Seraseq® BRCA1/2 Exon Deletions Reference Materials

Reference material for NGS-based BRCA assay development, validation, and routine QC use

INTRODUCTION

Genetic testing of the tumor suppressor genes BRCA1 and BRCA2 allows for the identification of DNA variants which are associated with an elevated lifetime risk of breast, ovarian, pancreatic and prostate cancer.

Accurate detection of pathogenic variants in BRCA1 or BRCA2 has a significant impact on the clinical management of disease, including determining a patient's eligibility for new PARP inhibitors. However, larger structural alterations—such as exon deletions involving one or more exons—are often missed by PCR-based methods and targeted next-generation sequencing (NGS) assays due to limitations such as primer binding, breakpoint identification, and coverage variability. Given the complexity of detecting these genomic alterations, there is a critical need for a comprehensive BRCA1/2 testing algorithm that includes reference materials incorporating such large pathogenic deletions.

To support clinical laboratories in developing, characterizing, validating, and routinely assessing BRCA assays, LGC Clinical Diagnostics has developed novel reference materials containing large exon deletions in the BRCA1 and BRCA2 genes.

This unique product includes BRCA1 exon 10 deletion and BRCA2 multi-exon deletion spanning exons 10 through 14 (Table1), engineered into large BRCA1 and BRCA2 synthetic constructs. It is formulated in a well-characterized genomic background (GM24385) at clinically relevant allele frequencies.

HIGHLIGHTS

High quality reference material containing exon level deletions in BRCA1 (exon10) and BRCA2 (exons 10-14) exons

Available in mutation mix format to develop, validate, monitor, and troubleshoot your assay

Manufactured under cGMP compliance in ISO 13485 certified facilities

FEATURES

- Develop, monitor, validate and challenge your BRCA NGS assays with confidence using reference material containing biomarkers important in BRCA-driven cancers.
- Contains two large pathogenic BRCA1/2 exon deletions
- Available as purified genomic DNA at ~60% allele frequencies
- Mutation targets quantitated by highly sensitive dPCR assays, and orthogonally analyzed by NGS
- All mutations are blended against the well-characterized GM24385 human genomic DNA as 'wild-type' background material.

ORDERING INFORMATION

Material #	Product	Conc.	Fill Size	Total Mass	VAF
0730-0570	Seraseq® BRCA1/2 Exon Deletions DNA Mix	15 ng/µL	25 µL	375 ng	~60%

*Concentration and Variant Allele frequency (VAF) as determined by Qiagen Qubit dsDNA BR Assay and digital PCR (dPCR; Bio-Rad QX200) respectively. See the Technical Product Report for more details.

To place an order, please contact us at +1.508.244.6400 and +1 800.676.1881 or email CDx-CustomerService@lgcgroup.com.

TABLE 1

Genes	Transcript	Necleotide Change	Protein Change	GRCh37 Location	GRC38 Location	Type of Nucleotide Alteration	Variatian Size (bp)
BRCA1	ENST00000 357654.9	c.671-56_4096+89del	p.(Ala224_ Leu1365del)	chr17: 41243363-41246933	chr17:43091346-43094916	Deletion - Exon 10	3.43kb
BRCA2	ENST00000 380152.8	c.794-97_7435+146del	p.(Gly265_ Leu2478del)	chr13: 32906312-32929571	chr13:32332175-32355434	Deletion - Exon 10-14	23.02kb

NOTE: Genomic coordinates use the 1-based coordinate system. Above list does not include variants present in the GM24385 background.
Target variant allele frequency (VAF) at 60%.

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.

IGV VISUALIZATION OF EXON-LEVEL DELETIONS IN BRCA1/2 CONSTRUCTS

This product contains large synthetic BRCA1 and BRCA2 DNA constructs, measuring 3.43 kb and 23.02 kb, respectively. IGV screenshots (Figures 1 and 2) derived from WES testing (~5x coverage) display the read alignments of the BRCA1 and BRCA2 constructs.

