



Introducing VSClinical AMP Guidelines: A Comprehensive Workflow for NGS Testing of Cancer

Gabe Rudy, VP Product & Engineering



20 Most Promising Biotech
Technology Providers



Hype Cycle for Life sciences

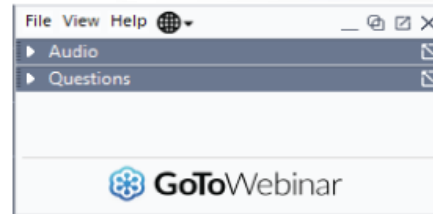


Top 10 Analytics
Solution Providers

Questions



Ask a question by typing them in
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NIH Grant Funding Acknowledgments

- Research reported in this publication was supported by the National Institute Of General Medical Sciences of the National Institutes of Health under:
 - Award Number R43GM128485-01
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 - Award Number 2R44 GM125432-01
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 - 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.

Who Are We?

Golden Helix is a global bioinformatics company
founded in 1998



Filtering and Annotation

ACMG Guidelines

Clinical Reports

CNV Analysis

Pipeline: Run Workflows



Variant Warehouse

Centralized Annotations

Hosted Reports

Sharing and Integration



CNV Analysis

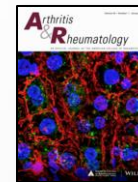
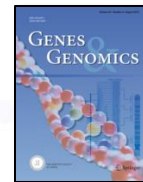
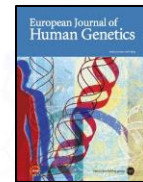
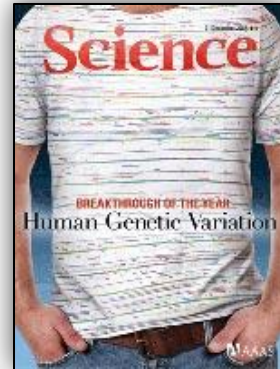
GWAS | Genomic Prediction

Large-N Population Studies

RNA-Seq

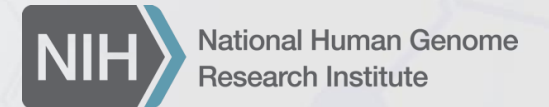
Large-N CNV-Analysis

Cited in 1,000s of Peer-Reviewed Publications



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GOLDEN HELIX
Enabling Precision Medicine



When you choose Golden Helix, you receive more than just the software



SOFTWARE IS VETTED

- 20,000+ users at 400+ organizations
- Quality & feedback



DEEPLY ENGRAINED IN SCIENTIFIC COMMUNITY

- Give back to the community
- Contribute content and support



SIMPLE, SUBSCRIPTION- BASED BUSINESS MODEL

- Yearly fee
- Unlimited training & support



INNOVATIVE SOFTWARE SOLUTIONS

- Cited in 1,000s of publications

BAM

VCF

VS-CNV[®]

Calling of CNVs

varSEQ[®]

Annotating, filtering & prioritizing of clinically relevant SNPs and CNVs

VS Clinical[®]

- Clinical interpretation of SNPs & CNVs
- ACMG & AMP guidelines assessing germline and somatic variations
- Clinical reporting

WORD
REPORT

PDF
REPORT

EXCEL
TABLE

Hallmarks of Cancer











Engines of Cancers

- Understanding cancer in a patient requires understanding its underlying biology
- Multiple hallmarks are required for tumorigenesis

A Disease of the Genome

- A given cancer gene plays a role in promoting or suppressing one or more of these hallmarks
- Genomic mutations enable hallmarks by:
 - Gain of function of a Oncogene
 - Loss of function of a Tumor Suppressor Gene (TSG)

Hallmarks for PTEN:

	P	S
 proliferative signalling		
 suppression of growth	■	
 escaping immune response to cancer		■
 cell replicative immortality		■
 tumour promoting inflammation		
 invasion and metastasis		■
 angiogenesis		
 genome instability and mutations		■
 escaping programmed cell death		■
 change of cellular energetics	■	

