Technical Specifications

FOUNDATIONONE®

FoundationOne® is a comprehensive genomic profiling assay for all solid tumors (including lung, colon, breast, melanoma, ovarian, etc.).

Methods

- Uses a hybrid-capture, next-generation sequencing test method.
- Identifies all four classes of genomic alterations (base substitutions, insertions and deletions, copy number alterations, and rearrangements) as well as select genomic signatures (tumor mutational burden and microsatellite instability).
- Covers a total of 322 unique genes—the entire coding region of 315 cancer-related genes, and select introns from 28 genes that are often rearranged or altered in cancer.
- Performs at a median depth of coverage of 500X.

PERFORMANCE SPECIFICATIONS			
Sensitivity	Base Substitutions	At Mutant Allele Frequency ≥10%	>99.9% (CI 99.6%-100%)
		At Mutant Allele Frequency 5-10%	99.3% (CI 98.3%-99.8%)
	Insertions/Deletions (1-40 bp)	At Mutant Allele Frequency ≥20%	97.9% (CI 92.5%-99.7%)
		At Mutant Allele Frequency 10-20%	97.3% (CI 90.5%-99.7%)
	Copy Number Alterations – Amplifications (ploidy <4, Amplification with Copy Number ≥8)	At ≥30% tumor nuclei	>99.0% (CI 93.6%-100%)
		At 20% tumor nuclei	92.6% (CI 66.1%-99.8%)
	Copy Number Alterations – Deletions (ploidy <4, Homozygous Deletions)	At ≥30% tumor nuclei	97.2% (CI 85.5%-99.9%)
		At 20% tumor nuclei	88.9% (CI 51.8%-99.7%)
	Rearrangements (selected rearrangements in specimens with ≥20% tumor nuclei)[1]		>90.0%[2] >99.0% for ALK fusion[3] (CI 89.1%-100%)
Specificity of all variant types		Positive Predictive Value (PPV)	>99.0%
Reproducibility		Average concordance between replicates	96.4% inter-batch precision 98.9% intra-batch precision
Immunotherapy Biomarkers		TMB[4], MSI[5]	
Specimen Type		FFPE block or slide (see Specimen Instructions for more details)	
Turnaround Time		2 Weeks[6]	

CI = Confidence Interval

Reporting

- Test results are provided in an interpretive report, curated by biomedical informatics scientists, and approved by on-site board-certified pathologists.
- Genomic findings are listed with clinically relevant targeted therapies, immunotherapies, 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.
- Pertinent negative results in certain disease-specific genes (e.g. *KRAS* in colon cancer, *EGFR* in lung cancer) are displayed on the front page if no known oncogenic alterations are found.
- Reports include tumor mutational burden (TMB) and microsatellite instability (MSI) status—biomarkers that may help predict response to checkpoint inhibitors.
- Test results are available via our online portal at www.foundationmedicine.com* or by fax.

