Summer 2020
–
Edition #03

Analyze, Interpret and Report NGS Data Faster than Ever Before

Reduce complex genomic analysis times from 20 hours to 30 minutes, while increasing diagnostic yield by 30%

Congenica

Enabling genomic medicine

Executive Summary

Next-generation sequencing has the potential to revolutionize healthcare outcomes, however the complex, lengthy and costly interpretation of sequenced data presents a bottleneck to widespread clinical use. The introduction of Congenica's clinical decision support platform delivers paradigm-shifting efficiency improvements in analysis and interpretation, making the healthcare of tomorrow a reality today.

The ability to generate genomic data has substantially outstripped the ability to analyze and interpret the data and its significance for an individual[1]. The resulting increase in demand for genomic analysis has put pressure on clinical laboratories and slowed the translation of genome sequencing into routine healthcare.

The Congenica clinical decision support platform meets these needs by providing rapid analysis, interpretation and reporting of genomic data that delivers paradigm-shifting improvements in workflow efficiency, diagnostic yield and confidence in your analysis.

An analysis of more than 2000 complex cases interpreted using the Congenica platform from the UK 100,000 Genomes Project shows that complex clinical analyses, which used to take 20 hours to interpret and report, can now be completed in an average of 30 minutes. This dramatic improvement in analysis, interpretation and reporting times enables significantly higher throughput of cases and saves resources and costs.

1. Horton RH, Lucassen AM. Recent developments in genetic/genomic medicine. Clin Sci (Lond). 2019;133(5):697–708. Published 2019 Mar 5. doi:10.1042/CS20180436

Reduce complex genomic analysis times from **20 hours** to **30 minutes** while increasing diagnostic yield by **30%**

Laboratories using the Congenica platform are able to increase their diagnostic yield across all sample types, by an average of 30%.[2,3]

The platform provides supporting evidence from millions of reference data sources to support decisions, empowering healthcare professionals to interpret data and identify actionable insights quickly and with confidence, even in the most complex cases.

Congenica

2. Konrad EDH et al., CTCF variants in 39 individuals with a variable neurodevelopmental disorder broaden the mutational and clinical spectrum. Genet Med. 2019 Dec; 21(12):2723-2733. doi: 10.1038/s41436-019-0585-z.
3. Yang L, Liu X, Li Z, et al. Genetic aetiology of early infant deaths in a neonatal intensive care unit. Journal of Medical Genetics 2020;57:169-177. http://dx.doi.org/10.1136/jmedgenet-2019-106221

Dr Tessa Homfray

Consultant in Medical Genetics

NHS

> Congenica is an absolute game changer, enabling us to be certain about our diagnoses for patients

