Expanded carrier screening

QIAGEN Clinical Insight (QCI®) Interpret

QIAGEN

Expanded carrier screening

Technological advancements now allow for the possibility of multi-disease, pan-ethnic screening, which we refer to as expanded carrier screening (ECS). Capable of detecting rare mutations across hundreds of genes, ECS panels are more efficient and informative than single assays, enabling more couples to understand their reproductive options.

The challenge

The enormous power of ECS in identifying novel variants has yielded an unpredicted abundance of rare variants with little or no information about their clinical significance. Unlike common variants that are easily recognized and well-documented, rare variants require meticulous literature searches that increase turnaround time and decrease accuracy.

QIAGEN Clinical Insight (QCI) Interpret for Expanded Carrier Screening

Clinical decision support software integrated with the industry's largest knowledge base, QCI Interpret for Expanded Carrier Screening reproducibly translates highly complex next-generation sequencing (NGS) data into concise, clinician-ready reports, using current clinical evidence and all 28 criteria of the ACMG/AMP published guidelines for the assessment of variants in genes associated with Mendelian diseases.
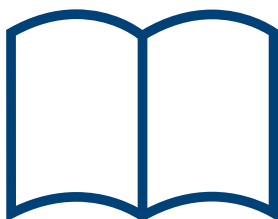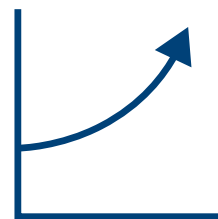
Delivers comprehensive variant pre-curation

Leverage the largest collection of expert-curated content to rapidly identify potentially pathogenic variants.

Provides full transparency to supporting evidence

Find links to the original articles that have been reviewed for accuracy by Ph.D. scientists certified in content curation.
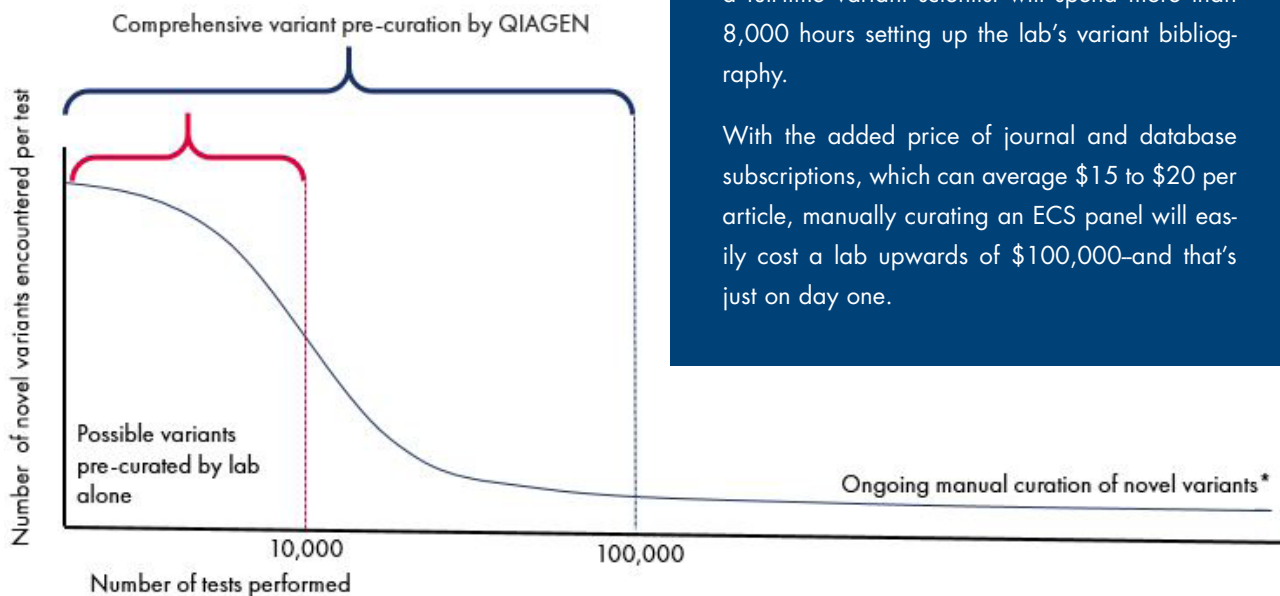
Scales for future growth and test menu expansion

Grow the future of your genetic testing lab with trusted, scalable, high-performance data solutionsand services.

