

Illumina Connected Insights

Enabling NGS data
interpretation through report
generation for oncology
applications and beyond

- Streamlined to save time and increase confidence by consolidating knowledge sources and automating routine tertiary analysis workflows
- Integrated for fewer touchpoints from sample to report with automatic information flow, regardless of assay or instrument
- Powered for growth, enabling clinical testing labs to keep pace with expanding test menus and dynamic case volumes

Introduction

Innovations in next-generation sequencing (NGS) technology have enabled deeper sequencing, higher throughput, and more comprehensive assessment of variant classes and biomarker types. Genomics-powered insights are helping to identify underlying causes of disease, optimize treatments, and create better outcomes for patients.

While accessible bioinformatic innovations for secondary analysis have kept pace with the massive amounts of data generated by NGS methods, many labs still struggle with scaling tertiary analysis, including interpreting genetic variants to extract biologically relevant meaning. This further increases the burden on lab personnel and makes variant interpretation a time-intensive, potentially manual process that requires numerous, repetitive steps and takes as long as seven hours per genome or for other comprehensive assay types.¹

Illumina Connected Insights helps labs address this data interpretation bottleneck as they bring NGS assays in house or scale existing workflows. This customizable platform enables tertiary analysis, from data upload to report generation, and streamlines the user experience through automatable user selections. Through application programming interface (API)-based calls, Connected Insights allows users to access variant information from > 45 sources for filtering and report generation. Connected Insights features functionality that is designed to decrease the time and effort required to extract biological insights

from genomic data while maximizing operational efficiency for routine, user-defined interpretation (Table 1).

Connected Insights is designed to serve multiple applications and areas of interest. In somatic oncology, Connected Insights can be configured to accept input data from a wide range of oncology assays, including comprehensive genomic profiling (CGP), from tissue or liquid biopsies, and hematological malignancy testing. The software supports variant types frequently identified in DNA and RNA tumor samples such as single nucleotide variants (SNVs), insertions/deletions (indels), fusions, structural variants (SVs), loss of heterozygosity (LOH), and others, and accepts and enables user interpretation for genome-wide biomarkers such as tumor mutational burden (TMB), microsatellite instability (MSI), and genomic instability score (GIS) to assess homologous recombination deficiency (HRD). Connected Insights is built on a futureproofed framework that will expand into additional applications within oncology and beyond.

Connected Insights integrates with and extends existing NGS workflows (Figure 1), enabling labs to implement standardized, user-defined workflows to interpret disease-relevant variants rapidly and generate reports summarizing the user's findings in a structured format. Connected Insights represents the final piece in the NGS workflow, enabling labs to streamline their tertiary analysis today, and scale operations for tomorrow.

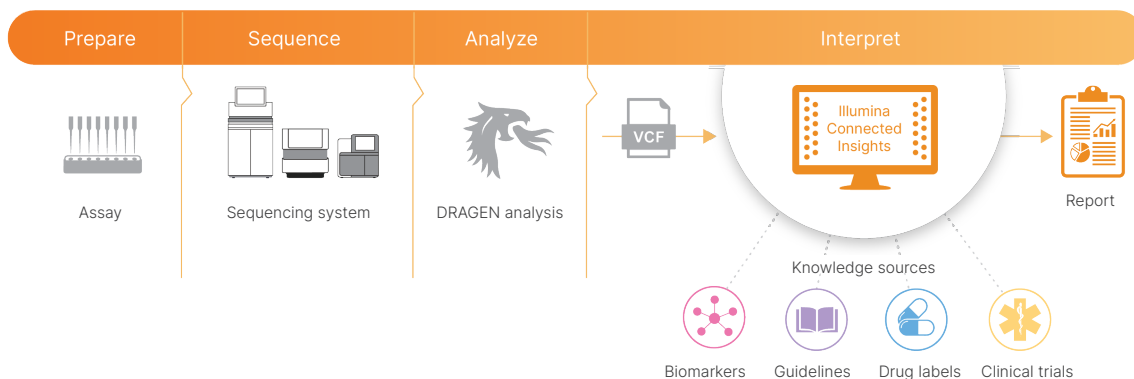


Figure 1: Connected Insights extends the NGS workflow—Enable variant interpretation and reporting across applications and areas of interest.

