DATA SHEET

Illumina Connected Insights-Research

Enabling NGS data interpretation for somatic oncology research applications

- Streamlined to save time and increase confidence by consolidating knowledge sources and automating routine tertiary analysis research workflows
- Integrated for fewer touchpoints from sample to research report with automatic information flow, regardless of assay or instrument
- Powered for growth, enabling clinical research labs to keep pace with new knowledge, expand assay menus, and scale projects

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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 methods and scale insights from population-size initiatives.

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-Research 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 research report generation, and streamlines the user experience through automatable user selections. Using application programming interface (API)–based calls, Connected Insights-Research allows users to access variant information from > 55 sources for filtering and insights generation. Connected Insights-Research 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-Research serves multiple research applications and areas of interest. In somatic oncology studies, Connected Insights-Research 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 assays. 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-Research is built on a future-proofed framework that will expand into additional application areas, within oncology and beyond.

Connected Insights-Research 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 findings in a structured format. Connected Insights-Research represents the final piece in the NGS workflow, enabling labs to streamline tertiary analysis and scale operations across research applications.

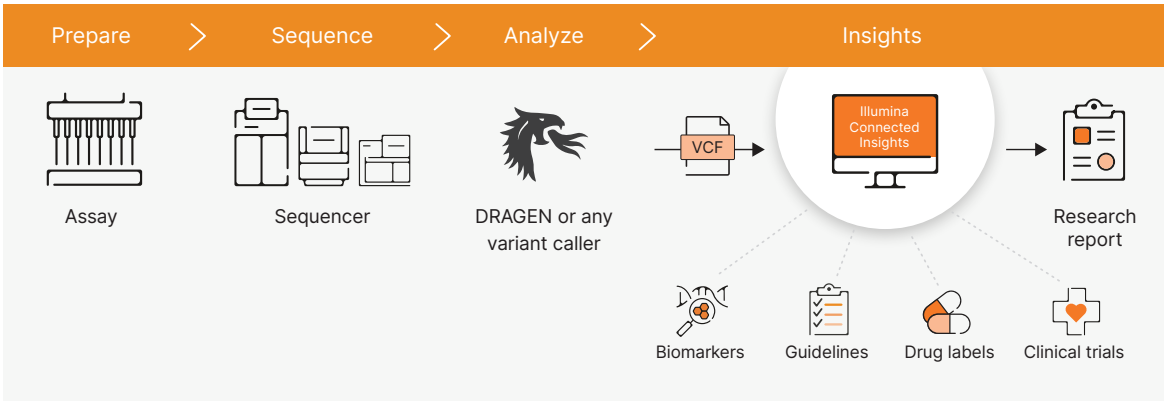

Figure 1: Connected Insights-Research extends the NGS workflow—Enables variant interpretation and reporting across research applications and areas of interest.

Table 1: Features of Illumina Connected Insights-Research

Feature	Specification
Platform compatibility	Broad spectrum of NGS instruments and robust APIs for implementing within digital ecosystems, including EHR/EMR
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 assays, liquid biopsy assays, 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
Internal knowledge base	Lab variant curation, ability to batch-load existing or acquired curated data
External knowledge sources	> 55 sources, including JAX-CKB, OncoKB, COSMIC, CIViC, ClinVar, LitVar, and Mastermind
Comprehensive filtering	Includes variant frequency, quality scores, read depth, variant type, functional impact, and others
Automation and classification	Supports variant filter presets for key test parameters, VICC guideline-based oncogenicity prediction, 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, fusion plots, and more
Multiplatform accessibility	Deployment available on cloudor on-premises via a DRAGEN server

CNV, copy number variant; EHR, electronic health record; EMR, electronic medical record; 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; VICC, Variant Interpretation for Cancer Consortium; WES, whole-exome sequencing; WGS, whole-genome sequencing

Streamlined operations

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

Automation for lab efficiency

With the Connected Insights-Research user interface, labs can 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 research 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 assay run 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-Research, labs have direct access to a network of > 55 external knowledge sources containing biologically relevant information to help assess a genomic alteration.