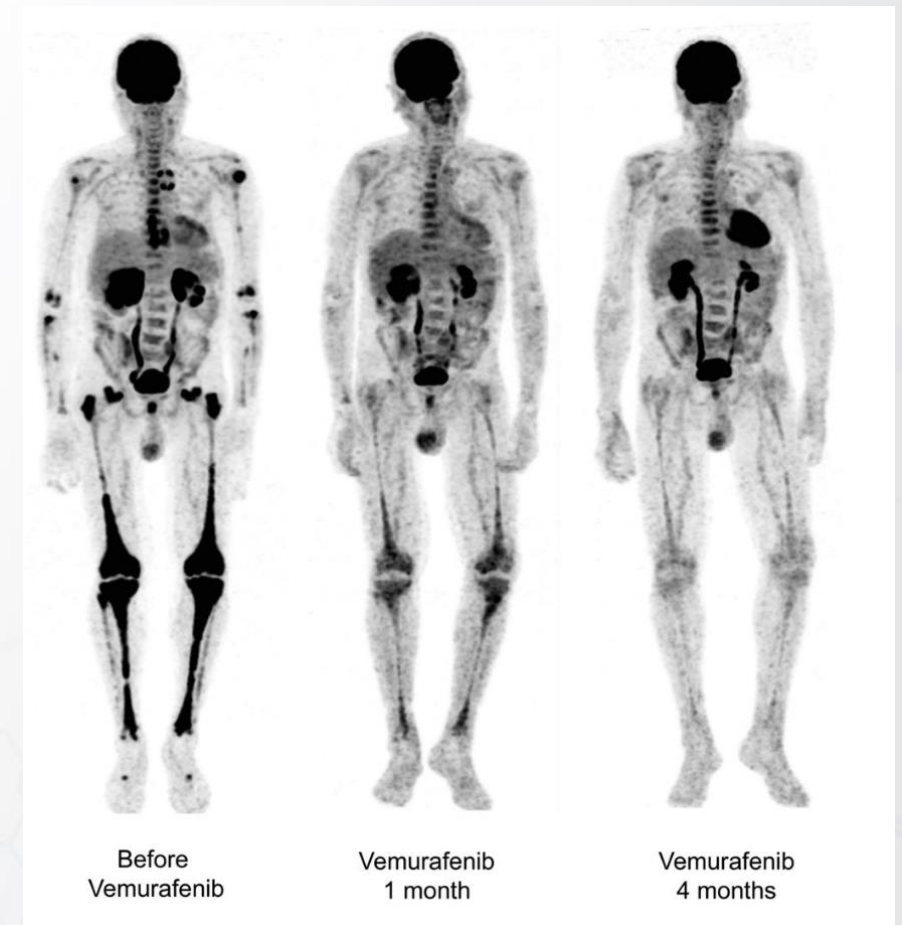
Biomarkers

■ Testable Biological Markers

- Biomarkers are biological states or measurements that provide indications for treatment, prognostic or diagnostic outcomes
- Range from presence or absence of proteins, antigens and specific genomic attributes of the tumor.

■ Common Cancer Biomarkers Examples

- HER2+: High levels of HER2 receptor protein
- MSI-H: Microsatellite instability-high
- BRAF^{V600E}: Presence of activating mutation V600E
- ERBB2^{Amp}: Amplification of ERBB2
- BCR-ABL1: Activation of ABL1 through fusion with BCR
- TP53^{WT}: No significant alterations of critical TSG



Haroche J. et al. Dramatic efficacy of vemurafenib in both multisystemic and refractory Erdheim-Chester disease and Langerhans cell histiocytosis harboring the *BRAF* V600E mutation. *Blood* 2013 121

Reporting Biomarkers

■ Reportable Biomarkers

- Molecular testing with NGS can detect many types of biomarkers.
- Activating Mutations for Oncogenes:
 - Missense mutations, CNV gains, gene fusions
- Inactivating of Tumor Suppressor Genes:
 - Truncating mutations, damaging missense mutations, CNV loss

■ Clinically Actionable Biomarkers

- Molecular genetics reports should provide actionable results with indications of the quality of the clinical evidence in the context of the patients tumor
- AMP Guidelines discuss best practices for clinical reporting and provides “Tier Levels” for rating the clinical evidence for drug response as well as prognostic and diagnostic implications.