Table 1: Features of Illumina Connected Insights

Feature	Specification
Platform compatibility	Broad spectrum of NGS instruments
Data input compatibility	VCF from DRAGEN software or any other secondary analysis solution with seamless data flow
Assay compatibility	Wide range of DNA or RNA assays with VCF output; supports solid tumor testing, liquid biopsy testing, hematological malignancy testing, panels, WES, WGS, and whole-transcriptome sequencing
Variant classes	Small variants (SNVs, indels), CNVs, SVs, fusions, LOH, and splice site variants
Genomic signatures	TMB, MSI, HRD (GIS), and tumor ploidy
Hereditary risk	Ability to report on hereditary risk in the context of the tumor
Sample quality	QC metrics, tumor purity, and VAF plot
MyKB	Lab variant curation, ability to batch-load existing or acquired curated data
External knowledge sources	> 45 sources, including JAX-CKB, COSMIC, CIViC, and ClinVar
Comprehensive filtering	Includes variant frequency, quality scores, read depth, variant type, functional impact, clinical information, and others
User-defined automation	Supports presets of key test parameters (eg, variant filters, report template) for convenient reuse and draft report generation
Variant curation and storage	Automatically stores variant interpretations to facilitate future use
User-friendly reporting	Enables generation of custom reports that can be optimized based on disease research focus
Multiple languages	Supports multiple languages for user interface and report generation
Visualizations	IGV, genome plots for SVs, CNVs, coverage and B-allele ratio, VAF distribution, and others

CNV, copy number variant; GIS, genomic instability score; HRD, homologous recombination deficiency; IGV, integrative genomics viewer; LOH, loss of heterozygosity; MSI, microsatellite instability; QC, quality control; SNV, single-nucleotide variant; SV, structural variant, TMB, tumor mutational burden; VAF, variant allele frequency; VCF, variant call format; WES, whole-exome sequencing; WGS, whole-genome sequencing

Streamlined operations

Connected Insights optimizes and automates variant interpretation to decrease time to report generation and achieve high accuracy and consistent performance. From enabling automation of user-defined presets to viewing content from multiple sources in one interface, Connected Insights offers powerful tools to accelerate day-to-day lab operations. Lab-specific variant curation allows labs to easily customize processes. Regional content drives an additional layer of functionality and relevance, helping labs produce comprehensive and meaningful results.

Automation for lab efficiency

The Connected Insights user interface allows labs to easily configure and automate interpretation workflows for greater efficiency:

- Flexible variant filters (Figure 2) allow for development of comprehensive filtering strategies; filters can be saved, locked, and shared, serving to streamline future analyses
- Report automation feature pregenerates draft report content based on user selections, such as a variant evidence level and presence in past reports
- The test definition feature stores key parameters (eg, variant filters, report template) for each test conducted in the lab; the ability to control who can edit the presets allows for consistency and efficiency of lab processes
- Team-based features, including tags, role-based permissions, logs, and workgroups, facilitate team coordination and collaboration

The entire workflow through custom report generation can be configured one time and automated to increase your team's tertiary analysis speed, breadth, and confidence.

Comprehensive knowledge base options all in one place

With API connections established by Connected Insights, labs have direct access to a network of > 45 external knowledge sources containing biologically and clinically relevant information to help assess a genomic alteration.

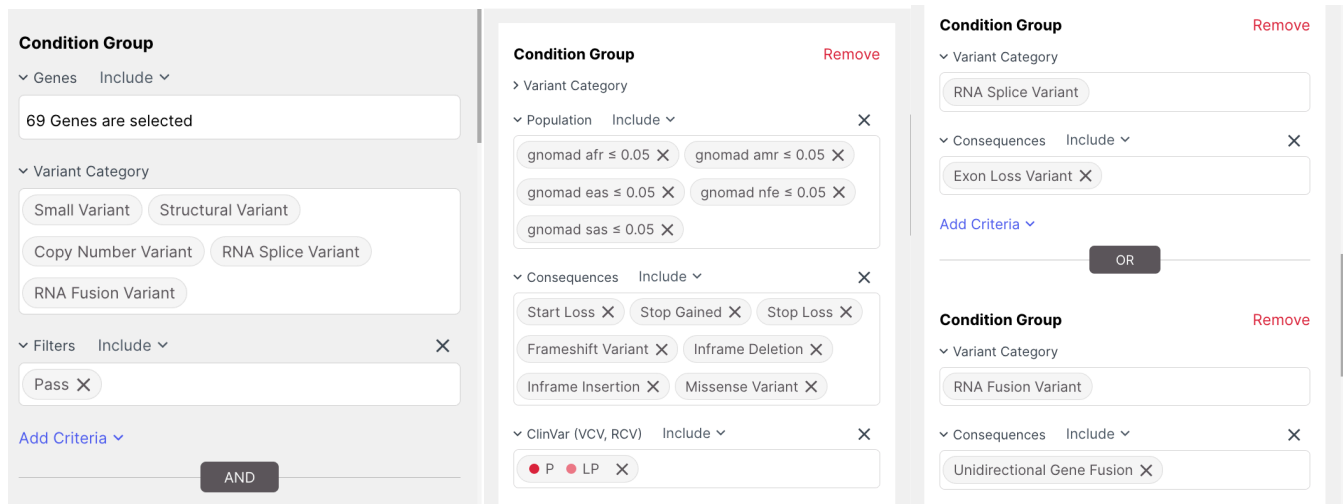


Figure 2: Filters in Connected Insights—Comprehensive filter sets enables rapid isolation of key variants that are relevant to the current case.