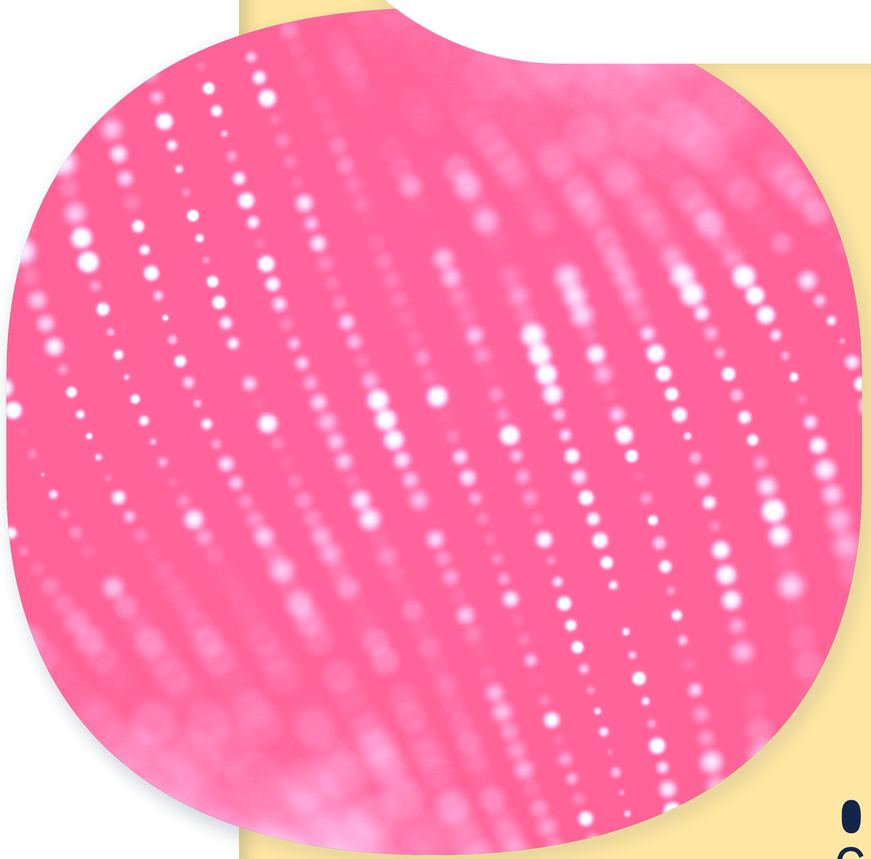
Congenica

The Efficiency Challenge

Ever since the completion of the Human Genome Project for $2.7 billion in 2003 there has been a belief that reducing the cost of sequencing to $1000 would make the promise of truly personalized genomic medicine a reality.

However, the costs and time required for sequencing and data interpretation made even next-generation sequencing (NGS) initially unsuitable for use in the clinic. In recent years however, advances in technology have enabled NGS of whole genomes to be conducted at population scale, as demonstrated by the UK 100,000 Genomes Project.

Yet, the ability to analyze and interpret NGS data and its significance for an individual has failed to keep pace with the increased ability to generate genomic data [1]. The greatest cost in NGS is currently still the sequencing,[4] but the interpretation of data is by far the most time consuming and resource-heavy step in the process.



Congenica

1. Horton RH, Lucassen AM. Recent developments in genetic/genomic medicine. Clin Sci (Lond) 2019;133(5):697–708. Published 2019 Mar 5. doi:10.1042/CS20180436

4. Schwarze, K., Buchanan, J., Fermont, J.M. et al. The complete costs of genome sequencing: a microcosting study in cancer and rare diseases from a single center in the United Kingdom. Genet Med 22, 85–94 (2020). https://doi.org/10.1038/s41436-019-0618-7

“By **2025**, over **60 million** people will have had their genome sequenced in a healthcare context”

Global Alliance for Genomics & Health
Collaborate. Innovate. Accelerate.

The Genomic Analysis Workflow

Genomic analysis includes numerous tasks, from the analysis of variant call format (VCF) onwards:

- Single nucleotide variants (SNV) calling
- Clinical analysis (known genes) – single nucleotide variants (SNVs)
- Copy number variations (CNV) calling
- Clinical analysis (known genes) – CNVs
- Research analysis (all genes)
- Second analyst review

Confirmation and reporting require additional time:

- Multidisciplinary team (MDT) review/report
- Variant Confirmation
- Primary report
- ACMG report (American College of Medical Genetics and Genomics)
- Archive data

Congenica streamlines all these steps with a single, intuitive solution designed by clinical experts, making interpretation and reporting headaches a thing of the past.

The interpretation challenge is likely to increase with The Global Alliance for Genomics and Health (GA4GH) predicting that by 2025, over 60 million people will have had their genome sequenced in a healthcare context, in order to attempt a disease diagnosis. This is an important development to prepare for: sequencing in healthcare is expected to surpass that on a research setting.

Congenica

Dr Gholson Lyon, M.D., Ph.D.

