TECHNICAL NOTE

Accelerating NGS workflows with Illumina Genomics Architecture

A standardized, modular, extensible framework that streamlines deployment and reduces turnaround times of DNA-to-data workflows

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Introduction

Illumina sequencing by synthesis (SBS) chemistry powers massively parallel next-generation sequencing (NGS) to deliver high-quality, accurate data. When combined with the speed and scalability enabled by the latest innovations in Illumina high-throughput sequencing technology, a broad array of applications in genomics, transcriptomics, and epigenomics become available.

The NGS workflow proceeds from library preparation to sequencing to data analysis and interpretation. The Illumina product portfolio encompasses a range of components throughout the workflow that address the many possible application areas. Because of the diversity of Illumina products, some new customers find that integrating individual components into an integrated solution, eg, isolation of genetic material through variant reporting, is laborious and time consuming. Also, while many Illumina workflows are compatible with automation, some customers are daunted by the technical expertise required to integrate and optimize automated methods into their existing practices.

Illumina Genomics Architecture (IGA) addresses these challenges by offering a standardized, modular, and flexible framework for rapidly adopting and implementing automation-compatible sample-to-answer NGS workflows for both research and clinical research applications. IGA was derived from experience gained in assisting customers implementing DNA-to-data workflows for whole-exome sequencing (WES), whole-genome sequencing (WGS), and Population Genomics (PopGen) programs. IGA currently supports components for WES and WGS and allows for future workflow enhancements.

This technical note presents an overview of IGA for research and clinical research labs who are either currently employing WES or WGS on the NovaSeq™ 6000 System and are seeking optimized integration with other Illumina products or labs seeking guidance before implementing WES or WGS on the NovaSeq 6000 System (Figure 1). This technical note also describes an example use case where a custom, modular implementation of IGA helped achieve a WGS run in 13.5 hours.

