Seraseq® NIPT Reference Materials

ASSAY VALIDATION AND DAILY-RUN QC MATERIAL FOR NON-INVASIVE PRENATAL TESTING (NIPT)

HIGHLIGHTS

PATIENT-LIKE: DERIVED FROM PREGNANT PATIENT SAMPLES AND CONTAINING MATERNAL & FETAL CFDNA

HIGH-QUALITY THIRD-PARTY QC MATERIAL TO DEVELOP, VALIDATE, MONITOR, AND TROUBLESHOOT YOUR NIPT ASSAY

CONVENIENT FULL-PROCESS CONTROL: SINGLE VIAL FORMAT OF PLASMA-LIKE MATERIAL TO SAVE TIME, COST, AND INCREASE QC CONSISTENCY

NGS TECHNOLOGY AGNOSTIC: COMPATIBLE WITH A BROAD RANGE OF NIPT ASSAYS

SAVES TIME AND COST PROCURING REMNANT SAMPLES OR PRODUCING HOMEBREW REAGENTS

Non-invasive Prenatal Testing (NIPT) of circulating cell-free DNA (cfDNA) present in the blood of pregnant women assesses the risk that the fetus will be born with a genetic abnormality such as Down Syndrome (trisomy 21). Given the clinical implications of the test result, it is extremely critical that NIPT assays report back presence or absence of aneuploidies in an accurate and consistent manner in order to reduce the number of false negatives, false positives or no-call results.

LGC SeraCare's matched maternal-fetal reference materials are biomimetic: they are derived from pregnant maternal plasma and thus maintain the characteristics of a clinical sample (patient-like). This enables accurate assessment of a broad range of NIPT assays, including those based on whole-genome sequencing or targeted approaches such as single nucleotide polymorphism (SNP)-based assays, microarrays, or those using bioinformatic pipelines based on difference in maternal and fetal cfDNA representations.

The portfolio includes the most frequent chromosomal aneuploidies (such as Trisomy 21, 18, and 13) as well as sex chromosome aneuploidies (SCAs) (Turner, Klinefelter, Jacobs), and the most frequent microdeletion: 22q11 which is associated with DiGeorge Syndrome. Supplied in our SeraCon Matribase (simulated plasma matrix), they are designed to be used in the same way as clinical samples and enable monitoring of the full NIPT process - from extraction to reporting results.

PRODUCT FEATURES

- Collection of common aneuploidies: trisomy 21, 18, 13, XO, XXY, XYY, 22q11 as well as euploid reference materials
- Proprietary method maintains native cfDNA size profile of ~170 bp size distribution and natural maternal-fetal size difference
- Long shelf-life product allows for repeated use of the same lot for training, validation, or assay performance assessment
- Ensure lot-to-lot consistency with materials manufactured in GMP-compliant and ISO 13485-certified facilities
- Scalable technology allows for easy customization of fetal fraction, concentration, and material formulation (either in plasma or fragmented DNA in buffer format)

PRODUCT DESIGN:

Our 2nd generation products are derived from real clinical samples rather than cell lines thus avoiding the inherent limitations of artificially made genomic DNA. They were developed using an innovative and proprietary technology (patent-pending) which utilizes source plasma material obtained from pregnant patients (through an external collaboration) with a known condition as confirmed by NIPT or amniocentesis. The DNA is amplified, encapsulated and formulated in plasma matrix which enables the material to be processed similarly to a patient specimen as well as increases the product stability.