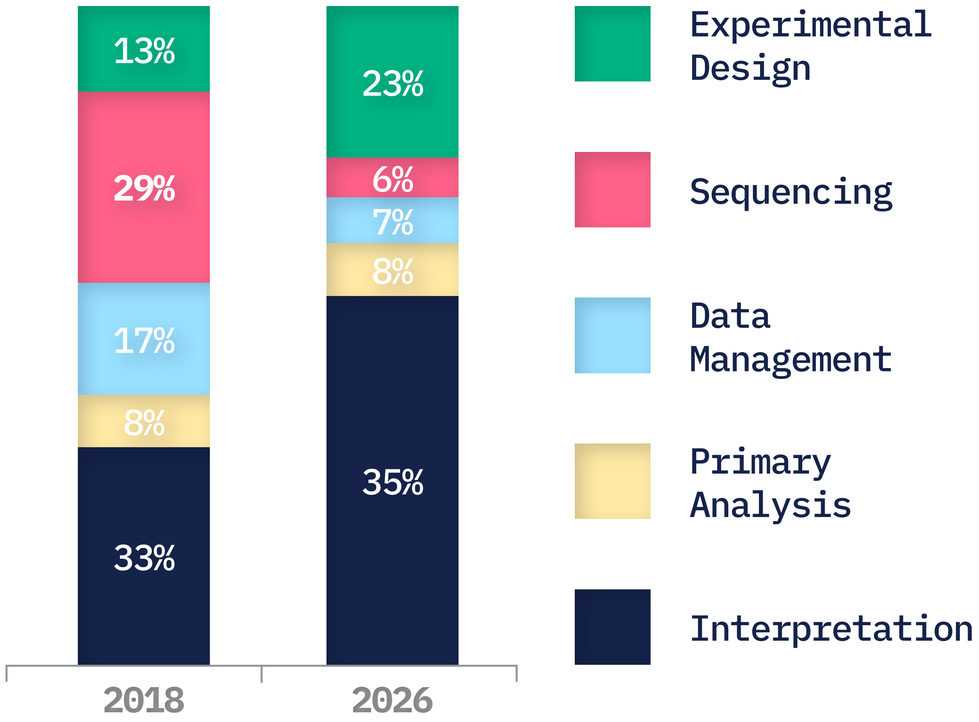
Principal Investigator and Clinician

Institute for Basic Research in Developmental Disabilities, New York State

> Congenica has been key in making our variant interpretation services a success.

Congenica

An Increasing Bottleneck



Implications of the interpretation bottleneck

- Low case throughout
- Increasing backlog of data to analyze
- Slow turn-around-times
- Extended diagnostic odysseys
- Staff and productivity burdens
- Limits a genomic service's ability to scale up

> Pathways for managing the output from genomic sequencing are still in their infancy. As the volume of genetic data grows, so too does the challenge of interpreting the data and aligning it with other biological marker data and electronic health records (EHR/EMR).[5]

5. Global NGS Informatics and Clinical Genomics Market - Analysis and Forecast, 2018-2028 BIS

Congenica

Sizing up to the Challenge

The scale of the challenge in analyzing NGS data becomes apparent when considering that sequencing a single whole genome generates between 100-200 GB of data.[5] On top of that, the volume of newly generated data from genomic research is currently doubling every seven months. It is estimated that by the end of 2025, the amount of genomic data generated per year will exceed 40 exabytes (40 million terabytes) thanks in part to the numerous national genomic-medicine initiatives and collaborative cross-country projects are currently underway.[6]

It is therefore crucial that genetic analysis platforms can scale to meet the extreme demands of analyzing such large volumes of data.

Congenica has been developed with scalability in mind with its secondary analysis pipeline capable of ingesting data from multiple whole genomes, exomes and panels using a powerful parallel cloud processing approach.

With Genomics England, Congenica has already demonstrated the ability to process 2700 analysis per week for a single client – with capacity for more. Genetic analysis on this scale has only been made possible by Congenica, with data from over 60,000 whole genome cases and more than 300,000,000 unique genetic variants already stored in its cloud infrastructure.

by the end of **2025**, the amount of genomic data generated per year will exceed **40** exabytes

