Seraseq®

FFPE MSI-High 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® FFPE MSI-High Reference Material product is a reference material formulated for use with Next Generation Sequencing (NGS) assays that detect microsatellites in human cancer patient samples. This product is intended for use as a reference material in the determination of the number of extended microsatellites in a cancer patient sample analyzed by 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`
0710-2236	Seraseq® FFPE MSI-High Reference Material

Product consist of one 10µm FFPE curl per vial.

WARNINGS AND PRECAUTIONS

For Research Use Only. Not for use in diagnostic procedures.
CAUTION: Handle Seraseq FFPE MSI-High Reference Material product as though it is capable of transmitting infectious agents. This product is formulated from a diseased uterine/cervical cancer cell line (https://www.atcc.org/products/htb-31).

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 FFPE MSI-High Reference Material product beyond the expiration date. Avoid contamination of the product when opening and closing the vial.

STORAGE INSTRUCTIONS

Store Seraseq FFPE MSI-High Reference Material at 2-8 °C. After opening, record the date opened and the expiration date on the vial.

PROCEDURE

Materials Provided

Seraseq FFPE MSI-High Reference Material consists of human diseased cells that were formalin treated and embedded in paraffin to create an FFPE block, and then sectioned into 10 µm curls. One 10 µm FFPE curl is provided per vial.

Materials Required but not Provided

Seraseq FFPE MSI-High Reference Material require 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 FFPE MSI-High Reference Material 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.

EXPECTED RESULTS & INTERPRETATION OF RESULTS

Seraseq FFPE MSI-High Reference Material is compatible with commercially available nucleic acid extraction methods commonly used for FFPE specimens. DNA extraction yields per FFPE curl (10 µm) when using either Promega's Maxwell RSC FFPE DNA kit or Qiagen's QIAamp DNA FFPE Tissue kit, quantitated by Thermo Fisher's Qubit dsDNA HS assay, are provided in Table 1 below

Table 1: Representative DNA extraction yield per 10µm FFPE curl.

	Yield per 10µm curl (ng)	
FFPE Block	**Qiagen QIAamp DNA FFPE Tissue (ng)**	**Promega Maxwell RSC DNA FFPE (ng)**
1	593	272
2	492	298
3	620	300
Average (ng)	**568 ± 117**	**290 ± 39**

Table 2 provides MSI analysis result for the Seraseq FFPE MSI-High Reference Material product as determined by the TSO500 assay. Detection of microsatellites may differ across different NGS panels, and concomitantly the MSI score and MSI-High determination for this product by other targeted NGS panels may differ. Each laboratory must establish an expected MSI score for the Seraseq FFPE MSI-High Reference Material. 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 are available by contacting us at CDx.Marketing@LGCGroup.com

LIMITATIONS OF THE PROCEDURE

Seraseq FFPE MSI-High Reference Material 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 FFPE MSI-High Reference Material 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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Table 2: MSI status determination for the Seraseq FFPE MSI-High Reference Material based on the TSO500 Assay.

Product Name	Material Number	Av. MSI Sites Detected	Av. Unstable MSI sites	Av. MSI Score*	MSI Call
Seraseq® FFPE MSI-High Reference Material	0710-2236	119 105	90 75	75.6 71.4	MSI-High MSI-High

**MSI score is the ratio of the unstable MSI sites to the total number of sites detected (expressed as a percentage). The value must be >20% for an MSI-High result.*

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Seraseq® Microsatellite Instability (MSI) Reference Materials

MICROSATELLITE INSTABILITY REFERENCE MATERIALS FOR DETECTION AND VALIDATION OF MSI BIOMARKERS IN CANCER PATIENT SAMPLES MEASURED BY PCR OR NGS.

HIGHLIGHTS

VALIDATE LOD OF MICROSATELLITE INSTABILITY ASSAYS WITH GROUND-TRUTH MSI BIOMARKERS AT TWO AF LEVELS.

APPLY PCR AND NGS TO QUANTITATE CANCER-ASSOCIATED MICROSATELLITES IN PATIENT SAMPLES.

HIGH-QUALITY MANUFACTURED REFERENCE MATERIAL; PROVIDES CONSISTENT GROUND TRUTH

INTRODUCTION

Microsatellites are regions of DNA repeats with different lengths, i.e., instability, highlighting DNA mismatch repair gene deficiencies. Typical repeat units are between 1-6 base pairs and the number of repeats vary from person to person such that each person has a set length of these microsatellites in their genome. Measurements of MSI have traditionally been performed using qPCR/CE fragment length analysis methods, or immunohistochemistry (IHC), but new methodologies such as digital droplet PCR (ddPCR) and Next Generation Sequencing (NGS) are now being applied to determination of MSI status of cancer patients. High incidence of microsatellite instability (MSI) has been linked to favorable outcomes in immuno-oncology (I-O) treatment response by patients with diseases such as Lynch Syndrome and colorectal cancer. Hence, determination of MSI status for cancer patients is important in I-O therapeutics management.