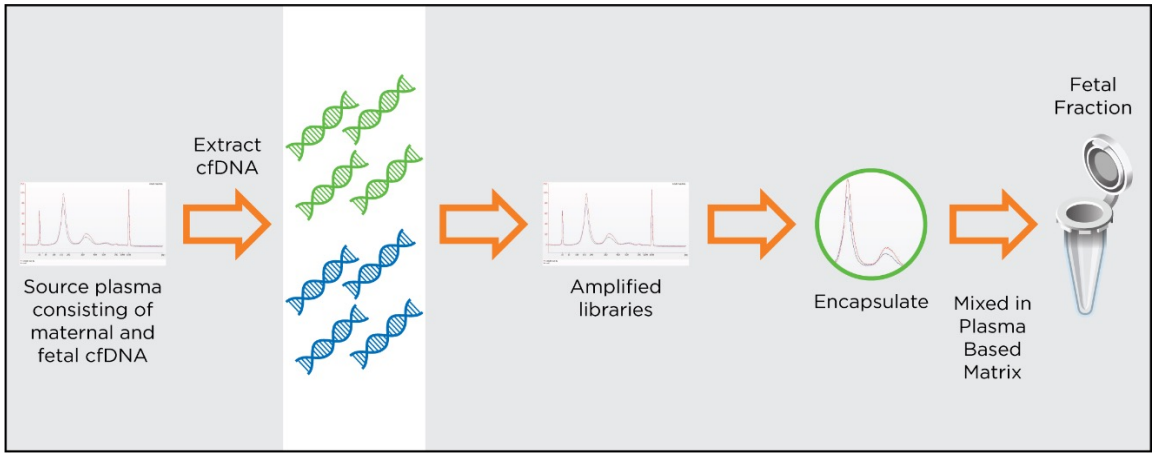

FIGURE 1: Creation of the NIPT reference materials: Matched materials prepared from a sample of maternal plasma containing maternal and fetal cfDNA. Plasma samples were collected from pregnant women, cfDNA was isolated, amplified via a proprietary method, encapsulated, and formulated in a plasma matrix.

