Seraseq®

BRCA1/2 Exon Deletions DNA Mix

Package Insert

NAME AND INTENDED USE

The Seraseq® BRCA1/2 Exon Deletions DNA Mix is a reference material intended for use in the development, validation, and evaluation of routine performance of Next Generation Sequencing (NGS) (and other amplified nucleic acid-based methods) that identify somatic and inherited (germline) variants in the genes *BRCA1* and *BRCA2* associated with cancers such as breast, ovarian, and prostate. This reference material is suitable for use by clinical laboratories, research institutions, and diagnostic assay developers to ensure consistent and reliable results across different sequencing runs and laboratory conditions.

The Seraseq BRCA1/2 Exon Deletions DNA Mix is not intended for use in patient diagnosis, treatment, or in any therapeutic procedures. It is intended for use by trained laboratory personnel proficient in NGS technologies and familiar with proper laboratory practices and quality control procedures.

For Research Use Only (RUO). Not for use in diagnostic procedures.

REAGENT PROVIDED

Seraseq BRCA1/2 Exon Deletions DNA Mix is a mixture of large synthetic DNA constructs spanning the whole gene sequences (Table 3) and genomic DNA extracted from the human cell line GM24385. It contains two (2) synthetic mutations in the BRCA1 and BRCA2 genes (not including those present in the GM24385 background) (Table 2). The product is formulated to contain each mutation at a 60% variant allele frequency (VAF), confirmed by digital PCR and measured by NGS.

Table 1. Seraseq BRCA1/2 Exon Deletions DNA Mix

Material No.	Product	Format
0730-0570	Seraseq® BRCA1/2 Exon Deletions DNA Mix	1x 25 µL

One (1) vial, 25 µL per vial, 375 ng total mass, at a nominal concentration of 15 ng/µL is provided. The product is formulated in a 1 mM Tris / 0.1 mM EDTA pH 8.0 aqueous buffer. Refer to the batch-specific Technical Product Report for exact concentration and VAF measured. Manufactured in the USA.

WARNINGS AND PRECAUTIONS

Safety and Handling Precautions

Handle Seraseq BRCA1/2 Exon Deletions DNA Mix and all materials derived from human blood products as though it is capable of transmitting infectious agents. 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. Avoid contamination of the product when opening and closing the vials. Dispose of all specimens and materials appropriately.

STORAGE INSTRUCTIONS

Store Seraseq BRCA1/2 Exon Deletions DNA Mix frozen at -20 °C or colder. Once opened, a vial can be thawed and re-frozen up to five (5) times. Sub-aliquoting of the product into low DNA binding tubes may be advisable to limit the number of freeze/thaw cycles to five (5) or less.

INDICATIONS OF REAGENT INSTABILITY OR DETERIORATION

Seraseq BRCA1/2 Exon Deletions DNA Mix 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 Required but not Provided

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

Instructions for Use

Allow the product vial to come to room temperature before use. Mix by vortexing to ensure a homogeneous solution and spin briefly. Seraseq BRCA1/2 Exon Deletions DNA Mix should be integrated into library preparation after the DNA isolation step; no further purification or DNA isolation is needed. If a DNA shearing step is part of the workflow, the reference material should be sheared and go through the target selection and library preparation in parallel with test specimens. Refer to standard assay procedures in order to determine the amount of material to use.

EXPECTED RESULTS & INTERPRETATION OF RESULTS

Table 2 lists the mutations included in the Seraseq BRCA1/2 Exon Deletions DNA Mix. While the presence and frequency of each variant in this product was confirmed during manufacture using digital PCR assays and NGS, observed allele frequencies may vary due to assay characteristics, and some mutations may not be detected by all assays due to their size or location. The product does not have assigned values for allele frequencies of the variants present. Furthermore, specific detection of variants and variant allele frequencies within the product 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 Seraseq BRCA1/2 Exon Deletions DNA 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 BRCA1/2 EXON DELETIONS MUST NOT BE SUBSTITUTED FOR THE MANDATORY POSITIVE AND NEGATIVE 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. Seraseq BRCA1/2 Exon Deletions DNA 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.

SPECIFIC PERFORMANCE CHARACTERISTICS

Seraseq BRCA1/2 Exon Deletions DNA Mix has been designed for use with NGS sequencing procedures for the purposes of evaluating assay performance. The product 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.

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Table 2. List of Mutations

Gene ID	Mutation Type	Nucleotide Change	Protein change	GRCh37 Location	GRCh38 Location	Transcript	Variant Length
BRCA1	Deletion - Exon 10	c.671-56_4096+89del	p.(Ala224_Leu1365del)	chr17: 41243363-41246933	chr17:43091346-43094916	ENST00000357654.9	3.43kb
BRCA2	Deletion - Exon 10-14	c.794-97_7435+146del	p.(Gly265_Leu2478del)	chr13: 32906312-32929571	chr13:32332175-32355434	ENST00000380152.8	23.02kb

NOTE: Above list does not include variants present in the GM24385 background. Target variant allele frequency (VAF) at **60%**.

Table 3. Genomic Content of Large Synthetic DNA Constructs

Construct	GRC37 Region	GRCh38 Region	Genes
BRCA1	chr17:41186868-?*	chr17:43034851-?*	BRCA1, NBR1, TMEM106A, CCDC200
BRCA2	chr13:32874606-33014361	chr13:32300469-32440224	BRCA2, N4BP2L1, N4BP2L2**

* The exact stop coordinate is unknown due to the repetitive nature of the region.

** Only the first 3 exons of N4BP2L2 are contained in the construct.

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.