

TruSight™ Oncology Controls Package Insert

FOR IN VITRO DIAGNOSTIC USE
FOR EXPORT ONLY

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Intended Use

The TruSight Oncology Controls, which consist of the TruSight Oncology DNA Control and the TruSight Oncology RNA Control, are intended for qualitative *in vitro* diagnostic use as a quality control to monitor analytical performance of the library preparation, sequencing, and analysis steps of Next Generation Sequencing (NGS) based molecular diagnostic assays used for the detection of select DNA and RNA variants. This product is also intended to help monitor performance of an NGS test system by detecting analytical deviations such as those that may arise from reagent or instrument variation in genetic testing.

Product Description

TruSight Oncology (TSO) Controls comprise two separately available products: TSO DNA Control and TSO RNA Control.

TSO DNA Control is a multiplexed blend of biosynthetic DNA in a background of DM24385 cell line DNA. It contains 40 variants across 28 genes representing single nucleotide variants, insertions, deletions, and rearrangements (Table 1).

Table 1 Variants Present in TSO DNA Control

COSMIC ID	Gene	Nucleotide Change	Amino Acid Change
COSM33765	AKT1	c.49G>A	p.E17K
COSM13127	APC	c.4348C>T	p.R1450*
COSM18561	APC	c.4666dup	p.T1556Nfs*3
COSM21924	ATM	c.1058_1059del	p.C353Sfs*5
COSM476	BRAF	c.1799T>A	p.V600E
COSM5664	CTNNB1	c.121A>G	p.T41A
COSM12378	EGFR	c.2310_2311insGGT	p.D770_N771insG
COSM6225	EGFR	c.2236_2250del	p.E746_A750del
COSM6224	EGFR	c.2573T>G	p.L858R
COSM6240	EGFR	c.2369C>T	p.T790M
COSM682	ERBB2	c.2313_2324dup	p.Y772_A775dup
COSM715	FGFR3	c.746C>G	p.S249C
COSM783	FLT3	c.2503G>T	p.D835Y
COSM33661	FOXL2	c.402C>G	p.C134W
COSM52969	GNA11	c.626A>T	p.Q209L
COSM28758	GNAQ	c.626A>C	p.Q209P
COSM27887	GNAS	c.2530C>T	p.R844C
COSM28747	IDH1	c.394C>T	p.R132C
COSM12600	JAK2	c.1849G>T	p.V617F
COSM1314	KIT	c.2447A>T	p.D816V
COSM521	KRAS	c.35G>A	p.G12D
COSM18918	MPL	c.1544G>T	p.W515L
COSM17559	NPM1	c.860_863dup	p.W288Cfs*12
COSM584	NRAS	c.182A>G	p.Q61R
COSM736	PDGFRA	c.2525A>T	p.D842V

COSMIC ID	Gene	Nucleotide Change	Amino Acid Change
COSM28053	PDGFRA	c.1694_1695insA	p.S566Qfs*6
COSM763	PIK3CA	c.1633G>A	p.E545K
COSM775	PIK3CA	c.3140A>G	p.H1047R
COSM12464	PIK3CA	c.3203dup	p.N1068Kfs*5
COSM5809	PTEN	c.800del	p.K267Rfs*9
COSM4986	PTEN	c.741 dup	p.P248Tfs*5
COSM965	RET	c.2753T>C	p.M918T
COSM14105	SMAD4	c.1394dup	p.A466Gfs*28
COSM6530	TP53	c.723del	p.C242Afs*5
COSM10648	TP53	c.524G>A	p.R175H
COSM10662	TP53	c.743G>A	p.R248Q
COSM10660	TP53	c.818G>A	p.R273H
COSM18610	TP53	c.267del	p.S90Pfs*33
N/A	NCOA4-RET	N/A	N/A
N/A	TPR-ALK	N/A	N/A

TSO RNA Control is a multiplexed blend of RNA transcripts in a background of GM24385 RNA. It contains 16 fusions across 26 genes and 2 splice variants across 2 genes (Table 2). For fusions, the 5' partner is listed first, and the 3' partner is listed after the hyphen.

Table 2 Variants Present in TSO RNA Control

Variant	Variant	Variant
CCDC6-RET	FGFR3-TACC3	SLC45A3-BRAF
CD74-ROS1	KIF5B-RET	TFG-NTRK1
EGFR-SEPT14	LMNA-NTRK1	TMPRSS2-ERG
EML4-ALK	NCOA4-RET	TPM3-NTRK1
ETV6-NTRK3	PAX8-PPARG	EGFR VIII
FGFR3-BAIAP2L1	SLC34A2-ROS1	MET Exon 14

Limitations

For *in vitro* diagnostic use.

Results presented in the labeling were obtained with a representative assay. Performance characteristics are provided for information purposes only. Variant detection results of the TruSight Oncology Controls might differ according to the library preparation method, sequencing method, and the bioinformatics pipeline. The end user is responsible for establishing their own performance criteria appropriate for their system.

Detection of NCOA4-RET and TPR-ALK in the TruSight Oncology DNA Control has not been evaluated by Illumina®.

Product Components

Product	Catalog Number	Quantity	Volume	Concentration*	Active Ingredients	Storage Temperature
TruSight Oncology DNA Control	20065041	1	25 µl	20 ng/µL	Synthetic DNA pool	-25°C to -15°C
TruSight Oncology RNA Control	20065042	1	25 µl	25 ng/µL	Synthetic RNA pool	-85°C to -65°C

*Minimum concentration is indicated. Actual concentration varies per lot and is indicated on the tube label.

Storage and Handling

TSO DNA Control, when stored at -15°C or below, is stable through the expiration date printed on the tube label and on the kit box. The tube can undergo 10 freeze-thaws from multiple uses of the tube. Use good laboratory practices to avoid contamination.

