Seraseq®
Carrier Screening DNA Mix

Package Insert

NAME AND INTENDED USE

The Seraseq® Carrier Screening DNA Mix is a reference material intended for use in the development, validation, and evaluation of routine performance of Next Generation Sequencing (NGS) carrier screening assays (and other molecular assays) that identify inherited (germline) variants in genes associated with monogenic diseases. 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 Carrier Screening 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 Carrier Screening DNA Mix is a mixture of synthetic DNA constructs and genomic DNA extracted from the human cell line GM24385. It contains 54 synthetic mutations in 48 genes (not including those present in the GM24385 background) associated with autosomal recessive disorders (Table 2). The product is formulated to simulate a heterozygous state for each mutation at a 50% variant allele frequency (VAF) confirmed by droplet digital PCR and measured by NGS.

Table 1. Seraseq Carrier Screening DNA Mix

Material No.	Product	Format
0730-0569	Seraseq Carrier Screening DNA Mix	1x 20 µL

One (1) vial, 20 µL per vial, 600 ng total mass, at a nominal concentration of 30 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 Carrier Screening 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 Carrier Screening 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 Carrier Screening 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 Carrier Screening 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 AND INTERPRETATION OF RESULTS

Table 2 indicates each of the mutations represented in the Seraseq Carrier Screening DNA Mix. While the presence and frequency of each variant in this product was confirmed during manufacture using digital PCR assays and NGS, there may be differences in observed allele frequencies due to assay characteristics. The Seraseq Carrier Screening DNA Mix 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 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 CARRIER SCREENING DNA MIX MUST NOT BE SUBSTITUTED FOR THE MANDATORY POSITIVE AND NEGATIVE CONTROL REAGENTS PROVIDED WITH MANUFACTURED TEST KITS.

Seraseq Carrier Screening DNA Mix is not compatible with MLPA (Multiplex ligation-dependent probe amplification) assays and NGS analysis methods based only on coverage depth, since the large genomic rearrangements do not reflect copy losses or gains across the whole DNA sequence.

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 Carrier Screening 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 Carrier Screening DNA Mix has been designed for use with NGS sequencing procedures for the purposes of evaluating assay performance. Seraseq Carrier Screening DNA Mix 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	HGVS Nomenclature	Amino Acid Change	Variant Length	Associated Syndrome
ABCC8	Substitution	c.3989-9G>A		1	Diabetes mellitus, permanent neonatal 3
ACADM	Large Insertion	c.136_158dup	p.F55fs	23	ACADM deficiency
ACADVL	Substitution	c.848T>C	p.V283A	1	VLCAD deficiency
AGXT	Insertion	c.823_824dup	p.S275fs	2	Hyperoxaluria, primary type I
ASL	Substitution	c.532G>A	p.V178Met	1	Argininosuccinate aciduria
ASPA	Large Deletion	c.437_449del	p.S146fs	13	Canavan disease
ATP7B	Deletion	c.2009_2015del	p.I669_Y670ins*	7	Wilson disease
BBS2	Large Insertion	c.256_278dup	p.V94fs	23	Bardet–Biedl syndrome 2/Retinitis pigmentosa 74
BCKDHB	Deletion	c.93_103del	p.A32fs	11	Maple syrup urine disease
BLM	Large Deletion	c.839_888del	p.E279_L280ins*	50	Bloom syndrome
CBS	Substitution	c.833T>C	p.I278T	1	Homocystinuria, B6 responsive and nonresponsive
CTFR	Deletion	c.1521_1523del	p.F508del	3	Cystic fibrosis
	Substitution	c.1624G > T	p.G542*	1	
	Large Indel	c.1973_1985delinsAGAAA	p.R658fs	13	
CLRN1	Substitution	c.300T>G	p.Y100*	1	Usher syndrome 3a
CPT2	Substitution	c.338C>T	p.S113L	1	Carnitine palmitoyltransferase II deficiency, infantile/lethal neonatal
CYP21A2	Deletion	c.332_339del	p.G111fs	8	21-hydroxylase deficient congenital adrenal hyperplasia (CAH)
DHCR7	Substitution	c.964-1G>T		1	Smith–Lemli–Opitz syndrome
DLD	Substitution	c.685G>T	p.G229C	1	Dihydrolipoamide dehydrogenase deficiency
DMD	Substitution	c.9568C>T	p.R3190*	1	Hemophilia A (HEMA)
ELP1	Substitution	c.2204+6T>C		1	Familial dysautonomia
ERCC2	Large Deletion	c.854_866del	p.Y285fs	13	Cerebrooculofacioskeletal syndrome 2/Trichothiodystrophy 1, photosensitive
FAH	Substitution	c.1062+5G>A		1	Tyrosinemia type I
FANCC	Substitution	c.456+4A>T		1	Fanconi anemia, complementation group C
FKTN	Insertion	c.1167dup	p.F390fs	1	Cardiomyopathy, dilated, 1X/Walker–Warburg congenital muscular dystrophy
FMR1	Indel	c.52-1_52delinsTA		2	Fragile X syndrome (FXS)
G6PC1	Insertion	c.379_380dup	p.Y128fs	2	Glycogen storage disease type IA
GAA	Substitution	c.-32-13T>G		1	Glycogen storage disease, type II (Pompe disease)
GALT	Deletion	c.-119_-116del		4	Galactosemia
GBA1	Large Deletion	c.1265_1319del	p.L422fs	55	Gaucher disease, type I/Gaucher disease, type II
GJB2	Deletion	c.35del	p.G12fs	1	Nonsyndromic hearing loss recessive 1A/dominant 3A

