GOLDEN HELIX

Enabling Precision Medicine

Workflows for Copy Number Variants in VarSeq
A Users Perspective

Steve Hystad – Field Application Scientist

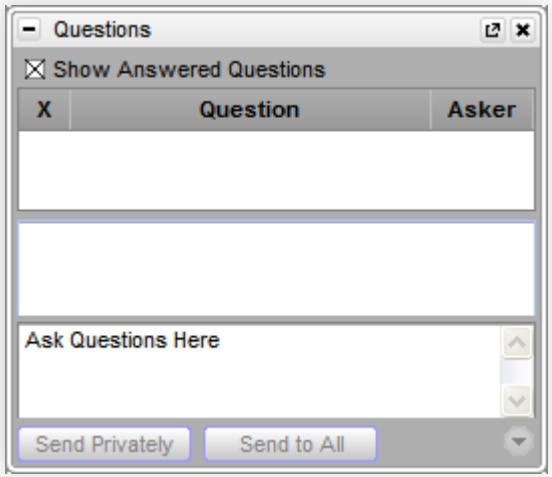
CIOReview
20 most promising Biotech Technology Providers

pharma TECH OUTLOOK
Top 10 Analytics Solution Providers

Gartner
Hype Cycle for Life sciences

Questions during the presentation

Use the Questions pane in your GoToWebinar window



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

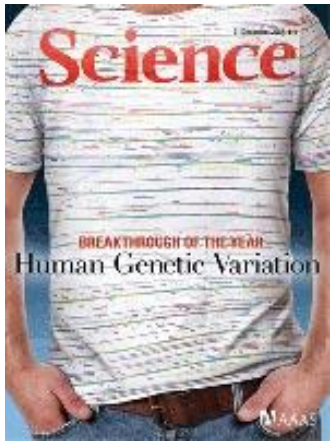
VARIANT WAREHOUSE

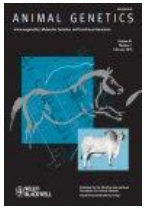
- Variant Warehouse
- Centralized Annotations
- Hosted Reports
- Sharing and Integration

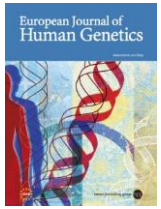
SNP & VARIATION SUITE

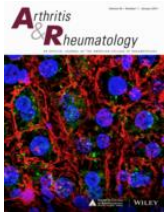
- GWAS
- Genomic Prediction
- Large-N-Population Studies
- RNA-Seq
- Large-N CNV-Analysis

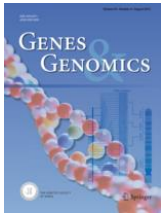
Cited in over 1100 peer-reviewed publications











