Quality and innovation you can count on

Invitae is dedicated to making high-quality genetic testing the standard of care.

INVITAE

Experience you can trust

3+ million patients have accessed their genetic information, thanks to Invitae testing.

Dedicated to the highest quality

1 in 7 pathogenic variants could be missed by standard next-generation sequencing workflows. Invitae's customized methods are optimized to detect these complex variants with high sensitivity.[1]

Committed to transparency

Invitae is the largest contributor to ClinVar with **> 1,000,000** submissions.[2]

Invitae's quality

Have confidence knowing that Invitae is committed to quality every step of the way.

1. **Comprehensive NGS panels**
2. **Thorough variant detection**
3. **Rigorous variant classification**

Make informed healthcare decisions with Invitae's affordable, high-quality testing.

1. Lincoln S, *et al. Genetics in Medicine.* 2021; 23:1673–1680.
2. As of May 2022. View ClinVar contributors at: http://www.ncbi.nlm.nih.gov/clinvar/docs/submitter_list
3. Cummings, *et al. Sci Transl Med.* 2017;9:1–11.
4. Abramowicz, Gos, *J Appl Genet.* 2018;59:253–268.
5. Truty, *et al. Am J Hum Genet.* Accepted.
6. Lee, *et al. Genet Med.* 2020;22:490–499.
7. Landrith, *et al. Nat Precis Onc.* 2020;4:4.
8. Nykamp, *et al. Genet Med.* 2017;19:1105–1117.
9. Invitae data on file
10. Sim NL, *et al. Nucleic Acids Res.* 2012;40:W452–W457.
11. Adzhubei IA, *et al. Nat Methods.* 2010;7(4):248–249.
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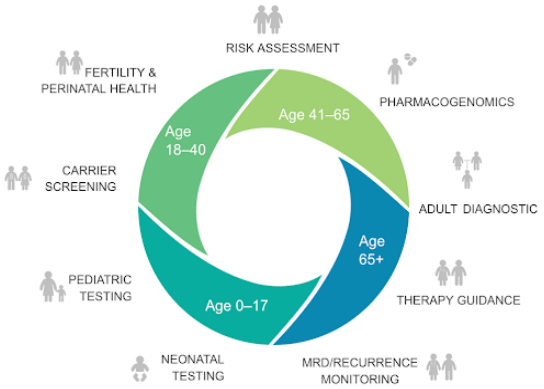
13. Invitae data on file

Committed to quality every step of the way

1 Comprehensive NGS panels

You can count on Invitae for the genetic tests your patients need at **all stages of life**, across a wide spectrum of conditions.

What's more, Invitae's genetics experts continually update our panels to reflect the latest research, so you know you're getting **comprehensive answers**.



2 Thorough variant detection

Invitae's **CLIA-certified** and **CAP-accredited** labs incorporate optimized and customized workflows to enable sensitive variant detection.[1]

Our **expanded reportable range** (+/-20 base pairs for most germline genes) means we delve deeper into the DNA sequence on either side of coding exons, capturing the majority of variants currently known to impact splicing. We also comprehensively report sequence changes and deletion/duplication events in intron/exon boundaries, splice sites, and other regions known to potentially harbor pathogenic variants.

To ensure thorough variant detection and interpretation, select hereditary cancer panels also include **RNA analysis** to help drive variant discovery,[6-7†] and interpret variants of uncertain significance.[3-5]

Case study: Expanded reportable range leads to detection of likely pathogenic variant[§]

Clinical history	Personal history of multiple cafe-au-lait spots & family history of possible clinical neurofibromatosis type 1; no molecular diagnosis
DNA result	*NF1*, c.2410-13A>G (intronic); in-vitro data suggests activation of a cryptic splice site, which introduces a premature stop codon
Evidence/ observed impact	Altered splicing, nonsense-mediated decay expected for loss-of-function gene
Final classification	Likely pathogenic

3 Rigorous variant classification

Invitae's highly refined variant interpretation process begins with **Sherloc**, a rigorous framework that:

- Systematically strives to remove subjectivity
- Ensures reproducibility in classifications
- Is peer-reviewed and published in *Genetics in Medicine*[8]

The latest advancement to Sherloc is Invitae's **Functional Modeling Platform**, which:

- Reduces variants of uncertain significance in real time[9]
- A pilot study showed FMP changed classification for 1 in 40 patients tested[9]
- Gives patients more definitive classifications

Case study: RNA sequencing leads to upgrade from VUS to likely pathogenic[§]

Clinical history	Family history of retinoblastoma and breast cancer
Initial classification based on DNA result	*RB1*, c.718+5G>T (intronic); predicted to result in loss of donor splice site 5 nucleotides away; classified as VUS
RNA result	Skipping event in exon 7 of RB1 mRNA, leading to in-frame deletion of 37 amino acids
Evidence/ observed impact	Loss of exon 7 is associated with retinoblastoma
Final classification	Likely pathogenic

How does this compare to what some other labs use?

Some other labs: Computational *(in silico)* evidence from publicly available models, such as PolyPhen2 and SIFT	**Invitae:** Computational *(in silico)* evidence from FMP incorporated into Sherloc
• Often outdated	• Dynamic and AI-enabled, continuously learning and improving with experience from Invitae's vast database of >3 million patients
• Single model for all genes: "one size fits all" approach	• Gene-specific: AI evaluates variants in each gene separately, taking gene-specific characteristics into account
• ~75–85% accuracy[10-12]	• >99% accuracy[13]

†RNA analysis currently available in select regions.

§Based on a real patient with identifiable information removed.

HEADQUARTERS | 1400 16th Street, San Francisco, CA 94103 | ONLINE | www.invitae.com | CONTACT | www.invitae.com/contact