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VeriSeq™ NIPT Analysis Software (16 Samples)

A fast, proven, CE-IVD marked solution for analyzing the status of key chromosomes in the fetus using whole-genome sequencing data.

Highlights

- **Reduce Informatics Burden**
  Easy-to-use, validated CE-IVD marked NIPT analysis software
- **Minimize Test Failure**
  Proven, whole-genome sequencing (WGS)–based NIPT analysis method[1-3]
- **Accelerate Turnaround Time**
  Fast analysis goes from sequencing data to NIPT results in 2 hours on a secure, onsite server

Introduction

Noninvasive prenatal testing (NIPT) provides important information about the status of key chromosomes in the fetus as early as 10 weeks gestation. NIPT performed with next-generation sequencing (NGS) offers a reliable, quick screen, generating high-sensitivity, high-specificity results.[2–4] Unfortunately, the bioinformatics aspect of analyzing NGS data can be a challenge for clinical laboratories interested in offering NIPT. The CE-IVD marked VeriSeq NIPT Analysis Software (16 Samples) removes this barrier for clinical labs (Figure 1, Table 1).

In just 2 hours, VeriSeq NIPT Analysis Software analyzes whole-genome sequencing (WGS) data to aid in the detection and differentiation of fetal aneuploidy status for chromosomes 21, 18, 13, X, and Y. Combining accessibility, accuracy, and speed, VeriSeq NIPT Analysis Software (16 Samples) provides a ready-to-use, affordable data analysis solution that enables clinical labs to expand their current offerings to include NIPT.

Accessible Solution

Clinical labs pursuing NGS-based assays traditionally required the services of highly trained bioinformaticians and a dedicated infrastructure to develop, validate, and perform data analysis. VeriSeq NIPT Analysis Software automates the bioinformatics analysis of NIPT data. Labs perform sample isolation and extraction, library preparation, and sequencing according to internal protocols and existing next-generation sequencing (NGS) system methods (Figure 2, Table 2).

Figure 1: VeriSeq NIPT Analysis Server (16 Samples)—With the VeriSeq NIPT Analysis Software (16 Samples), data analysis occurs on an onsite server, eliminating the need to send out samples for data analysis and protecting sample identity.

Table 1: VeriSeq NIPT Analysis Software (16 Samples) Features

Feature	Description
Method	WGS
No. of Samples	16 (scalable to 32 with addition of a second NGS instrument)
Time to Result	Approx. 2 hours
Analysis Offered	Aids in the detection and differentiation of fetal aneuploidy status for chromosomes 21, 18, 13, X, and Y

Proven Analysis

VeriSeq NIPT Analysis Software (16 Samples) uses NGS-based WGS, which has been shown to minimize test failures.[1-4] Generated WGS data are streamed to the VeriSeq NIPT Analysis Server where the software filters and aligns WGS reads to a reference genome. It then uses a sophisticated counting-based algorithm to detect over- or underrepresentation of test chromosomes, which are expressed as normalized chromosome value (NCV) scores. The NCV is equivalent to a statistical z-score.

Isolation and Extraction	Library Preparation	Sequencing	Data Analysis	Generate Report
Isolate plasma from maternal blood Extract cfDNA	Prepare libraries for sequencing	Load library on to the sequencing system	Demultiplex samples Align reads to genome	Analyze data for aneuploidy Generate report

Figure 2: NGS Workflow for NIPT—VeriSeq NIPT Analysis Software (16 Samples) fits easily into existing NGS workflows.

Table 2: NGS System Performance Requirements

Parameter	Specification
Read Length	1 x 36 bp
Sequencing File Type	.bcl file
Sequencing Output	300-400M reads
Run Time	7-8 hours
Multiplexing	16 samples per run (includes 1 negative and 1 process control)

NCV scores are generated for each sample for each of the 5 test chromosomes: 13, 18, 21, X, and Y. Built-in quality assessment (QA) of each sample ensures confidence in the obtained results. Clinical labs perform their own clinical validation studies to establish guidelines for calling aneuploidy based on the NCV scores and QA and then use the data to generate a clinical report.

Confident Quality Assessment

VeriSeq NIPT Analysis Software includes built-in QA of each sample to ensure the accuracy of generated results. Data input for each sample is assessed for DNA library yield, sequencing data quality and quantity, and quality and consistency of NCV calculations. Batch-level quality and consistency are also monitored.

Clear, Reliable Results

NCV scores from VeriSeq NIPT Analysis Software can be used to aid in the detection and differentiation of euploid and aneuploid samples (Figure 3). These scores reflect normalized coverage of the test chromosome. The algorithm used by the VeriSeq NIPT Analysis Software is an optimization of the counting method described by Sehnert AJ, et al.[5]

Fast Turnaround Time

Using VeriSeq NIPT Analysis Software, it takes just 2 hours to go from sequencing run data to NIPT results. This enables a 2-day turnaround time for the entire NIPT screen, from blood sample to analyzed results, when used with a 1-day sample and library preparation protocol and overnight sequencing run on an NGS system that meets the criteria outlined in Table 2.

