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GenepoweRx® Comprehensive testing

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Title: GenepoweRx® Comprehensive testing – an all-inclusive health management solution

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The **scope** and **usefulness** of an **individual's genomic information** extended beyond mere assertions and affirmed its strength in patient-centric care. Whether prescribing and using appropriate medications, making fitness recommendations or formulating feeding plans by physicians, genomics is the primary driver of the overall health plan. The GenepoweRx®'s Comprehensive test is an all-inclusive health management solution. This white paper aims to inform healthcare professionals on the importance of precision medicine in managing healthy life.

The GenepoweRx® comprehensive test:

- Helps to mitigate polypharmacy, optimize medication regimens, and give recommendations to optimize fitness training and performance based on the individual's genetic composition.
- Helps to give an idea of how the genetics of the individual affects metabolism and response to nutrients and other bioactive in food.
- Helps estimate the risk of developing metabolic disorders and cancers and reduce the risk of getting them by recommending lifestyle changes.

Our test helps identify patients who will not respond to certain drugs. Non-respondents might be offered other approved therapies, which will shorten the length of treatment if they were in standard-of-care clinical practice. Therefore, it is anticipated that the response rate for each individual to appropriate treatment within the population will increase. Consequently, more patients will quickly receive a remission or a good than under the current paradigm, improving patient outcomes and considerable savings in health costs.

Large amounts of complex genetic, clinical, and scientific data from extensive literature reviews and considerations for health care providers and patients are a substantial challenge. We have integrated the Pharmacogenomics Knowledge Base (PharmGKB) to collect and catalog scientific literature related to pharmacogenomics and used Pharmacogenetics Implementation Consortium (CPIC) peer-reviewed guidelines that are critical for providing the context and guidance necessary for implementing pharmacogenetics in clinical settings. The guidelines from CPIC are not designed for an end-to-end solution (from testing to careful considerations for providers) and are informative for specific gene-drug or phenotype-drug pairings only. We focus on the time-consuming process of curating and rendering substantial data within a software framework with broad user considerations. Information related to nutrigenomics, fitness, disease risk and cancer screening are also collected from various sources mentioned in figure 4.

General Variant Classification/ Assertion criteria

Variant documentation and elucidation are critical steps in making genetic diagnosis and personalized medicine a reality. The in-house method of variant classification at GenepoweRx® includes evidence from various sources like PharmGKB, ACMG, LitVar, PubMed, PubMedCentral, ClinVar.

Levels of evidence

PharmGKB guidelines

The assignment of clinical annotation levels of evidence (LOE) is primarily informed by the PharmGKB annotation scoring system for clinical annotations and variant annotations (Figure 1, Figure 2).

Figure 1: Level of evidence assigned by PharmGKB

PharmGKB annotation scoring system for clinical annotations and variant annotations			
LEVEL OF EVIDENCE	**STANDARD SCORING RANGE**	**RARE VARIANT SCORING RANGE**	**DESCRIPTION**
1A	≥80	≥80	Level 1A clinical annotations describe variant-drug combinations that have variant-specific prescribing guidance available in a current clinical guideline annotation or an FDA-approved drug label annotation. Annotations of drug labels or clinical guidelines must give prescribing guidance for specific variants (e.g. CYP2C9*3, HLA-B*57:01) or provide mapping from defined allele functions to diplotypes and phenotypes to be used as supporting evidence for a level 1A clinical annotation. Level 1A clinical annotations must also be supported by at least one publication in addition to a clinical guideline or drug label with variant-specific prescribing guidance.
1B	25 - 79.9375	10 - 79.9375	Level 1B clinical annotations describe variant-drug combinations with a high level of evidence supporting the association but no variant-specific prescribing guidance in an annotated clinical guideline or FDA drug label. Level 1B clinical annotations must be supported by at least two independent publications.
2A	8 - 24.9375 and variant in a Tier 1 VIP	3 - 9.9375 and variant in a Tier 1 VIP	Variants in Level 2A clinical annotations are found in PharmGKB's Tier 1 Very Important Pharmacogenes (VIPs). These variants are in known pharmacogenes, implying causation of drug phenotype is more likely. These clinical annotations describe variant-drug combinations with a moderate level of evidence supporting the association. For example, the association may be found in multiple cohorts, but there may be a minority of studies that do not support the majority assertion. Level 2A clinical annotations must be supported by at least two independent publications.
2B	8 - 24.9375	3 - 9.9375	Variants in Level 2B clinical annotations are not in PharmGKB's Tier 1 VIPs. These clinical annotations describe variant-drug combinations with a moderate level of evidence supporting the association. For example, the association may be found in multiple cohorts, but there may be a minority of studies that do not support the majority assertion. Level 2B clinical annotations must be supported by at least two independent publications.
3	0 - 7.9375	0 - 2.9375	Level 3 clinical annotations describe variant-drug combinations with a low level of evidence supporting the association. This association may be based on a single study annotated in PharmGKB, or there may be several studies that failed to replicate the association. The annotation may also be based on preliminary evidence (e.g., a case report, non-significant study, or in vitro, molecular, or functional assay evidence), resulting in a lower calculated score.

