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Illumina SeqLab

Delivering a comprehensive end-to-end solution for large-scale human whole-genome sequencing for the HiSeq X[™] Series of sequencing systems.

Highlights

- One Complete Solution for HiSeq X Series Operations End-to-end solution for planning and implementation of HiSeq X Series sequencing center operations
- Confidence in Laboratory Results Fully integrated solution provides positive sample tracking and streamlined laboratory workflows for maximum efficiency
- Optimized Software Solution for Rapid Data Analysis Fast and accurate data analysis for a full breadth of variants from whole-genome or tumor-normal sequencing data
- Acceleration of NGS Production and Expertise Customized recommendations to match the unique business needs of each laboratory for improved scalability

Introduction

The HiSeq X Series of sequencing systems brings population-scale human whole-genome sequencing (WGS) out of the realm of science fiction and into reality.¹ A high level of planning and preparation is required to deploy the HiSeq X Series and scale to this massive increase in throughput. The Illumina SeqLab is an integrative solution for implementing large-scale human whole-genome sequencing for the HiSeq X Series. The Illumina SeqLab is designed to provide the necessary tools for maximum laboratory efficiencies and improved scalability (Figure 1). Illumina SeqLab is a combination of products and services that includes:

- Illumina Automated Workflow Manager for Hamilton, Hamilton Microlab STAR Automation, and BaseSpace[®] Clarity LIMS X Edition—Out-of-the-box integration for automated laboratory workflows from sample accessioning to sequencing
- HiSeq Analysis Software v2.0—Fast, accurate data analysis for a broad range of variants; easily deployed on commodity hardware (Table 1), reducing IT infrastructure investments
- Illumina SeqLab Consulting Service—Best-in-class training and personalized consulting for successful scaling of NGS production with less start-up time and lower costs

For new high-throughput WGS laboratories, configuring the laboratory automation and software capabilities needed to process thousands of genomes per year can take several months or longer. The plug-and-play Illumina SeqLab allows customers to maximize laboratory efficiency, streamline data analysis, and build best-in-class laboratory practices to scale WGS operations successfully.

Automated Library Workflows with Positive Sample Tracking

Illumina offers preconfigured automation workflows and a first-class laboratory information management system (LIMS) optimized to support laboratories using the HiSeq X Series. The Illumina SeqLab offers full integration with laboratory equipment and procedures.







Figure 2: Illumina SeqLab Workflow – Seamless integration from sample accessioning to data analysis using Illumina methods and software: Illumina Automated Workflow Manager for the Hamilton Microlab STAR liquid-handling automation workstations, Illumina Automated Bridge Software for BaseSpace Clarity LIMS X Edition, and Illumina MicroPlate Analysis Reader Software for DNA quantification integrate with a defined reference architecture for auxiliary equipment. Positive sample tracking throughout the workflow provides confidence in WGS results while streamlined processes maximize efficiencies.

Key features include:

- Support for TruSeq[®] Nano DNA and TruSeq PCR-Free DNA library preparation workflows for reduced sample to sample variation
- Built-in QC logic to identify and requeue problematic samples automatically while processing successful samples efficiently
- Positive sample tracking with integrative BaseSpace Clarity LIMS X Edition, Hamilton Microlab STAR liquid-handling robotics, Illumina Automated Workflow Manager for Hamilton, and auxiliary laboratory equipment (Table 2)
- Illumina Automated Bridge Software and Illumina Microplate Analysis Reader Software enabling API driven integration with BaseSpace LIMS X Edition for sample traceability
- LIMS integration with the cBot[™] Cluster Generation System to ensure proper run set-up and tracking of sample association with flow cells
- LIMS integration with HiSeq X Series to set up runs easily, track reagents, and perform direct sample QC for streamlined processing
- Reagent tracking with LIMS
- Built-in reporting capabilities for audits and compliance requirements

The Illumina SeqLab workflow begins with sample accession into the BaseSpace LIMS X Edition system, allowing each lab to track sample inventory accurately (Figure 2). Following sample accessioning, customers use Illumina Automated Workflow Manager for Hamilton to complete laboratory workflows, from sample QC to clustering, with preconfigured automation methods on the Hamilton Microlab STAR workstations. The automated workflows are Illumina validated methods for use with the HiSeq X Series. Library preparation methods within the Illumina Automated Workflow Manager introduce extended fragment insert sizes of 450 bp to reduce overlapping reads with 2×150 bp read lengths. The workflow manager fully supports implementation and tracking of library pooling, enabling users to maintain traceability with multiplexed libraries. Moreover, the workflow manager streamlines processes for maximum utilization when clustering multiple flow cells simultaneously. With complete LIMS integration of auxiliary instrumentation, the cBot System, and HiSeq X Series, samples are positively tracked through every stage of the process.

