HiSeq X™ Series of Sequencing Systems
Maximum throughput and lowest cost for population- and production-scale human whole-genome sequencing.

Highlights
- **$1000 Genome is a Reality**
  HiSeq X Ten System is the first and only platform to break the $1000 barrier for 30x coverage human whole-genome sequencing
- **Population- and Production-Scale Human Whole-Genome Sequencing**
  HiSeq X Ten System delivers > 18,000 human genomes per year; HiSeq X Five System delivers > 9000 human genomes per year
- **Proven Performance**
  Take advantage of industry-leading data quality with the highly accurate Illumina sequencing by synthesis technology

Introduction
Through continuous innovation, Illumina has broken down barriers in human genome sequencing by increasing data throughput at an astounding rate—more than doubling each year—while dramatically reducing the price to sequence a human genome. Illumina technology enabled sequencing of the first genome at 30x coverage, the first cancer genome, and the first genome in a single day.1-3
Now, Illumina technology is helping researchers reach another milestone—the $1000 genome. The HiSeq X Ten System, a set of 10 HiSeq X instruments, is the first and only platform to deliver a $1000 human genome and generate tens of thousands of high-quality, high-coverage genome sequences (Figure 1). With its ultra-high throughput and unprecedented low price per genome, the HiSeq X Ten System makes population-scale human whole-genome sequencing (WGS) a reality (Table 1).

For laboratories wanting to take advantage of the power of the HiSeq X Ten System for production-scale sequencing, Illumina offers the HiSeq X Five System. Requiring a lower level of initial capital investment, the HiSeq X Five System provides accurate, accessible human WGS for thousands of samples per year at a slightly higher, yet still affordable, price per genome (Table 1). Laboratories that start with the HiSeq X Five System and then increase their capacity to 10 or more instruments can realize the throughput of the HiSeq X Ten System and the $1000 genome.

HiSeq X Ten System—Maximum Throughput, Lowest Cost Population-Scale WGS
The HiSeq X Ten System is the world’s first sequencing platform to break the $1000 barrier for 30x coverage of a human genome. When used at scale, the HiSeq X Ten delivers a $1000 genome, inclusive of instrument depreciation, sequencing consumables, DNA extraction, library preparation, and estimated labor for a typical high-throughput genomics laboratory.

Figure 1: The HiSeq X Ten System.
Table 1: HiSeq X System Sequencing Capacity

<table>
<thead>
<tr>
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<th>HiSeq X Ten System</th>
<th>HiSeq X Five System</th>
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<tbody>
<tr>
<td>Minimum Number of Instruments</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Annual Genome Capacity</td>
<td>&gt;18,000</td>
<td>&gt;9000</td>
</tr>
<tr>
<td>Price per 30x genome</td>
<td>&lt; $1000</td>
<td>&lt; $1500</td>
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When operating at scale, HiSeq X Ten and HiSeq X Five Systems generate a staggering level of throughput, sequencing thousands of genomes per year.

**Purpose-Built for Population-Scale Genome Sequencing**

Designed and optimized for population-scale human WGS, the 10 instruments of a HiSeq X Ten System generate a staggering level of throughput for processing tens of thousands of samples. Now, researchers can analyze the human genome like never before. Exploration of the human genome on this scale will bring the study of cancer and complex diseases to a new level.

**HiSeq X Five System—Maximum Throughout, Production-Scale WGS**

With a lower initial capital investment, but higher price per genome, the HiSeq X Five System provides access to HiSeq X patterned flow cell technology and production-scale human WGS at a cost and scale appropriate for large genome centers. The HiSeq X Five System consists of 5 individual HiSeq X instruments that, when operating at scale, have the capacity to sequence >9000 genomes a year. This level of throughput allows researchers to complete large human WGS projects rapidly, in their own lab.

**Innovative Technology, Proven Performance**

The HiSeq X Ten and HiSeq X Five Systems leverage proven Illumina sequencing by synthesis (SBS) chemistry, the most widely adopted next-generation sequencing technology. This chemistry ensures industry-leading data quality and gives researchers the utmost confidence in their results (Table 2). Building on this powerful foundation, the HiSeq X Series incorporate a new patterned flow cell technology to generate massive throughput. Patterned flow cells contain billions of nanowells at fixed locations, a design that provides even cluster spacing and uniform feature size to deliver extremely high cluster density (Figure 2). A proprietary clustering method, exclusion amplification, ensures that only a single DNA template binds and forms a cluster within a single well, resulting in high well occupancy and maximum data output.

**Integrated, End-to-End Solution**

Systems in the HiSeq X Series are available separately or as part of an integrated solution that includes laboratory best practices from sample preparation to variant detection (Figure 3).

**Superior Library Preparation**

To achieve exceptional genome coverage for accurate, comprehensive variant calling, the HiSeq X Ten and HiSeq X Five Systems support 2 library prep kits. The TruSeq® DNA PCR-Free Library Prep Kit provides a fast, gel-free protocol for preparing WGS libraries with superior coverage of areas that are traditionally difficult to sequence, such as high GC-rich regions, promoters, and repetitive content. PCR-free preparation reduces library bias and gaps, resulting in unsurpassed data quality for detecting the greatest number of variants. The TruSeq Nano DNA Library Prep Kit allows for efficient sequencing of samples with as little as 100 ng DNA. The enhanced workflow reduces the number and average size of typical PCR-induced gaps in coverage, minimizing library bias and improving coverage uniformity across the genome. Using the streamlined TruSeq Nano DNA protocol, libraries can be prepared in less than 1 day.