These sources include [The Jackson Laboratory Clinical Knowledgebase \(JAX-CKB™\)](#), which provides comprehensive solid and hematological cancer content, somatic gene variant annotations, and other related content. JAX-CKB is a trusted knowledge base of over 100,000 users worldwide. Other integrated sources include [Catalog of Somatic Mutations in Cancer \(COSMIC\)](#), [Clinical Interpretation of Variants in Cancer \(CIVIC\)](#), [ClinVar](#), the [Online Mendelian Inheritance in Man \(OMIM\)](#) catalog, variant frequency sources, functional impact resources, and other regularly updated databases. By aggregating information from multiple sources into a single hub, Connected Insights eliminates the need for manual searches for variant information across disparate online resources, streamlining the interpretation process and saving valuable time. Users can choose their knowledge sources, view aggregated content for a given variant, and examine in-depth information on the variant associations, including publication IDs, guidelines, and other forms of evidence. The software can populate a standardized, succinct report template with relevant draft information with high efficiency.

Regional content

By accessing the JAX-CKB, Connected Insights provides access to comprehensive regional content, enabling labs to address local needs. These sources include:

- Regionally specific drug labels by the US Food and Drug Administration (US FDA), the European

Medicines Agency (EMA), and the Therapeutic Goods Administration (TGA)

- Local clinical trials provided by [clinicaltrials.gov](#)
- Recommendations from the regional practice guidelines provided by the National Comprehensive Cancer Network (NCCN), the American Society of Clinical Oncology (ASCO), and the European Society for Medical Oncology (EMSO, includes Pan-Asian guidelines)

In addition to the regional content, Connected Insights users can customize their variant interpretation and reporting to follow any regional tiering guideline, for example, the framework developed by ASCO/Association for Molecular Pathology (AMP),² the ESMO Scale for Clinical Actionability of molecular Targets (ESCAT),³ or the [FDA approach](#). The biological classification used in some regions^{4,5} can be used with the tiering systems.

Lab-specific curation

Connected Insights features My Knowledge Base, a personalized, private repository for laboratory-curated data, including information about variants already interpreted in the lab and details of their inclusion in past reports. My Knowledge Base is used throughout Connected Insights to inform based on past decisions and autopopulate the draft report. Effectively integrating the curated data and cumulative, expanding knowledge from the laboratory can reduce the burden of interpretation

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DEMO_001_OVARIAN_DNA_RNA_TSO500_V3 • BRCA1 p.(Trp1815Ter) c.5444G>A

Biological Classification Actionability Clinical Trials ClinVar Variant Overview Gene Overview Cancer Datasets Computer Predictors Population

Biological Classification

Update Date	Source	Biomarker	HRD	Type	Classification	Disease(s)	Actions
2023-11-19	my KB	17-41199683 C > T Stop Gained, Loss of Function Variant	HRD+	Biological	Pathogenic	Malignant tumor of ovary	Report →

Actionability

Update Date	Source	Biomarker	HRD	Type	Classification	Direction	Therapy	Disease(s)	Actions
2023-11-09	my KB	BRCA1 Variant	HRD+	Therapeutic	Tier 1A	Responsive	Olaparib, Bevacizumab	Malignant tumor of ovary	Add
2023-10-13	CKB	BRCA1 Loss of Function Variant		Therapeutic	Tier 1A	Sensitive	Rucaparib	Ovarian cancer	Report →
2023-10-13	CKB	BRCA1 Loss of Function Variant		Therapeutic	Tier 1A	Sensitive	Olaparib, Bevacizumab	Ovarian cancer	Report →
2023-10-13	CKB	BRCA1 Variant		Therapeutic	Tier 1A	Sensitive	Olaparib	Ovarian cancer	Add
2023-10-13	CKB	BRCA1 Variant		Therapeutic	Tier 1A	Sensitive	Rucaparib	Ovarian cancer	Report →

Clinical Trials

Update Date	Source	Biomarker	HRD	Title	Phase	Location	Disease	Actions
2023-10-13	CKB	BRCA1 Variant		Niraparib in Tumors Metastatic to the CNS	Phase II	Boston, Massachusetts	Triple-receptor negative breast cancer, Malignant neoplastic disease	Report →

Also report as hereditary risk finding?

