Illumina solutions for genetic and rare disease

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Lab Director
ARUP Laboratories

Piece together
There are > 6000 known rare diseases, with more being discovered every year, affecting 2-6% of the global population. Individuals suspected of having a rare disease often face a long search for a diagnosis.

- Involve multiple tests
- Can take more than 5 years
- Result in 2-3 misdiagnoses
- Include up to 8 physicians

With up to 80% of rare diseases being genetic or having a genetic subtype, it is imperative that we interrogate the genome to find answers and shorten the diagnostic odyssey.

Illumina offers a wide range of NGS solutions, from robust library preparation kits to proven NGS instruments and highly accurate software solutions, that are built to deliver unparalleled insights into heritable genetic disease.
Illumina NGS systems, at the core of every rare disease workflow

Powered by proven NGS technology and sequencing by synthesis (SBS) chemistry, Illumina sequencing systems form the core of an integrated, sample-to-answer workflow. There is an Illumina system to help you answer the toughest questions in rare disease research (Table 1 and Table 2).

### TABLE 2

**KEY METHODS BY SYSTEM**

- **Powered by proven NGS technology and sequencing by synthesis (SBS) chemistry, Illumina sequencing systems form the core of an integrated, sample-to-answer workflow. There is an Illumina system to help you answer the toughest questions in rare disease research (Table 1 and Table 2).**

- **ILLUMINA MID- TO HIGH-THROUGHPUT SEQUENCING SYSTEMS**

  - **NovaSeq 6000 System**—scalable throughput for dynamic volume demands
  - **NovaSeq X Series**—breakthrough innovations for groundbreaking discoveries

### TABLE 1

**ILLUMINA MID- TO HIGH-THROUGHPUT SEQUENCING SYSTEMS**

<table>
<thead>
<tr>
<th>Method</th>
<th>NovaSeq 6000 System</th>
<th>NovaSeq X Series</th>
<th>NovaSeq X Plus</th>
</tr>
</thead>
<tbody>
<tr>
<td>WES</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Human exomes per run</td>
<td>4-50</td>
<td>100-200</td>
<td>500-1000</td>
</tr>
<tr>
<td>WGS</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Human genomes per run</td>
<td>4-128</td>
<td>4-128</td>
<td>4-128</td>
</tr>
<tr>
<td>Long-read WGS</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Human genomes per run</td>
<td>4-128</td>
<td>4-128</td>
<td>4-128</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Method</th>
<th>NextSeq 1000 and NextSeq 2000 Systems</th>
</tr>
</thead>
<tbody>
<tr>
<td>WES</td>
<td>●</td>
</tr>
<tr>
<td>Human exomes per run</td>
<td>100-1000</td>
</tr>
<tr>
<td>WGS</td>
<td>●</td>
</tr>
<tr>
<td>Human genomes per run</td>
<td>4-48</td>
</tr>
<tr>
<td>Long-read WGS</td>
<td>●</td>
</tr>
<tr>
<td>Human genomes per run</td>
<td>4-48</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Method</th>
<th>NextSeq™ 1000 and NextSeq 2000 Systems</th>
</tr>
</thead>
<tbody>
<tr>
<td>WES</td>
<td>●</td>
</tr>
<tr>
<td>Human exomes per run</td>
<td>100-1000</td>
</tr>
<tr>
<td>WGS</td>
<td>●</td>
</tr>
<tr>
<td>Human genomes per run</td>
<td>4-48</td>
</tr>
<tr>
<td>Long-read WGS</td>
<td>●</td>
</tr>
<tr>
<td>Human genomes per run</td>
<td>4-48</td>
</tr>
</tbody>
</table>

**NextSeq™ 1000 and NextSeq 2000 Systems—simplified workflow for various applications**

The NextSeq 1000 and NextSeq 2000 Sequencing Systems offer sequencing power for mid- to high-throughput methods for more moderate sample numbers. They offer innovative design features, DRAGEN™ onboard, an intuitive, simplified workflow, and flexibility of scale for various applications, all in a benchtop system.