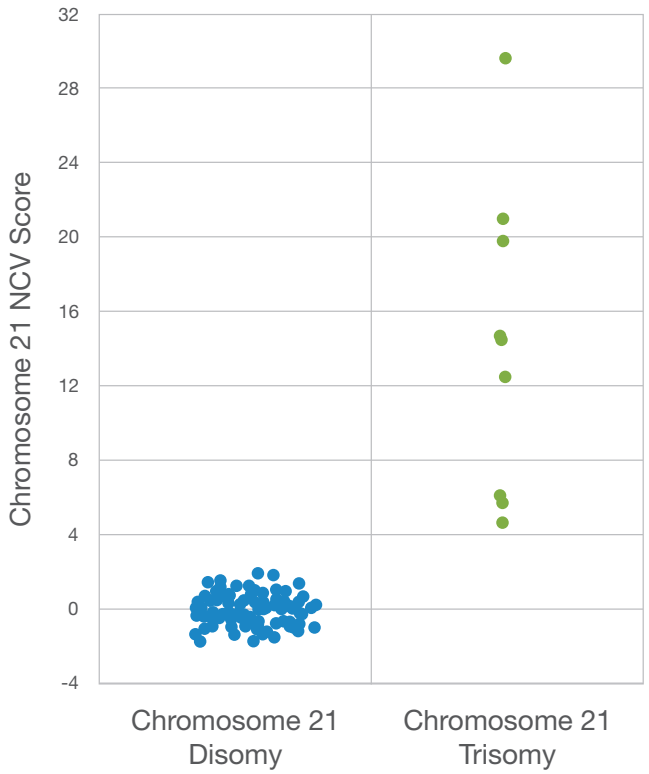

Figure 3: Distinct Identification of Aneuploidy Samples—Chromosome 21 NCV scores for a collection of 102 disomic 21 and 9 trisomic 21 samples generated by VeriSeq NIPT Analysis Software (16 Samples) based on WGS data from a compatible sequencing system. An NCV threshold of 4 was used in this study. Individual labs should perform their own clinical validation studies to establish NCV thresholds.

Flexible Throughput

VeriSeq NIPT Analysis Software is designed to support flexible throughput options. Analysis is based on batches of 16 samples. Labs can increase capacity by adding multiple NGS systems.

Dedicated Analysis Server

The CE-IVD marked VeriSeq NIPT Analysis Software runs on a dedicated VeriSeq NIPT Analysis Server. The onsite server offers secure data analysis that does not require an internet connection. Data remains on site and accessible only over a private network.

Supported Implementation

For seamless laboratory integration, the VeriSeq NIPT Analysis Software (16 Samples) and VeriSeq NIPT Analysis Server include installation by a skilled Illumina Field Service Engineer and 20+ hours of hands-on instruction. Knowledgeable Illumina scientists train laboratory personnel on data analysis and results interpretation. Consultation on NGS workflows is also available. When laboratories are up and running, continued support is provided by the Illumina Technical Support team.

Summary

Bringing NIPT analysis capabilities in house can require a sizable investment in bioinformatics expertise. The VeriSeq NIPT Analysis Software (16 Samples) provides a ready-to-use, accessible, onsite solution that overcomes this barrier.

Learn More

To learn more about the VeriSeq NIPT Analysis Software (16 Samples), visit www.illumina.com/NIPTsoftware.

References

1. Taneja PA, Snyder HL, de Feo E, et al. Noninvasive prenatal testing in the general obstetric population: clinical performance and counseling considerations in over 85 000 cases. *Prenat. Diagn.* 2015;Dec 30. doi: 10.1002/pd.4766. [Epub ahead of print].
2. Bianchi DW, Platt LD, Goldberg JD, Abuhamad AZ, Sehnert AJ, Rava RP. Genome-wide fetal aneuploidy detection by maternal plasma DNA sequencing. *Obstet Gynecol*. 2012;119(5):890-901.
3. Bianchi DW, Parker RL, Wentworth J, et al. CARE Study Group: DNA sequencing versus standard prenatal aneuploidy screening. *N Engl J Med.* 2014;370:799-808.
4. Yaron Y. The implications of non-invasive prenatal testing failures: a review of an under-discussed phenomenon. Prenat Diagn. 2016;Mar 4. doi: 10.1002/pd.4804. [Epub ahead of print].
5. Sehnert AJ, Rhees B, Comstock D, et al. (2011) Optimal detection of fetal chromosomal abnormalities by massively parallel DNA sequencing of cell-free fetal DNA from maternal blood. *Clin Chem.* 57:1042–1049.

Ordering Information

Product	Catalog No.
VeriSeq NIPT Analysis Server provided preloaded with the VeriSeq NIPT Analysis Software (16 Samples)	RH-400-1001

Server Specifications

Parameter	Specification
CPU Model	EMB XEON E5-2620 LGA2011
No. of CPUs	2
CPU Cores	6
CPU Speed (GHz)	2.0
Memory, Speed	64 GB 1333 MHz RAM
Raid Controller	LSI 8 Port 6 GB SAS
Hard Drive	8 x 1.0 TB 3.5' Enterprise SATA (2 OS RAID 1 drives, 6 data RAID 5 drives
Operating System	CentOS 6.4
Networking protocol	Samba SMB/CIFS
Enterprise Grade Disks	Yes
Safety and Security	Authentication-based access Redundant power supply Redundant cooling fans Hot swappable drives
Hard Disk Storage	4 TB (200 NIPT sequencing runs)
Data backup and archive	Customer supplied

Intended Use Statement

The VeriSeq NIPT Analysis Software (16 Samples) generates quantitative scores to aid in the detection and differentiation of fetal aneuploidy status for chromosomes 21, 18, 13, X, and Y by analyzing sequencing data generated from cell-free DNA (cfDNA) fragments isolated from maternal peripheral whole blood specimens in pregnant women of at least 10 weeks gestation. The quantitative scores are z-scores associated with under- or overrepresentation of a target chromosome relative to an expectation for a diploid genome.

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