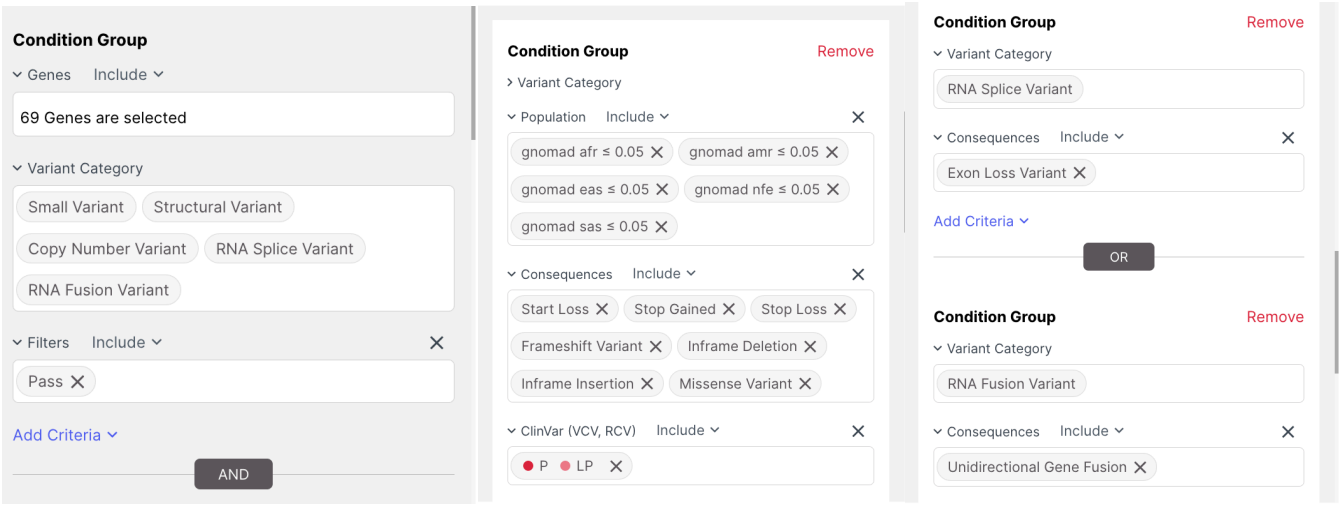

Figure 2: Filters in Connected Insights-Research—Comprehensive filter sets enables rapid isolation of key variants that are relevant to the research subject.

These sources include The Jackson Laboratory Clinical Knowledgebase (JAX-CKB™), a trusted knowledge base with over 100,000 users worldwide, providing comprehensive solid and hematological cancer content, somatic gene variant annotations, and other related content. Additionally integrated in Connected Insights-Research is OncoKB™, a precision oncology knowledge base from Memorial Sloan Kettering that includes FDA-recognized content. 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. Multiple article search tools, including LitVar 2.0,[2] Mastermind Genomic Intelligence Platform from Genomenon, Google Scholar, and more are integrated to enable retrieval of insights that are not yet in a curated knowledge base.

By aggregating information from multiple sources into a single hub, Connected Insights-Research 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 research report template with relevant draft information with high efficiency.

Regional content

By accessing the JAX-CKB, Connected Insights-Research provides access to comprehensive regional content. 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-Research users can customize their variant interpretation and research reporting to follow any regional tiering guideline, for example, the framework developed by ASCO/Association for Molecular Pathology (AMP),[3] the ESMO Scale for Clinical Actionability of molecular Targets (ESCAT),[4] or the FDA approach. The biological classification used in some regions[5,6] can be used with the tiering systems.

Automated oncogenicity classification

Standards for classifying somatic variant oncogenicity were defined from a joint set of guidelines by the Clinical Genome Resource (ClinGen), Cancer Genomics Consortium (CGC), and Variant Interpretation for Cancer Consortium (VICC)[7] to harmonize classification of variants across institutions. Connected Insights-Research automates guideline-based oncogenicity classification that is powered by AI algorithms, such as SpliceAI and PrimateAI. The logic and evidence behind the draft classification are fully transparent and interactive, presented in an evidence map (Figure 3). Users can override and edit draft, estimated classifications.

