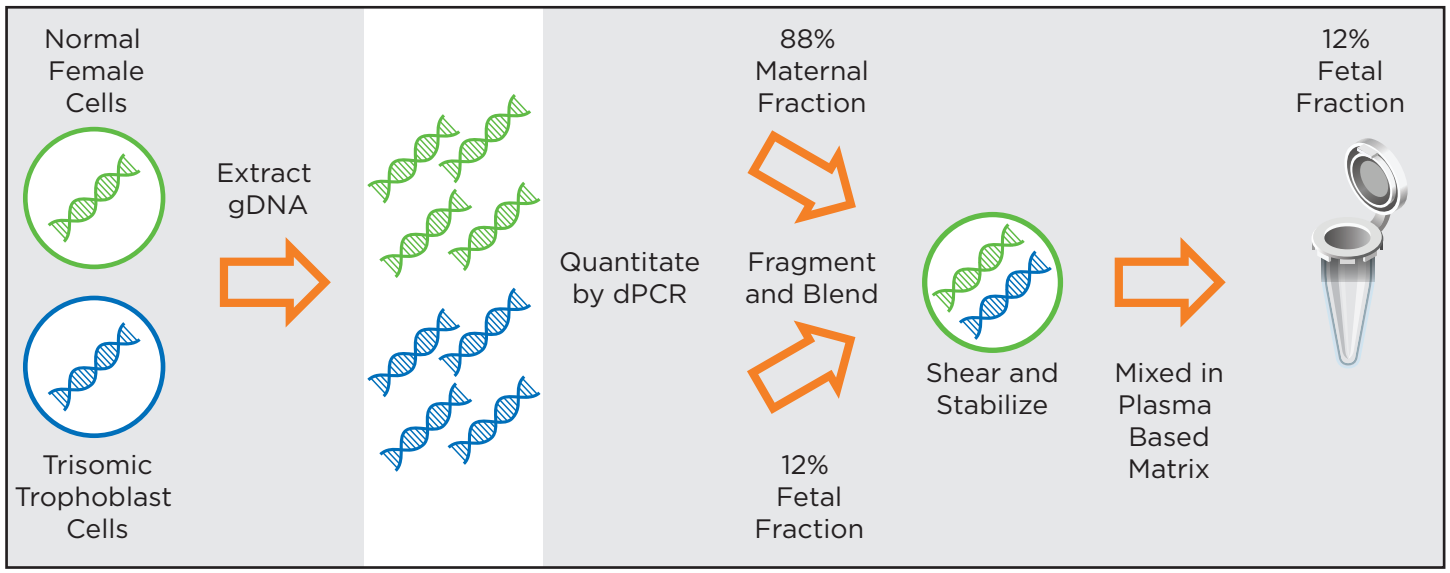
Seraseq™ Aneuploidy Reference Materials*

First cell-free fetal DNA aneuploidy reference material

As the non-invasive prenatal testing (NIPT) market continues to grow and more labs begin offering such assays, there is a need for reliable reference materials to ensure the accuracy of results. This is especially critical as labs scale up their operations and need to optimize, validate, and monitor ongoing assay performance. SeraCare has created a set of robust biosynthetic aneuploidy reference materials that alleviates the sourcing challenges and inherent variability in creating homebrew controls.

Seraseq Aneuploidy Reference Material is a mixture of cell-free fetal DNA (cfDNA) exhibiting one or multiple trisomies, and normal maternal DNA (unrelated) at specified fetal fractions.

- Fetal DNA derived from placental trophoblast cells exhibiting a trisomy
- Fragmented to ~170 bp to mimic cfDNA sizing for simplified library preparation
- DNA is encapsulated in a nucleosome-mimetic to maximize stability (and requiring extraction), and blended in plasma-based matrix for patient-like sample commutability



Seraseq Aneuploidy Reference Material is available in four positive formats (trisomy 21, 18, 13, and combined multi-analyte), a negative (euploid), as well as a linearity panel to assess your assay's limit of detection. Digital PCR was used to confirm trisomy status as well as establish fetal fraction concentration.