TSO RNA Control, when stored at -65°C or below, is stable through the expiration date printed on the tube label and on the kit box. The tube can undergo 10 freeze-thaws from multiple uses of the tube. Use good laboratory practices to avoid contamination.

Do not aliquot.

Warnings and Precautions

- ▶ Avoid cross-contamination.
- ▶ Follow proper laboratory practices when handling the product.
- ▶ Use fresh consumable labware and fresh pipette tips between samples and between dispensing products.
- ▶ Use aerosol resistant tips to reduce the risk of cross-contamination.
- ▶ Follow proper assay procedure and note safety, laboratory, and assay warnings and precautions.
- ▶ Use routine laboratory precautions. Do not pipette by mouth. Do not eat, drink, or smoke in designated work areas. Wear disposable gloves and laboratory coats when handling the product. Wash hands thoroughly after handling the product.
- ▶ Use nuclease-free microcentrifuge tubes, plates, pipette tips, and reservoirs.
- ▶ Use precision pipettes to ensure accurate product delivery. Calibrate regularly according to manufacturer specifications.
- ▶ Do not use TSO Controls beyond their stated expiration date on the tube label.

Instructions for Use

Instructions apply to both TSO DNA Control and TSO RNA Control.

- 1 Thaw contents on ice.
- 2 Gently vortex or invert the tube to mix, then briefly centrifuge the tube to collect contents to the bottom of the tube.
- 3 Dilute to the desired concentration in an appropriate buffer. Use the actual concentration on the tube label for a given lot of control when making dilution calculations, if dilutions are needed.
A suggested diluent for TSO DNA Control is Tris-EDTA (10 mM Tris, 1 mM EDTA, pH 8.0). A suggested diluent for TSO RNA Control is DNase and RNase free water.
- 4 Test the control like an assay sample alongside the assay samples.
- 5 Store at label conditions in between uses.

Performance Characteristics

TSO Controls were tested across multiple external sites, operators, and lots using TruSight Oncology Comprehensive (TSO Comprehensive) as the representative assay.

TSO DNA Control was tested with TSO Comprehensive. TSO DNA Control was diluted in Tris-EDTA buffer and 40 ng was used as sample input. At each of 3 external sites, 2 operators per site tested 3 lots of TSO DNA Control in combination with 3 lots of TSO Comprehensive assay kits. Libraries were sequenced on NextSeq 550Dx sequencers. In total, 112 sample results were generated for TSO DNA Control. There were 24 calls per sample for a total of 2688 evaluable expected calls.

A representative set of variants encompassing multiple variant types spanning a range of cancer related genes were selected for evaluation of reproducibility of the TSO DNA Control (Table 3).

Table 3 Selected TSO DNA Control Variants for Reproducibility

Variant	Variant	Variant	Variant
AKT1 E17K	EGFR E746_A750del	KIT D816V	PTEN P248Tfs*5
APC R1450*	ERBB2 Y772_A775dup	KRAS G12D	RET M918T
APC T1556Nfs*3	GNA11 Q209L	MPL W515L	SMAD4 A466Gfs*28
ATM C353Sfs*5	GNAQ Q209P	NRAS Q61R	TP53 R175H
CTNNB1 T41A	GNAS R844C	PDGFRA D842V	TP53 R248Q
EGFR L858R	JAK2 V617F	PIK3CA E545K	TP53 R273H

Results are summarized in Table 4. Correct calls were based on detection of the 24 variants in Table 3.

Table 4 External Site Evaluation of TSO DNA Control

Site	Site Operator	# of Runs	Total Expected Calls	% Observed Positive Calls
1	1	3	432	94.9%
1	2	3	432	94.4%
2	1	3	432	100%
2	2	3	432	100%
3	1	4	528	100%
3	2	3	432	100%
	Total	19 runs	2688 calls	98.3% correct

TSO RNA Control was tested with TSO Comprehensive. TSO RNA Control was diluted in RNase and DNase free water and 40 ng was used as sample input. At each of 3 external sites, 2 operators per site tested 3 lots of TSO RNA Control each with 4 lots of TSO Comprehensive assay kits. Libraries were sequenced on NextSeq 550Dx sequencers. In total, 96 sample results were generated for TSO RNA Control. There were 13 calls per sample for a total of 1248 evaluable expected calls.

A representative set of variants encompassing multiple fusions and a splice variant spanning a range of cancer related genes were selected for evaluation of reproducibility of the TSO RNA Control (Table 5).

Table 5 Selected TSO RNA Control Variants for Reproducibility

Variant	Variant	Variant	Variant
CCDC6-RET	FGFR3-BAIAP2L1	SLC45A3-BRAF	MET Exon 14*
CD74-ROS1	KIF5B-RET	TFG-NTRK1	N/A
EML4-ALK	NCOA4-RET	TMPRSS2-ERG	N/A
ETV6-NTRK3	PAX8-PPARG	TPM3-NTRK1	N/A

* MET Exon 14 is a splice variant. All other variants are gene fusions.

Results are summarized in Table 6. Correct calls were based on detection of the 13 variants in Table 5.

Table 6 External Site Evaluation of TSO RNA Control

Site	Site Operator	# of Runs	Total Expected Calls	% Observed Positive Calls
1	1	8	208	100%
1	2	8	208	100%
2	1	8	208	100%
2	2	8	208	100%
3	1	8	208	99%
3	2	8	208	100%
	Total	48 runs	1248 calls	99.8% correct

Revision History

Document	Date	Description of Change
Document # 200009919 v01	April 2022	Added FOR EXPORT ONLY marking.
Document # 200009919 v00	November 2021	Initial release.

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