Complete system and LIMS integration reduces the chance for inherent human error observed in standard manual processes. With built-in QC logic, users can quickly evaluate samples and direct next steps through LIMS. Illumina SeqLab streamlines processes and improves turnaround time by quickly highlighting QC failures within the LIMS. Users can rapidly make key decisions and requeue samples to begin reprocessing in a shorter amount of time. Moreover, as customers validate their processes for clinical sequencing operations, the LIMS system provides the necessary audit control to support regulated environments such as CLIA, CAP, and 21 CFR Part 11 compliance. The simple design and intuitive LIMS user interface allow ease of adoption and rapid personnel training.

The Illumina SeqLab with BaseSpace LIMS X Edition and Hamilton Microlab STAR automation is essential for laboratories scaling to thousands of genomes per year. It reduces cost per sample, minimizes production errors, and improves turnaround times, all while ensuring confidence in concordance between the samples received and the data generated.

HiSeq Analysis Software v2.0

Preventing data analysis bottlenecks in the sequencing workflow becomes critical as sequencing throughput increases and as the analysis of genetically driven diseases becomes more complex. Commercial analysis tools must provide high-quality data and increasingly sophisticated algorithms to have a significant impact on disease-related research and health care.

HiSeq Analysis Software v2.0 offers a fast, accurate solution for high-throughput WGS data analysis. With pipelines for WGS analysis and tumor–normal somatic variant analysis, the software provides a full range of variant types, including single nucleotide variants (SNVs), insertion-deletions (indels), structural variants (SVs), and copy number variants (CNVs) from BCL files. The pipelines harness a suite of proven algorithms including Isaac[™] Aligner,² Starling Small Variant Caller,² Manta Structural Variant Caller,³ Canvas Copy Number Variant Caller,⁴ Strelka Somatic Variant Caller,⁵ and the SENECA Copy Number Aberration Caller.⁶ Sequencing data and variants are delivered in standard file formats: archival BAM with aligned and unaligned reads, and variants in VCF and gVCF formats.

HiSeq Analysis Software v2.0 meets the speed and scalability requirements of the HiSeq X Series by providing results up to 6 times faster than existing analysis methods. By analyzing data faster than the rate of HiSeq X Series sequencing production, HiSeq Analysis Software v2.0 eliminates costly informatics bottlenecks while maintaining high data quality. To support HiSeq X Series laboratories, the software is easily deployed on commodity hardware, which lowers IT infrastructure costs (Table 1). With high-quality results and optimized analysis speed, customers can efficiently scale their HiSeq X WGS operations.

Table 1: Requirements for HiSeq Analysis Software v2.0

Feature	Requirements
Operating System	CentOS v6 standard libraries R statistical package
Network	10 Gb network
Dual Core Processors	10
Speed	Minimum 2.8 GHz
RAM Memory	128 GB
Local Storage	6x 1 TB with 500 MB
Ethernet Adapters	10 Gbits per sec

Illumina SeqLab Consulting Service

Experienced, Collaborative Guidance

Illumina SeqLab Consulting Service provides valuable knowledge and expertise allowing laboratories to rapidly scale, building best practices for long-term success. Illumina consultants leverage 15 years of sequencing operations experience across the globe and in-depth knowledge of Illumina sequencing systems to provide customized recommendations for process improvement. When deploying the HiSeq X Series, there are several factors to consider beyond sequencing technology. The increased genome output of the system requires customers to contemplate all workflow and laboratory operations holistically. To support implementation of HiSeq X Series systems, Illumina consultants guide customers through the entire process of establishing an efficient large-scale operation (Figure 3). Customized, expedient solutions aligned to the unique business objectives of the customer will be developed during collaborative consultations.



ILLUMINA SEQLAB CONSULTING SERVICE

Reduces Time and Resources for HiSeq X Deployment Accelerates NGS Production and Expertise

Figure 3: Illumina SeqLab Consulting Service – Experts in large-scale sequencing provide customized recommendations for establishing operations in HiSeq X Series laboratories.