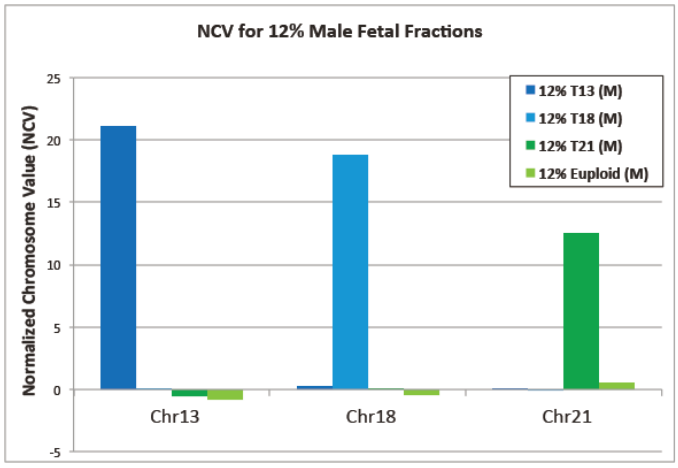
*Patent pending

Data from Early Laboratories

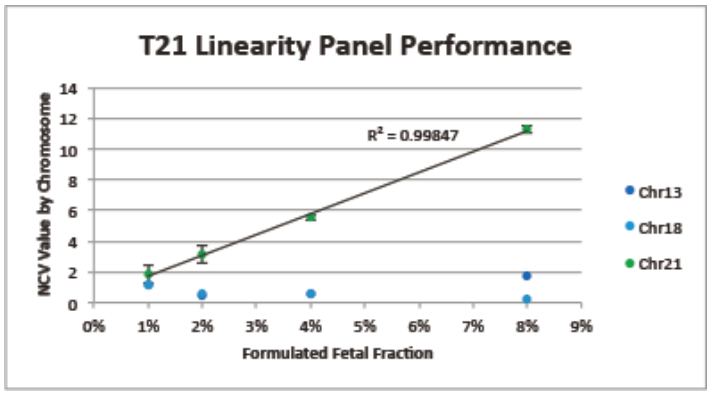
Seraseq Aneuploidy Reference Materials were evaluated by various laboratories across multiple NIPT assays and platforms following the same exact protocol as that used for their existing patient samples – from sample extraction through data analysis. The goal was to assess the utility and consistency of these reference materials as a known positive under existing workflows and run parameters. The typical measurement parameter (y-axis) for a positive call is a statistical value (such as NCV, Z-score or algorithm value), with greater values implying a higher probability of a trisomy event relative to a normal (euploid) reference set. Cutoff value to call a positive is typically around 3 or 4.

These results cumulatively demonstrate the utility of our biosynthetic reference materials as a robust positive material to validate and monitor run performance of the NIPT assays tested.

Massively Parallel Shotgun Sequencing (MPSS) Method on Illumina NGS Platform (Normalized Chromosome Value, or NCV, method)

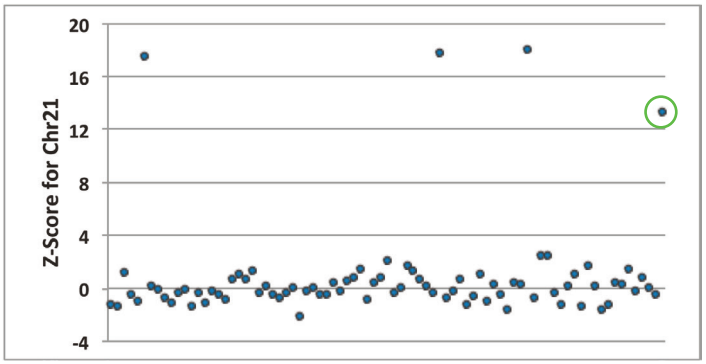


Results using an NCV method show positive trisomy calls (NCV >4) for each corresponding chromosome (while showing a very low score of NCV <4 for the other two chromosomes not being interrogated). The euploid (or negative) samples show a very low NCV score for all three chromosomes, as expected.

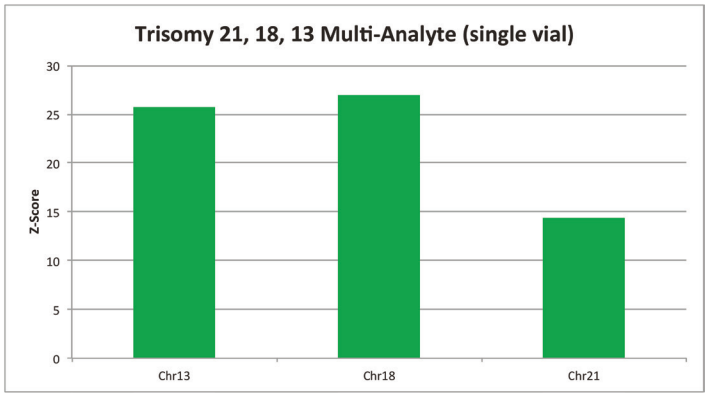


Plot of NCV versus formulated fetal fraction (as determined by digital PCR from various lots) for trisomy 21 (or T21). Linearity is observed from 1 – 8% fetal fraction with R^2 =0.9985. Chromosomes 18 and 13 show very low NCV values as expected (since only chromosome 21 is being interrogated).

