GOLDEN HELIX

Enabling Precision Medicine

Evaluating Splice Site Variants in VarSeq

Nathan Fortier, Ph.D. – Director of Research

CIOReview

20 most promising Biotech Technology Providers

pharma TECH OUTLOOK

Top 10 Analytics Solution Providers

Gartner

Hype Cycle for Life sciences

Q & A

Please enter your questions into your GoToWebinar Panel

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  - Award Number 2R44 GM125432-01
  - Award Number 2R44 GM125432-02
  - Montana SMIR/STTR Matching Funds Program Grant Agreement Number 19-51-RCSBIR-005
- **PI is Dr. Andreas Scherer, CEO Golden Helix.**
- **The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.**

Golden Helix – Who We Are

Golden Helix is a global bioinformatics company founded in 1998.

GlaxoSmithKline

VarSEQ

- Variant Calling
- Filtering and Annotation
- Clinical Reports
- CNV Analysis
- Pipeline: Run Workflows

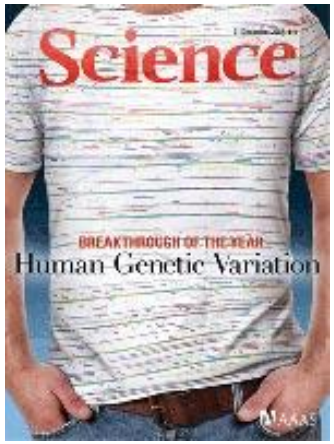
VariantWarehouse

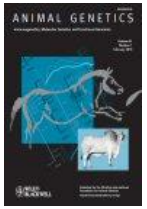
- Variant Warehouse
- Centralized Annotations
- Hosted Reports
- Sharing and Integration

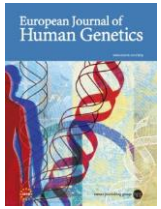
SNP & Variation Suite

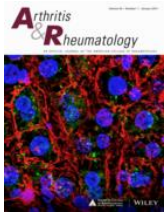
- GWAS
- Genomic Prediction
- Large-N Population Studies
- RNA-Seq
- CNV-Analysis

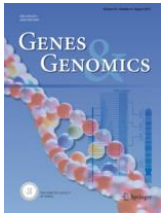
Cited in over 1,300 peer-reviewed publications











GOLDEN HELIX
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Over 400 customers globally

SickKids
THE HOSPITAL FOR SICK CHILDREN

Cincinnati Children's
Hospital Medical Center

The Children's Hospital of Philadelphia

Stanford University

UBC

Ucla

Yale

The Feinstein Institute for Medical Research
North Shore-Long Island Jewish Health System

North Shore LIJ

PREVENTION GENETICS
DISEASE PREVENTION THROUGH GENETIC TESTING

MAYO CLINIC

LINEAGEN

MOFFITT CANCER CENTER

Dartmouth-Hitchcock
NORRIS COTTON CANCER CENTER

BAYER

Lilly

abbvie

TEVA

NATIONAL CANCER INSTITUTE

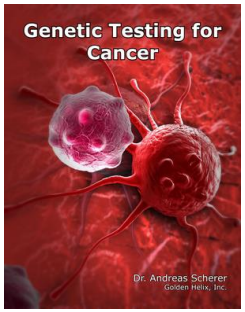
USDA
USDA Agricultural Research Service

FDA

Golden Helix – Who We Are

When you choose a Golden Helix solution, you get more than just software

- REPUTATION
- TRUST
- EXPERIENCE



- INDUSTRY FOCUS
- THOUGHT LEADERSHIP
- COMMUNITY

- TRAINING
- SUPPORT
- RESPONSIVENESS

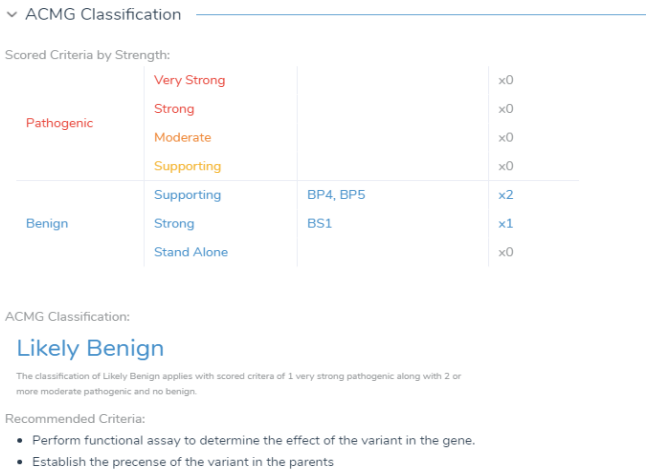
- INNOVATION and SPEED

PRODUCTS	BIOINFORMATICS PIPELINE	FUNCTION
DNAseq (Sentieon) TNseq (Sentieon) VS-CNV	FASTQ BAM VCF	▸ Single nucleotide variation ▸ Copy number variation & loss of heterozygosity ▸ Chromosomal aberration
Annotations	Annotated VCF	▸ Public & commercial annotations to enrich genomic data sets
VarSeq VSReports VSPipeline	Clinical Report	▸ Annotate & filter ▸ Visually inspect alignments ▸ Variant prioritization ▸ Clinical assessment
VSClinical	Automated ACMG Guidelines	▸ Clinical variant interpretation in concordance with ACMG Guidelines
VSWarehouse	Data Warehousing Web-Enabled Interface + Powerful API: JSON, XML, TSV, CSV, SQL, FHIR	▸ Clinical assessment catalog ▸ Advanced data querying ▸ Versioning ▸ Interoperability ▸ Compliance with HIPPA, CLIA & CAP data discovery