Gene ID	Mutation Type	HGVS Nomenclature	Amino Acid Change	Variant Length	Associated Syndrome
HBA1	Large Insertion	c.283_300+3dup		21	Alpha thalassemia
HBA2	Substitution	c.427T>C	p.*143Q	1	Alpha thalassemia
HBB	Substitution	c.20A>T	p.E7V	1	Sickle cell anemia β-thalassemia
HEXA	Insertion	c.1274_1277dup	p.Y427fs	4	Tay–Sachs disease
IDUA	Large Deletion	c.1525-11_1536del		23	Mucopolysaccharidosis, Ih (Hurler–Scheie S)
MCOLN1	Substitution	c.406-2A>G		1	Mucolipidosis type IV
MMACHC	Insertion	c.271dup	p.R91fs	1	Methylmalonic aciduria with homocystinuria cblC type
NEB	Substitution	c.3255+1G>A		1	NEB-related nemaline myopathy
NPHS1	Insertion	c.3250dup	p.V1084fs	1	Finnish congenital nephrotic syndrome
OTC	Large Deletion	c.72_77+18del		24	Ornithine Transcarbamylase Deficiency (OTC)
PAH	Large Deletion	c.707-12_711del		17	Phenylketonuria
PCDH15	Substitution	c.733C>T	p.R245*	1	Deafness, autosomal recessive 23/Usher syndrome, type 1F
PKHD1	Insertion	c.3463_3464dup	p.Q1155fs	2	Autosomal recessive polycystic kidney disease
PMM2	Substitution	c.422G>A	p.R141H	1	Carbohydrate-deficient glycoprotein syndrome type Ia
SLC26A4	Insertion	c.365dup	p.I124fs	1	Deafness autosomal recessive 4/Pendred syndrome
SMN1	Deletion	c.399_402del	p.E134fs	4	Spinal muscular/atrophy types: I, II, III, IV
	Large Insertion	c.770_780dup	p.G261fs	11	
	Large Deletion	c.835-21_*3+17del		92	
	Substitution	c.*3+80T>G		1	
	Substitution	c.*239G>A		1	
SMPD1	Deletion	c.996del	p.F333fs	1	Niemann–Pick disease, type A/ type B
TMEM216	Insertion	c.228dup	p.G77fs	1	Joubert syndrome 2/Meckel syndrome 2
XPC	Deletion	c.1643_1644del	p.V548fs	2	Xeroderma pigmentosum

NOTE: Above list does not include variants present in the GM24385 background. Target variant allele frequency is 50%. Substitution refers to a single nucleotide variant; Indel is defined as a deletion/insertion less than 10 base pairs, and large deletions or insertions are defined as longer than 10 base pairs.

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.

Human Genetic and Genomic Testing Using Traditional and High-Throughput Nucleic Acid Sequencing Methods. Third Edition. CLSI guideline MM09, 2023.