Cancer Gene Panels and Tumor-Normal Workflows

varSEQ

March 2, 2016

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GOLDEN HELIX
Accelerating the Quest for Significance™

Agenda

1. Overview Golden Helix
2. Introduction to VarSeq
3. Cancer Gene Panels
4. Tumor Normal Workflows

Golden Helix – Who We Are

Golden Helix is a global bioinformatics company founded in 1998.

gsk GlaxoSmithKline

varSEQ™

Filtering and Annotation
Clinical Reports
Pipeline
Data Warehousing

GOLDEN HELIX SNP & VARIATION SUITE

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

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

BabyGenes™

LINEAGEN

MOFFITT CANCER CENTER

Dartmouth-Hitchcock
NORRIS COTTON CANCER CENTER

BAYER

Lilly

abbvie

TEVA

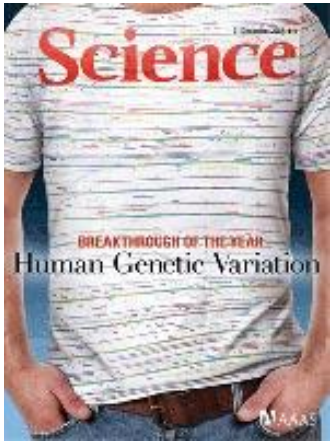
NATIONAL CANCER INSTITUTE

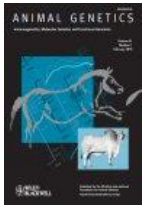
USDA
USDA Agricultural Research Service

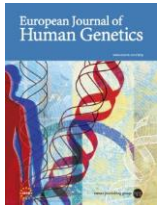
FDA

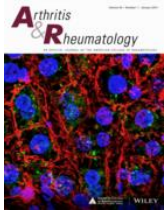
GOLDEN HELIX
Accelerating the Quest for Significance™

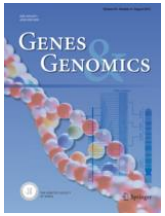
Cited in over 900 peer-reviewed publications