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

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Current Gene List†

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

ABL1	*ABL2*	*ACVR1B*	*AKT1*	*AKT2*	*AKT3*	*ALK*	*AMER1 (FAM123B)*	*APC*
AR	*ARAF*	*ARFRP1*	*ARID1A*	*ARID1B*	*ARID2*	*ASXL1*	*ATM*	*ATR*
ATRX	*AURKA*	*AURKB*	*AXIN1*	*AXL*	*BAP1*	*BARD1*	*BCL2*	*BCL2L1*
BCL2L2	*BCL6*	*BCOR*	*BCORL1*	*BLM*	*BRAF*	*BRCA1*	*BRCA2*	*BRD4*
BRIP1	*BTG1*	*BTK*	*C11orf30 (EMSY)*	*CARD11*	*CBFB*	*CBL*	*CCND1*	*CCND2*
CCND3	*CCNE1*	*CD274 (PD-L1)*	*CD79A*	*CD79B*	*CDC73*	*CDH1*	*CDK12*	*CDK4*
CDK6	*CDK8*	*CDKN1A*	*CDKN1B*	*CDKN2A*	*CDKN2B*	*CDKN2C*	*CEBPA*	*CHD2*
CHD4	*CHEK1*	*CHEK2*	*CIC*	*CREBBP*	*CRKL*	*CRLF2*	*CSF1R*	*CTCF*
CTNNA1	*CTNNB1*	*CUL3*	*CYLD*	*DAXX*	*DDR2*	*DICER1*	*DNMT3A*	*DOT1L*
EGFR	*EP300*	*EPHA3*	*EPHA5*	*EPHA7*	*EPHB1*	*ERBB2*	*ERBB3*	*ERBB4*
ERG	*ERRFI1*	*ESR1*	*EZH2*	*FAM46C*	*FANCA*	*FANCC*	*FANCD2*	*FANCE*
FANCF	*FANCG*	*FANCL*	*FAS*	*FAT1*	*FBXW7*	*FGF10*	*FGF14*	*FGF19*
FGF23	*FGF3*	*FGF4*	*FGF6*	*FGFR1*	*FGFR2*	*FGFR3*	*FGFR4*	*FH*
FLCN	*FLT1*	*FLT3*	*FLT4*	*FOXL2*	*FOXP1*	*FRS2*	*FUBP1*	*GABRA6*
GATA1	*GATA2*	*GATA3*	*GATA4*	*GATA6*	*GID4 (C17orf39)*	*GLI1*	*GNA11*	*GNA13*
GNAQ	*GNAS*	*GPR124*	*GRIN2A*	*GRM3*	*GSK3B*	*H3F3A*	*HGF*	*HNF1A*
HRAS	*HSD3B1*	*HSP90AA1*	*IDH1*	*IDH2*	*IGF1R*	*IGF2*	*IKBKE*	*IKZF1*
IL7R	*INHBA*	*INPP4B*	*IRF2*	*IRF4*	*IRS2*	*JAK1*	*JAK2*	*JAK3*
JUN	*KAT6A (MYST3)*	*KDM5A*	*KDM5C*	*KDM6A*	*KDR*	*KEAP1*	*KEL*	*KIT*
KLHL6	*KMT2A (MLL)*	*KMT2C (MLL3)*	*KMT2D (MLL2)*	*KRAS*	*LMO1*	*LRP1B*	*LYN*	*LZTR1*
MAGI2	*MAP2K1 (MEK1)*	*MAP2K2 (MEK2)*	*MAP2K4*	*MAP3K1*	*MCL1*	*MDM2*	*MDM4*	*MED12*
MEF2B	*MEN1*	*MET*	*MITF*	*MLH1*	*MPL*	*MRE11A*	*MSH2*	*MSH6*
MTOR	*MUTYH*	*MYC*	*MYCL (MYCL1)*	*MYCN*	*MYD88*	*NF1*	*NF2*	*NFE2L2*
NFKBIA	*NKX2-1*	*NOTCH1*	*NOTCH2*	*NOTCH3*	*NPM1*	*NRAS*	*NSD1*	*NTRK1*
NTRK2	*NTRK3*	*NUP93*	*PAK3*	*PALB2*	*PARK2*	*PAX5*	*PBRM1*	*PDCD1LG2 (PD-L2)*
PDGFRA	*PDGFRB*	*PDK1*	*PIK3C2B*	*PIK3CA*	*PIK3CB*	*PIK3CG*	*PIK3R1*	*PIK3R2*
PLCG2	*PMS2*	*POLD1*	*POLE*	*PPP2R1A*	*PRDM1*	*PREX2*	*PRKAR1A*	*PRKCI*
PRKDC	*PRSS8*	*PTCH1*	*PTEN*	*PTPN11*	*QKI*	*RAC1*	*RAD50*	*RAD51*
RAF1	*RANBP2*	*RARA*	*RB1*	*RBM10*	*RET*	*RICTOR*	*RNF43*	*ROS1*
RPTOR	*RUNX1*	*RUNX1T1*	*SDHA*	*SDHB*	*SDHC*	*SDHD*	*SETD2*	*SF3B1*
SLIT2	*SMAD2*	*SMAD3*	*SMAD4*	*SMARCA4*	*SMARCB1*	*SMO*	*SNCAIP*	*SOCS1*
SOX10	*SOX2*	*SOX9*	*SPEN*	*SPOP*	*SPTA1*	*SRC*	*STAG2*	*STAT3*
STAT4	*STK11*	*SUFU*	*SYK*	*TAF1*	*TBX3*	*TERC*	*TERT* (Promoter only)	*TET2*
TGFBR2	*TNFAIP3*	*TNFRSF14*	*TOP1*	*TOP2A*	*TP53*	*TSC1*	*TSC2*	*TSHR*
U2AF1	*VEGFA*	*VHL*	*WISP3*	*WT1*	*XPO1*	*ZBTB2*	*ZNF217*	*ZNF703*

Select Rearrangements‡

ALK	*BCL2*	*BCR*	*BRAF*	*BRCA1*	*BRCA2*	*BRD4*	*EGFR*	*ETV1*
ETV4	*ETV5*	*ETV6*	*FGFR1*	*FGFR2*	*FGFR3*	*KIT*	*MSH2*	*MYB*
MYC	*NOTCH2*	*NTRK1*	*NTRK2*	*PDGFRA*	*RAF1*	*RARA*	*RET*	*ROS1*
TMPRSS2								

The analytic validation of FoundationOne, published in Nature Biotechnology[7] in 2013, is based on a prior version of the assay (236 genes, 19 select rearrangements), and established the performance specifications required to deliver the high level of accuracy routinely obtained for all classes of genomic alterations by FoundationOne. This updated version of FoundationOne met these performance specifications by demonstrating high concordance with genomic profiles of ninety-four clinical specimens previously profiled on the validated version of FoundationOne.

Notes

1 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.

2 Based on analysis of coverage and re-arrangement structure in the COSMIC database for the solid tumor fusion genes where alteration prevalence could be established, complemented by detection of exemplar rearrangements in cell line titration experiments.

3 Based on ALK rearrangement concordance analysis vs. a standard clinical FISH assay described in: Yelensky, R. et al. Analytical validation of solid tumor fusion gene detection in a comprehensive NGS-based clinical cancer genomic test, In: Proceedings of the 105th Annual Meeting of the American Association for Cancer Research; 2014 Apr 5-9; San Diego, CA. Philadelphia (PA): AACR; 2014. Abstract nr 4699.

4 Chalmers ZR, et. al. "Analysis of 100,000 human cancer genomes reveals the landscape of tumor mutational burden". Genome Med. 2017;9(1):34.

5 Hall MJ, et al. Multigene Panels to Evaluate Hereditary Cancer Risk: Reckless or Relevant? J Clin Oncol. 2016 Dec;34(34):4186-4187.

6 Based on typical turnaround time from receipt of sample.

7 Frampton GM, et al. Development and validation of a clinical cancer genomic profiling test based on massively parallel DNA sequencing. Nat Biotechnol. 2013 Nov;31(11):1023-31.

† Current as of September 2017. Please visit www.foundationmedicine.com for the most up-to-date gene list.

‡ Select Introns only. Detailed list available upon request.

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