Figure 2: PharmGKB annotation scoring system for clinical annotations and variant annotations

ACMG/AMP guidelines

GenepoweRx® complies with the American College of Medical Genetics (ACMG) standards [1, 2]. GenepoweRx® designed internal criteria to refine ACMG/AMP guidelines based on the latest data available for assessing the strength of the variant and the most recent information specific to genes & gene-phenotype association. We devised standard internal guidelines to assess the robustness of publicly available information, gene-disease relationship, the clinical impact of nucleotide variations, the availability of treatments, and preventive measures [3-8].

GenepoweRx variant interpretation features a combination of open-source tools with automated in-house algorithms. There is a wide range of information retrieval from public resources and in-house databases through machine learning approaches, and a team of qualified professionals does an in-depth evaluation.

In the assessment of the variant classification, GenepoweRx® considers information and evidence that includes, but is not subjected to, the following five major parameters. The functional impact of the gene in causing the disease phenotype, functional impact of variation in the gene product based on *in silico*, *in vitro*, and *in vivo* studies, variant-disease association, prevalence and significance. All information derived from peer-reviewed

published literature, and in-house database testing, are considered when weighing a variant in favor of pathogenicity.

Variant Classification

GenepoweRx® classifies the variants into six groups as per ACMG guidelines and based on the above criteria. Consistency of the evidence is the key to categorizing each of the variants. It should be noted that documentation can make any early evidence obsolete.