**NovaSeq™ 6000 System—scalable throughput for dynamic volume demands**

The NovaSeq 6000 Sequencing System is a robust, scalable platform that has been adopted by leading hospital, commercial, and academic labs and featured in countless publications. Designed to adapt to your needs, it delivers deep and broad coverage and a flexible sequencing workflow for advanced applications.

**NovaSeq X Series—breakthrough innovations for groundbreaking discoveries**

The NovaSeq X and NovaSeq X Plus Sequencing Systems provide extraordinary sequencing power to fuel data-intensive methods like WGS, single-cell sequencing, and multiomics. Numerous technical innovations, including XLEAP-SBS™ chemistry and onboard DRAGEN analysis, enable maximum throughput and accuracy to deliver meaningful insights at scale.

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**TABLE 1**

<table>
<thead>
<tr>
<th>Method</th>
<th>NovaSeq X</th>
<th>NovaSeq X Plus</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5B</td>
<td>10G</td>
<td>25B</td>
</tr>
<tr>
<td>10G</td>
<td>10G</td>
<td>10B</td>
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<tr>
<td>16,000G</td>
<td>16,000G</td>
<td>1,000B</td>
</tr>
</tbody>
</table>

**TABLE 2**

**KEY METHODS BY SYSTEM**

- **Method**
- **NextSeq™ 1000 and NextSeq 2000 Systems**
- **NovaSeq™ 6000 System**—scalable throughput for dynamic volume demands
- **NovaSeq X Series**—breakthrough innovations for groundbreaking discoveries

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**Illumina Qualification Services**

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Illumina offers various library preparation kits, enabling researchers to examine DNA variation from small, targeted regions to the entire genome, including the most challenging sequences.

<table>
<thead>
<tr>
<th>Library prep kit</th>
<th>TruSight One Sequencing Panels</th>
<th>Illumina DNA with Exome 2.0 Plus Enrichment</th>
<th>Illumina DNA PCR-Free Prep</th>
<th>Illumina Complete Long-Read Prep, Human</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method</td>
<td>Targeted enrichment</td>
<td>WES, targeted enrichment</td>
<td>WGS</td>
<td>WGS</td>
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<tr>
<td>Hands-on time</td>
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<td>~7 hr</td>
<td>~45 min</td>
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<td>~9 hr</td>
<td>~15 hr</td>
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<td>50-1000 ng</td>
<td>25-300 ng</td>
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<tr>
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<td>gDNA, blood, saliva</td>
<td>gDNA</td>
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<td>Yes</td>
<td>Automation capable</td>
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<td>Yes</td>
<td>No</td>
<td>No</td>
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<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Fragmentation included?</td>
<td>Yes-on bead</td>
<td>Yes-on bead</td>
<td>Yes-on bead</td>
<td>Yes-on bead</td>
</tr>
</tbody>
</table>

**VERSATILE LIBRARY PREP KITS**

**WGS**

Illumina DNA PCR-Free Prep

Highly accurate WGS without PCR-induced bias to provide highly uniform coverage, even in genomic regions with uneven base composition.

Learn more

Illumina Complete Long Read Prep, Human

Makes accurate and comprehensive WGS easily accessible by enabling both long and short reads on the same instrument, with included DRAGEN on BaseSpace™ Sequence Hub analysis.

Learn more

**Targeted enrichment**

TruSight™ One Sequencing Panels

Two enrichment panel options target < 6700 disease-associated genes in exonic regions.

Learn more

**WES**

Illumina DNA Prep with Exome 2.0 Plus Enrichment

Focused enrichment of up-to-date exome content for comprehensive, reliable human WES.

Learn more
Illumina Connected Software—
The final piece in finding an answer

Illumina offers comprehensive software solutions to help reduce bioinformatics bottlenecks and streamline genomics workflows. Whether a lab is just getting started or in rapid scale mode, Illumina Connected Software unlocks the power of your rare disease data.