Congenica

5. Global NGS Informatics and Clinical Genomics Market - Analysis and Forecast, 2018-2028 BIS

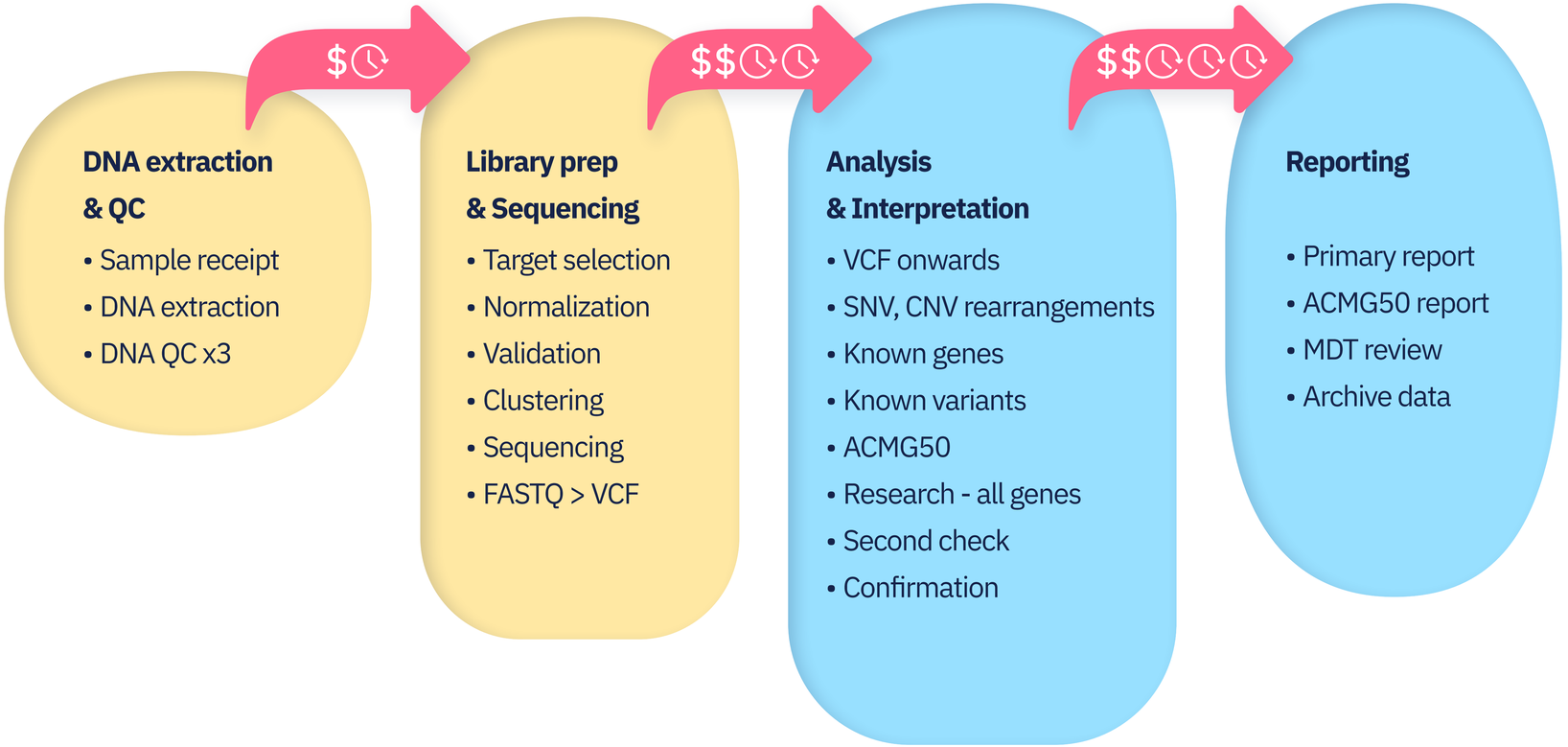
6. Zornitza Stark et al., Integrating Genomics into Healthcare: A Global Responsibility. The American Journal of Human Genetics, 3 January 2019, Pages 13-20 https://doi.org/10.1016/j.ajhg.2018.11.014

Breaking Down the Costs

While claims have been made that the cost of sequencing a human genome has fallen below $1000, these figures tend to only take into account the cost of consumables and ignore the overall costs of the sequencing and analysis process.[4]

To understand the real cost of genomic sequencing, Schwarze et al. performed a micro costing study of Illumina-based genome sequencing in a UK National Health Service (NHS) laboratory processing 399 whole genome samples per year. The researchers collected cost data for all steps in the sequencing pathway, including library preparation, bioinformatics analysis, interpretation and reporting of results.[4]

The NGS pipeline - from sample to report



Congenica

4. Schwarze, K., Buchanan, J., Fermont, J.M. et al. The complete costs of genome sequencing: a microcosting study in cancer and rare diseases from a single center in the United Kingdom. Genet Med 22, 85–94 (2020). https://doi.org/10.1038/s41436-019-0618-7

Staffing costs previously accounted for **15%** of total costs, with **>70%** of the staffing time being spent on clinical interpretation and reporting

Analyzing the Cost of Progress

This analysis revealed that genome sequencing, analysis and reporting costs totaled £6841 per cancer case (comprising matched tumor and germline samples) and £7050 per rare disease case for three sample trios. The consumables used during sequencing proved to be the most expensive component of testing (68–72 % of the total cost).