Comprehensive variant pre-curation

With QCI Interpret, genetic testing labs can leverage the knowledge equivalent of having performed 100,000 tests on day one of implementation. The expansive rare variant bibliography contains the most comprehensive collection of expertly curated content for all the known variants of each gene.
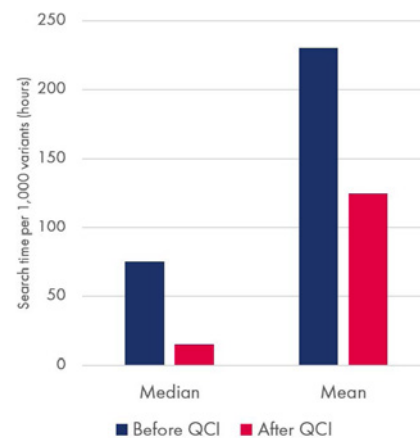

Comprehensive variant pre-curation by QIAGEN

Number of novel variants encountered per test

Possible variants pre-curated by lab alone

Ongoing manual curation of novel variants*

10,000 100,000

Number of tests performed

*Even after analyzing and interpreting100,000 samples, a lab using a 200 gene panel will continue to encounter one to three novel variants per test.

When a genetic testing lab uploads NGS data to QCI Interpret, the software computes variant classifications according to the ACMG/AMP variant interpretation guidelines.

QCI Interpret bases variant classifications on evidence manually curated from full-text articles and public and private data sources. This critical feature—automated curation of manually sourced content—gives QCI Interpret the ability to present evidence for all 28 levels of the ACMG/AMP criteria.

In 2017, a high-throughput population screening laboratory adopted QCI Interpret and reported an 80% boost in efficiency and test turnaround time (Cox et al. 2017).

The value

From a 200 gene panel, approximately 5,000 variants will be detected.

If there are five papers per variant, and it takes approximately 20 minutes to read each paper, a full-time variant scientist will spend more than 8,000 hours setting up the lab's variant bibliography.

With the added price of journal and database subscriptions, which can average $15 to $20 per article, manually curating an ECS panel will easily cost a lab upwards of $100,000–and that's just on day one.

Comparison of time savings pre- and post-QCI Interpret in a CLIA laboratory

Search time per 1,000 variants (hours)

250
200
150
100
50
0

Median   Mean

■ Before QCI   ■ After QCI
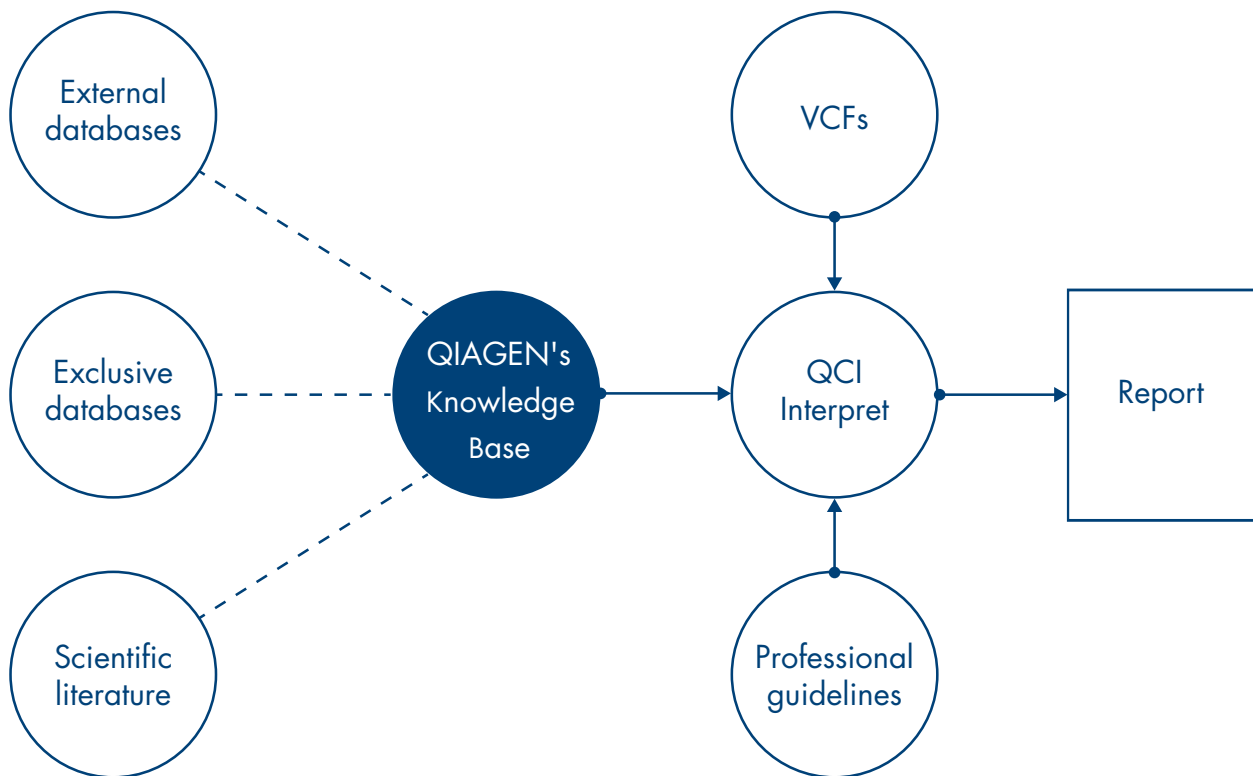
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When it comes to classifying rare and complex variants, having full transparency and traceability of clinical evidence is critical. QCI Interpret captures both confirmatory and contradictory findings and includes the source publication and context, ensuring users have all the supporting evidence required to assess the pathogenicity of a specific variant.