GOLDEN HELIX
Enabling Precision Medicine

Over 350 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

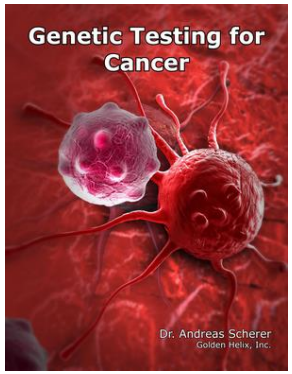
FDA

GOLDEN HELIX
Enabling Precision Medicine

Golden Helix – Who We Are

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

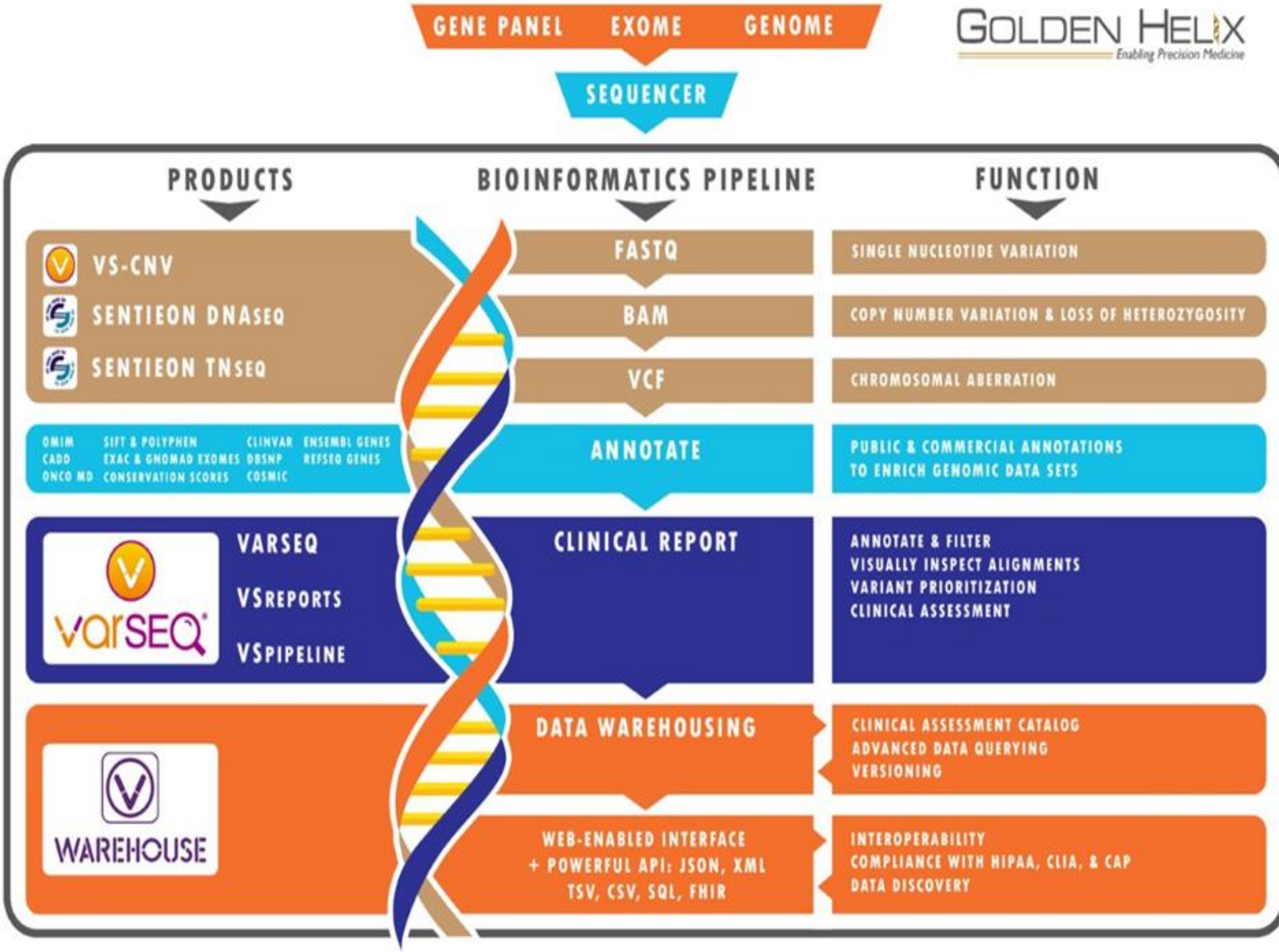
- REPUTATION
- TRUST
- EXPERIENCE



- INDUSTRY FOCUS
- THOUGHT LEADERSHIP
- COMMUNITY

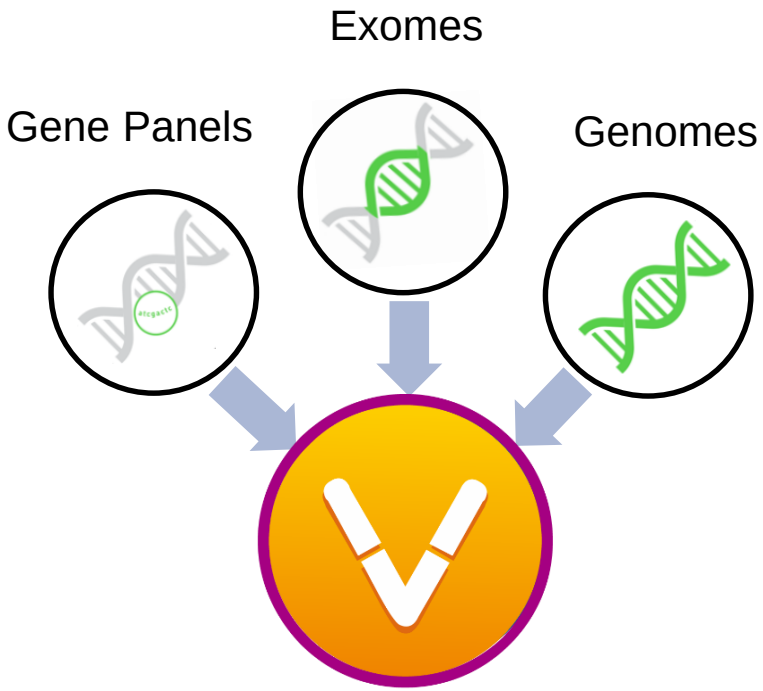
- TRAINING
- SUPPORT
- RESPONSIVENESS

- INNOVATION and SPEED
- CUSTOMIZATIONS


GENE PANEL
EXOME
GENOME
SEQUENCER
GOLDEN HELIX
Enabling Precision Medicine
PRODUCTS
BIOINFORMATICS PIPELINE
FUNCTION
VS-CNV
SENTIEON DNASEQ
SENTIEON TNSEQ
FASTQ
BAM
VCF
SINGLE NUCLEOTIDE VARIATION
COPY NUMBER VARIATION & LOSS OF HETEROZYGOSITY
CHROMOSOMAL ABERRATION
OMIM
CADD
ONCO MD
SIFT & POLYPHEN
EXAC & GNOMAD EXOMES
CONSERVATION SCORES
CLINVAR
DBSNP
COSMIC