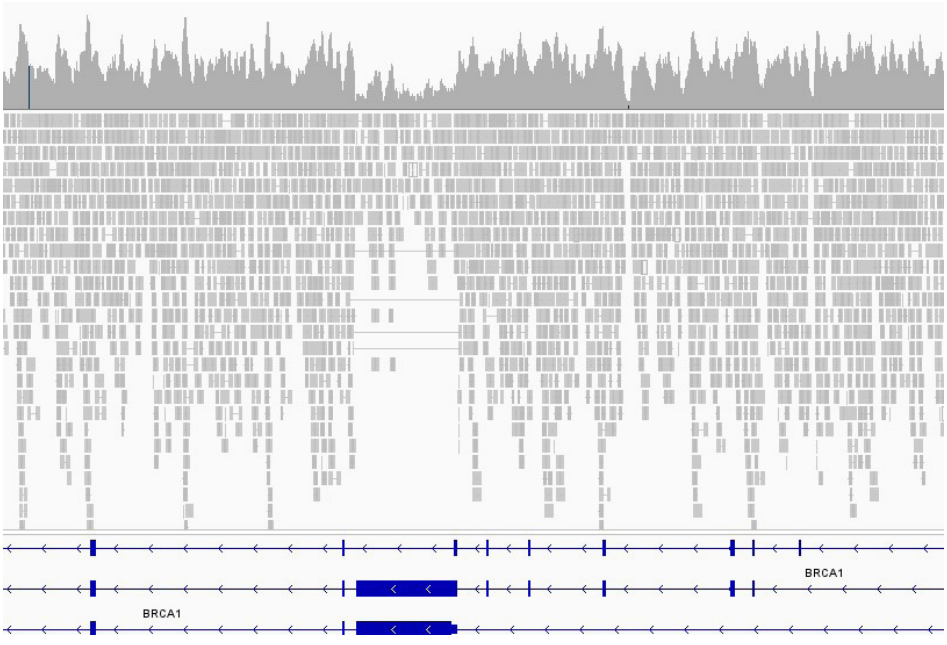

FIGURE 1: IGV visualization of read alignments to the synthetic BRCA1 construct from NGS sequencing highlighting exon deletions. The track shows clear gap in coverage indicating the missing exon 10.

IGV VISUALIZATION OF EXON-LEVEL DELETIONS IN BRCA1/2 CONSTRUCTS continued

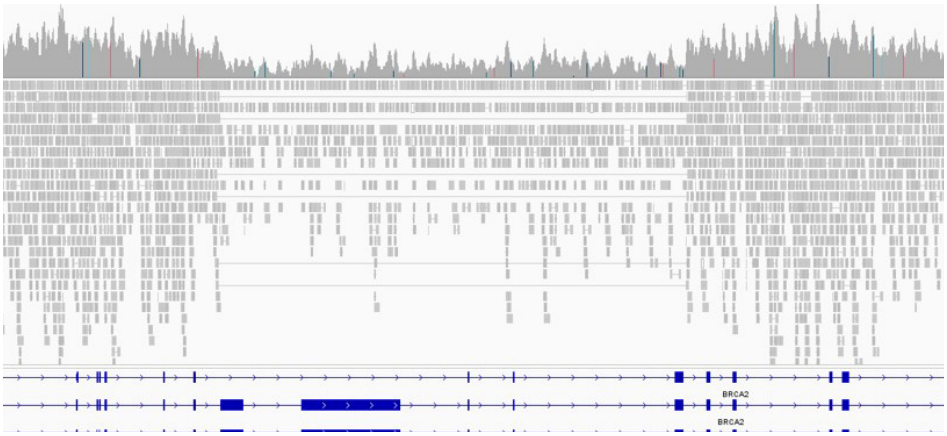

FIGURE 2: IGV visualization of read alignments to the synthetic BRCA2 construct from NGS sequencing highlighting exon deletions. The track shows clear gap in coverage indicating the deletion of exons 10-14.

ABOUT US

SeraCare offers a comprehensive portfolio of reference materials for oncology and reproductive health, designed and manufactured to meet the precision demanded by NGS assays. The portfolio includes high quality ground-truth RNA, ctDNA and genomic DNA-based reference materials that are NGS platform agnostic for tumor profiling, immuno-oncology, liquid biopsy, NIPT and germline cancer assay workflows. **For more information visit seracare.com**

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