Evidence Levels and Tiers

Tier I: Variants of Strong Clinical Significance

Therapeutic, prognostic & diagnostic

Level A Evidence

FDA-approved therapy
Included in professional guidelines

Level B Evidence

Well-powered studies with consensus from experts in the field

Tier II: Variants of Potential Clinical Significance

Therapeutic, prognostic & diagnostic

Level C Evidence

FDA-approved therapies for different tumor types or investigational therapies

Multiple small published studies with some consensus

Level D Evidence

Preclinical trials or a few case reports without consensus

Tier III: Variants of Unknown Clinical Significance

Not observed at a significant allele frequency in the general or specific subpopulation databases, or pan-cancer or tumor-specific variant databases

No convincing published evidence of cancer association

Tier IV: Benign or Likely Benign Variants

Observed at significant allele frequency in the general or specific subpopulation databases

No existing published evidence of cancer association

VSClinical AMP Workflow

- Evaluate Which Variants to Report
- Classify Evidence Following AMP Guidelines
- Your Interpretations Saved & Re-Used
- Built In Auto-Scoring of Somatic & Germline (ACMG Guideline) Variants
- Integrated Reporting
- Results: **Comprehensive, Consistent, Efficient**

Clinical
Report
Outline

Results

Biomarkers

Secondary Germline

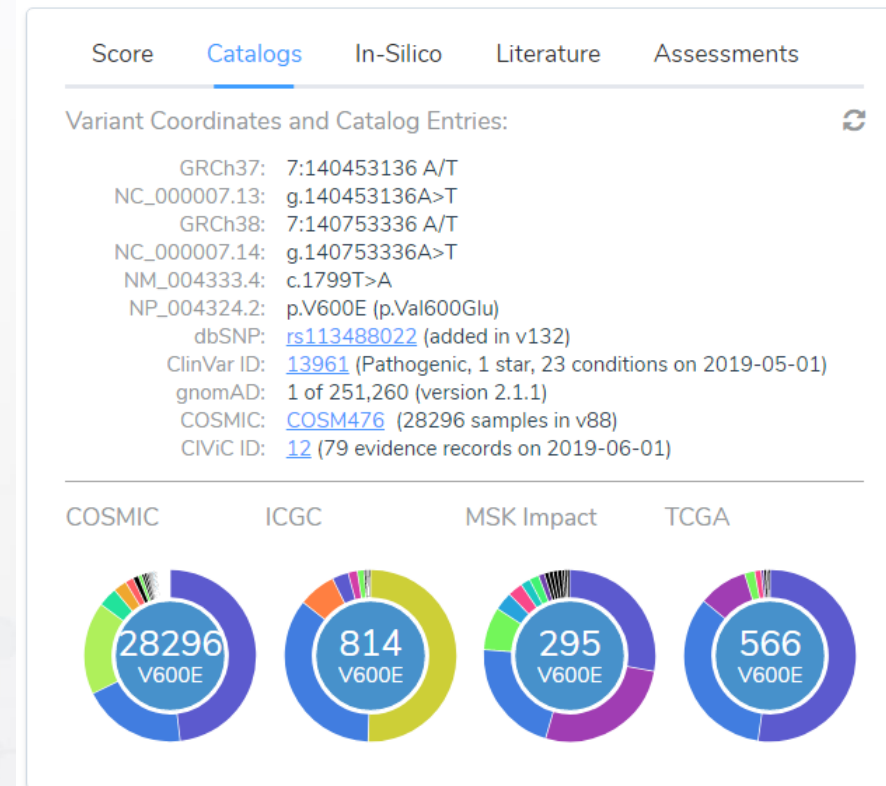
Variants of Unknown
Significance

Coverage Report

References

Integrated Data Sources

- COSMIC
 - Mutations
 - Fusions
 - Gene Census
 - Hallmarks of Cancer
- Clinical Evidence Sources:
 - DrugBank
 - CIViC
 - PMKB
- Golden Helix **CancerKB** Interpretation Knowledgebase (Beta)
 - Jump start your interpretations
 - Can contribute back anonymized interpretations
 - Provides well cited interpretations for most common biomarkers
- Others:
 - Genetic Home Reference
 - Clinical Genomic Database
 - CPDB Pathways
 - InterPro Protein Domains
 - ICGC Somatic Variants
 - MSK-Impact Somatic Variants
 - TCGA Somatic Variants
 - Cancer Hotspot Regions