Table 2: HiSeq X System Performance Parameters.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<tbody>
<tr>
<td>Output per Run</td>
<td>Dual flow cell: 1.6-1.8 Tb</td>
</tr>
<tr>
<td>Single Reads Passing Filter</td>
<td>Dual flow cell: 5.3-6 billion</td>
</tr>
<tr>
<td>Supported Read Length</td>
<td>2 × 150 bp</td>
</tr>
<tr>
<td>Run Time</td>
<td>&lt; 3 days</td>
</tr>
<tr>
<td>Quality</td>
<td>≥ 75% of bases above Q30 at 2 × 150 bp</td>
</tr>
<tr>
<td>Supported Library Preparation</td>
<td>TruSeq DNA PCR-Free Library Prep Kit</td>
</tr>
<tr>
<td></td>
<td>TruSeq Nano DNA Library Prep Kit</td>
</tr>
</tbody>
</table>

_a_ Specifications based on Illumina PhiX control library at supported cluster densities (1255–1412 K clusters/mm²) on 1 HiSeq X System. Supported library preparation kit includes TruSeq Nano DNA Kit and TruSeq PCR-Free DNA Kit with 350 bp target insert size and HiSeq X Reagent Kit v2. The HiSeq X System was designed, optimized, and licensed for human WGS. Other applications and species are not permitted.
High Operational Efficiency
To drive operational efficiency for HiSeq X laboratories, Illumina, together with select third-party vendors, has developed best-in-class tools, including high-throughput liquid-handling robotics fully integrated with a laboratory information management system (LIMS), WGS analysis software, and personalized consulting. Each component is optimized specifically for the HiSeq X Five and HiSeq X Ten Systems to maximize quality, throughput, and cost efficiency, while minimizing turnaround time.

Fully Integrated LIMS
Illumina has partnered with GenoLogics to offer a first-class LIMS solution, the Clarity LIMS X Edition, tuned to the power of the HiSeq X Series. Clarity LIMS X Edition is fully integrated with Hamilton MICROLAB STAR liquid-handling robotics and defined auxiliary equipment to provide complete positive sample tracking. It is preconfigured to support both the TruSeq DNA PCR-Free and TruSeq Nano DNA workflows. The intuitive user interface allows quick system adoption for immediate process tracking and scalability.

Fast, Accurate WGS Analysis
Illumina redefines WGS analysis with the HiSeq® Analysis Software (HAS) v2.0. Offering a fast, accurate solution to high-throughput WGS, HAS v2.0 processes data up to 5× faster than existing analysis methods. It uses the proven Isaac™ workflow to provide a full spectrum of variant types, including single nucleotide variants (SNVs), indels, structural variants (SVs), and copy number variants (CNVs) from BCL and FASTQ files. The pipeline can be run through the Illumina BaseSpace® genomics cloud-computing environment or through command-line on commodity hardware, reducing the need for significant IT infrastructure investment. By analyzing data faster than the rate of HiSeq X sequence acquisition, HAS v2.0 eliminates costly informatics bottlenecks while maintaining exceptional data quality.

Custom High-Throughput Implementation Consulting
Illumina professional services provide a suite of custom high-throughput implementation solutions for the HiSeq X Series. Personalized consulting engagement delivers accurate and expedient solutions aligned to each customer’s unique business objectives and operation environment in a collaborative manner. This enables each facility to realize the full potential of their HiSeq X Systems and achieve operational excellence. The comprehensive solution includes a full spectrum of guidelines for running a successful production sequencing operation, including capacity planning, fleet management, risk mitigation, performance and QC trending, troubleshooting, bioinformatics, data management, and IT infrastructure. At the end of the consultation, Illumina provides personalized recommendations and customized solutions to implement production-scale sequencing operations expeditiously and at a low total cost of ownership.

Figure 2: Advanced Patterned Flow Cell Design Enables Maximum Throughput. Patterned flow cells contain billions of nanowells at fixed locations providing even cluster spacing and uniform feature size to deliver extremely high cluster density.

Figure 3: A Complete WGS Sequencing Solution. Illumina offers a complete workflow for population- and production-scale sequencing on the HiSeq X Series of sequencing systems.
Summary

The HiSeq X Ten and HiSeq X Five Systems continue to break down sequencing barriers, reshaping the economics of human genome sequencing and laying the foundation for visionary scientists, institutions, and nations working to perform groundbreaking research that will forever change our understanding of the human genome.

Just as true population-scale human genome sequencing projects are beginning to take shape around the world, the HiSeq X Series delivers the first truly affordable human genome—on a massive scale. By providing the capacity to sequence thousands to tens of thousands of genomes, the HiSeq X Series will bring genome sequencing to an inflection point. They will pave the way to a comprehensive catalog of human variation, forge population-based references, drive far-reaching discoveries, and accelerate a deeper understanding of human biology and genetic disease.

We’ve taken sequencing to the next level. Now it’s time to make your vision for human health and genome science a reality.

Learn More

To learn more about the HiSeq X Series, visit www.illumina.com/hiseqxseries.

References