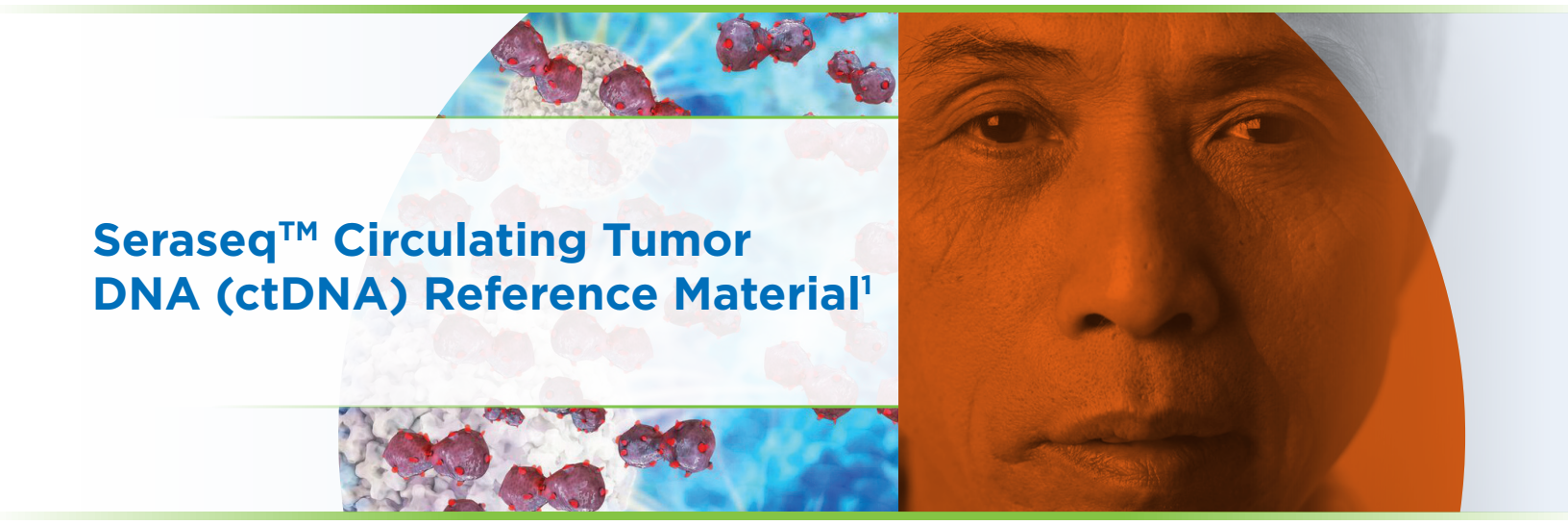

Seraseq™ Circulating Tumor DNA (ctDNA) Reference Material[1]

Introducing an early-access product for oncology circulating tumor DNA assays

An area of great interest in translational cancer research and clinical application is circulating tumor DNA analysis. This is at times given the term 'liquid biopsy'[2]; however, this term is also applied to circulating tumor cell analysis in addition to circulating tumor DNA. The ability to detect and monitor specific mutations in cell-free DNA at very low-levels (often less than 1%) offers diagnostic, prognostic, and predictive potential[2], however is not yet routinely performed as a clinical application. Having a stable source of precisely quantified circulating tumor DNA is vital for assay development and verification processes.

The amount of circulating free DNA (cfDNA) in plasma can be limiting, on the order of 30 nanograms per 5 mL of plasma sample[3]; in addition, 10 nanograms represents only about 3,000 copies of the human genome, and assays to detect at a 1% level means only 30-copy detection sensitivity. At 0.1% variant allele frequency, there are only about 3 copies present to detect.[3]

Designed for both next-generation sequencing-based and digital PCR-based assays, the Seraseq Circulating Tumor DNA-I Reference Material is a set of 9 DNA mutations at specific percentage ratios against a background of well-characterized genomic DNA (GM24385) (Table 1). The material is fragmented (similar to the circulating DNA found naturally, around 170 base-pairs in length), stabilized via a proprietary method, and blended into a matrix containing human proteins to mimic natural plasma (Figure 1). Careful titration and measurement of the target mutation yields minor allele frequencies of 5%, 1.25%, 0.625%, and 0.125%, and wild-type (0%).

Table 1: List of actionable circulating tumor DNA (ctDNA) targets in the Seraseq Circulating Tumor DNA-I Reference Material.