Assertion 1

Automation

Assertion 2

Automation

Level Gene (BRCA1)

Consequences

HRD

Type Therapeutic

Classification Tier 1A

Direction Sensitive

Therapy Olaparib

Disease Ovarian cancer

Summary

Lynparza (olaparib) is included in guidelines as a maintenance therapy following response to a platinum-based therapy in ovarian cancer patients with BRCA mutations (ESMO Guidelines, PMID: 31046081).

Notes

NA

Actions Remove from report

Create New Assertion Remove All

Figure 3: Lab-specific curation in Connected Insights—A lab's repository of curated data can serve as a knowledge source for retrospective discovery research and efficiency gains for future case studies.

and curation for additional efficiency gains (Figure 3). My Knowledge Base allows users to:

- Upload past variant interpretations from the lab when adopting Connected Insights
- Clone and edit variant records created in the lab or by external sources
- Use any oncology tiering framework, including a fully custom one
- Use biological classification for oncogenic interpretation
- Interpret genome-wide biomarkers such as TMB, MSI, and HRD (GIS)
- View a summary of past variants used including reports

Concise, customizable reports

Connected Insights provides powerful and flexible capabilities for clear and concise variant reporting. Users can choose to use a default report template or create and

store multiple customized templates using a simple word-processor-like editing feature. In addition to report naming and logo changes, common customizations include display of the sample and subject information, updates of report sections, and more. Reports can be exported in PDF or JSON format (Figure 4).

Visualizations for deeper insights

Connected Insights includes several visualization features (Figure 5) to facilitate:

- Variant QC (eg, IGV, coverage plots, VAF plot)
- Understanding of identified variants (genome plots for SVs, CNVs, coverage and B-allele ratio)
- Variant interpretation (variant distribution plots across tissues and tumor histologies)

