Seraseq® ctDNA ESR1 Reference Materials

Accelerate breast cancer liquid biopsy assay validation and clinical implementation with a comprehensive reference material

INTRODUCTION

As liquid biopsy assays gain acceptance for a growing variety of clinical applications, an acute need for highly multiplexed reference materials bearing a broad range of clinically relevant variant types has arisen. Acquiring useful patient specimens is prohibitively time-consuming, and cell lines bearing single mutations are inefficient and add unnecessary expense.

The *ESR1* gene is frequently mutated in metastatic breast cancer (MBC), with 15-50% of all metastatic breast cancer patients harboring *ESR1* mutations. *ESR1* mutations develop in response to selection pressure during treatment and are typically undetectable in the primary tumor. The recent emergence and approval of drug therapy specific to *ESR1* mutations in metastatic breast cancer have led to the updated guidance to monitor MBC patients for mutations in both *ESR1* and *PIK3CA* to guide treatment decisions. Such mutations are often polyclonal and co-occurring, and most easily tracked in circulating tumor DNA (ctDNA) in liquid biopsy samples.

Seraseq ctDNA *ESR1* reference materials can help confirm the presence of clinically relevant *ESR1* and *PIK3CA* variants including ones in the druggable ligand binding domain of *ESR1*. Care has been taken in the design of this reference material to include all DNA alterations which lead to the relevant changes to the amino acid sequence of the *ESR1* protein to confirm detection of different variant types.

HIGHLIGHTS

22 variants in the clinically relevant portions of *ESR1* and *PIK3CA* genes

Improved manufacturing to reduce background noise

Consistently performing with batch-specific VAF information provided

FEATURES AND BENEFITS

- 22 clinically relevant mutations in *ESR1* and *PIK3CA*
- All variants present at 1% variant allele frequency (VAF) with WT sample available to dilute and challenge limit of detection
- All DNA mutations leading to clinically relevant amino acid substitutions in the ligand binding domain of *ESR1* (e.g. 3 different DNA sequences leading to a Y537S amino acid substitution) are present
- Variants precisely quantitated with digital PCR and orthogonally validated by NGS
- Blended with well-characterized GM24385 human genomic DNA as background wild-type material
- Manufactured in cGMP-compliant, ISO 13485 certified facilities.

ORDERING INFORMATION

Material #	Product	Concentration*	Fill Volume	Total Mass
0710-3565	Seraseq ctDNA ESR1 Mutation Mix AF1%	10 ng/µL	25 µL	250 ng
0710-3564	Seraseq ctDNA ESR1 Mix WT	10 ng/µL	25 µL	250 ng

*Concentration targets are based on the Qubit dsDNA BR Assay.

MUTATIONS PRESENT IN SERASEQ® ctDNA ESR1 1%

#	Gene	Nucleic Acid Change	Amino Acid Change	Variant Type
1	ESR1	c.1138G>C	E380Q	SNV
2		c.1387T>C	S463P	SNV
3		c.1603C>A	P535T	SNV
4		c.1607_1608delinsAT	L536H	INDEL
5		c.1607T>A	L536H	SNV
6		c.1607T>C	L536P	SNV
7		c.1607T>G	L536R	SNV
8		c.1607_1608delinsAG	L536Q	INDEL
9		c.1610_1611delinsCA	Y537S	INDEL
10		c.1609_1610delinsAG	Y537S	INDEL
11		c.1610A>C	Y537S	SNV
12		c.1609T>A	Y537N	SNV
13		c.1608_1609delinsTA	Y537N	INDEL
14		c.1610A>G	Y537C	SNV
15		c.1609T>G	Y537D	SNV
16		c.1613A>G	D538G	SNV
17		c.1610_1615dupATGACC	D538_L539insHD	INDEL
18		c.1625A>G	E542G	SNV
19	PIK3CA	c.1624G>A	E542K	SNV
20		c.1633G>A	E545K	SNV
21		c.3140A>G	H1047R	SNV
22		c.3203dupA	p.N1068Kfs*5	INDEL

NOTE: Above list does not include variants present in the GM24385 background. Indels are defined as deletion/insertions less than 10 base pairs.

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