Invitae Boosted Exome

EXPERTISE AND QUALITY YOU CAN TRUST

The Invitae Boosted Exome provides a rigorous analysis of an individual's exome through a systematic evaluation of genetic variants informed by the patient's clinical presentation and medical history. We use highly advanced next-generation sequencing (NGS) capture technology with boosted coverage of medically relevant genes, custom-built bioinformatics solutions to support variant analysis, a phenotype ontology-based tool that uses clinical information to generate a list of relevant genes, the option to add additional genes to the list of genes to be analyzed, analytical solutions to identify other relevant genes through inheritance patterns or impact on gene function, and a team of board-certified geneticists to provide expert interpretation and clearly explained reports.

THE INVITAE BOOSTED EXOME INCLUDES:

- **Advanced NGS capture technology** with boosted coverage of medically relevant genes
- **Gene coverage data**, providing full transparency prior to placing an order
- Personalized analysis of your patient's exome through an Invitae-developed online **phenotype selection tool** so you can collaborate in selecting the genes to analyze
- **Customized capture baits** to enhance the coverage of hard-to-sequence areas of the exome and allow detection of intragenic copy number variants (learn more in the metrics table on reverse)
- **Rigorous bioinformatics** and **expert interpretation** that you can trust
- **Average turnaround time** of only **8–12 weeks**

The Invitae Boosted Exome is a customized, in-depth analysis of the human exome that integrates your knowledge of a patient's clinical history and presentation with the variants we find within his/her exome. We will analyze:

- Variants identified in genes associated with Mendelian conditions that correspond to the patient's presentation and additional genes you indicate, **plus**
- Variants in any gene identified as possibly causing premature truncation events and interfering with canonical splice sites, thereby interfering with gene expression, **plus**
- For a trio analysis (when samples from both parents are provided for analysis), variants shown to be de novo in the patient or variants segregating as x-linked or autosomal recessive

These variants will be analyzed and reported according to a validated and published interpretation framework called Sherloc, which is Invitae's further refinement of the American College of Medical Genetics and Genomics standards and guidelines. This assay evaluates currently known nuclear genes associated with mitochondrial dysfunction, but not the genes encoded by mitochondrial DNA at this time.

For more information, please visit **www.invitae.com/exome**.

INVITAE BOOSTED EXOME METRICS

Sequencing parameters	Variants interpreted	Report provided
Proband	**Proband**	**Proband**
■ Average 150x coverage (per base) across all exons with >99.4% of reportable exons covered at ≥20x ■ Invitae's high-quality variant calling detects: • single nucleotide variants • small deletions/insertions <50 bp • intragenic copy number variants* ■ Standard variant calling	■ All variants in the gene list derived from clinical history, plus ■ Variants predicted to cause loss of function	■ A clinical summary describing relevant findings ■ Detailed information including: • list of analyzed genes • all identified pathogenic, likely pathogenic, and variants of uncertain significance • description of relevant variants with citations • in-depth description of technical coverage ■ Optional secondary findings report (based on the latest ACMG recommendations) for all sequenced individuals
Trio	**Trio**	**Trio**
■ Exome sequencing of all three samples with joint calling	■ Everything interpreted in the proband, plus ■ Variants segregating as X-linked or autosomal recessive, plus ■ De novo variants	■ Inheritance patterns associated with all reported variants

* In contrast to Invitae's gene panel sequencing where single-exon del/dups are detected, the greater variability in depth of coverage across an exome permits reliable detection of del/dups spanning 4 exons or more with high confidence; smaller events may be detected and will be reported when sufficient resolution exists.

TURNAROUND TIME: 8–12 weeks on average

SPECIMEN TYPES: Blood or saliva

PRICE: Proband $2,500; Duo/Trio $4,500, with insurance billing, institutional billing, and patient pre-pay options available

INVITAE BOOSTED EXOME TEAM: COMMITTED TO QUALITY

DR. ROBERT NUSSBAUM, M.D.
Chief Medical Officer
Harvard Medical School M.D.

Dr. Nussbaum is a world-renowned pioneer in genetics who co-discovered the first inherited form of Parkinson's disease. Before Invitae, he served as chief of the genomic medicine division in the UCSF Department of Medicine. He is a past president of the ASHG and a member of the National Academy of Medicine.

DR. SWAROOP ARADHYA, PH.D., FACMG
Director of Medical Affairs
Baylor College of Medicine Ph.D.

Dr. Aradhya is a molecular geneticist and cytogeneticist who has helped shape professional practices and technology applications in clinical genetic testing. Before Invitae, he was director of neurogenetics and clinical microarray services at GeneDx. He has helped identify and characterize various genetic disorders and participated in the Human Genome Project.

DR. TINA HAMBUCH, PH.D., FACMG
Medical Director, Pediatrics
UC Berkeley Ph.D.

Dr. Hambuch is board-certified in clinical molecular genetics, with a focus on pediatrics. Prior to Invitae, she led the launch of the first CLIA-certified, CAP-accredited laboratory offering clinical genome sequencing at Illumina. She has co-authored over 20 publications on clinical applications of exome and genome sequencing, and served on several national working groups for clinical exome and genome applications.

DR. KRISTIN MCDONALD GIBSON, PH.D., DIPL. ABMGG
Assistant Medical Director, Pediatrics
Duke University Ph.D.

Dr. McDonald Gibson is board-certified in clinical molecular genetics, with experience launching exome tests. Prior to Invitae, she helped develop The Children's Hospital of Philadelphia's clinical exome as well as an analysis pipeline for exome sequencing while at Duke. She also served as a member of a neonatal genomics exome sequencing group at Duke.

Questions? Our team is ready to assist you! Please contact us at 800-436-3037 or clientservices@invitae.com.

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