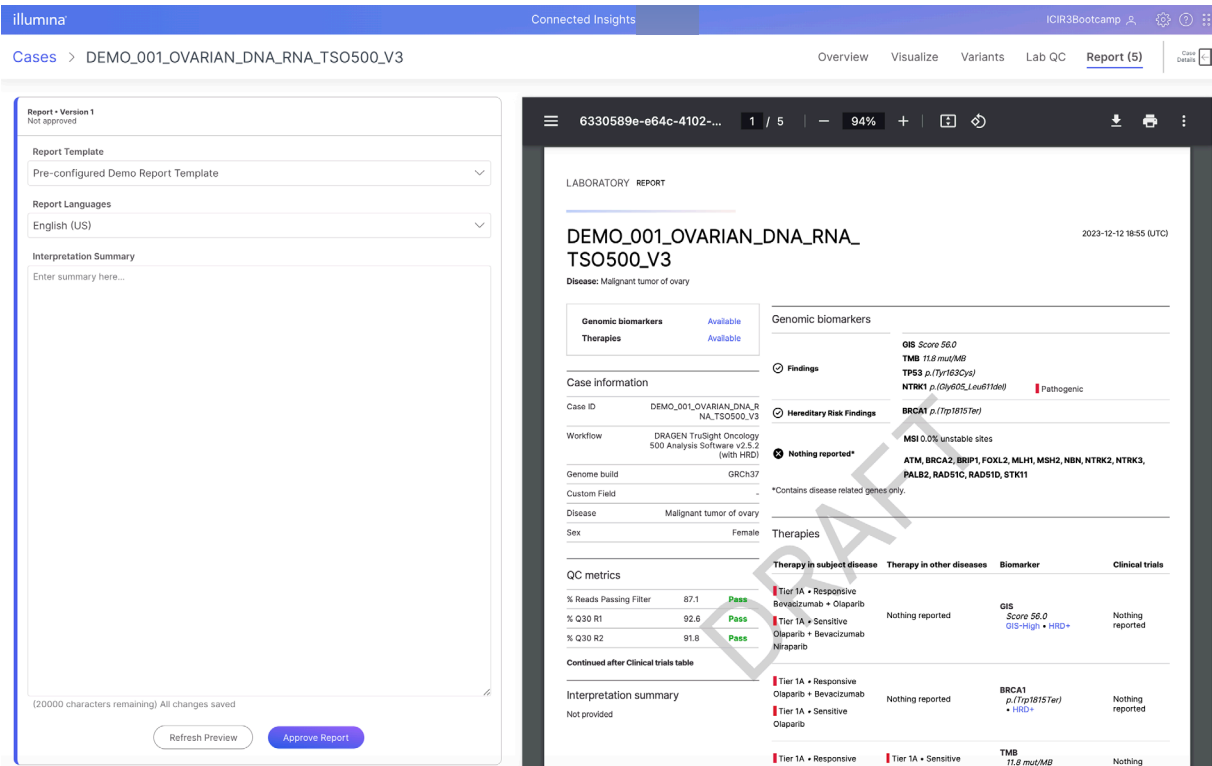


Figure 4: Flexible reporting capabilities enable clear and concise variant interpretation reporting with preconfigured templates—Templates are customized by the lab in a word processing-like template for ease. Templates reflect what the lab is doing and draft reports are editable and amenable in any way for full control by the lab.



Figure 5: Connected Insights powerful, clear visualization tools—Users can see complexities, perform variant QC, and interpret data in a single view. (A) Gene and exon coverage for DNA and RNA. (B) Genome view covering SVs, CNVs, coverage, and B-allele ratio.

Integrated solution

Connected Insights integrates with existing NGS workflows to streamline tertiary analysis and enable variant interpretation. The software is compatible with the VCF output of virtually any variant caller for maximum flexibility, allowing labs to take advantage of a single-vendor solution for their NGS workflow. Connected Insights is compatible with any Illumina sequencing system, and connects directly with the Illumina Connected Software ecosystem, designed to be a streamlined, holistic set of analysis and data management solutions that can be deployed out of the box or customized to meet specific needs.

DRAGEN™ secondary analysis

Connected Insights can be configured to work with VCF data files output from any secondary analysis platform. With the option to connect to DRAGEN (Dynamic Read Analysis for GENomics) secondary analysis upstream of Connected Insights, labs of any size can take advantage of the proven performance and accuracy of variant calling across multiple variant types.

Illumina Connected Analytics

Connected Insights can integrate directly with Illumina Connected Analytics for automated data import and consolidated data storage. Connected Analytics is a comprehensive, cloud-based bioinformatics platform that empowers researchers to manage and process large volumes of genomic data in a secure, scalable, and flexible environment. The software empowers labs performing deep data science across population cohorts and supports data sharing with collaborators on a secure platform compliant with international data privacy regulations.

Powered for growth

Connected Insights enables labs to keep pace with evolving science and technology and scale operations to meet demand.

Trusted support and service partner

Illumina is committed to ensuring that the user community is empowered to serve their mission and definition of growth. Illumina provides a world-class support team that comprises experienced scientists who are experts in library prep, sequencing, and analysis. Technical support is available by phone and email, 24/5 worldwide; support uses a follow-the-sun model based on local business hours, Monday through Friday.

Dedicated to your success, Illumina also provides customers with an Informatics Services team, bringing a staff of bioinformaticians, data scientists, and designers to help you customize and optimize your analysis workflow and minimize your development burden.

In addition, Illumina offers a complete professional services option to support customized implementation needs, upstream and downstream of Connected Insights.

Typical service projects span software implementation according to lab standard operating procedures (SOPs), past variant data aggregation and upload, data flow setup including laboratory information management system (LIMS) connectivity, electronic health/medical record integration (EHR/EMR), connecting collaborators with role-based permissions, and more. This service makes sure that your resources remain focused on mission-critical work while applying the expertise of Illumina and partnered system integrators to connect and test your optimized data flow.

Security and compliance at the core

Security is of paramount importance when operating with genomics data for research, clinical therapeutics, and human diagnostics. Connected Insights employs various digital and administrative measures to meet even the most demanding data security requirements.



Connected Insights is a global platform that adheres to local data residency requirements. To learn more, read the [Security, privacy, and compliance with Illumina Connected Insights technical note](#).

Summary

Connected Insights streamlines tertiary analysis and variant interpretation workflows by connecting external knowledge sources via API-calling and enabling highly tunable user-defined workflow automation. Connected Insights is designed to serve across multiple applications and areas of interest. While the software is compatible with the output of any secondary analysis variant caller, when integrated into the Illumina NGS workflow, users can take advantage of proven Illumina sequencing technology and the accuracy of DRAGEN secondary analysis. Connected Insights enables labs to streamline tertiary analysis today, and scale operations for tomorrow.

Learn more

[Illumina Connected Insights](#)

Ordering information

Available in select countries.

For qualified inquiries, Illumina offers a supported evaluation experience, allowing customers to work with example cases available in Connected Insights or upload and evaluate their own cases within the software. Contact an Illumina sales representative for more information.



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