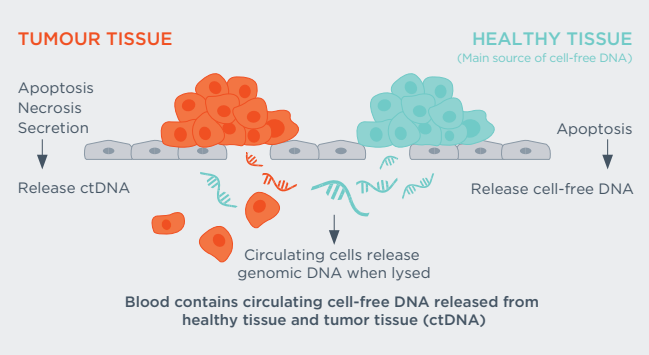
FOUNDATIONONE®LIQUID

Technical Specifications

FoundationOne®Liquid is a liquid biopsy test for solid tumours that analyses circulating tumour DNA (ctDNA) in blood.

Clinical Background

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



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

Methods

FoundationOne®Liquid:

- Analyses blood samples from patients with solid tumours 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 artefacts from bona fide mutations.
- Identifies four classes of genomic alterations (base substitutions, insertions and deletions, copy number alterations, and rearrangements), and reports high microsatellite instability.
- Evaluates select clinically relevant genomic alterations in 70 commonly altered oncogenes.
- Features an optimized laboratory process to achieve high sensitivity and specificity, with enhanced extraction methodology to generate a large amount of high quality ctDNA.
- Utilizes proprietary technology to accurately identify unique ctDNA fragments from plasma

PERFORMANCE SPECIFICATIONS[1]			
	Mutant Allele Frequency (MAF) / **Tumour Fraction**[2]	**Sensitivity**[3]	**Positive Predictive Value** (PPV)[3]
Base substitutions	> 0.5%	99.9% (CI 99.7% – 99.9%)	100% (CI 99.9% – 100%)
	0.25% – 0.5%	95.8% (CI 94.5% – 96.9%)	99.8% (CI 99.3% – 99.9%)
	0.125% – 0.25%	68.4% (CI 65.7% – 70.9%)	96.1% (CI 94.8% – 97.1%)
Insertions/Deletions (Indels) (1–40bp)	> 0.5%	99.7% (CI 98.7% – 99.9%)	100% (CI 99.3% – 100%)
	0.25% – 0.5%	87.7% (CI 81.1% – 92.2%)	98.8% (CI 95.4% – 99.8%)
	0.125% – 0.25%	60.5% (CI 52.7% – 67.7%)	96.8% (CI 92.3% – 98.8%)
Rearrangements[4]	> 0.5%	100% (CI 85.9% – 100%)	100% (CI 85.9% – 100%)
	0.25% – 0.5%	89.4% (CI 65.5% – 98.2%)	100% (CI 77.1% – 100%)
	0.125% – 0.25%	68.4% (CI 43.5% – 86.4%)	100% (CI 71.7% – 100%)
Copy Number Amplifications (CNA)[4]	≥ 20%	95.3% (CI 82.9% – 99.2%)	97.6% (CI 85.9% – 99.9%)
	< 20%	Varies depending on amplitude of CNA and ctDNA fraction	
Microsatellite Instability (MSI)[6]	> 2.0%	92.0% (CI 72.5% – 98.6%)	100% (CI 82.2% – 100%)
Reproducibility (average concordance between replicates)		97.7% inter-batch precision 95.9% intra-batch precision	
Specimen Type		Peripheral whole blood (see Specimen Instructions for details)	
Turnaround Time[7]		< 2 Weeks	

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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, immunotherapies, and clinical trials.
- Reported alterations may indicate response or lack of response to therapy (approved or in clinical trials), or may be drivers of oncogenesis based on reported scientific knowledge.
- Reports include microsatellite instability (MSI) status, a biomarker that may help predict response to checkpoint inhibitors.
- 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).

Visualization of MAF

The clinical report includes a graphic representation of MAF. If multiple FoundationOne®Liquid tests are ordered in the patient's treatment journey, the graphic will show the relative change in MAF which will allow treating physicians to better understand the evolution of a patient's disease and may help to inform the next steps in patient care.

Current Gene List†

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

APC	*AR*	*ATM*	*BRCA1*	*BRCA2*	*CCND1*	*CD274* (PD-L1)	*CDH1*	*CDK4*
CDK6	*CDK12*	*CDKN2A*	*CHEK2*	*CRKL*	*EGFR*	*ERBB2*	*ERRFI1*	*FGFR1*
FGFR2	*FOXL2*	*KRAS*	*MDM2*	*MET*	*MYC*	*MYCN*	*NF1*	*PALB2*
PDCD1LG2 (PD-L2)		*PTEN*	*PTPN11*	*RB1*	*SMO*	*STK11*	*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*	*ROS1*	*TERT*	

Select Rearrangements

ALK	*EGFR*	*FGFR2*	*FGFR3*	*PDGFRA*	*RET*	*ROS1*

To learn more about our analytical validation based on a prior version of the test called FoundationACT (62 genes), see our publication in the Journal of Molecular Diagnostics:§ "Analytical validation of a hybrid capture–based next-generation sequencing clinical assay for genomic profiling of cell-free circulating tumour DNA".

References

1. Data on file.
2. Copy number amplifications were calculated using tumour fraction.
3. 95% confidence interval.
4. 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.
5. Copy number ≥8.
6. Reported when MSI is determined to be high.
7. Based on typical turnaround time from receipt of sample..

* Visit foundationmedicine.com to create an online account.

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

‡ Detailed list available upon request.

§ Clark TA, et al. Analytical validation of a hybrid capture–based next-generation sequencing clinical assay for genomic profiling of cell-free circulating tumour DNA. J of Mol Diagn. 2018;published online ahead of print.

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