Seraseq®

Blood TMB Mix Score 7, 13, 20 & 26 Products — 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® Blood TMB Mix products are reference materials formulated for use with Next Generation Sequencing (NGS) assays that detect somatic mutations in human cancer patient samples. These products are intended for use as reference materials in the determination of the number of somatic mutations per genome 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	Blood TMB Reference Materials
0710-2087	Seraseq® Blood TMB Mix Score 7
0710-2088	Seraseq® Blood TMB Mix Score 13
0710-2089	Seraseq® Blood TMB Mix Score 20
0710-2090	Seraseq® Blood TMB Mix Score 26

Each item consists of 3 vials at tumor fractions of 0%, 0.5% and 2%; 3x10 ng/µl concentration; 3x20 µl fill volumes; and 3x200 ng total mass.

WARNINGS AND PRECAUTIONS

For Research Use Only. Not for use in diagnostic procedures.
CAUTION: Handle Seraseq Blood TMB Mix product as though it is capable of transmitting infectious agents. This product consists of purified and fragmented DNA from diseased (lung or breast cancer, i.e., tumor) and SNP-matched non-diseased (i.e., normal) human cell lines.

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 Blood TMB Mix product beyond the expiration date. Avoid contamination of the product when opening and closing the vial.

STORAGE INSTRUCTIONS

Store Seraseq Blood TMB Mix frozen at -20°C. After opening, record the date opened and the expiration date on the vial. Aliquoting of the product into low DNA binding tubes may be advisable to limit the number of freeze-thaw cycles.

INDICATIONS OF REAGENT INSTABILITY OR DETERIORATION

Seraseq Blood TMB Mix products are formulated as tumor-normal reference materials derived from expanded/cultured human cell lines of diseased (tumor) and matching non-diseased (normal) patients, and 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

Each Seraseq Blood TMB Mix consist of 3 vials of fragmented (~188bp size, see Figure 1) and purified DNA from human cell lines (diseased and normal), blended at tumor fractions of 0% (WT), 0.5% and 2%. 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. Each vial of the Seraseq Blood TMB 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

Tissue TMB values were assigned using Whole Exome data for the matched parental tumor and normal DNA cell lines, which uses a VAF 5% cutoff for non-synonymous TMB variant detection. Applying the same criteria for Blood TMB is a challenge because at VAF 5% and 100% tumor, a 2% tumor fraction results in a VAF cutoff of 0.1%, which is below the claimed LoD of many cfDNA NGS assays.
https://www.q2labsolutions.com/en/genomics-laboratories/tso500-plasma

Blood TMB scores for each tumor fraction of the Seraseq Blood TMB Mix products were determined by a targeted NGS assay (TSO500 plasma) and analyzed by the associated bioinformatics pipeline. Results are shown in Table 1. Detection of somatic mutations may differ across different NGS panels, and concomitantly the Blood TMB scores determined by targeted NGS panels for the Seraseq Blood TMB Mix products may differ. The matched normal DNA that comprises ≥98% of total DNA in each product, contains some low frequency variants which should be treated as clonal hematopoiesis and subtracted from the Blood TMB Scores determined for the 2% and 0.5% blends. Each laboratory must establish an expected Blood TMB score for each of the Seraseq Blood TMB Mix products. 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 (VCFs of filtered mutations from analysis pipeline) are available by contacting us at CDx-info@LGCgroup.com

LIMITATIONS OF THE PROCEDURE

Seraseq Blood TMB Mix 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 Blood TMB Mix 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.

SeraCare Life Sciences, Inc. | 37 Birch Street, Milford, MA 01757 USA
Phone: +1 508.244.6400 | Toll Free (US Only) 800.676.1818
info@seracare.com | www.seracare.com

13829-03 August 2021

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.

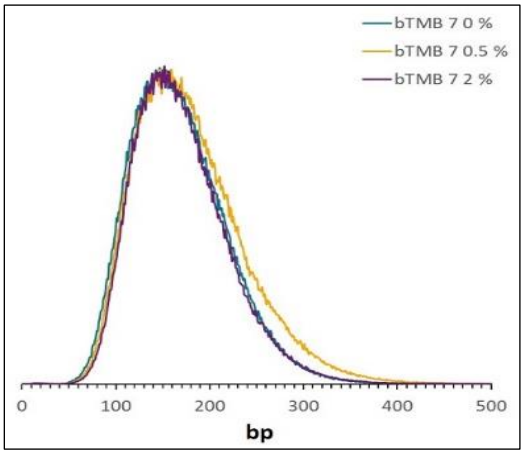

Figure 1: Example DNA fragment sizing in the Seraseq® Blood TMB Mix Score 7 for TF 0%, 0.5% and 2%.

Table 1: Targeted NGS assay[1] determination of Blood TMB Scores for the Seraseq Blood TMB Mix products.

Blood TMB Reference Materials	Material Number	Blood TMB Score TF 0%[2]	Blood TMB Score TF 0.5%[2]	Blood TMB Score TF 2%[2]	Adjusted[3] Blood TMB Score (TF 0.5%)	Adjusted[3] Blood TMB Score (TF 2%)
Seraseq® Blood TMB Mix Score 7	0710-2087	7.5 ± 1.7	13.1 ± 2.6	17.9 ± 1.3	5.6 ± 0.9	10.4 ± 0.4
Seraseq® Blood TMB Mix Score 13	0710-2088	4.6 ± 0.5	18.7 ± 2.1	24.6 ± 0.8	14.1 ± 2.2	20.0 ± 0.9
Seraseq® Blood TMB Mix Score 20	0710-2089	7.5 ± 1.4	26.0 ± 2.3	35.6 ± 1.0	18.5 ± 2.7	28.1 ± 1.7
Seraseq® Blood TMB Mix Score 26	0710-2090	6.0 ± 0.5	20.7 ± 5.5	30.4 ± 1.8	14.7 ± 5.0	24.4 ± 1.3

[1]Analysis was performed using the ILMN TSO500 plasma assay, on a Novaseq 6000 NGS system.
[2]Averaged from three technical replicate measurements.
[3]Subtracts the TF 0% Blood TMB variant contributions (~5-7.5) for the tumor-derived (adjusted) scores.