Staffing costs accounted for 15% of total costs, with >70% of the staffing time being spent on clinical interpretation and reporting.[4]

While automation can help streamline library preparation and sequencing stages of the NGS pipeline, many laboratories experience a significant bottleneck in the data analysis and interpretation steps. This challenge is hard to overcome due to the difficulty of recruiting and training clinical experts to perform the essential work of translating complex sequenced data into actionable information that can inform life-changing answers.

Congenica

4. Schwarze, K., Buchanan, J., Fermont, J.M. et al. The complete costs of genome sequencing: a microcosting study in cancer and rare diseases from a single center in the United Kingdom. Genet Med 22, 85–94 (2020). https://doi.org/10.1038/s41436-019-0618-7

Dr Simon Ramsden, PhD FRCPath

Consultant Clinical Scientist

Centre for Genomic Medicine, Manchester

> Congenica has allowed us to scale our operation to accommodate the explosion in genomic analysis. Congenica offers us an opportunity to collate the information, perform the analysis, and then make decisions within a single piece of software, making our whole system far more efficient.

Congenica

Shifting the Paradigm

Data interpretation is by far the most time-consuming and resource-intensive step of the NGS workflow. Any time savings that can be found have a significant impact on overall costs and sample throughput.

This is where the next generation clinical decision support platform from Congenica comes in. Congenica enables rapid analysis, interpretation and reporting of complex genomic data to aid the understanding and characterization of genetic diseases and the identification of other genetic variants that are important for human health. It also enables a significant reduction in interpretation time and cost, as well as increasing diagnostic yield.

In fact, an analysis of more than 2000 complex rare disease cases from the 100,000 Genomes Project shows that analysis which used to take 20 hours can now be completed in an average of 30 minutes using Congenica

What's more, the use of the platform enabled the 100,000 Genome Project to achieve these staggering efficiencies while increasing diagnostic yields by >50%.

Maximizing Lab Efficiency

Without Congenica

Average time per sample in leading UK NHS laboratory processing 399 samples/year[1]

17-22 hours from data to report

With Congenica

Average time per sample*

30 mins from data to report

20x faster analysis and interpretation

95% reduction in interpretation costs

*Times based on 2,000 complex cases analysed as part of the 100,000 Genomes Project

Congenica

1. Genet Med. (2019)doi:10.1038/s441436-019-0618-7

Find out why Genomics England, chose Congenica as the exclusive clinical decision support solution to help deliver a ground breaking Genomic Medicine Service across the UK National Health Service (NHS)

Download the case study

100,000 Genomes and Beyond

The 100,000 Genomes Project was established to sequence 100,000 genomes from patients affected by a rare disease or cancer. To date, actionable findings have been found for 20-25% of rare disease patients.

The Congenica platform played an integral role in the success of the 100,000 Genomes Project and enabled clinical scientists to reach decisions more than 20 times faster on average, even in complex cases, and achieve interpretation cost savings of up to 95%.

The project has led to the creation of a new nationwide Genomic Medicine Service for the UK NHS.

Following a rigorous evaluation of the leading 16 genomic data analysis solutions, Congenica was selected as the exclusive decision support platform for use by the Genomic Medicine Service by the NHS and Genomics England.