MPSS Method on Illumina NGS (Z-score method)

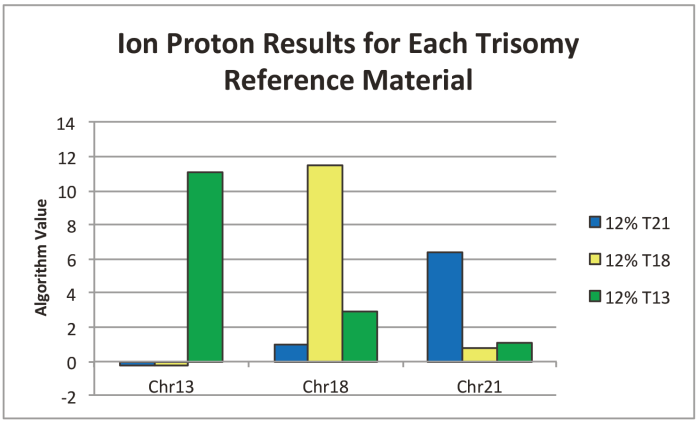


Distribution of Z-scores in a 96-sample customer run consisting of a mix of normal samples, actual trisomy positives, and Seraseq T21 Reference Material (circled in green). Results indicate a clear difference between normal (negative) samples (Z-score < 4) and positive trisomy samples (Z-score >4). They also clearly illustrate the similarity of our reference material to actual positive patient samples.

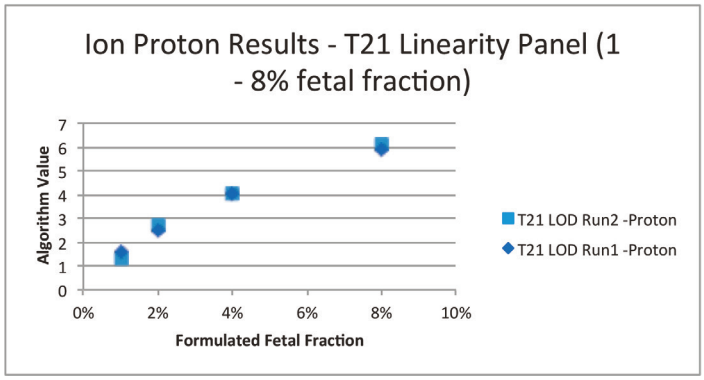


Results from using our multi-analyte product (which combines trisomy 21, 18, and 13 in a single vial at 12% fetal fraction) show positive calls (Z-score >4) for all three chromosomes.

New MPSS Assay Development - Ion Proton™ Platform



Results on a new Ion Proton MPSS assay show positive calls (algorithm value >3) for each corresponding chromosome at 12% fetal fraction, while showing a very low score (algorithm value <3) for the other two chromosomes not being interrogated.



Results on a new Ion Proton NGS assay across two runs using the Trisomy 21 Linearity Panel (with 1, 2, 4, and 8% fetal fraction) to assess the limit of detection during development. Cutoff value for a positive call is algorithm value > 3.

Available Products

Part Number	Material Description
0720-0019	Seraseq T21 Aneuploidy Reference Material (12% fetal fraction)
0720-0018	Seraseq T18 Aneuploidy Reference Material (12% fetal fraction)
0720-0017	Seraseq T13 Aneuploidy Reference Material (12% fetal fraction)
0720-0002	Seraseq T21, T18 & T13 Multi-Analyte Aneuploidy Reference Material (single vial at 12% fetal fraction)
0720-0020	Seraseq Aneuploidy Negative (Euploid) Reference Material
0720-0052	Seraseq T21 Aneuploidy Linearity Panel (4 vials - 1, 2, 4, & 8 % fetal fraction)

About SeraCare

With over 25 years of manufacturing experience and full cGMP compliance in ISO 9001- and ISO 13485-certified facilities, SeraCare has provided routine testing laboratories worldwide consistent and reliable infectious disease reference standards with our ACCURUN® line for assay monitoring. We now offer that same quality for fetal aneuploidy detection with Seraseq Aneuploidy Reference Material.

Visit precisionmedicine.seracare.com to enroll in our Seraseq sample program.

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Passion. Innovation. Precision.

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