GOLDEN HELIX
Enabling Precision Medicine

Oncogenicity Scoring in VSClinical

Dr. Nathan Fortier, Director of Research

CIOReview
20 Most Promising Biotech Technology Providers

Gartner
Hype Cycle for Life sciences

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Top 10 Analytics Solution Providers

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NIH Grant Funding Acknowledgments

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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
Enabling Precision Medicine

Golden Helix is a global bioinformatics company founded in 1998

varSEQ™
Filtering and Annotation
ACMG Guidelines
Clinical Reports
CNV Analysis
Pipeline: Run Workflows

VARIANT WARE-HOUSE
Variant Warehouse
Centralized Annotations
Hosted Reports
Sharing and Integration

SNP & VARIATION SUITE
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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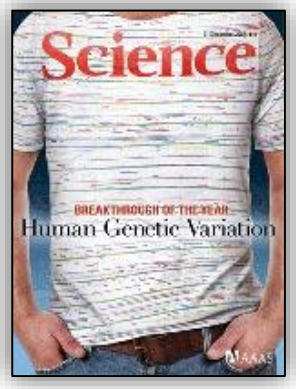

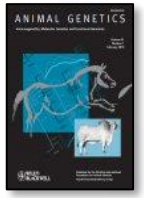

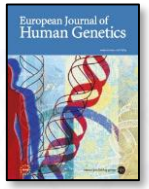

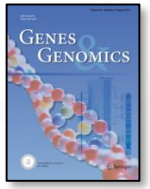

Over 400 Customers Globally

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

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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

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- Yearly fee
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INNOVATIVE SOFTWARE SOLUTIONS

- Cited in 1,000s of publications

BAM

VCF

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VS-CNV®	Calling of CNVs
varSEQ™	Annotating, filtering & prioritizing of clinically relevant SNPs and CNVs
VSClinical®	- Clinical interpretation of SNPs & CNVs - ACMG & AMP guidelines assessing germline and somatic variations - Clinical reporting