ENSEMBL GENES
REFSEQ GENES
ANNOTATE
PUBLIC & COMMERCIAL ANNOTATIONS
TO ENRICH GENOMIC DATA SETS
varSEQ
VARSEQ
VSREPORTS
VSPIPELINE
CLINICAL REPORT
ANNOTATE & FILTER
VISUALLY INSPECT ALIGNMENTS
VARIANT PRIORITIZATION
CLINICAL ASSESSMENT
WAREHOUSE
DATA WAREHOUSING
CLINICAL ASSESSMENT CATALOG
ADVANCED DATA QUERYING
VERSIONING
WEB-ENABLED INTERFACE
+ POWERFUL API: JSON, XML
TSV, CSV, SQL, FHIR
INTEROPERABILITY
COMPLIANCE WITH HIPAA, CLIA, & CAP
DATA DISCOVERY

VarSeq CNV

- **VS-CNV**
  - Call CNVs from Gene Panels
- **VS-CNV 2.0**
  - Call large and small CNVs & LOH on Exome datasets
- **Whole Genome Sequence CNV Caller**
  - Call CNVs from low and ultra low read depth datsets.
  - Call CNVs from the command line
- **CNV annotations**
  - Quickly examine clinically relevant CNVs
  - Reduce false positives and filter out common CNVs
  - Capture and store clinical CNV assessments