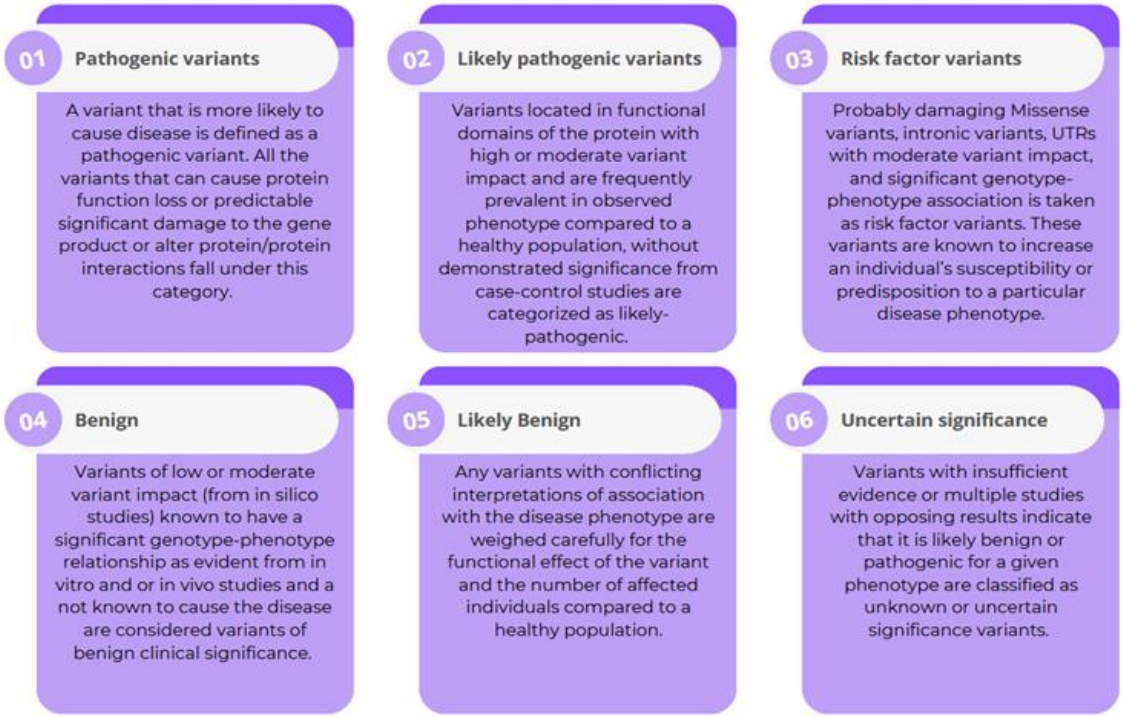

Figure 3: Variant classification of GenepoweRx

For rare disorders, proportionally lower allele frequencies are accepted as stand-alone criteria relative to the disease incidence. Open source population databases like 1000 Genomes, NHLBI Exome Sequencing Project (ESP), Exome Variant Server, and Exome Aggregation Consortium (ExAC) are screened for frequency of the variant in a control population. Additional databases, computational tools, and in-house algorithms are tested and considered as new sources of information become available.

Extensive interactions between the variant classification team, molecular biologists, bioinformaticians, and genetic counselors ensure continual progress in variant classification quality that facilitates the accuracy of classification results. All variant classifications are re-assessed at defined intervals for relevant updates that may influence the interpretation of the final report. Final reports are reviewed and approved according to clinical indications from the research director.

Review process

The Bioinformatics and Clinical Team at GenepoweRx® employs a rigorous process involving a stepwise extraction of published literature to examine genetic variants that potentially impact the pharmacokinetics and pharmacodynamics of a medication. The team conducts a systematic literature search of databases like PubMed, OMIM, and others using precise keywords to retrieve information regarding a specific medication and related genes/variants of interest. Figure 4 summarizes key sources of information used for curating data.