LGC SeraCare has developed microsatellite instability (MSI) reference materials that support qPCR and NGS assays that target a range of short tandem repeat regions commonly analyzed for microsatellite instabilities. For assays that target specific mono and dinucleotide repeats such as BAT-25, BAT-26, NR-21, NR-24, MONO-27, we have created MSI reference materials containing these markers blended at two different allele frequency (AF) levels – 5% and 20%. Additionally, for NGS MSI assays that analyze for a large number of microsatellite loci across the human genome, we have a human diseased cell line-based MSI-High reference material for such analysis. These products are quantitated by PCR (qPCR/CE and ddPCR) and by targeted NGS assays to support all product claims.

MICROSATELLITE BIOMARKERS AND GENOMIC LOCATIONS IN THE SERASEQ® MSI REFERENCE PANEL MIX AF5% AND AF20%

Marker	Gene	Chromosome	Position (hg19 based)	Comment
BAT-25	KIT (intron16)	chr4	55598211	25T -> 19T
BAT-26	MSH2 (intron5)	chr2	47641559	27A -> 17A
NR-21	SLC7A8 (5'UTR)	chr14	23652346	21A -> 13A
NR-24	ZNF2 (3'UTR)	chr2	95849361	23T -> 17T
MONO-27[1]	MAP4K3 (intron 3)	chr2	39573062	27A -> 21A
	MAP4K3 (intron13)		39536689	

1 There is ambiguity in the literature on the MONO-27 locus so two constructs are included in the product to ensure compatibility (see, Bacher J, Halberg R, Kent-First M, Wood KV. "Methods and kits for detecting mutations" US Patent US20090068646A1 issued March 12, 2009; and Pino MS, Chung DC. "Application of molecular diagnostics for the detection of Lynch syndrome." Expert review of molecular diagnostics vol. 10,5 (2010): 651-65. doi:10.1586/erm.10.45).

ABOUT LGC SERACARE

TRUSTED SUPPLIER TO THE DIAGNOSTIC TESTING INDUSTRY FOR OVER 30 YEARS

HIGH-QUALITY CONTROL PRODUCTS, RAW BIOLOGICAL MATERIALS, AND IMMUNOASSAY REAGENTS

INNOVATIVE TOOLS AND TECHNOLOGIES TO PROVIDE ASSURANCE IN DIAGNOSTIC ASSAY PERFORMANCE AND TEST RESULTS

FOR MORE INFORMATION, PLEASE VISIT OUR WEBSITE: WWW.SERACARE.COM

TARGETED NGS ASSAY DETERMINATION OF MICROSATELLITE INSTABILITY STATUS OF THE SERASEQ® MSI-HIGH PRODUCTS

Product Name	NGS Assay	Av. MSI Sites Detected*	Av. Unstable MSI sites*	Av. MSI Score*	MSI Call
Seraseq® gDNA MSI-High Mix	TSO500	106	81	77.1	High
Seraseq® FFPE MSI-High RM	TSO500	119	90	75.6	High
		105	75	71.4	High

**MSI measurements are from replicate runs on the TSO500. MSI score is the ratio of the unstable MSI sites to the total number of sites detected (expressed as a percentage). The value must be >20% for an MSI-High result.*

FEATURES AND BENEFITS

1. Cell line or plasmid-based MSI reference material mix for analysis in molecular assays or NGS
2. Offered as tumor-only (MSI-High) or tumor-normal (AF5% and AF20%) options
3. Support MSI assay validation, LoD determination, and routine detection of MSI markers in cancer patient samples
4. Variant AFs (AF5% and AF20% products) quantitated by ddPCR and qPCR/CE fragment length analysis assays
5. Normal background DNA is a highly characterized GM24385 human genomic DNA known to be microsatellite stable (MSS)
6. Manufactured within cGMP compliant and ISO 13485 certified facilities

ORDERING INFORMATION

Product Description	Kit Composition	Material No.	Concentration	Fill Volume	Total Mass
Seraseq gDNA MSI-High Mix	gDNA - Tumor	0710-1670	25 ng/µl	20 µl	500 ng
Seraseq® FFPE MSI-High RM	FFPE - Tumor	0710-2236	1 FFPE curl	10 µm	>200 ng*
Seraseq MSI Reference Panel Mix AF5%	gDNA – Tumor	0710-1675	2 x 20 ng/µl	2x 15 µl	2 x 300 ng
	gDNA - Normal				
Seraseq MSI Reference Panel Mix AF20%	gDNA – Tumor	0710-1676	2 x 20 ng/µl	2x 15 µl	2 x 300 ng
	gDNA - Normal				

**QIAamp DNA FFPE Tissue kit or Promega Maxwell RSC FFPE DNA kit and Qubit dsDNA HS kit.*

FOR RESEARCH USE ONLY. NOT FOR USE IN DIAGNOSTIC PROCEDURES.

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