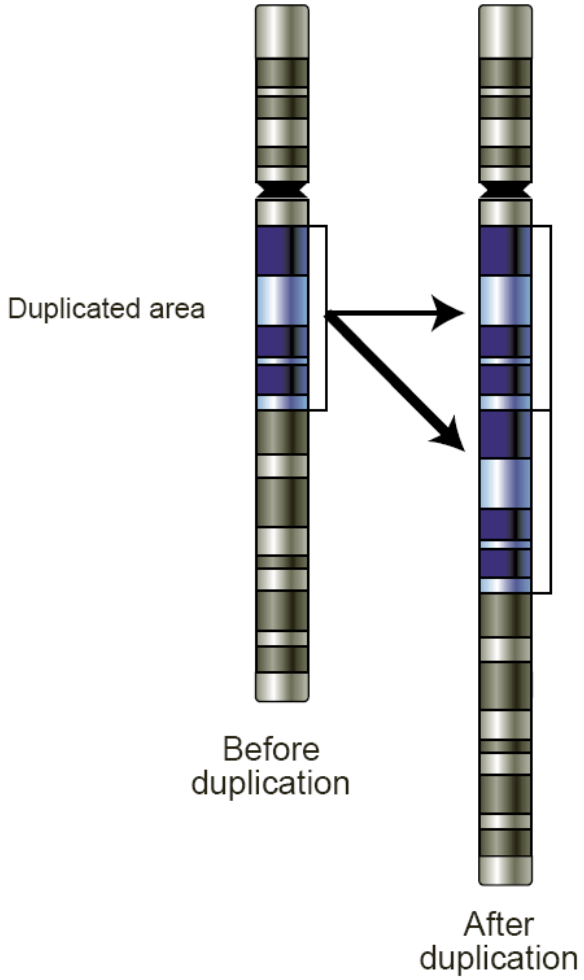


Annotate and Filter

VS-CNV

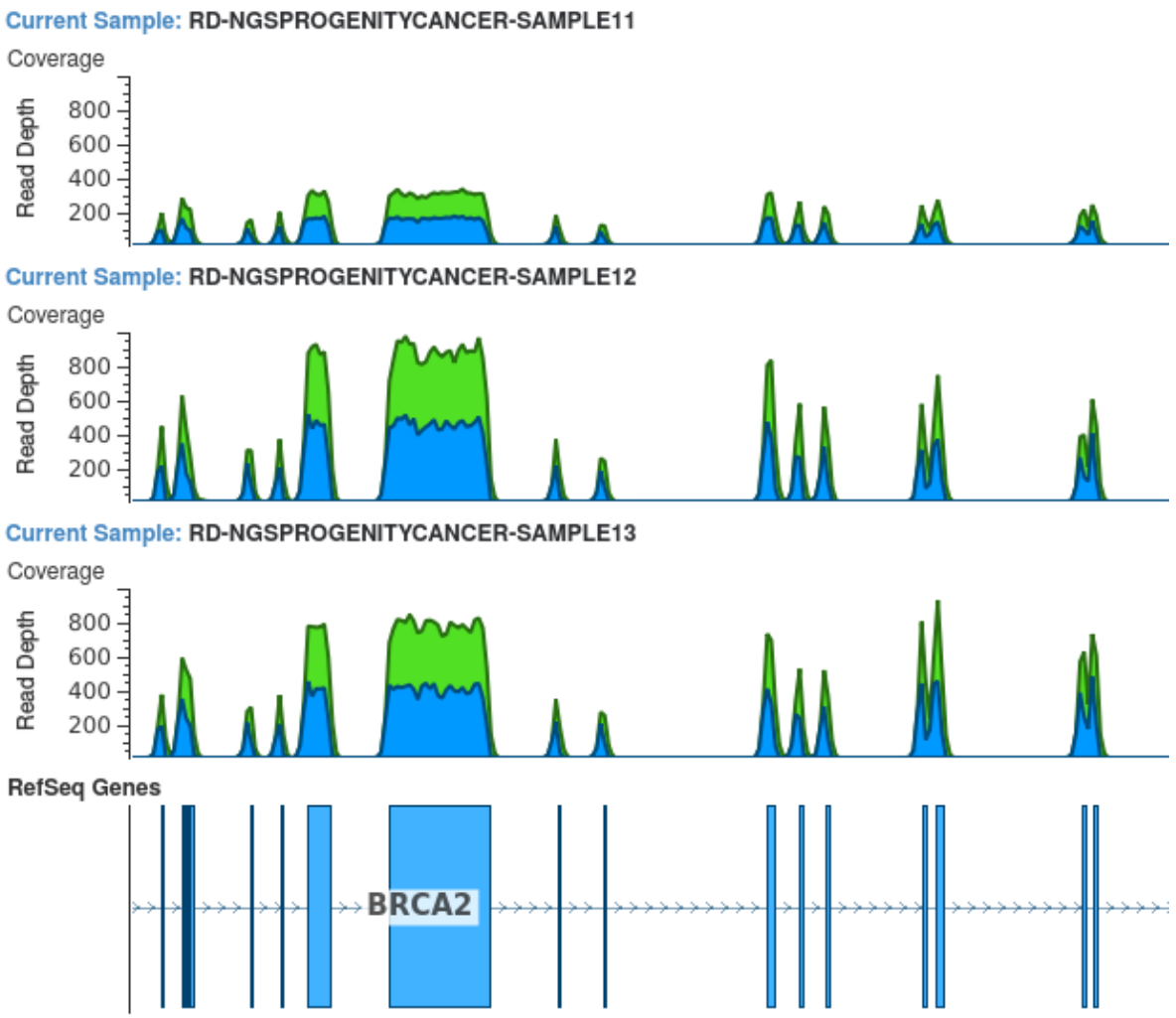
CNV Detection

- **Chromosomal microarray**
  - Current best practice
  - Slow
  - Additional expense
  - Only detects large events
- **CNV calling from NGS data**
  - Calls from existing coverage data
  - Detects small single-exon events