OVERVIEW

Clarity LIMS™ software
Innovative laboratory information management system (LIMS) enabling labs using Illumina sequencing systems to run samples faster, track them easily, and more. It is easy to use, implement, and configure.

Illumina Connected Analytics
A secure genomics data platform that operationalizes informatics and drives scientific insights. A central component for labs using Illumina sequencing systems, Connected Analytics enables users to build and customize analysis pipelines, execute production workflows at scale, and explore and share data and results.

DRAGEN secondary analysis
Highly accurate sequencing by synthesis (SBS) chemistry plus DRAGEN secondary analysis deliver award-winning germline and somatic variant calling. With onboard DRAGEN analysis available on select instruments, users can gain significant cost savings for accurate, comprehensive, and efficient NGS analysis. DRAGEN secondary analysis pipelines are also available on Illumina cloud platforms and as a server.

Emedgene™ software
Emedgene software is an explainable artificial intelligence (XAI)-powered platform enabling high-throughput, user-defined interpretation workflows for rare disease research. Delivering a streamlined experience and dramatic reductions in data interpretation time, Emedgene provides a highly configurable and automatable platform for evidence-backed insights.

Trusted technology partners
Dedicated to your success, the Illumina Informatics Services team brings a staff of bioinformaticians, data scientists, and designers to help you customize and optimize your analysis workflow and minimize your development burden.

High standards for data privacy
To meet the most stringent security requirements, our software products are built with security and compliance at the core. Data sharing security and governance, audit trails with encryption, and controlled sharing ensure your data are kept safe and secure.

Simplified lab optimization
Large-scale data management and analysis
Accurate secondary analysis
Explainable AI-powered interpretation

Lab Run Analytics Insights

Clarity LIMS Instrument Software DRAGEN secondary analysis Connected Analytics Emedgene

Illumina Connected Software
Balancing approachability with customization, Illumina Connected Software offers data analysis, exploration, and management for a variety of bioinformatics expertise levels. From single sample analysis through population-wide studies, Connected Software is seamlessly integrated with Illumina sequencing systems for a highly efficient lab ready to scale.
INTEGRATED solutions for meaningful insights

Example workflows for genetic disease research:

**WGS**
Achieve uniform coverage and exceptional variant calling performance

Prepare library
> Sequence
> Analyze
> Interpret

- **Prepare library**
  - Illumina DNA
    - PCR-Free Prep

- **Sequence**
  - NovaSeq 6000

- **Analyze**
  - DRAGEN Germline app

- **Interpret**
  - Emedgene

For more information about these products, click the links above.

**WGS WITH LONG READS**

Call variants in challenging regions, phase haplotypes, and more

Prepare library
> Sequence
> Analyze
> Interpret

- **Prepare library**
  - Illumina Complete Long Read Prep, Human

- **Sequence**
  - NovaSeq X

- **Analyze**
  - DRAGEN ICLR Analysis in BaseSpace Sequence Hub

- **Interpret**
  - Emedgene

For more information about these products, click the links above.

**WES**
Focus sequencing efforts on protein-coding regions for variants reported in public databases

Prepare library
> Sequence
> Analyze
> Interpret

- **Prepare library**
  - Illumina DNA Prep with Exome 2.0 Plus Enrichment

- **Sequence**
  - NextSeq 2000

- **Analyze**
  - DRAGEN Enrichment app

- **Interpret**
  - Emedgene

For more information about these products, click the links above.

**Example workflows for genetic disease research:**

WES
Focus sequencing efforts on protein-coding regions for variants reported in public databases
Illumina genomic in vitro diagnostic (IVD) solutions empower clinical laboratories to find the answers they’re looking for to directly impact patient outcomes. Our wide range of products, encompassing the entire NGS workflow, are built to withstand the rigor and precision of the IVD world.

**The Illumina IVD instrument portfolio**

With easy-to-follow workflows and integrated software, the MiSeq™Dx, NextSeq 550Dx, and NovaSeq 6000Dx instruments deliver accurate, reliable screening and diagnostic testing. They are built with the same proven NGS technology and SBS chemistry as our research use only (RUO) platforms.