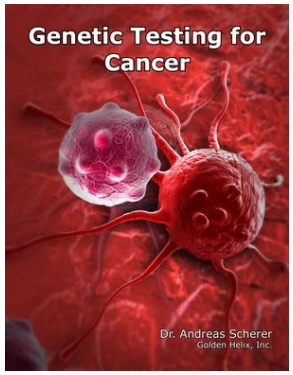




Golden Helix – Who We Are

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

- REPUTATION
- TRUST
- EXPERIENCE



- INDUSTRY FOCUS
- THOUGHT LEADERSHIP
- COMMUNITY

- TRAINING
- SUPPORT
- RESPONSIVENESS

- TRANSPARENCY
- INNOVATION and SPEED
- CUSTOMIZATIONS

Questions during the presentation

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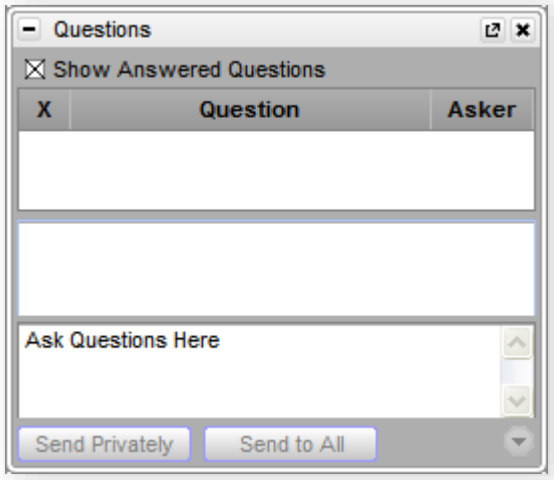
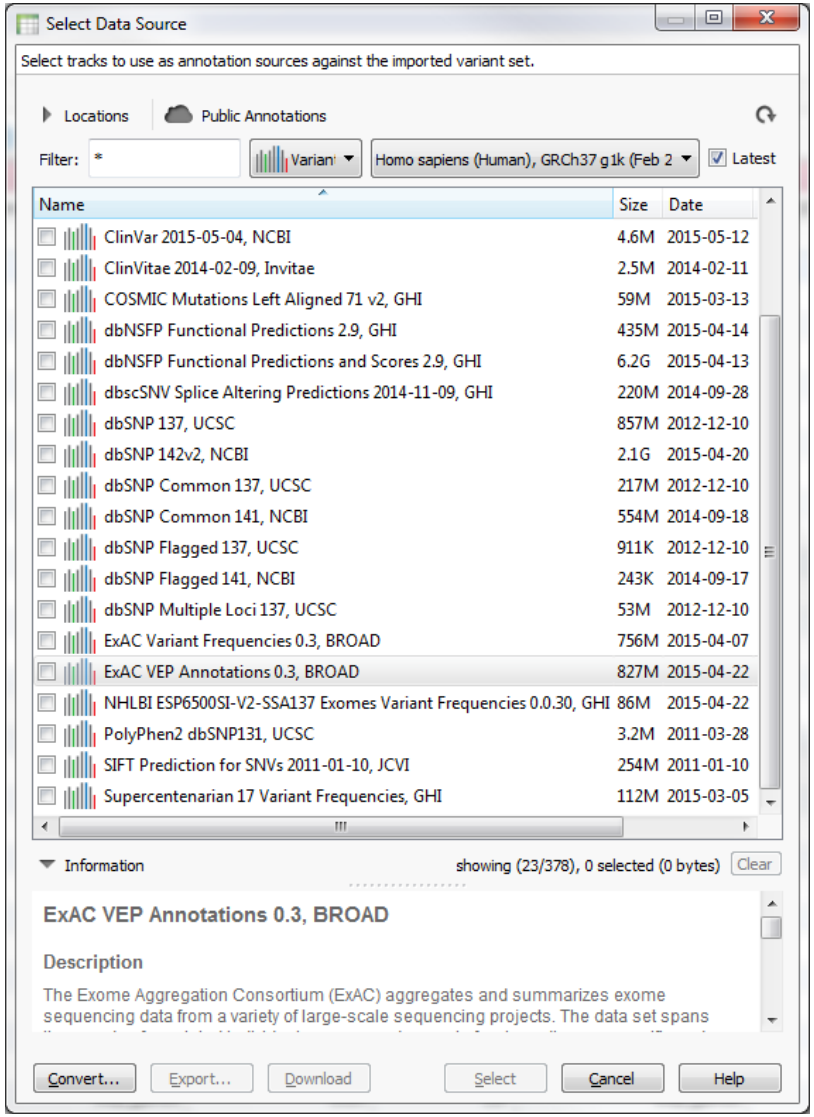


What is VarSeq?

- **Variant annotation, filtering and ranking**
- **Repeatable workflows**
- **Rich visualizations with GenomeBrowse integration**
- **Powerful GUI and command-line interfaces**