  - Provides faster results, simplified clinical workflow



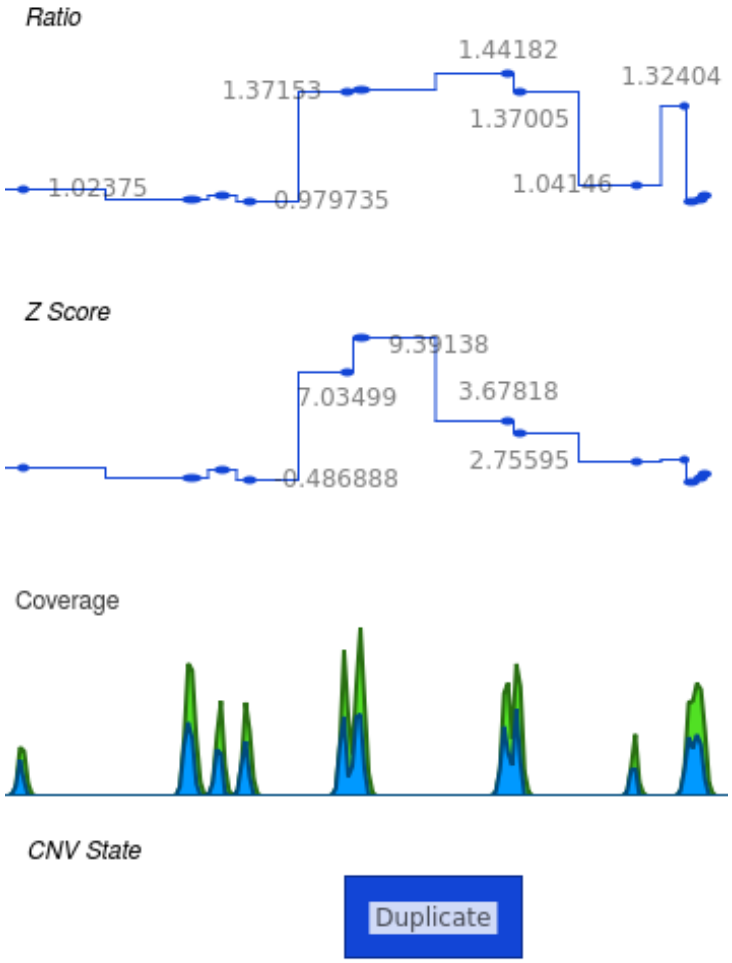
CNV Detection via NGS

- **CNVs are called from coverage data**
- **Challenges**
  - Coverage varies between samples
  - Coverage fluctuates between targets
  - Systematic biases impact coverage
- **Solutions**
  - Data Normalization
  - Reference Sample Comparison