<table>
<thead>
<tr>
<th>MiSeqDx Reagent</th>
<th>NextSeq 550Dx High-Output Reagent Kit v2.5 (300 cycles)</th>
<th>NextSeq 550Dx High-Output Reagent Kit v2.5 (70 cycles)</th>
<th>NovaSeq 6000Dx S2 Reagent v1.5 Kit (300 cycles)</th>
<th>NovaSeq 6000Dx S4 Reagent v1.5 Kit (300 cycles)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Read length</td>
<td>2 × 300 bp</td>
<td>2 × 75 bp</td>
<td>2 × 150 bp</td>
<td>2 × 150 bp</td>
</tr>
<tr>
<td>Clusters passing filter (per flow cell)</td>
<td>25M</td>
<td>400M</td>
<td>400M</td>
<td>41B</td>
</tr>
<tr>
<td>Maximum output</td>
<td>15 Gb</td>
<td>120 Gb</td>
<td>30 Gb</td>
<td>1.7b</td>
</tr>
<tr>
<td>Run time</td>
<td>&lt; 56 hr</td>
<td>&lt; 35 hr</td>
<td>&lt; 11 hr</td>
<td>≤ 40 hr</td>
</tr>
<tr>
<td>Data quality (Q30)</td>
<td>≥ 80%</td>
<td>&gt; 75%</td>
<td>&gt; 80%</td>
<td>&gt; 85%</td>
</tr>
</tbody>
</table>

**Illumina diagnostic solutions**

Illumina offers NGS-based IVD assays and kits enabling clinical labs to apply the power of genomics to genetic disease testing.

**TruSight Cystic Fibrosis**

A fully integrated molecular testing solution for cystic fibrosis on the MiSeqDx instrument. This assay detects 139 clinically relevant CFTR variants or enables comprehensive sequencing of all protein coding regions of the CFTR gene.

Learn more

**Illumina DNA Prep with Enrichment Dx**

A library preparation and enrichment solution that is compliant with European Union (EU) IVD Regulation (IVDR) 2017/746. As part of an NGS workflow compatible with any Illumina IVD instrument, it enables clinical labs to add targeted enrichment panels to their menu of diagnostic applications.

Learn more

**DRAGEN for Illumina DNA Prep with Enrichment Dx App**

The DRAGEN for Illumina DNA Prep with Enrichment Dx App performs alignment and variant calling in DNA for somatic and germline mutations.

**Example IVD-compliant workflows for genetic disease testing**

Illumina offers integrated solutions for clinical labs to deliver results that will impact patient outcomes.

**Cystic Fibrosis testing**

Perform cystic fibrosis screening with comprehensive coverage of known disease-associated variants or the ability to sequence all protein-coding regions and intron/exon boundaries of the CFTR gene.

To learn more, read “Confirming cystic fibrosis diagnosis in neonates using TruSight Cystic Fibrosis.”

**Flexible support for content**

Expand your menu of diagnostic offerings with support for panels that meet the required specifications, including Illumina or third-party fixed and custom panels of varying sizes, such as those designed for WES.

To learn more, read “High-quality variant calling with the NovaSeq 6000Dx instrument.”
Welcome to a world of support
Illumina service and support begin when your Illumina instrument is delivered. Our scientists and engineers are ready to assist with instrument installation and laboratory setup. In addition to onsite support, courses are available to train users on various workflows. Illumina scientists are available 24 hours a day, five days a week globally to answer questions every step of the way.

Illumina Qualification Services
Meet compliance requirements by taking advantage of Illumina comprehensive qualification services.

Illumina Training
Get high-quality results on Illumina technology even faster with instructor-led, hands-on courses and web-based training options.

Contact Illumina
Contact your Illumina sales representative to find out more about our solutions.

Learn more

References
We are always available for questions, insights, and conversation.

Visit us at illumina.com

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