Source of Data	Description
CPIC	**Clinical Pharmacogenetics Implementation Consortium** (CPIC®) is an international consortium that is a collaboration between PharmGKB and the Pharmacogenomics Research Network (PGRN) in 2009. CPIC recommendations are indexed in PubMed as clinical guidelines, validated by ASHP and ASCPT, and referenced in ClinGen and PharmGKB. (https://cpicpgx.org/)
PharmGKB	The **PharmGKB** is a pharmacogenomics database. https://www.pharmgkb.org/
Google Scholar	**Google Scholar** helps to search for scholarly literature. https://scholar.google.com/
Ensembl	**Ensembl** (http://www.ensembl.org/) is a comprehensive source of stable automatic annotation of individual genomes and a framework for the integration of any biological data that can be mapped onto features derived from the genomic sequence.
PubMed	**PubMed®** encompasses more than 34 million citations for biomedical literature from MEDLINE, life science journals, and online books. https://pubmed.ncbi.nlm.nih.gov/
PubMedCentral	**PubMed Central®** (PMC) is a free full-text archive of biomedical and life sciences journal literature at the U.S. National Institutes of Health's National Library of Medicine (NIH/NLM). https://www.ncbi.nlm.nih.gov/pmc/
dbSNP	**dbSNP** consists of publication, population frequency, molecular consequence, and genomic and RefSeq mapping information pertaining single nucleotide variations, microsatellites, and small-scale insertions and deletions for both common variations and clinical mutations. https://www.ncbi.nlm.nih.gov/snp/
ClinVar	**ClinVar** aggregates information about genomic variation and its relationship to human health. https://www.ncbi.nlm.nih.gov/clinvar/
LitVar	**LitVar** helps retrieve variant pertinent information from the biomedical literature and displays key biological relations between a variant and its close related entities (e.g. genes, diseases, and drugs). https://www.ncbi.nlm.nih.gov/CBBresearch/Lu/Demo/LitVar/
FDA list of pharmacogenomic biomarkers and drug labeling	https://www.fda.gov/drugs/science-and-research-drugs/table-pharmacogenomic-biomarkers-drug-labeling
PharmVar	The Pharmacogene Variation (PharmVar) Consortium is a central repository for pharmacogene (PGx) variation that addresses haplotype structure and allelic variation. https://www.pharmvar.org/
OMIM	Online Mendelian Inheritance in Man is a catalog of human genes and genetic disorders and traits, with emphasis on the gene-phenotype relationship. https://www.omim.org/
MedGen	Organizes information related to human medical genetics, such as attributes of conditions with a genetic contribution. https://www.ncbi.nlm.nih.gov/medgen/
dbVar	dbVar is NCBI's database of human genomic Structural Variation — large variants >50 bp https://www.ncbi.nlm.nih.gov/dbvar/

Figure 4: Source of Literature for Pharmacogenomic reporting

A team of designated curators with experience in pharmacogenomics, nutrigenomics, fitness genomics, disease predictions, cancer risk screening, and literature analysis queries each source and prepares a complete and exhaustive summary of current evidence for individual drugs.

The team mines the evidence from related scientific articles including but is not limited to the following information: the comprehensive pharmacologic and clinical drug profile comprising generic drug name, indications, drug class, formulations (route of administration), the activity of parent compound, and metabolites, metabolism pathway and enzymes involved, mechanism of action, documented drug-to-drug interactions, inhibitor or inducer status, alternative medications, genes of interest, existing pharmacogenomic guidelines, and current pharmacogenomic evidence in the literature, affected status, clinical significance, the origin of allele, haplotypes where applicable, regions of regulatory importance. Information regarding immunity profile, nutrigenomics and fitness profile, blood factors, and risk assessment of various metabolic disorders and conditions like cancer are also described in detail along with possible management. All this information is consolidated in our in-house database.

Special attention is given to the impact on pharmacodynamic and pharmacokinetic properties of the medication by candidate genes/variants.

This comprehensive summary is then reviewed by a team of bioinformaticians, clinicians, pharmacologists, molecular biologists, and scientists, with a specialization in genetics and/or pharmacogenomics.

The comprehensive information for reporting and interpretation is then determined for inclusion, and documentation, and further added to a database, and specific algorithms are developed in parallel to ensure reproducible results.

Comprehensive Report Generation: Compiling Genetic, Clinical, and Drug-related information

- A medication interacts with multiple enzymes and receptors in the body in order to undergo pharmacokinetic and pharmacodynamic processes.
- Genetic variants in genes encoding more than one enzyme or receptor the drug interacts with can impact its pharmacology.
- In order to provide comprehensive information to providers, a multi-gene approach to data review and interpretation is utilized where applicable.
- Relevant literature is analyzed individually to deduce the predicted impact of each gene, followed by the designation of a unique level of evidence for each gene-drug interaction per burden of proof in order to determine the genes with the highest evidence on which to provide interpretation.
- The clinically relevant genetic variants isolated in the review process are then weighted proportional to their overall contribution and clinical impact in a combinatorial manner to provide a single, patient genotype-specific interpretation.
- The genomic data processing module processes the drug associations for the variants on a computing device and provides information regarding how effective associated drugs are for the user.

Here, the custom database (Custom DB) is a database comprising information on the regular drugs associated with the specific condition and helps in identifying the most effective drug for the user.