Congenica

Dr Anne-Karin Kahlert

The Institute of Immunology and Genetics, Germany

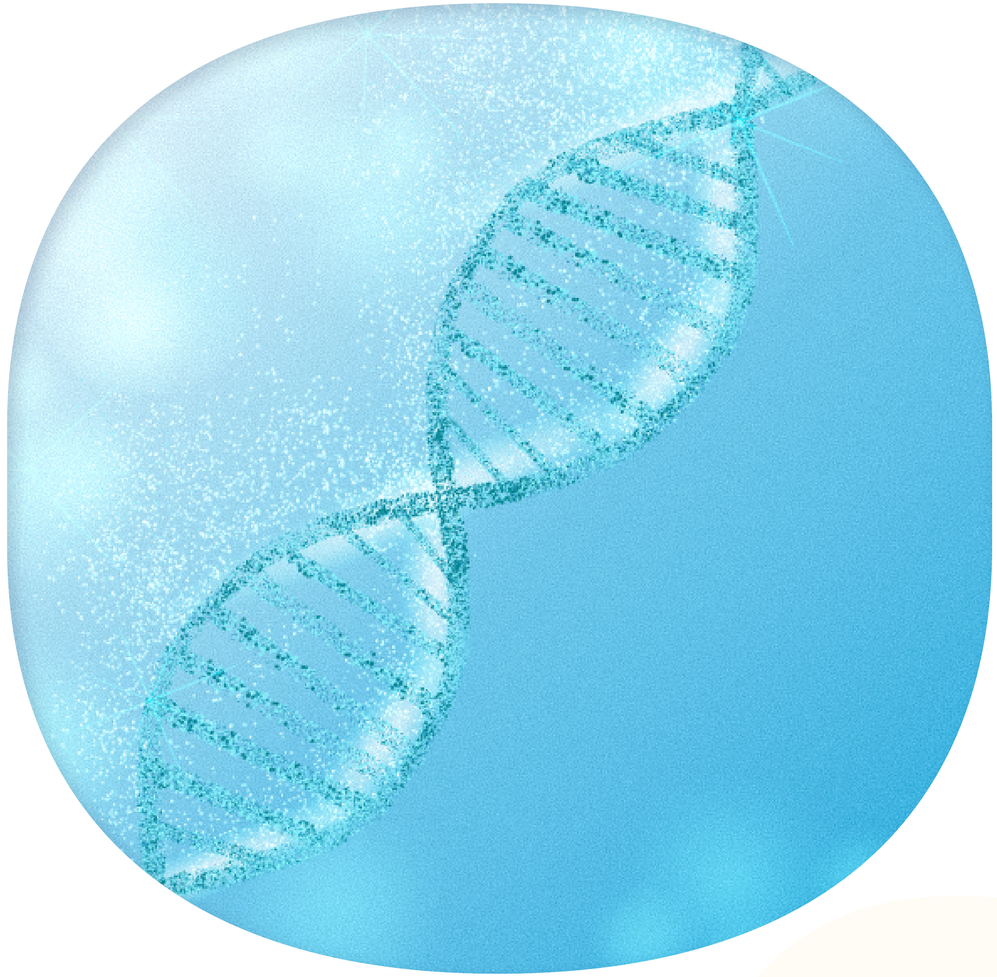
> Congenica is an outstanding technology for the interpretation of NGS data. We can now achieve incredibly short turnaround times, which is of great benefit to our patients.

Congenica

So how does Congenica do it?

Congenica performance is driven by three groups of features:

1. Workflow: The ability to support the user to run a cost effective, efficient and quick analytical process
2. Diagnostic Yield: The ability to detect a disease-causing DNA variation more often than competitive platforms
3. Confidence: The ability to be accurate and fast using a Quality platform with QC tools and audit capability



Congenica

Workflow

Congenica is able to simplify and speed-up the workflow in a busy clinical genomics laboratory through the use of automation, a scalable design and by supporting integration into other existing systems.

Automated

By automating the manual processes from sequencer to report including the identification of known variants and associated supporting clinical evidence, Congenica provides fast, accurate reporting that enables high throughput of cases and lets clinical specialists focus on the most complex cases.

Scalable

From small laboratories to National Programs, Congenica meets customer needs for robust performance systems no matter how small or large. The platform was uniquely developed with a genome-first approach, capable of consistently processing multiple whole genome, whole exome or gene panel samples without impacting performance.

Integrated

Congenica is setup with a published API library to fully integrate for inbound and outbound data into any third-party system, which enables fast, accurate processes delivering information directly where it is needed.

Congenica

Diagnostic Yield

Congenica delivers a high diagnostic yield because of three core capabilities built into the system: access to the best comparison data, effective DNA variant analysis and prioritization, and a design that makes it easier to sort through complex decisions.

Data

Congenica contains the widest range of variants (SNV, Indel, CNV, SV, Mitochondrial, STR, UPD) and datasets - with 40+ data-points annotated per variant and access to a comprehensive range of reference data sources including the Mastermind database of over 6 million published variants across all genes. This enables granular data manipulation and fine tuning of data to significantly improve analytical options and the ability to rapidly identify supporting evidence, all within a single interface.

Design

Congenica has been designed by teams of clinical scientists and bioinformaticians to replicate and streamline NGS analysis workflows. Packaging everything into a single user interface, Congenica improves consistency and speed of analysis for improved diagnostic yield and case throughput.