QCI Interpret leverages QIAGEN's Knowledge Base, a repository of expertly curated biological interactions and functional annotations created from millions of individually modeled relationships between proteins, genes, complexes, cells, tissues, drugs, and diseases.

The curated content in the Knowledge Base is structured into an ontology that makes information computationally accessible and ensures semantic and linguistic consistency across concepts, making QIAGEN's Ingenuity Knowledge Base distinctive and unparalleled by any other database.

>20 million knowledge base findings	**>1 million** samples analyzed
>35,000 publications	**>33,000** disease classes
>35 integrated databases	**>5,500** new findings per day

QIAGEN is the world's leading provider of Bioinformatics Solutions for Research and Clinical applications.

Sample ECS report

YOUR LAB

Sample ID: 1234-12345678
Description: East Asian, Female
Date Collected: 02-Apr-2019
Date Analyse: 03-Apr-2019

> Customize your report according to your lab's specifications, offerings and preferences.

Expanded Carrier Screening for Hereditary Diseases
RESULT: CARRIER

The PreConcept™ expanded carrier screening test is a Next Generation Sequencing genetic test that tests for 200 carrier conditions to identify mutations within a population for the prevalence of a specific rare disease

FINDINGS OVERVIEW

Cystic fibrosis
Inheritance: Autosomal recessive

Reproductive risk: 1 in 110

CFTR
NM_000492
c.1521_1523delCTT
p.Phe508del

Interpretation | The tested individual is a carrier of cystic fibrosis. Carriers generally do not experience symptoms. Disease phenotype is dependent on, but not necessarily predicted by, the combination of variants inherited.

HOW COMMON IS CYSTIC FIBROSIS?

According to the National Institutes of Health, CF is the most common deadly inherited condition among Caucasians in the United States. Disease-causing mutations in the CFTR gene are more common in some ethnic populations than others.

Ethnic Group	Carrier Rate	Affected Rate
French Canadian	1 in 16	1 in 900
Caucasian	1 in 28	1 in 3,000
Ashkenazki Jewish	1 in 28	1 in 3,000
Hispanic	1 in 46	1 in 8,300
African American	1 in 66	1 in 17,000
Asian	1 in 87	1 in 30,000

Inheritance: Autosomal recessive

Unaffected   Affected
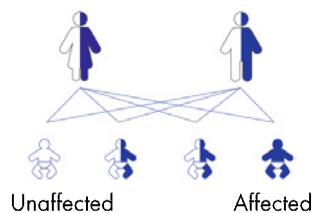
APPROVAL

Your signature

Electronically signed on: 05-May-2019
This report has been reviewed and approved by Dr. Simon Yong, YL Genetics Lab

Scale for future growth and test menu expansion

Accelerate time to launch with clinical informatics services focused on expanding and differentiating your test menu.

QIAGEN Clinical Informatics Services deliver complete end-to-end testing solutions, fully customizable and capable of supporting a broad range of indications both now and in the future.

While QCI Interpret helps you keep pace with publications, QIAGEN Clinical Informatics Services ensures your automated IT infrastructure runs smoothly, efficiently and securely.

- Scale NGS without limits with managed services
- Focus on your research and not IT infrastructure management
- Customize your pipeline and reporting solutions
- Save valuable time and resources

Go to **www.digitalinsights.com/qci-interpret** to learn more.

"QCI has already proven a valuable resource for increasing the efficiency of [our lab's] inhouse curation. Work is underway to additionally incorporate QIAGEN's continually-updated bibliographies into the automated components of our variant classification workflows."

Cox et al . (2017)
"Evaluation of QIAGEN Clinical Insight as a content resource for variant curation in a CLIA laboratory"

References

Cox S, Karimi K, Moyer K, Kang HP, Evans E, Tanenbaum S, Richards D. Evaluation of QIAGEN Clinical Insight as a content resource for variant curation in a CLIA laboratory. ClinGen 2017. [Poster]