- The clinical significance data use the VCF information and classify records based on ClinVar annotations. Information from the ClinVar database is added for each genetic record.
- Information of each record after ClinVar annotation regarding drug-related info is added from the Custom DB.
- the variants along with normal response data to a drug response calculator from the pharmacogenomics module
- Classifying the response of a drug by the drug response calculator for a specific ailment into categories like poor, good, or intermediate
- Gathering information from the transient database to a nutrigenomics module for clinically significant information and also the one or more input files
- Querying, retrieving, and matching information of significant genes with a user's genomics information by the nutrigenomics module
- Interpreting records and phenotypic data of the user by the nutrigenomics module and documenting nutritional recommendations
- Persisting the clinical significance data along with the VCF information in a transient database which facilitates other modules – fitness genomics module, disease risk module, cancer risk module – to work with clinically significant data
- Using the interpretations of the records and the phenotypic data of the patient by a nutrigenomics module and recommendations are documented
- Calculating the strength of the response using a chi-square technique after determining the response score for each category

- The classified records are sent to a demystification module from the clinical significance module to simplify the process of interpretation and evaluation of the record's significance for a doctor (Figure 5)

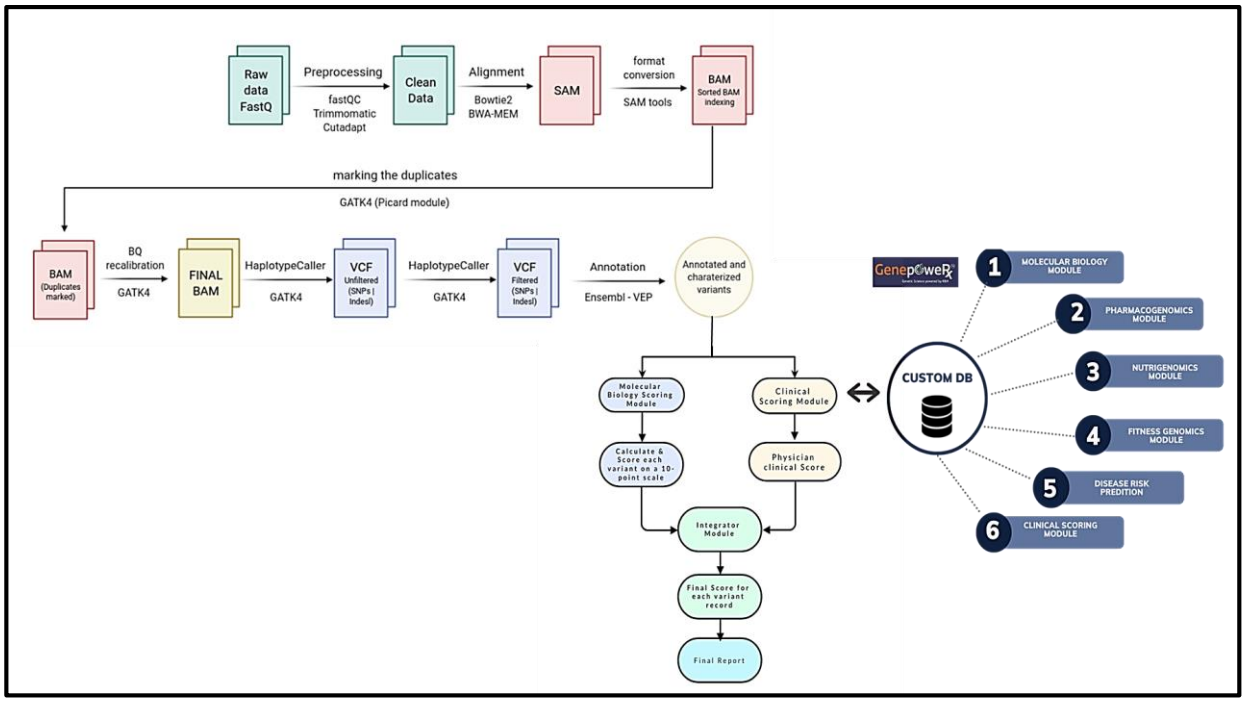

Figure 5: GenepoweRx in-house bioinformatics and reporting pipeline

Interpretation Methodology of GenepoweRx® Comprehensive genomics Test

1. Value allocation to disease-specific variants includes the assignment of values based on 10 different attributes of the variant, to derive a single score for each variant.