Lab-specific curation

Connected Insights-Research features My Knowledge Base (MyKB), a personalized, private repository for laboratory-curated data, that includes information about variants already interpreted in the lab and details of their inclusion in past reports. My Knowledge Base is used throughout Connected Insights-Research 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 and curation for additional efficiency gains (Figure 4).

My Knowledge Base allows users to:

- Upload past variant interpretations from the lab when adopting Connected Insights-Research
- 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

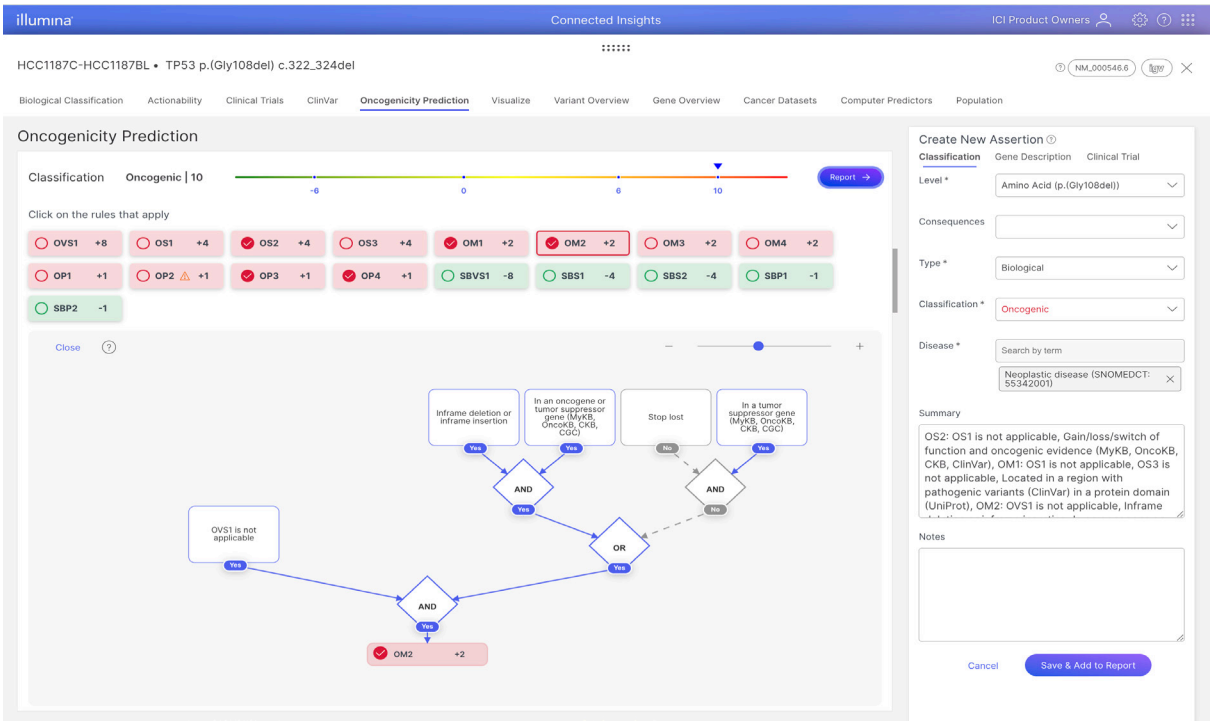

Figure 3: Oncogenicity draft classification and evidence map— An estimated oncogenicity score based on guidelines is automated; transparent display of logic and evidence.