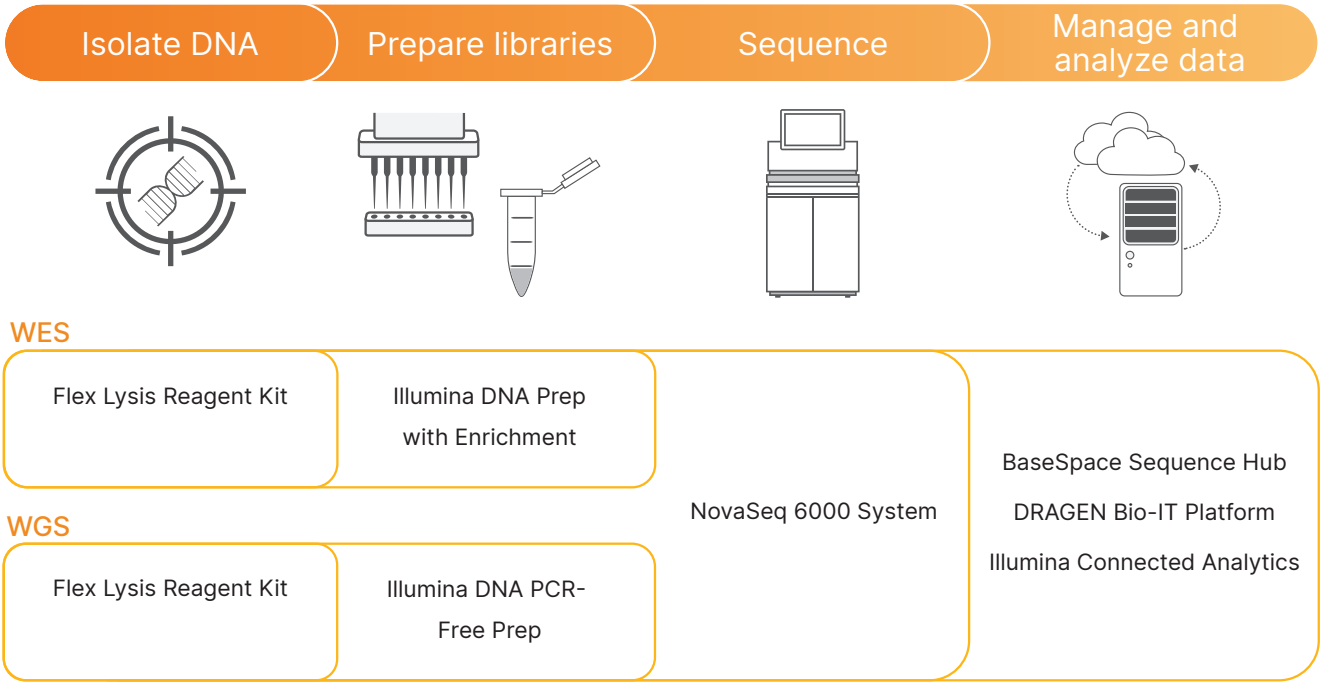

Figure 1: IGA sample-to-answer NGS workflows—IGA currently supports optimized, DNA-to-data workflows for WES and WGS. Individual components used in each step of the NGS workflow can be specific to a method or shared across methods.

The IGA framework

For the purposes of optimization, the NGS workflow is divided into four main process steps: isolation of genetic material, library preparation, sequencing, and data analysis and interpretation. Individual components used at each step can be specific to each method or shared across methods (Figure 1). IGA is comprised of a combination of hardware and software that enables:

- Accelerated deployment of NGS workflows
- Rapid adoption through intuitive user-guided interfaces
- Improved workflow management and sample tracking
- Increased throughput with less user intervention
- Simplified integration of future workflow components

Hardware includes an automated liquid-handling platform and the NovaSeq 6000 System. Software includes BaseSpace™ Clarity LIMS (Laboratory Information Management System), BaseSpace Sequence Hub, DRAGEN™ Bio-IT Platform, and Illumina Connected Analytics (Figure 2). After a lab has procured all hardware, software, and appropriate reagent components, IGA reduces the time to integrate and deploy WES or WGS workflows from approximately one year to only a few months.

Optimizing NGS workflows with IGA

Preconfigured IGA workflows within BaseSpace Clarity LIMS and instrument integration reduce turnaround times, minimize human interaction and potential errors, and increase sample throughput. The modularity and flexibility of IGA enable both WES and WGS to be performed using the same labware, hardware, and software by simply using the appropriate IGA workflow and library prep kit. This reduces lengthy liquid-handling deck layout reconfiguration and allows for continuous sample processing from one application to another with minimal differences. IGA workflows are provided through the Illumina Preset Protocols (IPP) collection.

BaseSpace Clarity LIMS guides users through the workflow and provides orchestration between the user, liquid handler, sequencing system, and data analysis. The user begins by initiating a project and accessioning samples from within BaseSpace Clarity LIMS using the IGA WES or WGS workflow. BaseSpace Clarity LIMS then directs the user to load samples into the automated liquid-handling platform to perform DNA isolation and library preparation, while tracking workflow progress.

After library preparation is complete, BaseSpace Clarity LIMS directs the liquid-handling platform to perform bulk pooling, sample denaturation, and loading of the library tube or flow cell for standard or Xp workflows, respectively. After the user loads the reagent cartridge onto the NovaSeq 6000 System, BaseSpace Clarity LIMS sends the required information to start the sequencing run automatically. Data from the NovaSeq 6000 System is streamed through BaseSpace Sequence Hub to Illumina Connected Analytics (ICA), a comprehensive cloud-based platform for storage, management, and analysis.