VSClinical

- **Complete Support for ACMG Guideline Workflow:**
  - Implements a guided workflow for following the ACMG guideline scoring and classifying
  - Place criteria into conceptually related groups, paired with their opposites, and formatted as answerable question.
- **Aggregate and Automate:**
  - Questions have supporting evidence presented with rich and interactive visuals
  - Automatically computed recommendations for questions that have explicit bioinformatic evidence, with supporting reasons for each answer.
- **Expert and Beginner Friendly:**
  - Start with descriptive summaries and recommendations for a variant
  - Deep dive into Population Catalogs, Gene Impact, Published Studies and Clinical tabs
  - Integrated documentation, readings on scoring criteria and citations

VSClinical®



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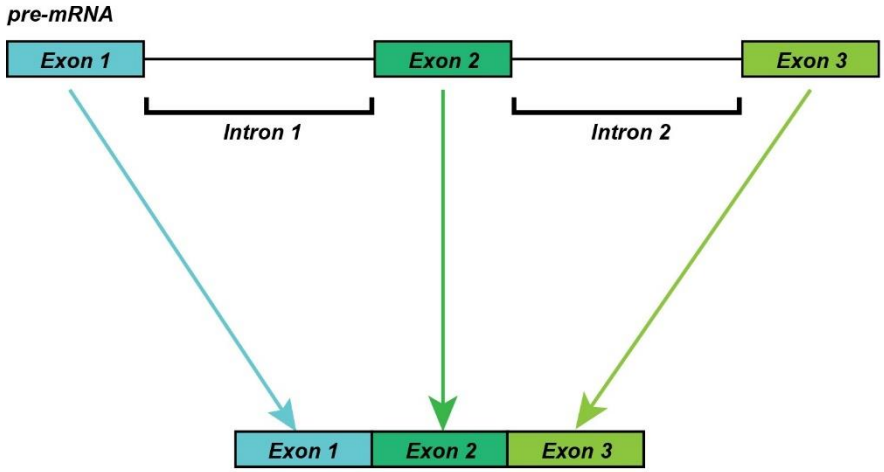
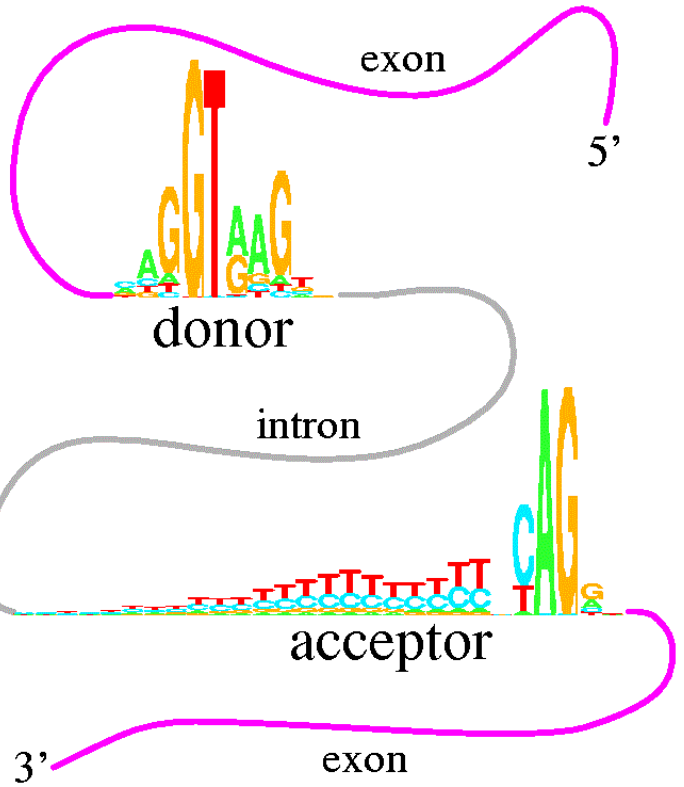
Splice Sites

- Understanding a variant's impact on splicing is crucial
- Synonymous variants can disrupt existing splice sites or introduce novel splice sites
- Such variants can cause exon skipping or truncation



Splice Sites

- **Introns have distinct nucleotide pairs at each end**
  - GT at the 5’ end (Donor Site)
  - AG at the 3’ end (Acceptor Site)
- **Area surrounding nucleotide pair is defined by a splice motif**
- **Sequences around splice sites are highly variable**
- **Machine learning and probabilistic methods are used to identify sites**



Algorithms

- **VSClinical supports four splice site prediction algorithms**
  - PWM: Uses position weight matrix similar to SpliceSiteFinder and Human Splice Finder
  - MaxEntScan: Approximates sequence motifs using Maximum Entropy Distribution
  - NNSplice: Identifies splice sites using neural networks
  - GeneSplicer: Uses Markov models combined with maximal dependence decomposition

[Demo in VarSeq]

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