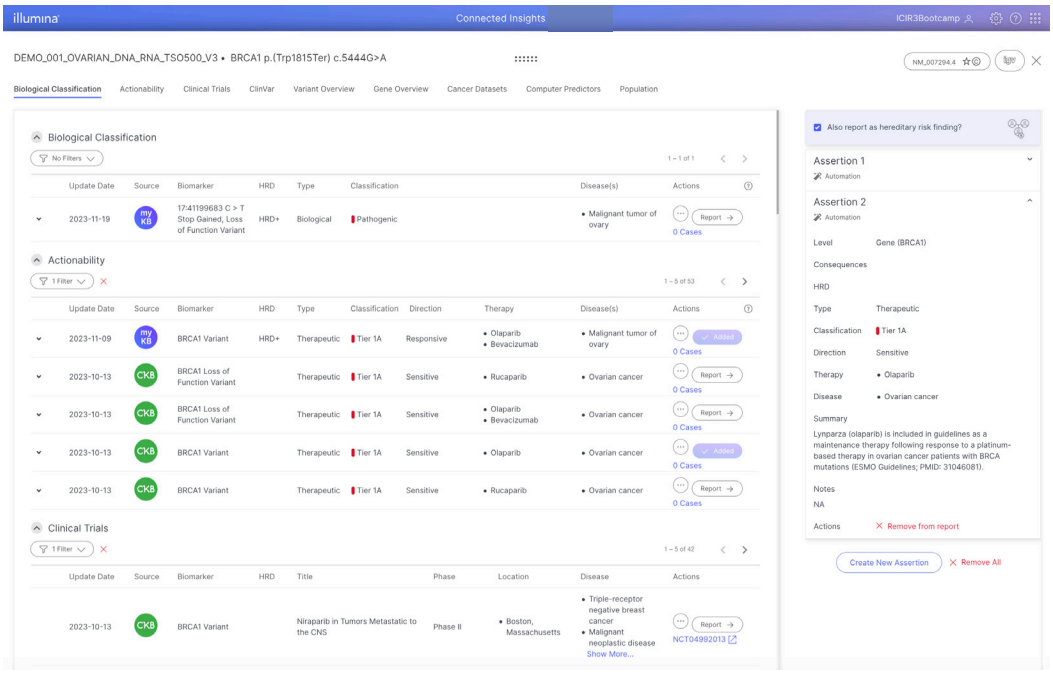

Figure 4: Lab-specific curation in Connected Insights-Research—A lab's repository of curated data can serve as a knowledge source for future cases, reducing the burden of interpretation and curation and resulting in additional efficiency gains.

Concise, customizable research reports

Connected Insights-Research provides powerful, flexible capabilities for clear and concise variant reporting. Users can choose 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 5).

Visualizations for deeper insights

Connected Insights-Research includes several visualization features (Figure 6) to facilitate:

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

Integrated solution

Connected Insights-Research 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-Research is compatible with any Illumina sequencing system, connecting directly with the Illumina Connected Software ecosystem, and 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

Users have the option to connect DRAGEN secondary analysis pipelines to Connected Insights-Research directly in the cloud or via a local DRAGEN server. With seamless integration, labs of any size can pair Connected Insights-Research with the proven performance and accuracy of DRAGEN variant calling across multiple variant types.