WORD REPORT

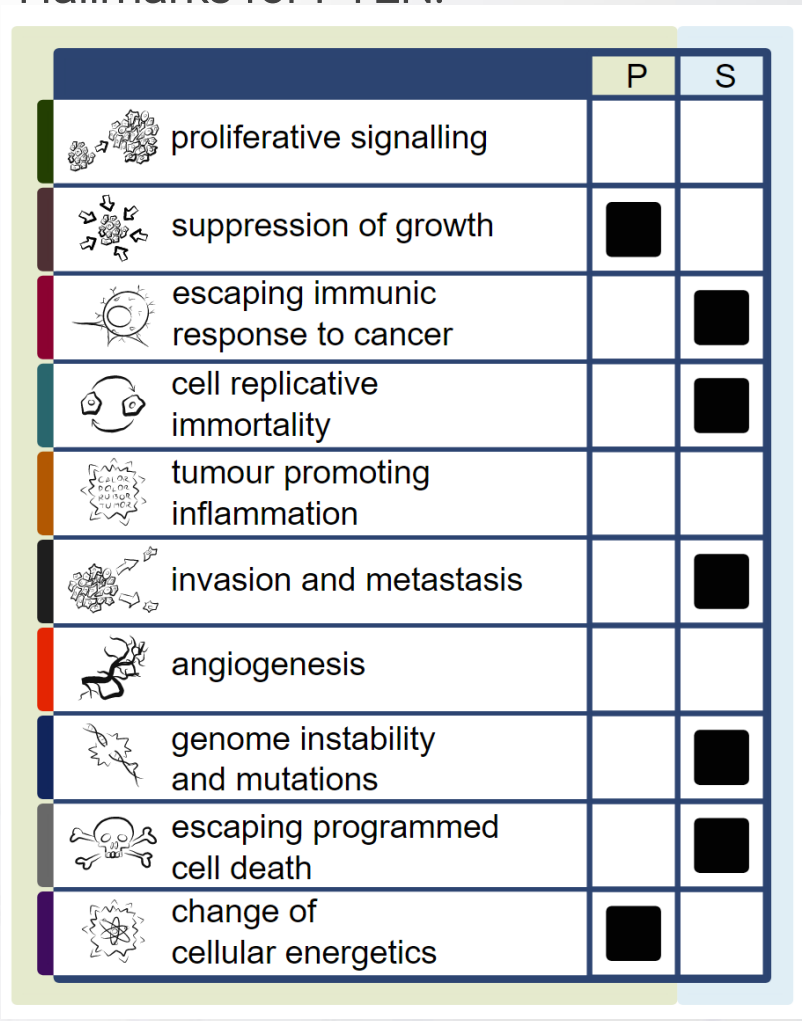
PDF REPORT

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)

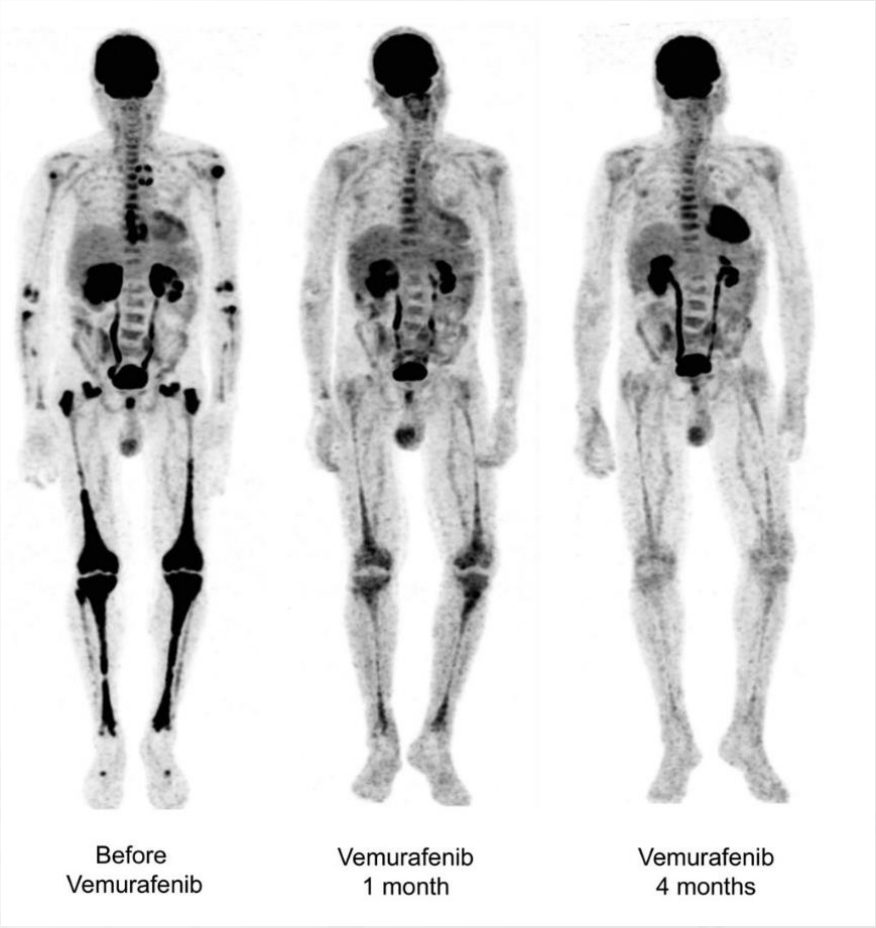
Hallmarks for PTEN:



Hanahan D., Weinberg R.A. **Hallmarks of Cancer: The next generation**. Cell . 2011; 144:646–674
Tate J et al. **COSMIC: the Catalogue Of Somatic Mutations In Cancer**, Nucleic Acids Research, Volume 47, Issue D1, 08 January 2019

