

# **Definitive answers** for more patients

## **Expert-driven**, AI-enabled

Invitae strikes a balance between a comprehensive team of genetics experts and new technologies, including artificial intelligence (AI). This allows our team of highly experienced genetic counselors, scientists and lab directors to make the most impact.

More than 300,000+ patients have received a definitively classified result thanks to these 7 new technologies<sup>1</sup>

- **Invitae Population Frequency** 1 Modeling<sup>™</sup>: This Invitae developed, machine learning algorithm estimates the probability of a variant's pathogenicity based on information from the gnomAD population database.<sup>3,4</sup>
- 2 SpliceAI: An open-source deep learning splicing predictor developed by Illumina5 that has higher accuracy than Alamut splicing predictors.1
- Large-scale functional/experimental 3 datasets: We rigorously assessed 5 datasets (BRCA1, BRCA2, TP53, MSH2, SCN5A) generated by academic labs to determine how much weight to give functional evidence and have integrated this data into variant classification.<sup>6-12</sup>
- Cellular evidence modeling: Invitae 4 has generated large-scale functional/ experimental datasets for 19 genes using single-cell RNA expression profiling.<sup>13</sup>

References:

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- Submitters and their submissions. National Center 2 for Biotechnology Information. Accessed July 17, 2023. https://www.ncbi.nlm.nih.gov/clinvar/docs/ submitter\_list
- Invitae Population Frequency Modeling white paper. Published March 2023. Available at: https://view. publitas.com/invitae/wp131\_population-frequency-modeling\_white-paper
- Karczewski et al. Nature 581, 434-443 (2020) 4.
- 5. Jaganathan et al. Cell 176, 535-548 (2019)

- Evolutionary model of variant effect 5 (EVE): Developed by researchers at Harvard Medical School and Oxford University,<sup>14</sup> the EVE deep learning algorithm uses evolutionary sequence conservation to predict variant pathogenicity with high accuracy.
- AlphaFold protein structures: The AlphaFold database, developed by DeepMind and EMBL-EBL,<sup>15</sup> uses AI to 6 predict the 3D structure of proteins. These predictions are incorporated into in-silico models developed by Invitae that predict the functional effect of missense variants.

Invitae Evidence Modeling<sup>™</sup> Platform: 7 A machine-learning platform developed at Invitae and designed for generating, validating and standardizing new types of evidence for variant classification. To date, this platform includes evidence for more than 10 million unique variants from more than 3,000 genes.<sup>1</sup>

- Findlay et al. Nature 562, 217-222 (2018) 6.
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  - Glazer et al. Am J Hum Genet 107(1), 111-123 (2020)



### We're the company that:

#### tested over 4 million patients<sup>1</sup>

classified over 2 million unique variants<sup>1</sup>

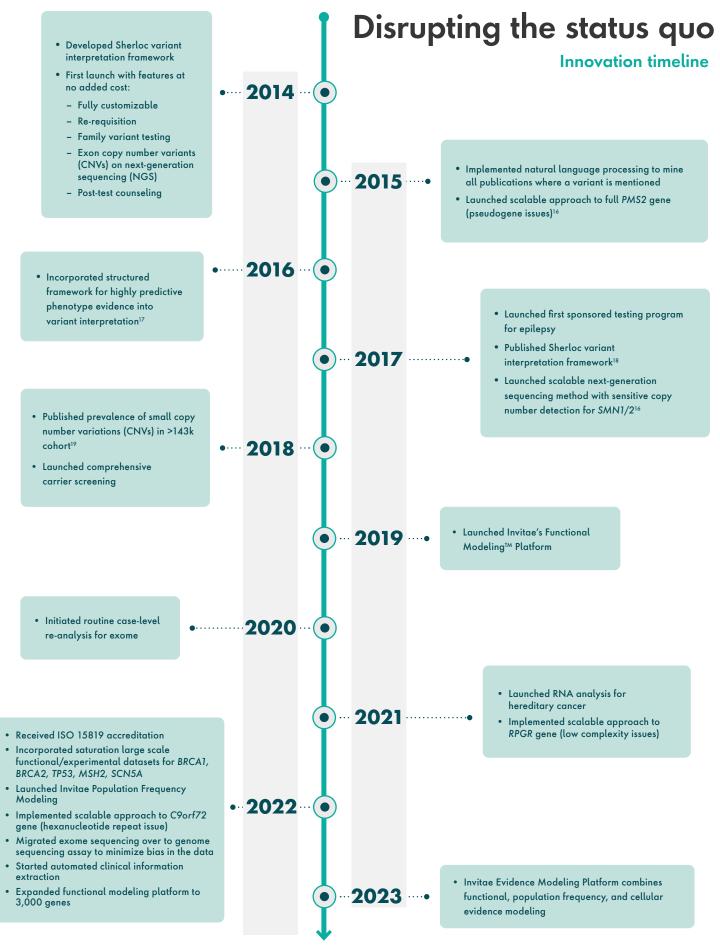
submitted >1,300,000 variants to ClinVar<sup>2</sup>

implemented 7 new technologies in the last 2 years<sup>1</sup>

#### led and collaborated on more than 100 research publications<sup>4</sup>

- 13. Invitae cellular evidence modeling platform white paper. Published March 2023. Available at: https:// view.publitas.com/invitae/wp134\_whitepaper\_cellular-evidence-platform
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- Senior et al. Nature. 2020; 577, 706-710 15
- Rojahn et al. Molecular Genetics & Genomic Medicine. 16. 2022: 10:e2072.
- Johnson et al. Am J Med Genet A. 2022; 188:2642-17. 2651
- Nykamp et al. Genet Med. 2017; 19:1105-1117. 18
- Truty R, et al. Genetics in Medicine. 2019; 21:114-123. 19.

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#### invitae.com

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