Seraseq®

Solid Tumor FFPE DNA Reference Material

Package Insert

PLEASE NOTE:
THESE REAGENTS MUST NOT BE SUBSTITUTED FOR THE MANDATORY POSITIVE AND NEGATIVE CONTROL REAGENTS PROVIDED WITH MANUFACTURED TEST KITS.

NAME AND INTENDED USE

The Seraseq® Solid Tumor FFPE DNA Reference Material (RM) is a full process reference material formulated for use with Next Generation Sequencing (NGS) assays that detect mutations in key oncogenes and tumor suppressor genes associated with solid tumors. It is intended for use in the development, validation, and routine performance monitoring of laboratory tests designed to detect solid tumor gene variants by NGS assays under a given set of bioinformatics pipeline parameters.

For Research Use Only. Not for use in diagnostic procedures.

SUMMARY

A well-designed quality control program can provide confidence in the reliability of results obtained from unknown specimens. The use of independent reference products may provide valuable information concerning assay accuracy and bioinformatics pipeline analysis.

PRINCIPLES OF THE PROCEDURE

Seraseq Solid Tumor FFPE DNA RM is a full process reference material requiring extraction. The product consists of one 10 µm Formalin-Fixed Paraffin Embedded (FFPE) curl per vial. This reference material should follow the same workflow as unknown samples.

Seraseq Solid Tumor FFPE DNA RM contains 74 mutations (not including those present in the GM24385 background) that are associated predominantly with druggable mutations relevant to solid tumors (Table 2). Variant allelic frequency (VAF) is measured by targeted NGS and/or digital PCR (dPCR).

REAGENTS

Table 1. Seraseq Solid Tumor FFPE DNA RM

Material No.	Product
0710-3634	Seraseq® Solid Tumor FFPE DNA RM

Product consists of one 10 µm FFPE curl per vial.

WARNINGS AND PRECAUTIONS

For Research Use Only. Not for use in diagnostic procedures.
CAUTION: Handle Seraseq Solid Tumor FFPE DNA RM product as though it is capable of transmitting infectious agents. This product is formulated using an engineered human cell line derived from GM24385, which is a B-lymphocytic, male cell line from the Genome in a Bottle (GIAB) Project.

Safety Precautions

Use Centers for Disease Control and Prevention (CDC) recommended universal precautions for handling reference materials and human specimens[1]. Do not pipette by mouth; do not smoke, eat, or drink in areas where specimens are being handled. Clean any spillage by immediately wiping up with 0.5% sodium hypochlorite solution. Dispose of all specimens and materials used in testing as though they contain infectious agents.

Handling Precautions

Do not use Seraseq Solid Tumor FFPE DNA RM product beyond the expiration date. Avoid contamination of the product when opening and closing the vials.

STORAGE INSTRUCTIONS

Store Seraseq Solid Tumor FFPE DNA RM at 2-8°C. After opening, record the date opened and the expiration date on the vial.

INDICATIONS OF REAGENT INSTABILITY OR DETERIORATION

Seraseq Solid Tumor FFPE DNA Reference Material contains one 10 µm FFPE curl. It should appear as a white solid form. Alterations in this appearance may indicate instability or deterioration of the product and vials should be discarded.

PROCEDURE

Materials Provided

Seraseq Solid Tumor FFPE DNA RM consists of engineered cells which have been formalin treated and embedded in paraffin to create an FFPE block. Blocks are then sectioned into 10 µm curls. One 10 µm FFPE curl is provided per vial. This product only contains DNA variants and is not suitable for RNA or Proteomic analysis of targets.

Materials Required but not Provided

Seraseq Solid Tumor FFPE DNA RM requires extraction. Refer to instructions supplied by manufacturers of the extraction kit to be used.

Instructions for Use

Allow the product vial to come to room temperature before use. Seraseq Solid Tumor FFPE DNA RM must go through an extraction process. Refer to your assay procedures in order to determine the amount of extracted material to use in library preparation.

INTERPRETATION OF RESULTS

Seraseq Solid Tumor FFPE DNA RM is compatible with commercially available nucleic acid extraction methods commonly used for FFPE specimens. The product is designed to give a minimum yield of 100 ng DNA per curl when using AutoGen XTRACT Genomic DNA FFPE One-Step Kit (AutoGen, Cat. # XK405-72) or QIAamp DNA FFPE Tissue Kit (QIAGEN, Cat. # 56404) and ThermoFisher's Qubit dsDNA HS Assay.

For additional information on FFPE extraction methods refer to our blog here https://blog.lgcclinicaldiagnostics.com/ffpe.