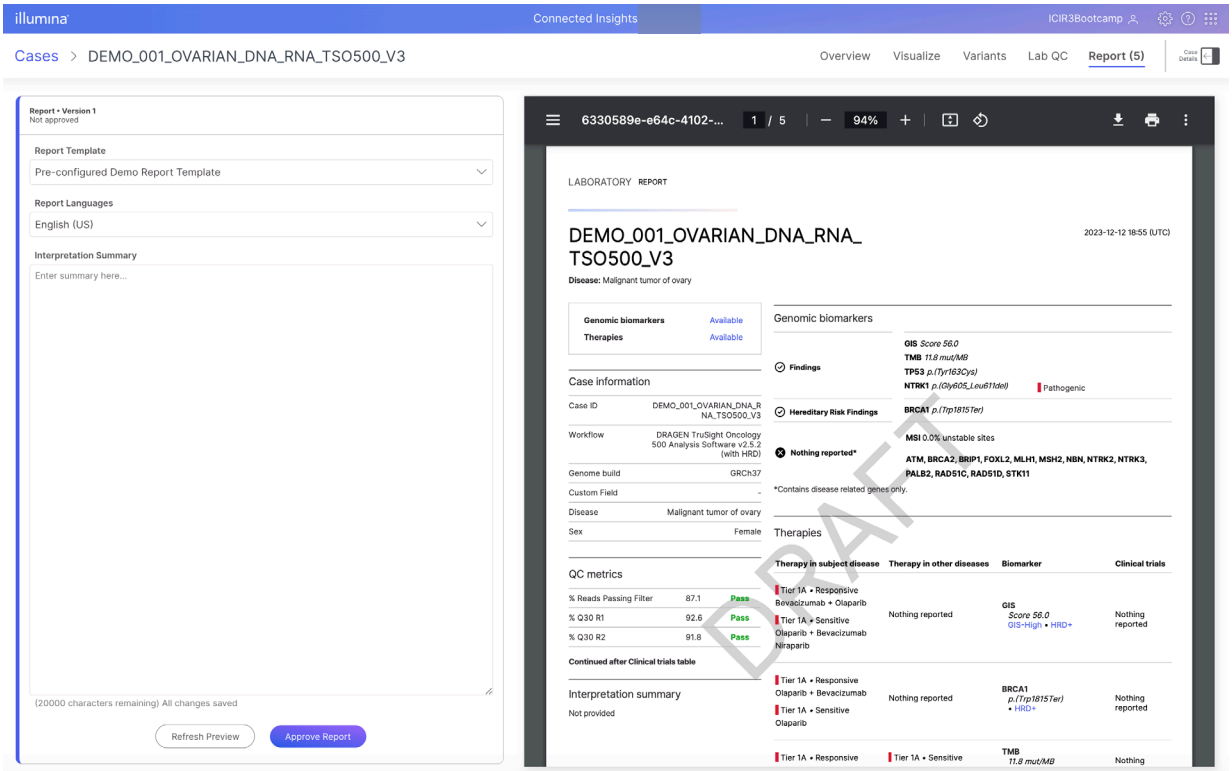

Figure 5: Connected Insights-Research flexible reporting capabilities enable clear and concise variant interpretation reporting for research applications with preconfigured templates

Illumina Connected Analytics

Connected Insights-Research 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-Research 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.

Figure 6: Connected Insights-Research 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, (C) fusion plot.

Dedicated to your success, Illumina 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-Research. 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.

Multiplatform accessibility

Connected Insights-Research meets users where their data are, offering multiple deployment options. Connected Insights-Research is available on cloud or on-premises via a DRAGEN server to meet the varying compliance and regulatory needs of different laboratories.

Security and compliance at the core

Security is of paramount importance when operating with genomics data. Connected Insights-Research employs various digital and administrative measures to meet even the most demanding data security requirements.

Connected Insights-Research is a global platform that adheres to local data residency requirements. To learn more, read the Security, privacy, and compliance with Illumina Connected Insights-Research security brief.

Summary

Connected Insights-Research streamlines tertiary analysis and variant interpretation research workflows by connecting external knowledge sources via API calling and enabling highly tunable user-defined workflow automation. Connected Insights-Research serves 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-Research enables labs to streamline tertiary analysis today, and scale operations for tomorrow.

Learn more

Illumina Connected Insights-Research

Ordering information

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

Product	Catalog no.
Illumina Connected Insights-Research—Oncology Genome Equivalent Sample—VCF	20090138
Illumina Connected Insights-Research Starter Implementation Package	20071787
Illumina Connected Insights-Research Expanded Implementation Package	20071787 (as scoped)
On-premises Illumina Connected Insights-Research Local—Oncology Genome Equivalent Sample—VCF	20112915

Any additional items required for the lab will be included in the prepared quotation.

References

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5. Horak P, Griffith M, Danos AM, et al. Standards for the classification of pathogenicity of somatic variants in cancer (oncogenicity): Joint recommendations of Clinical Genome Resource (ClinGen), Cancer Genomics Consortium (CGC), and Variant Interpretation for Cancer Consortium (VICC) [published correction appears in Genet Med. 2022 Sep;24(9):1991]. *Genet Med*. 2022;24(5):986-998. doi:10.1016/j.gim.2022.01.001.
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