Prioritization

The platform includes Exomiser – a class-leading variant prioritization application that identifies potential disease-causing variants from whole-exome or whole-genome sequencing data. Exomiser comprises a suite of algorithms that prioritizes variants by leveraging information on variant frequency, predicted pathogenicity, and gene-phenotype associations derived from human diseases, model organisms, and protein–protein interactions[7].

Congenica uses an optimized version of the variant prioritization application, calibrated for optimum performance by its original developers, Dr Damian Smedley and Dr Jules Jacobsen. Its performance is not only superior to other variant interpretation software but is also designed to integrate into existing workflows through secure API connections to enable high-throughput analysis.

Congenica

7. Smedley, D., Jacobsen, J., Jäger, M. et al. Next-generation diagnostics and disease-gene discovery with the Exomiser. Nat Protoc 10, 2004–2015 (2015). https://doi.org/10.1038/nprot.2015.124

Confidence

Congenica is a high-quality product that ensures users can operate quickly with a high level of confidence.

Compliant

The platform's cloud and on-premise hosting options have been developed under a certified ISO 27001 Information Security Management System and a certified ISO 13485 Quality Management System.

Reliable

The platform calculates coverage statistics for all genes so users can be confident that the data used are consistent and reliable.

Quality

Quality assurance includes detailed quality control at every step of the process and a full audit trail of the analysis performed for every case, including clinical, phenotypic, family, quality and variant data for review. This gives users visibility of all details relating to a case, and traceability for future reference.

Congenica

Summary

The ability to sequence genomes and generate genomic data has substantially outstripped the ability to analyze and interpret the data and its significance for an individual, [1] putting pressure on laboratories and slowing the translation of genome sequencing into routine healthcare.

Implementation of the Congenica clinical decision support platform enables laboratories to maximize the efficiency of their service, reduce interpretation costs of genomic analysis by up to 95% and translate NGS data from sequencer to report 20 times faster – even in the most complex cases.

In addition, services using the Congenica platform are able to increase diagnostic yields across sample types by an average of 30%.

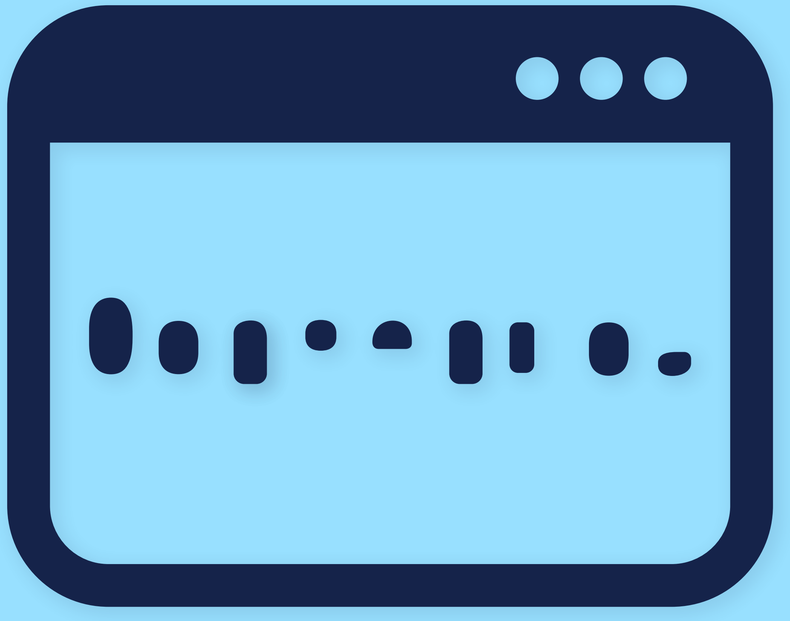
20x Faster analysis and interpretation

95% Reduction in interpretation costs

30% Increase in diagnostic yield

Congenica

1. Horton RH, Lucassen AM. Recent developments in genetic/genomic medicine. Clin Sci (Lond). 2019;133(5):697–708. Published 2019 Mar 5. doi:10.1042/CS20180436



Click here to demo Congenica

Are you interpreting genomic data as efficiently as possible? Visit **congenica.com** for further information and talk to our specialists

info@congenica.com

congenica.com

Congenica

Enabling genomic medicine