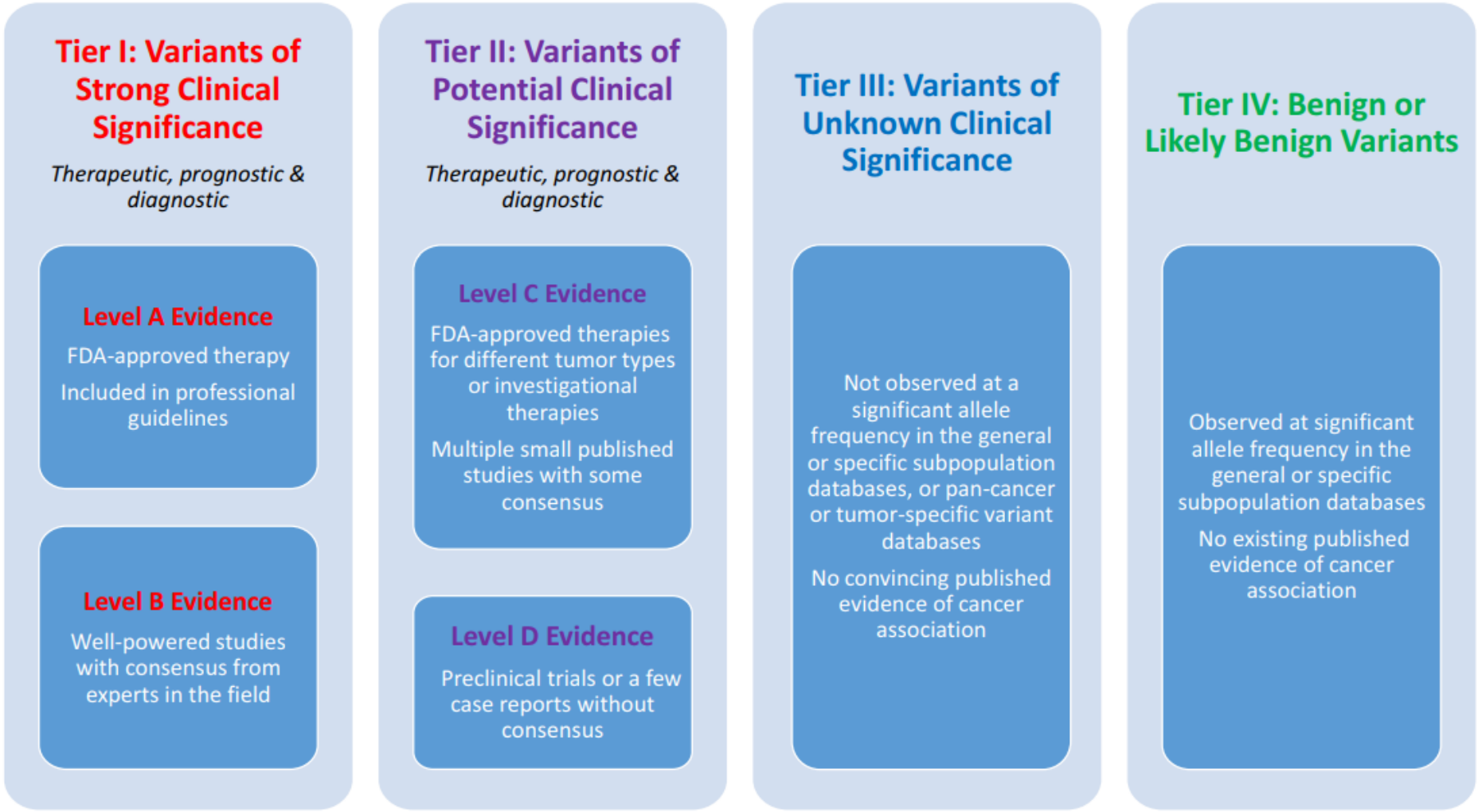
Biomarkers

- **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*

Evidence Levels and Tiers



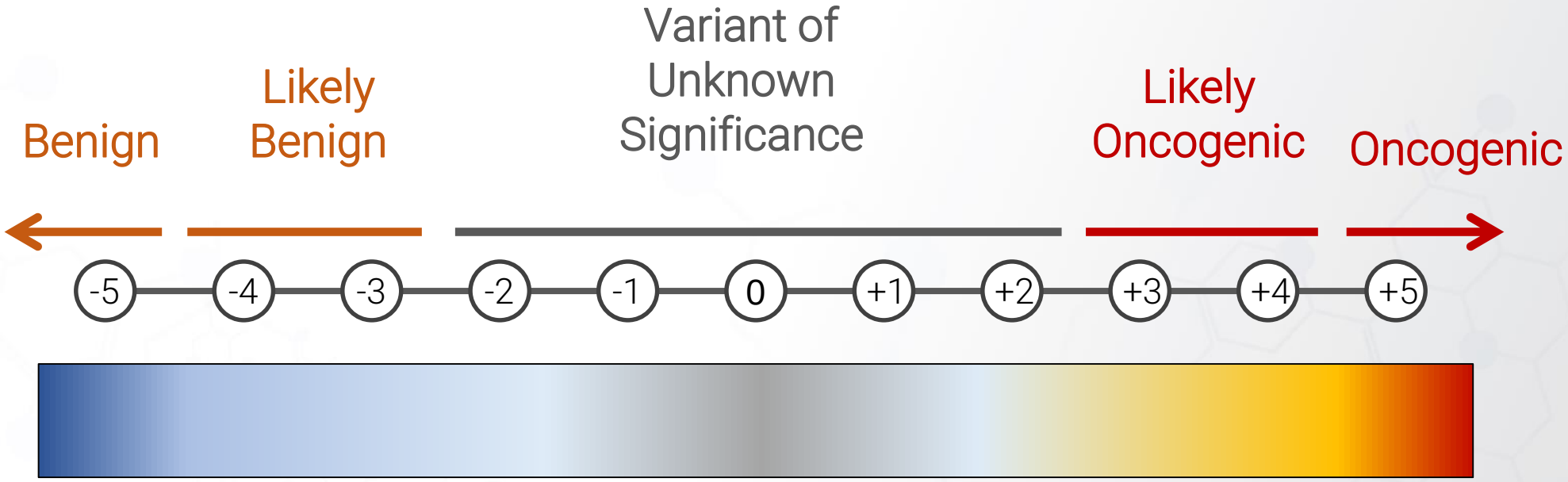
VSClincial AMP Workflow

- 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

Oncogenicity Scale



- Germline Population Catalogs
- In-Silico Functional/Splicing
- Previous / Clinical Evaluations

- Somatic Catalogs
- Domain / Hotspot Analysis
- Gene Affinity to Variant Type

Oncogenicity Scoring

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Applies To	Criteria	-5B	-3B	-2B	-1B	+1O	+2O	+3O
All	Population Frequency	-5	-3		-1			
	Homozygous in Controls			-2	-1			
	In Somatic Catalogs					+1	+2	+3
	Relevant Variant Assessments				-1		+2	+3
Null	Damaging LoF					+1	+2	
	LoF are Oncogenic Mutations in Gene					+1		
Missense	Nearby Pathogenic Missense Variants						+2	
	In-Frame not in Repeat Region					+1		
	Somatic Hotspot & Active Binding Sites					+1	+2	
Non-Null	Computational Evidence				-1	+1		
All	Splice Site Prediction					+1	+2	
Non-Coding	Silent, Intronic, UTR, Intergenic Variants w/ No Splice Effect		-3					

