



Illumina releases SpliceAI2 to help advance rare disease research

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In a rare disease research dataset, SpliceAI2 identified 17% more disease-relevant variants compared to other splicing models

Illumina's genomic AI models now collectively enable researchers to identify 2x as many variants with predicted biological impact

SAN DIEGO, Oct. 8, 2026 /PRNewswire/ -- Illumina, Inc. (NASDAQ: ILMN) today introduced SpliceAI2, a new genomic AI model designed to address one of the central challenges in genomics: understanding the functional consequences of genetic variation. SpliceAI2 helps researchers identify disease-relevant splice variants that otherwise may go unnoticed. Predicting splice effects is key to resolving variants of uncertain significance in rare disease research, hereditary cancer testing research, and drug discovery. When applied to a rare disease research dataset, SpliceAI2 identified 17% more disease-relevant variants compared to other splicing models.



"Variant effect prediction tools, such as SpliceAI2, are among the key areas of focus for the BioInsight AI Lab," said Rami Mehio, senior vice president and general manager of BioInsight at Illumina. "As researchers work to elucidate the effect of mutations, we are uniquely positioned to unite genomic data and scientific expertise at scale, delivering the AI tools that can advance discovery and human health."

The BioInsight AI Lab focuses on three main areas of scientific impact: generating genomic and multiomic data to power AI tools; developing genomic AI models for variant effect prediction and prioritization; and training biological foundation models.

"Illumina is advancing AI to systematically shrink the portion of the genome that remains uninterpretable," said Kyle Farh, vice president of Illumina's BioInsight AI Lab. "Genomics has driven some of the most consequential genetic disease breakthroughs of the past two decades. Today, we are equipping researchers with the next generation of technology to help understand the underlying causes of disease."

SpliceAI2, PromoterAI, and PrimateAI-3D form a suite of genomic AI models designed to help researchers assess the functional impact of genetic variation across a broad spectrum of variant effect types, including splice, promoter, and missense variants. Together, these genomic AI models now collectively enable researchers to identify up to twice as many variants with predicted biological impact.

SpliceAI2 enables state-of-the-art variant interpretation across rare disease and population health research

Accurate interpretation of the functional consequences of genetic variation remains a central challenge for life science research. Splicing is the process by which RNA transcripts are assembled before protein production. Splice variants can disrupt transcripts, alter gene function, and interfere with protein function. Cryptic splice sites contribute to a significant burden of rare disease cases but are challenging to identify through traditional approaches. SpliceAI2 improves researchers' ability to identify and interpret these variants and provides accurate prediction of cell type-specific splicing.

A [newly released preprint](#) from Illumina's BioInsight AI Lab evaluated SpliceAI2's performance against the original SpliceAI and alternative splice prediction models. According to analyses of matched DNA and disease phenotype data from Genomics England

cohorts, SpliceAI2 identified 17% more disease-relevant splice variants than other models. Analysis of matched whole genome and RNA sequencing data from the NIH's Genotype-Tissue Expression Portal showed that SpliceAI2 improved quantification of splice site usage by 34% compared to the next best model. SpliceAI2 results also aligned more closely with downstream protein effects seen in UK Biobank proteomic datasets and better captured the effects of splice variants across multiple population genomics datasets.

Researchers worldwide already use genomic AI from Illumina to drive deeper insights into their sequencing data. The first generation of SpliceAI has become the splice variant prediction tool of choice for researchers, cited in over 3,400 publications to date. It is incorporated into guidelines from ClinGen, a clinical research body that sets standards for clinical genomics, for splice variant interpretation. Trained on a dataset that is 100 times larger than the original SpliceAI, SpliceAI2 advances the model through significantly improved prediction of splice variants, enabling the detection of more disease-relevant variants while reducing the overall number of variants requiring review.

Customers on the frontline of rare disease and drug discovery research can easily access SpliceAI2 through Illumina's BioInsight applications, including DRAGEN Annotation for AI-powered and traditional variant annotation, and Emedgene for germline research.

BioInsight is Illumina's data, software, informatics, and AI business, helping researchers, healthcare organizations, and biopharma companies transform genomic and multiomic data into biological insights. BioInsight enables customers to accelerate discovery, identify and validate drug targets, deepen understanding of disease biology, and advance precision medicine. BioInsight's growing portfolio includes the groundbreaking BioInsight AI Lab as well as resources such as the Billion Cell Atlas, which helps biopharma partners connect genetic signals to cellular mechanisms and biological function.

Learn more about SpliceAI2 [here](#)

Read the full preprint [here](#)

About Illumina

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Contacts

Investors:
Illumina Investor Relations
858-291-6421
IR@illumina.com

Media:
Christine Douglass
PR@illumina.com

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