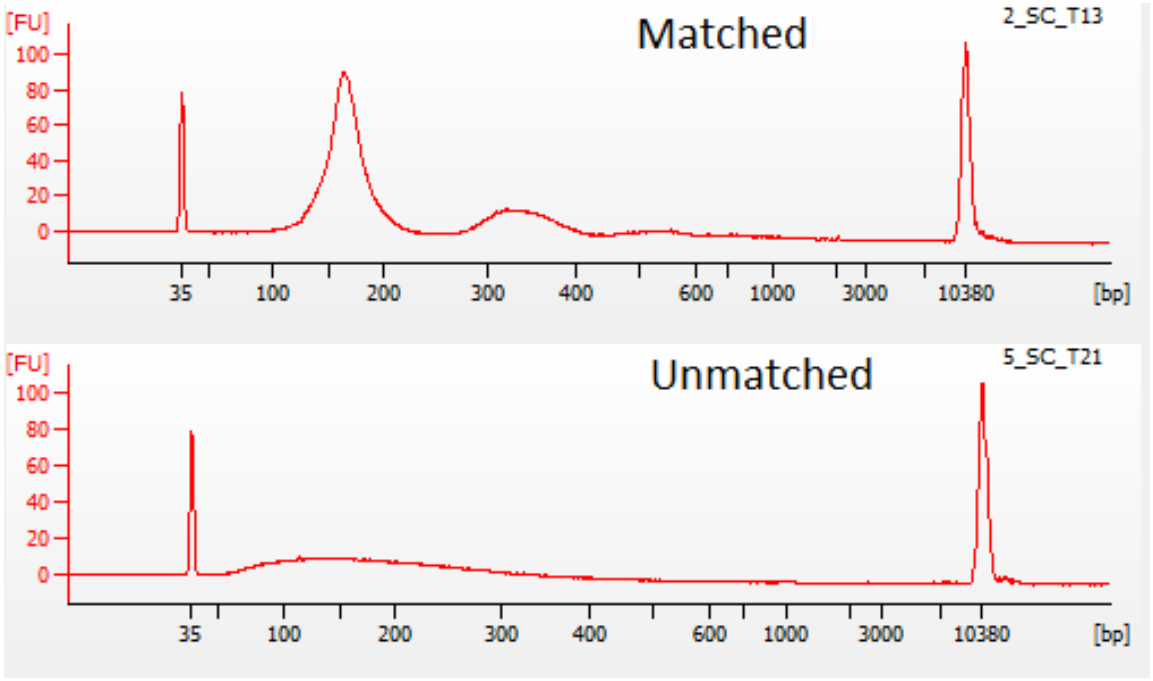

FIGURE 2: cfDNA size distribution difference between Seraseq Matched and Unmatched Reference Materials. Representative cfDNA size distribution of Seraseq® T13 Matched Reference Material (2nd generation, patient-derived) compared to a cell-line derived T21 reference material. X-axis represents base pairs; Y-axis represents relative fluorescence units. Peak size was observed between 150 and 200 bp. Samples were run on the Agilent 2100 Bioanalyzer by an external laboratory. A study has shown that maternal and fetal cfDNA fragment size distributions show a series of peaks, including a main peak of 166 bp and a small peak of 143 bp [2]. This shows that Seraseq matched reference materials have a similar cfDNA size distribution to clinical samples unlike reference materials made from fragmented cell line-derived DNA.

REAL-WORLD APPLICATION OF THE NIPT REFERENCE MATERIALS

The Seraseq NIPT reference materials have been successfully used in numerous labs across the world for a variety of applications ranging from new assay development to proficiency assessment and routine run QC.

Assay Development

- Enables sensitivity, specificity, limit of detection (LOD) studies and more
- Test range validity thanks to our customizable technology which allows for specific volume, concentration and fetal fraction
- Expedite new assay development and protocol optimization

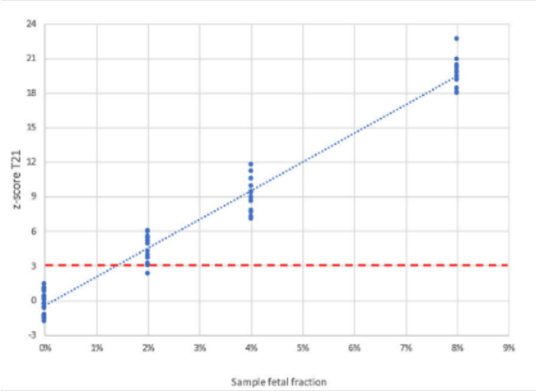

FIGURE 3A: Trisomy 21 Reference Materials at fetal fractions 0%, 2%, 4% and 8% were analyzed to evaluate ability to measure samples with low fetal fraction (Vanadis). Those were cell-line derived materials which are available on request or as custom).

Analytical Validation

- Confirm analytical performance and ability to correctly identify all the chromosomal aneuploidies (Figure 3B)
- Perform External Quality Assessment (EQA) and proficiency to ensure accuracy and comparability of routine clinical assays
- Conduct new assay installation and training

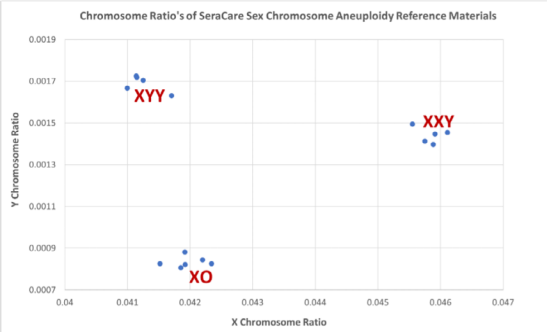

FIGURE 3B: Plot of X and Y chromosome ratios observed with our Sex Chromosome Aneuploidies matched reference materials (XYY, XXY, XO) by ADL Health laboratory using a whole-genome pair-end NGS NIPT assay.