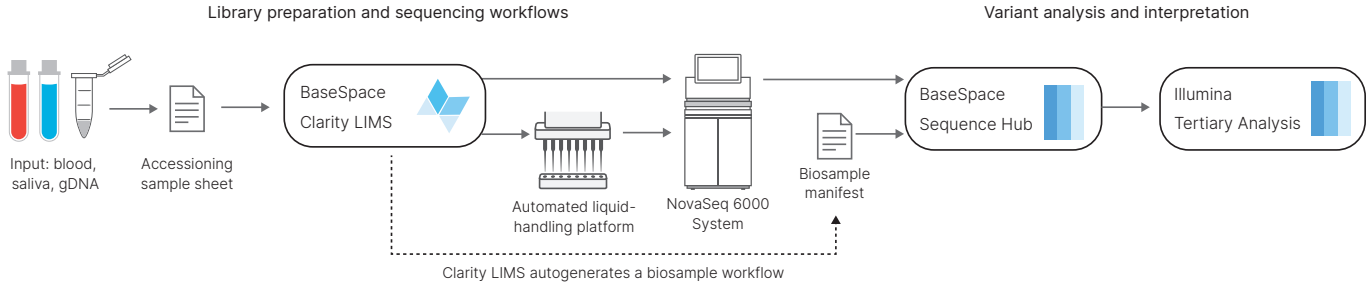

Figure 2: IGA framework—IGA framework consists of hardware, including a liquid-handling platform and the NovaSeq 6000 System, and software, including BaseSpace Clarity LIMS, BaseSpace Sequence Hub, Illumina Connected Analytics, and the DRAGEN Bio-IT Platform, that coordinate to provide a DNA-to-data workflow for WES and WGS.

ICA is a security-first environment, built to enable data privacy and compliance. It interfaces directly with the DRAGEN Bio-IT Platform to deliver rapid, automated primary (BCL to FASTQ conversion) and secondary (mapping, alignment, and variant calling) analyses. With ICA, users have access to powerful tools and machine-learning models to aid in tertiary analysis (variant prioritization and interpretation).

Example use case

In the field of genomic medicine, WGS has the potential to aid in the detection of variants associated with rare disease. Rady Children's Institute for Genomic Medicine (RCIGM) worked with Illumina to implement IGA and provide a WGS DNA-to-data solution that reduced their workflow turnaround time while maintaining a high level of performance. Specifically, RCIGM adopted IGA with the following modifications:

- Illumina DNA PCR Free library preparation was accelerated
- Ultrafast custom sequencing recipes were used with the NovaSeq 6000 System
- Onsite data analysis was performed using a DRAGEN Server

RCIGM used this customized IGA WGS workflow to perform variant analysis of a 5-week-old, previously healthy male proband. WGS was performed in just 13.5 hours, a significant reduction from the previous world record for fastest molecular diagnosis using WGS in 19.5 hours (held by RCIGM).[1] Results led to detection of a variant associated with thiamine metabolism dysfunction syndrome 2 (THMD2).[2]

With IGA, RCIGM accelerated implementation of a custom, DNA-to-data workflow that reduces user touch points and turnaround time, dramatically accelerating WGS. Given the built-in scalability of IGA, RCIGM is looking to take advantage of the liquid-handling automation component of their workflow to scale from proband sequencing only to sequencing of trios.

Summary

IGA enables rapid adoption and implementation of sample-to-answer NGS workflows for various research applications. Although IGA currently supports WES and WGS, it allows for future workflow enhancements and can be easily extended to other applications, including transcriptomics and epigenomics. In addition to accelerating deployment of NGS workflows, IGA offers improvements in turnaround time and reduces manual touchpoints in the workflow, lowering the risk of user error. IGA ultimately enables customers to obtain results faster by providing an efficient, accurate, sample-to-answer workflow.

Learn more

Illumina Genomics Architecture, support-docs.illumina.com/SHARE/IlluminaGenomicsArchitecture/Content/SHARE/FrontPages/IGA.htm

or contact your Field Application Scientist to begin implementing Illumina Genomics Architecture

Clarity LIMS Support, support-docs.illumina.com/SW/ClarityLIMS/ClarityIPP/Content/SW/FrontPages/ClarityLIMS_IPPs.htm

References

1. Saunders CJ, Miller NA, Soden SE, et al. Rapid whole-genome sequencing for genetic disease diagnosis in neonatal intensive care units. *Sci Transl Med.* 2012;4(154):154ra135. doi:10.1126/scitranslmed.3004041.
2. Owen MJ, Niemi AK, Dimmock DP, et al. Rapid sequencing-based diagnosis of thiamine metabolism dysfunction syndrome. *N Engl J Med.* 2021;384(22):2159-2161. doi:10.1056/NEJMc2100365.

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