CNV calling in VarSeq

- **Reference samples used for normalization**
- **Metrics**
  - Z-score: number of standard deviations from reference sample mean
  - Ratio: sample coverage divided by reference sample mean
  - VAF: Variant Allele Frequency
- **For Gene Panels and Exomes**
  - Probabilistic model used to call CNVs
  - Segmentation identifies large cytogenetic events
- **For Whole Genome Data**
  - Targets segmented using Z-scores
  - Events called based on Z-score and Ratio thresholds



Annotations

- **Genes**

NCBI RefSeq Ensembl UCSC GENCODE

- **Clinical Assessments**

ClinGen Clinical Genome Resource ClinVar OMIM CADD

- **Population Frequencies**

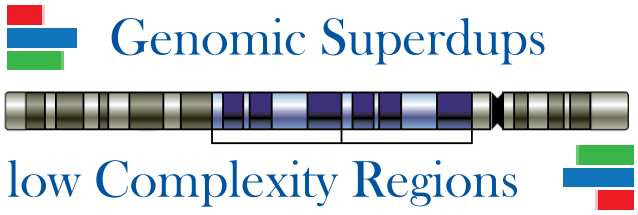
NIH National Heart, Lung, and Blood Institute IGSR BROAD INSTITUTE

- **Cancer**

ICGC OncoMD COSMIC Catalogue Of Somatic Mutations In Cancer CIViC Clinical Interpretations of Variants in Cancer

- **CNV**

DGV



ExAC CNV ClinGen Clinical Genome Resource ClinVar IGSR

Sample Data for Single Exome Analysis

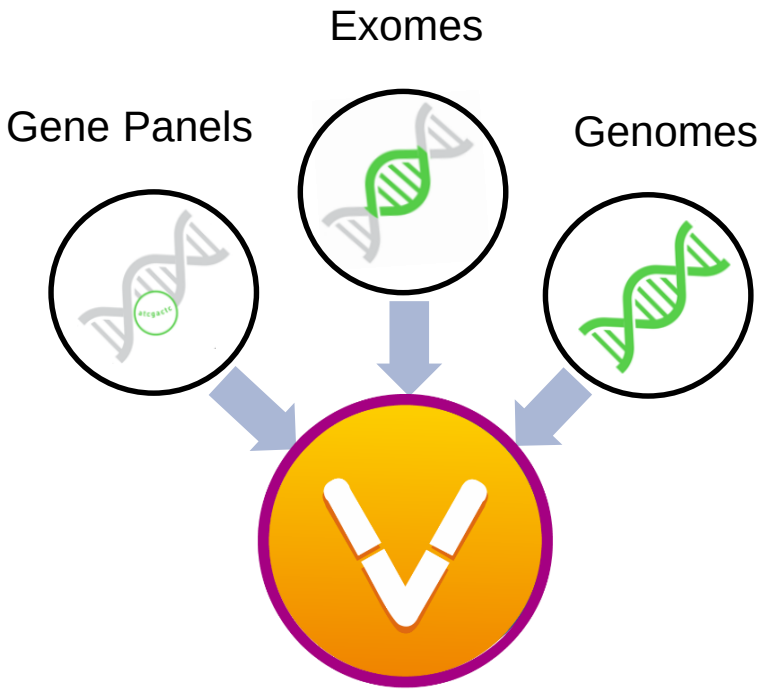
- **Four Single Exome Samples**
- **BAM files from 1000 Genomes Phase 3 Illumina Exome Alignment**
- **Used Sentieon tools for variant calling.**

Sample CRExome-18 has chronic history of stomach ulcers and reported hearing impairment phenotype.