Table 2 lists the DNA variants presented in the Seraseq Solid Tumor FFPE DNA Reference Material. Although VAFs are examined during manufacture using NGS assays and/or dPCR, the product does not have assigned values for mutation frequencies. There may be differences in observed allelic frequencies due to assay characteristics. Each laboratory must establish an assay-specific expected value for each mutation and lot of the Seraseq Solid Tumor FFPE DNA RM prior to its routine use. When results for the product are outside of the established acceptance range, it may indicate unsatisfactory test performance. Possible sources of error include deterioration of test kit reagents, operator error, faulty performance of equipment, contamination of reagents, or changes in bioinformatics pipeline parameters.

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LIMITATIONS OF THE PROCEDURE

Seraseq Solid Tumor FFPE DNA RM MUST NOT BE SUBSTITUTED FOR THE CONTROL REAGENTS PROVIDED WITH MANUFACTURED TEST KITS.

TEST PROCEDURES and *INTERPRETATION OF RESULTS* provided by manufacturers of test kits must be followed closely. Deviations from procedures recommended by test kit manufacturers may produce unreliable results. LGC does not claim that others can duplicate test results exactly. Seraseq Solid Tumor FFPE DNA RM is not a calibrator and should not be used for assay calibration. Adverse shipping and storage conditions or use of outdated product may produce erroneous results.

EXPECTED RESULTS

Specific detection of variants and variant allele frequencies will vary among different assays, different procedures, different lot numbers, and different laboratories. Each laboratory should establish its own acceptance criteria. For example, the acceptable range for each variant might include all values within two standard deviations of the mean of 20 data points obtained in 20 runs[2]. Table 2 lists the variants (SNV, insertions, deletions and translocations) in the product (verified by NGS and/or digital PCR).

SPECIFIC PERFORMANCE CHARACTERISTICS

Seraseq Solid Tumor FFPE DNA RM has been designed for use with NGS sequencing procedures for the purposes of evaluating assay performance. Seraseq Solid Tumor FFPE DNA RM does not have assigned values. Procedures for implementing a quality assurance program and monitoring test performance on a routine basis must be established by each individual laboratory.

REFERENCES

1. Siegel JD, Rhinehart E, Jackson M, Chiarello L, and the Healthcare Infection Control Practices Advisory Committee, 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings.
2. Statistical Quality Control for Quantitative Measurements: Principles and Definitions; Approved Guideline– Fourth Edition. CLSI document C24, 2016.

Table 2: List of DNA Mutations Incorporated

Gene	Transcript	Nucleotide Change	COSMIC ID	Variant Type
AR	NM_000044.6	c.2623C>T	COSM238555	SNV
ATM	NM_000051.4	c.1058_1059del	COSM21924	Deletion
BRCA1	NM_007294.4	c.1961del	COSM219054	Deletion
BRCA2	NM_000059.4	c.7934del	COSM1738241	Deletion
CDKN2A	NM_000077.5	c.9_32dup	COSM13442	Insertion
CHEK1	NM_001114122.3	c.676del	COSM1352376#	Deletion
CHEK2	NM_007194.4	c.1116_1117delinsGT	COSM384945	INDEL
EGFR	NM_005228.5	c.2303G>T	COSM6241	SNV
EGFR	NM_005228.5	c.2310_2311insGGT	COSM12378	Insertion
EGFR	NM_005228.5	c.2369C>T	COSM6240	SNV
EGFR	NM_005228.5	c.2389T>A	COSM6493937	SNV
ERBB2	NM_004448.4	c.2313_2324dup	COSM20959	Insertion
ESR1	NM_000125.4	c.1613A>G	COSM94250	SNV
FGFR3	NM_000142.5	c.746C>G	COSM715	SNV
HRAS	NM_005343.4	c.182A>G	COSM499	SNV
HRAS	NM_005343.4	c.37G>C	COSM486	SNV
IDH1	NM_005896.4	c.394C>T	COSM28747	SNV
IDH2	NM_002168.4	c.419G>A	COSM41590	SNV
IDH2	NM_002168.4	c.515G>A	COSM33733	SNV
KIT	NM_000222.3	c.2361+67_2361+72delTTTTTT	N/A	Deletion