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Project Demonstration

Upcoming Webcasts

- *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
  - Dr. Eli Sward, Field Application Scientist
- *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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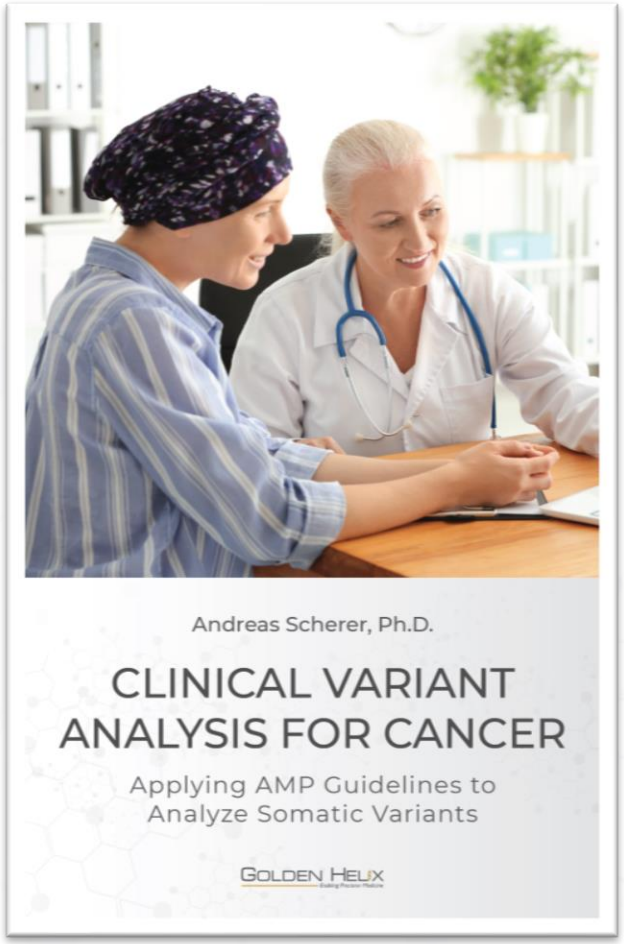
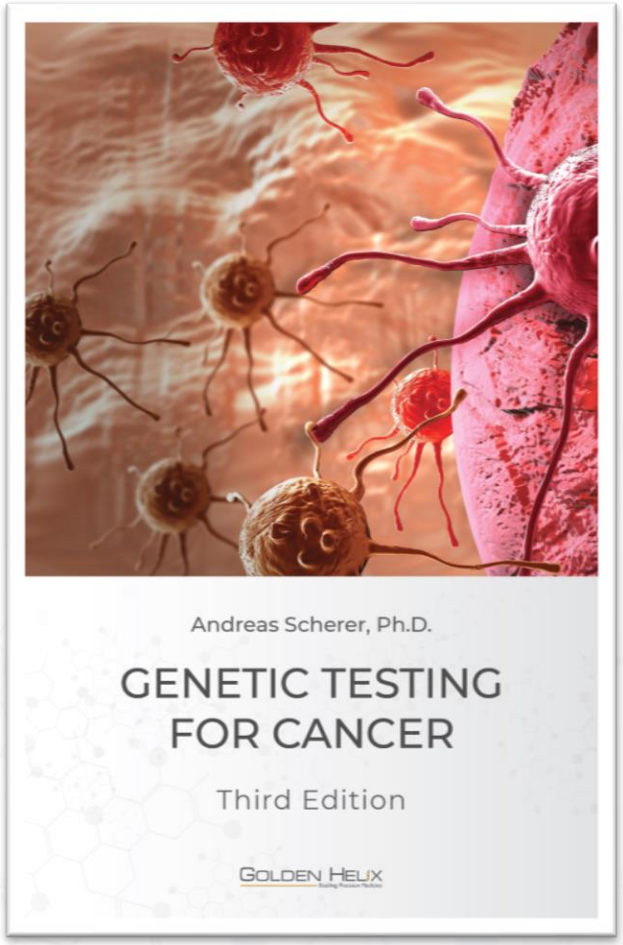
New eBooks





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