Gene	Mutation	Type	COSMIC ID
BRAF	V600E	SNV	COSM476
EGFR	T790M	SNV	COSM6240
EGFR	p.D770_N771insG	INDEL	COSM12378
EGFR	p.E746_A750delELREA	INDEL	COSM6226
PIK3CA	p.H1047R	SNV	COSM775
PIK3CA	p.N1068fs*4	INDEL	COSM12464
NRAS	p.Q61R	SNV	COSM584
KRAS	G12D	SNV	COSM521
KIT	D816V	SNV	COSM1314

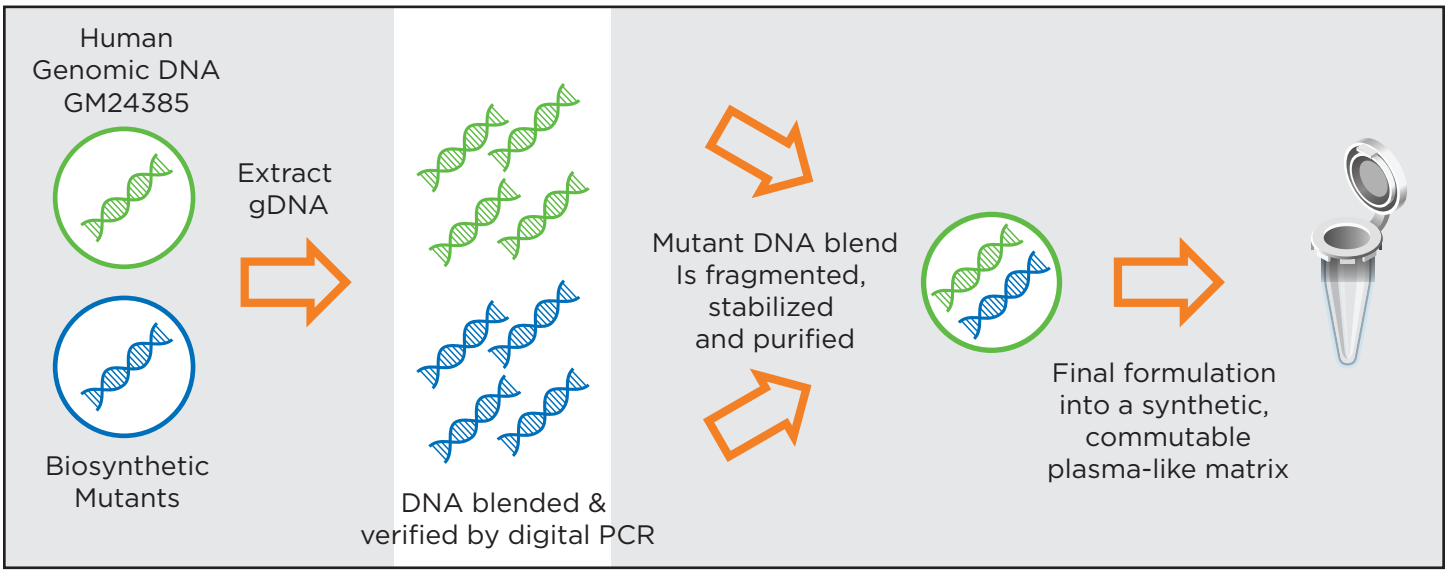

Figure 1: Preparative methodology of the Seraseq Circulating Tumor DNA-I Reference Material.

For those who need purified DNA for assay development, SeraCare also offers the Seraseq Circulating Tumor DNA-I Mutation Mix Kit (AF5-WT), which is a set of six vials containing nine mutations with the same allele frequencies (5%, 1.25%, 0.625%, 0.12% and wild-type) as the reference material.

With over 30 years of supplying the highest quality reference and disease-state materials to in-vitro diagnostic manufacturers worldwide, SeraCare's cGMP compliance, ISO 9001 and ISO 13485 certified facilities assure consistent high-quality products that you can depend upon.

Ordering Information

Product	Item Number
Seraseq Circulating Tumor DNA-I (AF5) Reference Material	0710-0012
Seraseq Circulating Tumor DNA-I (AF1.2) Reference Material	0710-0014
Seraseq Circulating Tumor DNA-I (AF0.6) Reference Material	0710-0015
Seraseq Circulating Tumor DNA-I (AF0.1) Reference Material	0710-0016
Seraseq Circulating Tumor DNA-I (WT) Reference Material	0710-0017
Seraseq Circulating Tumor DNA-I Mutation Mix Kit (AF5-WT)	0710-0018

References

1. Patent Pending
2. Heitzer E, Ulz P, Geigl JB. Circulating tumor DNA as a liquid biopsy for cancer. Clin Chem. 2015 61(1):112-23. doi: 10.1373/clinchem.2014.222679. Review. PubMed PMID: 25388429.
3. Mussolin L, Burnelli R, Pillon M, Carraro E, Farruggia P, Todesco A, Mascarin M, Rosolen A. Plasma cell-free DNA in paediatric lymphomas. J Cancer. 2013 Apr 16;4(4):323-9. doi: 10.7150/jca.6226. Print 2013. PubMed PMID: 23678368; PubMed Central PMCID: PMC3654488.

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