Routine run QC

- Produces patient-like performance for monitoring daily run performance
- As shown in Figure 3C, when used as run controls, they cluster together with the patient samples (for both trisomy and euploid) providing a clear indication that these materials behave like patient samples
- Detect, monitor, and mitigate or troubleshoot issues at each step of the workflow

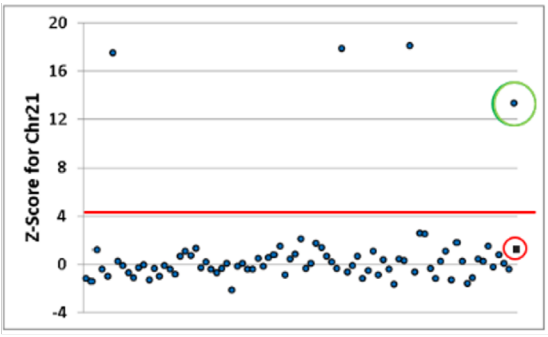

FIGURE 3C: Plot of samples run at the Cerba laboratory demonstrating majority of NIPT results being euploid with only 4 being T21 positive. The samples circled represent SeraCare T21 & euploid cell-line-made reference materials (1st generation, available on request) and their similarity to actual specimens.

ABOUT LGC SERACARE

TRUSTED SUPPLIER TO THE DIAGNOSTIC TESTING INDUSTRY FOR OVER 30 YEARS

HIGH-QUALITY CONTROL PRODUCTS, RAW BIOLOGICAL MATERIALS, AND IMMUNOASSAY REAGENTS

INNOVATIVE TOOLS AND TECHNOLOGIES TO PROVIDE ASSURANCE IN DIAGNOSTIC ASSAY PERFORMANCE AND TEST RESULTS

FOR MORE INFORMATION, PLEASE VISIT OUR WEBSITE: WWW.SERACARE.COM

RELIABLE, CONSISTENT REFERENCE MATERIAL

As a manufactured control reference material, developed under cGMP compliance in ISO 13485 certified facilities, Seraseq NIPT Reference Materials ensure a reliable, lot-to lot consistent supply. This eliminates the need to obtain, characterize, blend, and document your own mixes of cell lines, saving you time and resources in your assay development and validation efforts. Not for In Vitro Diagnostic Use. Research Use Only.

ORDERING INFORMATION

Matched NIPT Reference Materials

Condition	Material	Product	Fill Size
Euploid	0720-0169	Seraseq® Euploid Male Matched Reference Material	1 vial x 1 mL
	0720-0170	Seraseq® Euploid Female Matched Reference Material	
T21	0720-0167	Seraseq® Trisomy 21 Male Matched Reference Material	
	0720-0168	Seraseq® Trisomy 21 Female Matched Reference Material	
T18	0720-0171	Seraseq® Trisomy 18 Male Matched Reference Material	
	0720-0172	Seraseq® Trisomy 18 Female Matched Reference Material	
T13	0720-0779	Seraseq® Trisomy 13 Male-Matched Reference Material	
22q11	0720-0173	Seraseq® 22q11 Male - Matched Reference Material	
Sex Chromosome Aneuploidies	0720-0952	Seraseq® Turner Syndrome (XO) Reference Material	
	0720-0953	Seraseq® Klinefelter Syndrome (XXY) Reference Material	
	0720-0954	Seraseq® Jacobs Syndrome (XYY) Reference Material	

Custom NIPT Materials

The above products can be customized with regard to fetal fraction level, concentration, volume and format (DNA mix or plasma). Other conditions are available. Please contact LGC SeraCare for details.	Custom

LEARN MORE

To learn more about Seraseq NIPT Reference Materials and LGC SeraCare's product offering for reproductive health, visit https://www.seracare.com/nipt.

Contact us at (+1) 508.244.6400 and 800.676.1881 or email CDx-info@lgcgroup.com.

REFERENCES

1. *Dahl, F et al. (2018) Imaging single DNA molecules for high precision NIPT. Scientific Reports 8:4549*

2. *Lo, Y. M et al. (2010). Maternal plasma DNA sequencing reveals the genome-wide genetic and mutational profile of the fetus. Science translational medicine, 2(61), 61ra91.*

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