

High-quality panel testing, simplified



Invitae is committed to delivering high-quality, affordable testing, with the goal of improving patients' lives while also saving the healthcare system valuable dollars.

Experience the difference by creating an account today at www.invitae.com.

Technology		Invitae Advantage
Industry leading methodology	<ul style="list-style-type: none">■ Invitae's customized biochemical and bioinformatics methods reduce costs and improve accuracy over standard next-generation sequencing (NGS)	High quality, low cost testing
Comprehensive coverage	<ul style="list-style-type: none">■ At least 50x minimum coverage at all positions—the main determinant of accuracy¹—and 350x average coverage■ The use of multiple hybridization assays provides uniform coverage without gaps or bias issues■ Specialized NGS methods tackle difficult regions and variants (e.g., PMS2 exons 12–15)	Accurate, thorough assessment
Advanced deletion/duplication methods	<ul style="list-style-type: none">■ Invitae conducts del/dup analysis by NGS, reducing the need for multiple assays that increase cost and time■ Multiple algorithms provide equivalent sensitivity to traditional del/dup techniques for events as small as one exon and can detect complex events invisible to traditional techniques²	Innovative technology to improve patient care
Confirmation	<ul style="list-style-type: none">■ PacBio and Sanger technology used to confirm variants using a validated process■ CNV events confirmed by array	Validated two-step confirmatory approach
Testing safeguards	<ul style="list-style-type: none">■ Robust safeguards to prevent sample mix-ups and clerical errors including 2 step verification, barcode scanning, and more	In good hands
Test Design		Invitae Advantage
Comprehensive assays	<ul style="list-style-type: none">■ Full gene sequencing and del/dup analysis is included with every test■ Invitae tests the full coding sequence plus 10 bases into each intron (more for certain genes, such as BRCA1/2, which covers 20 bases)■ Promoters and intronic regions known to harbor pathogenic mutations are also assayed	All-inclusive analysis in a single report
Curated gene panels	<ul style="list-style-type: none">■ Invitae's panels are expertly curated to produce informative results for specific indications and clinical scenarios■ Clinicians have the ability to customize panels based on their needs and each patient's indication	7 disease areas. 175+ panels. 1000+ genes. Your choice.

¹Not only is minimum coverage the main determinant of accuracy, but excessive coverage has no benefit on accuracy. See Ajay *et al.*, *Genome Res.* 2011. Any targets not meeting Invitae's 50x minimum, which are very rare, are reviewed by a lab director and filled in as needed with alternate methods. In addition, any assay limitations are clearly documented on reports.

²For example, Alu insertions and breakpoints within an exon. Invitae's algorithms are both read-depth and split-read based, following the approach taken by Nord *et al.* (*BMC Genomics* 2011) with improvements.

Classification

Guidelines-based variant classification

- Invitae's 5-tier variant classification begins with **the most recent (2015) ACMG guidelines¹** and builds on them to generate rigorous variant interpretations
- Invitae's stringent procedures provide **reproducibility** and reduce subjectivity through rigorous, critical evaluation of all applicable evidence of pathogenicity
- Every Invitae report is reviewed by two or more PhD scientists, a medical geneticist lab director, and a genetic counselor

Ongoing data sharing

- Invitae is **one of the largest contributors to ClinVar²**, allowing peer review of all of our variant classifications
- Invitae participates in **patient registries** to help define the medical impact of new genes and interventions

Invitae Advantage

Rigorous classification backed by experts

Improving care through open collaboration

Validation

Demonstrated 100% analytic sensitivity and specificity

- Invitae's **>1000 patient, peer-reviewed study** showed equivalence to traditional genetic testing technologies, even on challenging classes of variants³
- Ongoing studies continue to show **100% sensitivity and 100% specificity** across the full Invitae test menu

99.8% BRCA1/2 classification concordance

- **99.8% concordance** was observed between Invitae's variant classifications and those from Myriad Genetics (including Myriad's amended reports), in Invitae's published validation study of BRCA1/2³
- Invitae provides **specific evidence with each classification**; because Myriad does not do so, it is not possible to determine which classification is most appropriate in the remaining 0.2% of cases
- Ongoing studies confirm this result in an even larger population⁴

Proven clinical utility

- Invitae published the **first systematic clinical utility study** of panel testing for hereditary cancer, based on recent updates to the NCCN guidelines⁵

Fully accredited and licensed

- Invitae is **CLIA approved** and **CAP accredited**

Invitae Advantage

Validated performance across variant types

Proven equivalence in a published head-to-head comparison

Dedicated to improved patient outcomes

Results you can trust

¹Richards *et al.*, *GIM* 2015.

²For a list of the largest contributors to ClinVar, visit http://www.ncbi.nlm.nih.gov/clinvar/docs/submitter_list.

³Lincoln *et al.*, *JMD* 2015.

⁴Lincoln *et al.*, ACMG 2016 Annual Meeting, platform presentation #14, using variants from approx. 20,000 patients.

⁵Desmond *et al.*, *JAMA Oncol.* 2015.