Gene	Transcript	Nucleotide Change	COSMIC ID	Variant Type
KRAS	NM_004985.5	c.34G>T	COSM516	SNV
MAP2K1	NM_002755.4	c.370C>T	COSM235614	SNV
MAP4K3	NM_003618.4	c.246-2475_246-2470delTTTTTT	N/A	Deletion
MAP4K3	NM_003618.4	c.998-35_998-30delAAAAAA	N/A	Deletion
MET	NM_001127500.3	c.3082+1del	COSM6947926	Deletion
MLH1	NM_000249.4	c.232_243delinsATGTAAGG	N/A	INDEL
MSH2	NM_000251.3	c.1662-12_1677del	N/A	Deletion
MSH2	NM_000251.3	c.942+20_942+29delAAAAAAAAAA	N/A	Deletion
MSH6	NM_000179.3	c.2056_2060delinsCTTCTACCTCAAAAA	N/A	INDEL
MTOR	NM_004958.4	c.6644C>A	COSM20417	SNV
NF1	NM_001042492.3	c.3738_3747del	COSM510741	Deletion
NTRK1	NM_002529.4	c.1783G>A	COSM9113104	SNV
NTRK2	NM_006180.6	c.1915G>A	N/A	SNV
NTRK3	NM_001012338.3	c.1867G>A	COSM6951362	SNV
PALB2	NM_024675.4	c.839del	COSM1376815	Deletion
PDGFRA	NM_006206.6	c.2525A>T	COSM736	SNV
PIK3CA	NM_006218.4	c.3140A>G	COSM775	SNV
PIK3CA	NM_006218.4	c.3203dup	COSM249879	Insertion
PIK3CA	NM_006218.4	c.1633G>A	COSM763	SNV
PIK3R1	NM_181523.3	c.1727_1729del	COSM35737	Deletion
PMS2	NM_000535.7	c.861_864del	COSM5547641	Deletion
PTCH1	NM_000264.5	c.2307_2308delinsTT	COSM17587	INDEL
PTEN	NM_000314.8	c.741dup	COSM4986	Insertion
PTEN	NM_000314.8	c.800del	COSM5809	Deletion
RAD51C	NM_058216.3	c.242C>A	N/A	SNV
RAD51C	NM_058216.3	c.338dup	N/A	SNV
RAD51D	NM_002878.4	c.392dup	N/A	SNV
RAD51D	NM_002878.4	c.271A>T	N/A	SNV
RAF1	NM_002880.4	c.770C>T	COSM181063	SNV
RB1	NM_000321.3	c.751C>T	COSM878	SNV
RET	NM_020975.6	c.2753T>C	COSM965	SNV
SLC7A8	NM_012244.4	c.-231_-224delTTTTTTTT	N/A	Deletion
SMARCB1	NM_003073.5	c.118C>T	COSM1002	SNV
STK11	NM_000455.5	c.734+1G>T	COSM51523	SNV
TERT	NM_198253.3	c.-124C>T	N/A	SNV
TERT	NM_198253.3	c.-146C>T	N/A	SNV
TP53	NM_000546.6	c.524G>A	COSM10648	SNV
TP53	NM_000546.6	c.723del	COSM6530	Deletion

Gene	Transcript	Nucleotide Change	COSMIC ID	Variant Type
TP53	NM_000546.6	c.743G>A	COSM10662	SNV
TP53	NM_000546.6	c.818G>A	COSM10660	SNV
TSC1	NM_000368.5	c.1263+1G>T	COSM1738312	SNV
TSC2	NM_000548.5	c.2640-1G>A	COSM3361675	SNV
VHL	NM_000551.4	c.481C>T	COSM17612	SNV
ZNF2	NM_021088.4	c.*1525_*1530delTTTTTT	N/A	Deletion
CD74::NRG1	Intron 6::Intron 5	NM_001025159.3::NM_013964.5	Translocation	N/A
CD74::ROS1	Intron 6::Intron 34	NM_001025159.3::NM_001378902.1	Translocation	N/A
COL1A1::PDGFB	Intron 25::Intron 1	NM_000088.3::NM_002608.3	Translocation	N/A
EML4::ALK	Intron 13::Intron 19	NM_019063.5::NM_004304.5	Translocation	N/A
ETV6::NTRK3	Intron 5::Intron 14	NM_001987.5::NM_002530.4	Translocation	N/A
FGFR2::BICC1	Intron 17::Intron 2	NM_000141.5::NM_001080512.3	Translocation	N/A
FGFR3::TACC3	Exon 18::Intron 7	NM_000142.5::NM_006342.3	Translocation	N/A
NCOA4::RET	Intron 7::Intron 11	NM_001145263.2::NM_020975.6	Translocation	N/A
PML::NTRK2	Intron 2::Intron 12	NM_002675.4::NM_006180.6	Translocation	N/A
TPM3::NTRK1	Intron 7::Intron 9	NM_153649.4::NM_002529.4	Translocation	N/A

#COSMIC uses transcript ENST00000427383.6

NOTE: Above list does not include variants present in the GM24385 background. SNV refers to single nucleotide variant; INDEL is defined as insertion/deletion. Genomic coordinates use the 1-based coordinate system.