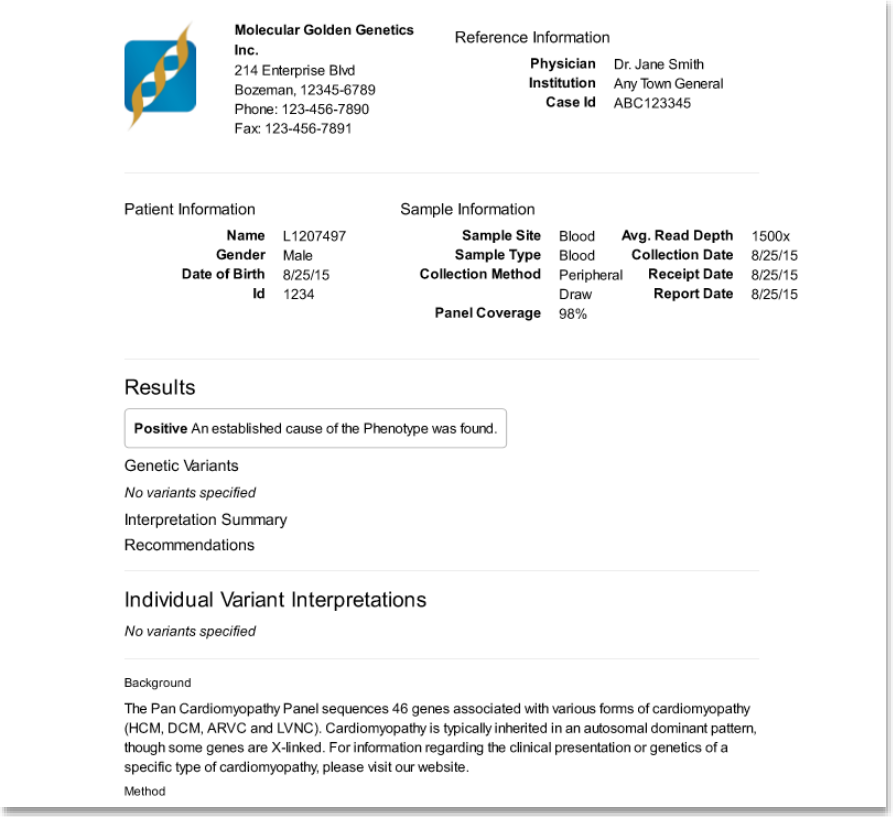
Data Curation of Annotation Sources

- **VarSeq is backed by an extensive list of curated data sources**
  - 1kG Phase3 Variant Frequencies
  - ClinVar, NCBI
  - ClinVitae, Invitae
  - COSMIC
  - dbNSFP Functional Predictions
  - dbSNP
  - ExAC
  - RefSeq Genes, NCBI
  - Supercentenarian 17 Variant Frequencies
- **Your workflows lock down specific versions**
- **MedGenome OncoMD provides curated drug targeted mutations for Cancer, supporting clinical trials and functional evidence.**
- **OMIM Genes, Phenotypes, and Variants**



VarSeq Reports

- **Prepared "Templates"**
  - ACMG Standard Germline Report
  - Configurable Global Settings
    - Logo
    - Lab Information
    - Test Description / Disclaimers
- **Customizable Sample Inputs**
  - Patient Information
  - Test Results
- **Selected Variants Added**
  - Per-variant information
- **Customizable**
  - Default values are scriptable
  - Rendering is entirely programmatic



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214 Enterprise Blvd
Bozeman, 12345-6789
Phone: 123-456-7890
Fax: 123-456-7891

Reference Information

Physician	Dr. Jane Smith
Institution	Any Town General
Case Id	ABC123345

Patient Information

Name	L1207497
Gender	Male
Date of Birth	8/25/15
Id	1234

Sample Information

Sample Site	Blood	**Avg. Read Depth**	1500x
Sample Type	Blood	**Collection Date**	8/25/15
Collection Method	Peripheral Draw	**Receipt Date**	8/25/15
		Report Date	8/25/15
Panel Coverage	98%		

Results

Positive An established cause of the Phenotype was found.

Genetic Variants

No variants specified

Interpretation Summary

Recommendations

Individual Variant Interpretations

No variants specified

Background

The Pan Cardiomyopathy Panel sequences 46 genes associated with various forms of cardiomyopathy (HCM, DCM, ARVC and LVNC). Cardiomyopathy is typically inherited in an autosomal dominant pattern, though some genes are X-linked. For information regarding the clinical presentation or genetics of a specific type of cardiomyopathy, please visit our website.

Method

Motivation

- **Next-Gen sequencing provides the ability to:**
  - Understand mutations associated with cancer
  - Discover new arrangements in the cancer genome
  - Provide personalized diagnosis and management of cancer
- **We will cover two type of panels:**
  - Cancer Gene Panels
  - Tumor/Normal Workflows

“Cancer is a disease of the genome” – Theodor Boveri

Sample Data for Cancer Gene Panels

- **Illumina TruSight Cancer Sequencing Panel**
  - Six reference samples including one HapMap sample NA12878 sequenced following standard protocols set forth by Illumina
- **Comprehensive coverage of 94 genes associated with a predisposition for various cancers**
- **BAM and VCF files for each replicate are available**
- **High Coverage, average read depth over the targeted regions**
  - For the six samples the average read depth is 574 reads

VarSeq Demonstration

Sample Data for Tumor-Normal Pair Analysis

- **Exome sequence data from a Gastric Cancer Study**
  - An exome pair (Normal-N990005 and Tumor-T990005) from the study ***Exome sequencing of gastric adenocarcinoma identifies recurrent somatic mutations in cell adhesion and chromatin remodeling genes*** published in *Nature Genetics*.

    http://www.nature.com/ng/journal/v44/n5/full/ng.2246.html
- **BAM and VCF files for each sample**
  - Sequencing data was downloaded from the NCBI Sequence Read Archive (SRA) then batch variant calling for single samples was done using BWA + GATK through the Seven Bridges Genomics, Inc. pipeline
- The study for this dataset identified 661 genes that contained non-silent somatic point mutations and this list was used for filter criteria.

Questions or more info:

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

Questions?

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