Seraseq®
ctDNA MRD Panel Mix

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® ctDNA MRD Panel Mix product is a reference material formulated for use with Next Generation Sequencing (NGS) assays that detect somatic mutations in human cancer patient samples. This product is intended for use as a reference material in the development and validation of laboratory tests used to monitor cancer disease progression or treatment response by cfDNA NGS assays under a given set of bioinformatics pipeline parameters. Product is *For Research Use Only. Not for use in diagnostic procedures.*

REAGENTS

Material Number	Product Name
0710-2146	Seraseq® ctDNA MRD Panel Mix

Product consist of four (4) ctDNA vials blended at tumor fractions of 0%, 0.5%, 0.05% and 0.005%; 4x10 ng/µl concentration; 4x20 µl fill volumes; and 4x200 ng total mass.

WARNINGS AND PRECAUTIONS

For Research Use Only. Not for use in diagnostic procedures.
CAUTION: Handle Seraseq ctDNA MRD Panel Mix product as though it is capable of transmitting infectious agents. This product consists of purified and fragmented DNA from a diseased cell line, its SNP-matched normal human cell line, and DNA plasmids of biosynthetic constructs.

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 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 ctDNA MRD Panel Mix product beyond the expiration date. Avoid contamination of the product when opening and closing the vial.

STORAGE INSTRUCTIONS

Store Seraseq ctDNA MRD Panel Mix frozen at -20°C. After opening, record the date opened and the expiration date on the vial. Aliquoting of the product into low DNA binding tubes may be advisable to limit the number of freeze-thaw cycles.

INDICATIONS OF REAGENT INSTABILITY OR DETERIORATION

Seraseq ctDNA MRD Panel Mix is formulated from a combination of tumor-normal reference standard derived from expanded/cultured human cell line of diseased (tumor) and matching non-diseased (normal) patient, as well as biosynthetic DNA variant spike-ins, and should appear as a clear liquid. Alterations in this appearance may indicate instability or deterioration of the product and vials should be discarded.

PROCEDURE

Materials Provided

Each Seraseq ctDNA MRD Panel Mix consists of 4 vials of fragmented (to a size range consistent with cfDNA) and purified DNA from human cell lines (diseased and normal) and biosynthetic DNA variant spike-ins, blended at tumor fractions of 0% (WT), 0.5%, 0.05% and 0.005%. Each purified DNA is present in a 1 mM Tris, 0.1 mM EDTA, pH 8.0 aqueous buffer, and ready to use in NGS assays in steps that follow DNA isolation. No further purification or DNA isolation is needed.

Materials Required but not Provided

Refer to instructions supplied by manufacturers of the test kits to be used.

Instructions for Use

Thaw the product vial on ice. Mix by vortexing to ensure a homogenous solution and spin briefly. Each vial of the Seraseq ctDNA MRD Panel Mix may be input directly into library preparation following procedures used for clinical specimens. Refer to your assay procedures in order to determine the amount of material to use.

EXPECTED RESULTS & INTERPRETATION OF RESULTS

Table 1 lists the additional 22 DNA plasmid variants included in the Seraseq ctDNA MRD Panel Mix product. Figure 1 shows the ctDNA fragment sizing for all tumor fractions. Detection of somatic mutations may differ across different NGS panels, and concomitantly the VAFs determined by targeted NGS panels for the Seraseq ctDNA MRD Panel Mix product may differ. Each laboratory must establish an expected VAF for the somatic variants in the Seraseq ctDNA MRD Panel Mix product. 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. Additional support documents (VCFs of all variants detected in the 0%, 0.5%, 0.05% and 0.005% tumor fractions are available by contacting us at CDx-TechnicalSupport@LGCGroup.com

LIMITATIONS OF THE PROCEDURE

Seraseq ctDNA MRD Panel Mix MUST NOT BE SUBSTITUTED FOR THE CONTROL REAGENTS PROVIDED WITH MANUFACTURED TEST KITS. *TEST PROCEDURES* provided by manufacturers must be followed closely. Deviations from procedures recommended by test kit manufacturers may produce unreliable results. This product is offered for Research Use Only. Not for use in diagnostic procedures. Data are provided for informational purposes. SeraCare Life Sciences does not claim that others can duplicate test results exactly. Seraseq ctDNA MRD Panel Mix is not a calibrator and should not be used for assay calibration. These materials are not whole-process controls and do not evaluate the methods used for specimen extraction. Adverse shipping and/or storage conditions or use of outdated product may produce erroneous results.

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.

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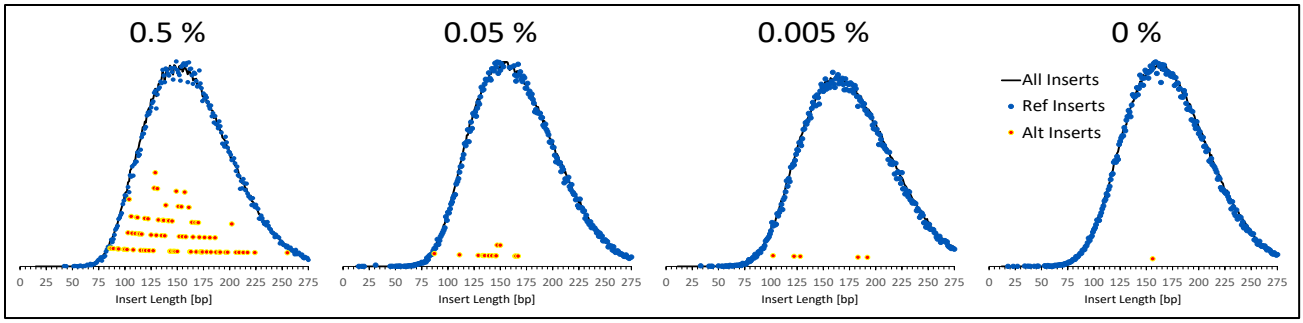

Figure-1: Post processing analysis of ctDNA fragment sizes for all reads (black lines), reference sequence-containing reads (blue dots), and variant-containing reads (red/yellow dots) after error correction.

Table 1: List of additional 22 biosynthetic spike-ins combined into the Seraseq ctDNA MRD Panel Mix product.

	Gene	COSMIC ID	Amino acid change
1	AKT1	COSM33765	p.E17K
2	ALK	COSM144250	p.G1202R
3	ALK	COSM28055	p.F1174L
4	BRAF	COSM476	p.V600E
5	BRCA1	COSM1383519	p.K654fs*47
6	BRCA2	COSM1738242	p.R2645fs*3
7	CD74-ROS1	N/A	Translocation
8	EGFR	COSM12370	p.L747_P753>S
9	EGFR	COSM6223	p.E746_A750delELREA
10	EGFR	COSM6224	p.L858R
11	EGFR	COSM6240	p.T790M
12	EGFR	COSM6256	p.S752_I759delSPKANKEI
13	EML4-ALK	N/A	Translocation
14	ERBB2	COSM20959	p.A775_G776insYVMA
15	KIT	COSM1314	p.D816V
16	KRAS	COSM516	p.G12C
17	KRAS	COSM521	p.G12D
18	KRAS	COSM554	p.Q61H
19	NCOA4/RET	N/A	Translocation
20	NRAS	COSM584	p.Q61R
21	PIK3CA	COSM12464[1]	p.N1068fs*4
22	PIK3CA	COSM775	p.H1047R

[1]As of June 2019, this mutation is no longer listed in the COSMIC database.