Project Demonstration

Upcoming Webcasts

- **July: Scoring of Somatic Variants for Oncogenicity with VSClinical**
 - Present scoring similar to ACMG for classifying somatic variants rigorously
 - Dr. Nathan Fortier, Director of Research
- **August: Using VSClinical AMP Guidelines to Perform Cancer Testing**
 - Reporting Secondary Germline findings using ACMG guidelines
 - Customizing clinical report to match the requirements of your lab
 - Darby Kammeraad and Dr. Eli Sward, Field Application Scientists
- **September: Cancer Interpretation Reuse and Golden Helix CancerKB**
 - Saving and re-using interpretations with your own lab knowledgebase
 - Starting with 80% of your report written with Golden Helix CancerKB
 - Gabe Rudy, VP Product & Engineering

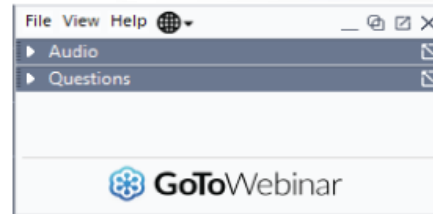
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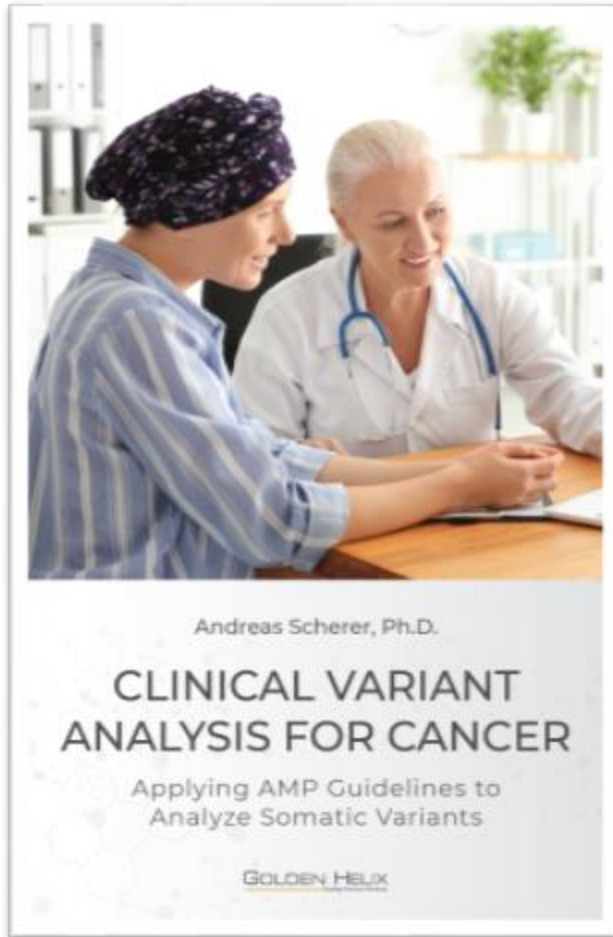
Limited Time Offer

15-months of VSClinical +Cancer Add-On
with a one-year license purchase

Ends on June 30th

To learn more, mention it in the Q&A pane, reach out to your Area Director, or email info@goldenhelix.com.

New eBooks



We released two new eBooks last week –
download your complimentary copies!

bit.ly/ghiebooks

Heading to ESHG in Sweden!



We will be demoing VSClinical, along with all our other software solutions! Stop by the Golden Helix booth to see it for yourself and pick up a free t-shirt!

Booth #368

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