Considerations for Large-Scale Sequencing

There can be significant growing pains when ramping from a small core lab to a large sequencing center. Illumina consultants can provide guidance in the following key areas:

- Lab Management—Assess upstream sample acquisition and downstream data analysis requirements
- Capacity Planning—Develop a custom analysis of capacity based on systems and bottleneck principles in the laboratory environment
- Staffing and Communication Examine qualities to look for when hiring an individual for specific roles in the production environment
- Risk Reduction Assess risk to the facility based on the business focus, which is explored in the custom risk management plan
- Inventory Management—Develop Kanban-based systems designed to detect and respond to demand dynamically, ensuring inventory availability
- Troubleshooting and Trending—Establish troubleshooting and trending techniques for fleet of instruments
- Computing Architecture Help determine optimal IT infrastructure and data storage capacity in collaboration with our Customer Information Systems group
- Data Analysis and Delivery—Identify key performance indicators when analyzing genomic data; discussions include a review of established market standards for genome analysis

Working with experienced Illumina consultants ensures that customers adopt best-in-class procedures, enabling rapid scaling to thousands of genomes per year.

Table 2: Required Instrument Reference Architecture for Illumina SeqLaba

	Product	Vendor	Minimum Quantity ^b	Recommended Quantity ^b
Sequencing Platform	HiSeq X Series Instrument	Illumina	5	5+
Liquid-Handling Workstations ^c	Microlab STAR	Hamilton	2	4
DNA Quantification ^d	SpectraMax M Series Microplate Reader	— Molecular Devices	1	2
	SpectraMax Gemini XPS Microplate Reader			
DNA Shearing	LE220 Focused-Ultrasonicator	Covaris	1	2
Library Quantification	LightCycler 480 Real-Time PCR System	Roche	1	2
Library Insert Size QC	LabChip GX Touch	PerkinElmer	1	2
Cluster Generation	cBot Cluster Generation System	Illumina	5°	5
LIMS License	BaseSpace LIMS X Edition	GenoLogics, an Illumina Company	1	1

a. The reference architecture described in Table 1 is qualified by Illumina to support the Illumina SeqLab.

b. Minimum quantities are required for large-scale WGS operations while recommended quantities provide reduced laboratory risk to manage production efficiently.

c. Minimum quality requires 1 liquid-handling instrument control computer for each of the prelab and postlab workspaces.

d. DNA quantification requires either the MSeries or Gemini Microplate Reader. It is not required to use both readers.

e. Assumes full capacity use of the HiSeq X Five System at a minimum.

Summary

The HiSeq X Series breaks barriers by offering the first truly affordable human genome sequencing on a massive scale. Users must consider all facets of laboratory processes as they prepare for large-scale sequencing operations. Illumina SeqLab delivers an end-to-end solution with integrative automation using BaseSpace Clarity LIMS X Edition and Hamilton Microlab STAR, fast and accurate WGS analysis with HiSeq Analysis Software v2.0, and personalized consulting with Illumina SeqLab Consulting Service. Unlike homebrew solutions that piece-meal systems and services together, Illumina SeqLab provides a single turnkey solution with all required components to achieve operational excellence. With the Illumina SeqLab, users can establish maximum efficiencies, manage production escalation, and accelerate toward achieving business objectives and research goals.

Learn More

To learn more about the Illumina SeqLab, visit www.illumina.com/illuminaseqlab.

To learn more about HiSeq Analysis Software v2.0, visit www.illumina.com/systems/hiseq-x-sequencing-system/software.html.

References

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- Canvas Copy Number Variant Caller (support.illumina.com/downloads/ whole_genome_sequencing_service_user_guide.html).
- Saunders CT, Wong WS, Swamy S, Becq J, Murray LJ, Cheetham RK. Strelka: accurate somatic small-variant calling from sequenced tumornormal sample pairs. *Bioinformatics*. 2012;28:1811-1817.
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Ordering Information

Component ^a	Vendor	Catalog No.		
Illumina SeqLab	Illumina	SW-480-1001		
BaseSpace LIMS X Edition	GenoLogics	CLX1000		
Microlab STAR LIquid Handling Workstation	Hamilton	95300-1		
HiSeq Analysis Software v2.0	Illumina	SW-470-2001		
Illumina SeqLab Consulting Service	Illumina	SV-475-1001		
a. Illumina SeqLab requires all items listed and Illumina instrumentation to support HiSeq X				

Series workflows. Components must be ordered individually.

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