Seraseq®
gDNA BRCA1/2 LGR Inherited Mutation 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® gDNA BRCA1/2 LGR (Large Genomic Rearrangement) Inherited Mutation Mix contains 20 variants across the BRCA1 and BRCA2 genes in the genomic background of GM24385 (Table 2).

Seraseq gDNA BRCA1/2 LGR Inherited Mutation Mix is intended for use with Next Generation Sequencing (NGS) assays or amplified nucleic acid-based methods that identify somatic and inherited (germline) variants in the genes *BRCA1* and *BRCA2* under a given set of bioinformatics pipeline parameters. This product is intended for use as a quality reference material in the development, validation, and evaluation of routine performance of laboratory tests.

REAGENTS

Table 1. Seraseq® gDNA BRCA1/2 LGR Inherited Mutation Mix

Material No.	Product
0730-0568	Seraseq® gDNA BRCA1/2 LGR Inherited Mutation Mix

Product consist of 1 vial, 15 ng/µl concentration, 25 µl fill volume, and 375 ng total mass.

WARNINGS AND PRECAUTIONS

For Research Use Only. Not for use in diagnostic procedures.
CAUTION: Handle Seraseq gDNA BRCA1/2 LGR Inherited Mutation Mix 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/the Personal Genome Project offered by the NIGMS Human Genetic Cell Repository (https://catalog.coriell.org/1/NIGMS).

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

Avoid contamination of the product when opening and closing the vials.

STORAGE INSTRUCTIONS

Store Seraseq gDNA BRCA1/2 LGR Inherited Mutation Mix frozen at -20°C. Do not use the product beyond the expiration date.

INDICATIONS OF REAGENT INSTABILITY OR DETERIORATION

Seraseq gDNA BRCA1/2 LGR Inherited Mutation Mix is a mixture of human genomic DNA and synthetic DNA constructs. It 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

Seraseq gDNA BRCA1/2 LGR Inherited Mutation Mix consists of DNA purified from a reference cell line, GM24385, plus constructs containing variants mixed at defined allele frequencies. The purified DNA is present in a 1 mM Tris, 0.1 mM EDTA, pH 8.0 aqueous buffer. Material is 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. Seraseq gDNA BRCA1/2 LGR Inherited Mutation 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 2 indicates each of the mutations represented in the Seraseq gDNA BRCA1/2 LGR Inherited Mutation Mix. While the presence and frequency of each variant in this product was confirmed during manufacture using digital PCR assays and/or NGS, there may be differences in observed allele frequencies due to assay characteristics. The Seraseq gDNA BRCA1/2 LGR Inherited Mutation Mix does not have assigned values for allele frequencies of the variants present. Furthermore, specific detection of variants and variant allele frequencies within Seraseq gDNA BRCA1/2 LGR Inherited Mutation Mix will vary among different assays, different procedures, different lot numbers, and different laboratories.

Each laboratory must establish an assay-specific expected value and acceptance range for each variant and lot of the Mutation Mix 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 change in bioinformatics pipeline parameters.

LIMITATIONS OF THE PROCEDURE

Seraseq gDNA BRCA1/2 LGR Inherited Mutation Mix 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 instructions may produce unreliable results. LGC Clinical Diagnostics does not claim that others can duplicate test results exactly. Seraseq gDNA BRCA1/2 LGR Inherited Mutation Mix 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.

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: List of 20 DNA variants in Seraseq® gDNA BRCA1/2 LGR Inherited Mutation Mix

Gene ID	Variant Type	Nucleotide change	Protein change	GRCh37 Location	GRCh38 Location	Transcript	Variant Length (bp)
BRCA1	Deletion	c.4487_4675+2del	Splice variant	17:41226346_41226536	17:43074329_43074519	NM_007294.4	191
BRCA1	Insertion	c.4186_4357dup	p.R1397Yfs*2	17:41234421_41234592	17:43082404_43082575	NM_007294.4	172
BRCA1	Deletion	c.2071_2171del	p.R691*	17:41245377_41245477	17:43093360_43093460	NM_007294.4	101
BRCA1	Deletion	c.4987_5074del	p.V1665Sfs*8	17:41219625_41219712	17:43067608_43067695	NM_007294.4	88
BRCA1	Deletion	c.5279_5332del	p.I1760_D1778delinsN	17: 41203080_41203133	17: 43051063_43051116	NM_007294.4	54
BRCA1	Indel	c.5209_5248delinsTC	p.R1737Sfs*80	17:41209098_41209137	17:43057081_43057120	NM_007294.4	40
BRCA1	Indel	c.2820_2830delinsAAGATAAGCCAGTTTGATAA	p.D940_C944delinsER*	17:41244718_41244728	17:43092701_43092711	NM_007294.4	11
BRCA1	Deletion	c.1961del	p.K654Sfs*47	17:41245587	17:43093570	NM_007294.4	1
BRCA1	SNV	c.4327C>T	p.R1443*	17:41234451	17:43082434	NM_007294.4	1
BRCA1	SNV	c.441+2T>G	Splice variant	17:41256137	17:43104120	NM_007294.4	1
BRCA2	Deletion	c.8757-2_9023del	Splice variant	13:32953452_32953956	13:32379315_32379819	NM_000059.4	505
BRCA2	Deletion	c.2886_3144del	p.H962Qfs*6	13:32911378_32911636	13:32337241_32337499	NM_000059.4	259
BRCA2	Deletion	c.68_316del	p.D23_L105del	13:32893214_32893462	13:32319077_32319322	NM_000059.4	249
BRCA2	Indel	c.5150_5226delinsTACTTAATACTTATTAAGTATTA	p.E1717_N1742delinsVLNTY*	13:32913642_32913718	13:32339505_32339581	NM_000059.4	77
BRCA2	Indel	c.891_899delinsGATACTTCAG	p.T298Ifs*7	13:32906506_32906514	13:32332369_32332377	NM_000059.4	9
BRCA2	Deletion	c.5436del	p.E1812Dfs*3	13:32913927	13:32339790	NM_000059.4	1
BRCA2	SNV	c.8167G>C	p.D2723H	13:32937506	13:32363369	NM_000059.4	1
BRCA2	SNV	c.8331+2T>A	Splice variant	13:32937672	13:32363535	NM_000059.4	1
BRCA2	SNV	c.910G>T	p.E304*	13:32906525	13:32332388	NM_000059.4	1
BRCA2	Insertion	c.2407dup	p.Y803Lfs*2	13:32910898	13:32336761	NM_000059.4	1

NOTE: Above list does not include variants present in the GM24385 background.
Substitution refers to single nucleotide variant; Indels are defined as deletion/insertions less than 10 base pairs, and LGRs (deletions or insertions) are larger than 10 base pairs.