Seraseq™

Cardiomyopathy 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™ Cardiomyopathy Reference Material is intended for use with Next Generation Sequencing (NGS) assays that identify germline variants that represent pathogenic and likely pathogenic mutations for hypertrophic cardiomyopathy. The Seraseq Cardiomyopathy Reference Material is intended as a quality reference material for translational and disease research testing and monitors library preparation, sequencing, and variant allele detection 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 added confidence in the reliability of results obtained for unknown specimens. The use of independent reference products may provide valuable information concerning assay sensitivity and bioinformatics pipeline analysis.

PRINCIPLES OF THE PROCEDURE

Seraseq Cardiomyopathy Reference Material is ready-to-use in Next Generation Sequencing (NGS) assays in steps that follow DNA isolation; no further purification or DNA isolation is needed. The reference materials should follow the same workflow as unknown samples. The product contains DNA at a concentration of 50 ng/µL. The Reference Material is formulated in 1 mM Tris / 0.1mM EDTA pH 8.0, which is a buffer that is compatible with both PCR-based target amplification and hybridization-based target selection methods.

Seraseq Cardiomyopathy Reference Material contains ten (10) mutations that are pathogenic or likely pathogenic mutations for hypertrophic cardiomyopathy (Table 1). The product is formulated to simulate the heterozygous state and the 50% variant allele frequency is confirmed by droplet digital PCR.

REAGENTS

Item No. 0740-0021. 1 vial, 200 µL per vial, 50 ng/µL concentration.

WARNINGS AND PRECAUTIONS

For Research Use Only. Not for use in diagnostic procedures.
CAUTION: Handle Seraseq Cardiomyopathy Reference Material and all materials derived from human blood products as though it is capable of transmitting infectious agents. Seraseq Cardiomyopathy Reference Material is manufactured using genomic DNA extracted from the human cell line GM24385, which is a B-lymphocytic, male cell line from the Personal Genome Project offered by the NIGMS Human Genetic Cell Repository (https://catalog.coriell.org/1/NIGMS). Purified genomic DNA is formulated in a 1 mM Tris / 0.1mM EDTA pH 8.0 aqueous buffer.

Safety Precautions

Use Center 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 Cardiomyopathy Reference Material frozen at -20 ºC or colder. Once opened, a vial can be thawed and re-frozen up to five (5) times. Sub-aliquoting of the product in 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 Cardiomyopathy Reference Material 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 Cardiomyopathy Reference Material is a mixture of human genomic DNA and synthetic DNA constructs in a 1mM Tris / 0.1mM EDTA pH 8.0 buffer. Two hundred (200) µL is provided per tube and the concentration is 50 ng/µL.

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 Cardiomyopathy Reference Material should be integrated into library preparation after the DNA isolation step. If a DNA shearing step is part of the workflow, Seraseq™ Cardiomyopathy 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.

Quality Control

Although Seraseq Cardiomyopathy Reference Material is designed to simulate a heterozygous state and offered at a target mutation frequency of 50%, the product does not have assigned values for mutation frequencies. There are many reasons why assays may observe deviation from the representative data which may or may not be of significance. It is therefore recommended that each laboratory qualify the use of Seraseq Cardiomyopathy Reference Material with each assay system prior to its routine use.

INTERPRETATION OF RESULTS

Detection of the variants within Seraseq Cardiomyopathy Reference Material may vary with different types of tests and different test kit lots. Since the reference material does not have an assigned value, the laboratory must establish a range for each lot of Seraseq™ Cardiomyopathy 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 change in bioinformatics pipeline parameters.

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LIMITATIONS OF THE PROCEDURE

Seraseq Cardiomyopathy Reference Material 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. Seraseq Cardiomyopathy Reference Material 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. Table 1 lists the variants in the product and their target allele frequencies (verified by digital PCR).

SPECIFIC PERFORMANCE CHARACTERISTICS

Seraseq Cardiomyopathy Reference Material has been designed for use with NGS sequencing procedures for the purposes of assessing assay performance. Seraseq Cardiomyopathy Reference Material 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. CDC Recommendations for prevention of HIV transmission in health care settings. MMWR 36 (supp.2), 1987.

Table 1: List of mutations incorporated

Name	Mutation Type	Gene	Variant Allele Frequency
MYBPC3 c.1504C>T	SNV	myosin binding protein C, cardiac	50%
MYBPC3 c.2373_2374insG	Small insertion		50%
MYBPC3 c.3628-41_3628-17del	Large Deletion (in repetitive region)		50%*
MYH7 c.1988G>A	SNV	myosin, heavy chain 7, cardiac muscle, beta	50%
MYH7 c.1357C>T	SNV		50%
MYH7 c.1750G>C	SNV		50%
TNNI3 c.532_534delAAG	Small Deletion	troponin I type 3 (cardiac)	50%
TNNI3 c.575G>A	SNV		50%
TNNT2 c.487_489delGAG	Small Deletion (in repetitive region)	troponin T type 2 (cardiac)	50%
TPM1 c.574G>A	SNV	tropomyosin 1 (alpha)	50%

* As a large deletion, MYBPC3 c.3628-41_3628-17del shows severely depressed allele frequency by NGS using SureSelect^{XT} Target Enrichment System for Illumina Paired-End Multiplexed Sequencing methods.

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