Invitae Exome Sequencing

Up-to-date analysis and reanalysis for every patient

The Invitae exome combines continuously updated gene and variant curation with expert evaluation for an accurate and comprehensive exome interpretation.

Why choose Invitae Exome Sequencing?

- Robust sequencing coverage of the whole exome ensures high sensitivity and specificity: 150x average sequencing depth and >99.4% of reportable bases covered at ≥20x depth
- Customized capture baits boost coverage of hard-to-sequence areas of the exome and allow detection of intragenic copy number variants
- Results available in 6 to 8 weeks, on average
- Automated reanalysis reduces burden on clinicians and patients
- Annotated supplemental reports are available upon request, which include all rare variants (<1% frequency)

Accurate, fast exome interpretation utilizing Moon

Moon, Invitae's artificial intelligence (AI)-powered software, weighs clinical and genetic information to quickly identify the variants most relevant to each patient's case. Moon works by first ranking potential causative variants based on weighted parameters including patient phenotype, gene-disease associations, predicted molecular effects, and family information. The software then sifts through the exome sequence to provide scientists, board-certified genetic counselors, and board-certified laboratory geneticists with a list of potential positives that they review and clinically evaluate within our proven variant-interpretation framework, Sherloc.[1]

Moon is trusted by genomic medicine pioneers at University of Liège, Uppsala University Hospital, and Rady Children's Institute for Genomic Medicine—and others like them, who use the software to power their clinical exome analyses.[2-4]

Automated disease gene curation utilizing Apollo

New gene and disease associations are discovered and published at a rapid pace. To allow our teams to stay on top of these latest advancements, Invitae integrated the Apollo database, an up-to-date gene disease knowledge base that performs daily automated literature searches using natural language processing algorithms. Information is gathered, then weighted to prioritize the phenotypic features most often observed with disease. The results are manually curated and annotated by expert scientists and genetic counselors. Apollo's continuously growing knowledge base guarantees a comprehensive, up-to-date analysis for every patient.

Turnaround time: 6–8 weeks on average

Specimen types: Blood, buccal, saliva, or gDNA

Price: Proband $1,250; Duo/Trio $2,500, with insurance billing, institutional billing, and patient-pay options available. View full billing options at www.invitae.com/billing.

Reanalysis and reevaluation, at no additional charge

Exome reanalysis is critical in the search for a diagnosis and has been shown to increase the diagnostic yield by as much as 20%, with the highest yields achieved >1 year after reanalysis.[5,6]

Case-level reanalysis provides a re-review of all reported and unreported variants in an exome to ensure that newly discovered gene-disease associations are considered in a patient's case.

Invitae's exome reanalysis includes:

- Automatic case-level reanalysis **every 6 months**, at no additional charge, with reporting of new positive findings for 3 years after the initial exome report
- An additional one-time, provider-initiated reanalysis within 3 years of the initial exome report

With Invitae's exome reanalysis program, there is no need to remember to request reanalysis or decide on the best time to ask for reanalysis. Patients can be reassured that they will continually receive the most up-to-date information about their genetics.

Variant-level reevaluation occurs, in general, when there are known variant classification changes. Corresponding cases are reviewed and reports are updated. Invitae has always offered variant-level reevaluation and will continue to offer this service.

Beyond sequencing—accurate and reproducible variant classification and reporting

- Invitae's 5-tier variant classification framework, called Sherloc, begins with the most recent American College of Medical Genetics and Genomics (ACMG) guidelines and builds on them to generate rigorous variant interpretations. Invitae's stringent procedures provide reproducibility and reduce subjectivity through critical evaluation of all applicable evidence of pathogenicity.[1,7]
- Invitae's exome analysis also draws on the advanced capabilities of our functional modeling platform (FMP), which uses machine learning techniques to create gene-specific biochemical, cellular, and computational data models to predict variant pathogenicity. FMP helps to resolve variants of uncertain significance (VUS) and improve test results across all clinical areas in accordance with ACMG guidelines.
- Our user-friendly clinical exome reports summarize the most salient information, focusing on variants that are likely to have medical implications for the patient. We provide a detailed description of gene-disease associations and evidence for variant classification for each reported variant.

Questions? Our team is ready to assist you!
Reach us at www.invitae.com/contact.

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2. Lumaka A, Race V, Peeters H, *et al.* A comprehensive clinical and genetic study in 127 patients with ID in Kinshasa, DR Congo. *Am J Med Genet A.* 2018;176(9):1897-1909.
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4. Clewemar P, Hailer NP, Hailer Y, *et al.* Expanding the phenotypic spectrum of osteogenesis imperfecta type V including heterotopic ossification of muscle origins and attachments. *Mol Genet Genomic Med.* 2019;7(7):e00723.
5. Deignan JL, Chung WK, Kearney HM, *et al.* Points to consider in the reevaluation and reanalysis of genomic test results: a statement of the American College of Medical Genetics and Genomics (ACMG). *Genet Med.* 2019;21(6):1267-1270.
6. Liu P, Meng L, Normand EA, *et al.* Reanalysis of Clinical Exome Sequencing Data. *N Engl J Med.* 2019;380(25):2478-2480.
7. Richards S, *et al.* Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med.* 2015;17(5):405-24.

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