provided in an interpretive report, curated by biomedical informatics scientists, and approved by 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.

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).

<i>BRCA1</i>	<i>BRCA2</i>	<i>CCND1</i>	<i>CD274 (PD-L1)</i>	<i>CDH1</i>	<i>CDK4</i>	<i>CDK6</i>	<i>CDKN2A</i>	<i>CRKL</i>
<i>EGFR</i>	<i>ERBB2</i>	<i>ERF1</i>	<i>FGFR1</i>	<i>FGFR2</i>	<i>FOXL2</i>	<i>KRAS</i>	<i>MDM2</i>	<i>MET</i>
<i>MYC</i>	<i>MYCN</i>	<i>NF1</i>	<i>PDCD1LG2 (PD-L2)</i>	<i>PTEN</i>	<i>PTPN11</i>	<i>SMO</i>	<i>TP53</i>	<i>VEGFA</i>

Select Exons[‡]

<i>ABL1</i>	<i>AKT1</i>	<i>ALK</i>	<i>ARAF</i>	<i>BRAF</i>	<i>BTK</i>	<i>CTNNA1</i>	<i>DDR2</i>	<i>ESR1</i>
<i>EZH2</i>	<i>FGFR3</i>	<i>FLT3</i>	<i>GNA11</i>	<i>GNAQ</i>	<i>GNAS</i>	<i>HRAS</i>	<i>IDH1</i>	<i>IDH2</i>
<i>JAK2</i>	<i>JAK3</i>	<i>KIT</i>	<i>MAP2K1 (MEK1)</i>	<i>MAP2K2 (MEK2)</i>	<i>MPL</i>	<i>MTOR</i>	<i>MYD88</i>	<i>NPM1</i>
<i>NRAS</i>	<i>PDGFRA</i>	<i>PDGFRB</i>	<i>PIK3CA</i>	<i>RAF1</i>	<i>RET</i>	<i>TERT</i>		

Select Rearrangements

<i>ALK</i>	<i>EGFR</i>	<i>FGFR3</i>	<i>PDGFRA</i>	<i>RET</i>	<i>ROS1</i>
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References

* Visit foundationmedicine.com to create an online account.

† Current as of May 2018. Please visit foundationmedicine.com for the most up-to-date gene list.

‡ Detailed list available upon request.