VarSeq Demonstration

Lets Review

- **VS-CNV**
  - Call CNVs from Gene Panels, Exomes, and WGS
- **CNV annotations**
  - Quickly examine clinically relevant CNVs
  - Reduce false positives and filter out common CNVs
- **CNV algorithms**
  - Complete control over annotations
  - Match Gene linked to Phenotype
  - CNV Phorank!
- **CNV Assessment Catalogs**
  - Build knowledge base
  - Plot, Annotate, and Repeat



Annotate and Filter

VS-CNV

CNV Resources

- **Webcasts**
  - **CNV Analysis in VarSeq** – December 7th 2016
  - **Calling Large LOH and CNV Events with NGS Exomes** – March 8th 2017
  - **CNV Analysis in VarSeq – A User's Perspective** – April 19th 2017
  - **Comprehensive Clinical Workflows for CNVs in VarSeq** – Sept 27th 2017

- **Tutorials**
  - VarSeq CNV Caller Tutorial

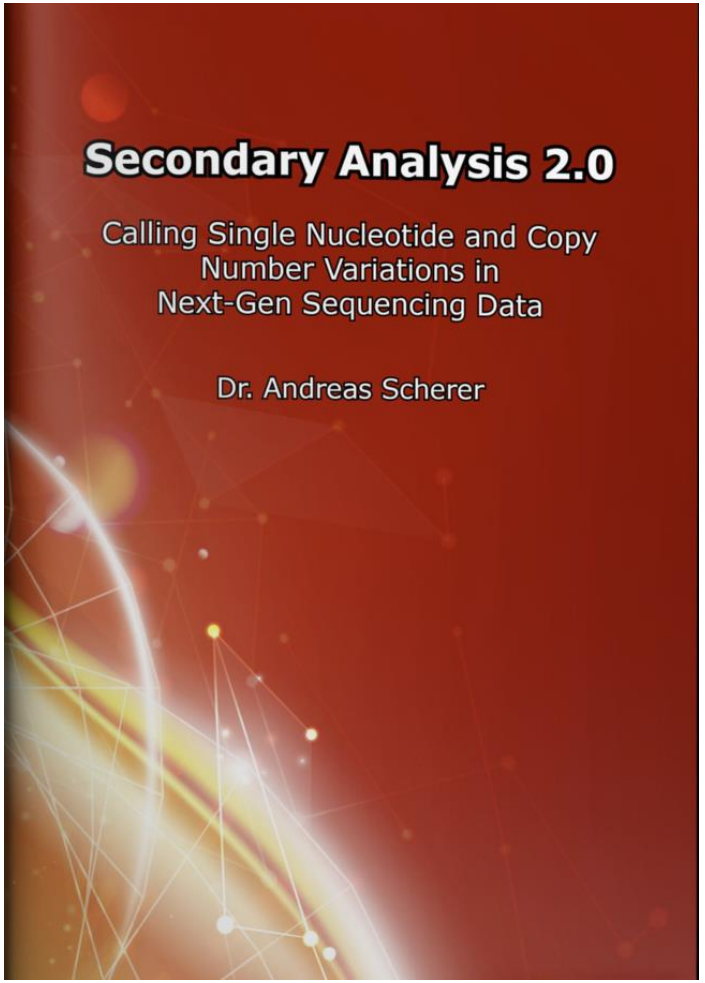
- **Support from Field Application Scientists**
  - Support@Goldenhelix.com

Additional Information

- **Secondary Analysis ebook**
  - Calling SNVs & CNVs from NGS data

- **Golden Helix at ASHG 2017!**
  - Booth 902
  - Come see demos and ask us questions!

- **VarSeq CNV Powerpack (end Oct)**
  - *VarSeq + VSCNV + Sentieon + VSReports - $ 15,995*
- **SVS & VarSeq Bundle**
  - CADD & OMIM included - $7,995
- **Small Lab Warehouse + VS-CNV**
  - 2 users $36,00



Questions or more info:

- Email info@goldenhelix.com
- Request an evaluation of the software at www.goldenhelix.com