2. Normalization of the variant scores based on the disease conditions

3. The statistical significance is calculated and the ambiguous SNPs which do not attain the statistical significance are excluded. [statistics used: (t-tests and subsequent Z-scores (for determining the importance of each component when predicting this set))]

4. Analyze data statistically to derive FDR values and eliminate the false positives according to the FDR threshold

5. Identify cumulative frequency for final risk estimation

6. Repeat the steps for Molecular scoring and Physician clinical score

7. Load end values on a 10-point scale

8. Any records with no clinical significance are further checked through online analytics platforms about their genotypic and phenotypic information

Phenotypes follow CPIC's proposed standard nomenclature, where defined. For genes with no proven standards, phenotype outlines are stated based on existing literature on the functional impact of each SNP (https://www.pharmgkb.org/, https://www.omim.org/, https://www.ncbi.nlm.nih.gov/projects/SNP/, https://www.ncbi.nlm.nih.gov/clinvar/) [8,9].

Pharmacogenomics reporting categories

Medicines appearing on the GenepoweRx® Comprehensive Test are classified under categories, which are associated with colors to help visually and intuitively inform providers of the overall pharmacogenetic impact of the individual's genotype results on that medication. Medicines with gene-drug associations meeting a level of evidence of "2C" or higher, and having genotype results for all required genes associated, will appear on the Pharmacogenomics Test categorized into one of three levels of gene-drug interaction. Drug categories and associated colors, legend definition, and criteria for categorization are summarized in the following figures.

GLOSSARY

- **Pathogenic Variant** - This gene variant is more likely to cause disease
- **Risk Variant** - This gene variant is a risk factor for the disease
- **Benign Variant** - This gene variant has not shown to cause disease in the studies so far.
- **Homozygous** - Each gene has 2 copies in our body. Homozygous refers to inheriting 2 similar copies of a gene from the parents
    - Every person has two copies of same chromosome or DNA. Homozygous Normal refers to having same healthy gene in both copies of the DNA. Homozygous mutant refers to having mutated or altered DNA in both the copies of the gene.
- **Heterozygous** - Indicates 2 non identical or mismatched copies of a gene. i.e One normal copy and one mutated copy.
- The mutations can be Inherited from the parents or acquired (due to various exposures) during one's lifetime.

You have multiple structural variants, risk variants and a few benign variants for **Parkinson's Disease-Mild to Moderate chances. Multiple studies have shown that Gastrointestinal conditions are a precursor for Parkinson's disease.**	• **Strictly monitor your diet.** • **Please follow the dietary recommendations in the nutrition recommendation's part.**	
You have multiple mutations, mostly benign for **Cataract-**	• **Recommend yearly eye check up.**	
Few benign and risk variants for **mood disorders-**	• **Recommend meditation for at least 15 minutes every day.**	

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YOUR CURRENT MEDICAL CONCERNS

Concern – High Blood Pressure Few risk variants seen, a few benign variants seen- Likely a combination of genetic predisposition and lifestyle factors	• **Genes seen- ACAT1, WNK1, CYP11B1** • **Monitor BP at home every day and maintain a log.** • **DASH guidelines- Include more vegetables in your diet, Reduce Salt in diet**	
Concern- Diabetes A few benign mutations and risk variants seen- **Less likely to have uncontrolled diabetes and complications.**	• **Please monitor your HbA1C every 6 months.** • **Your carbohydrate sources should be complex carbs whole grains (Brown Rice, Hand Pounded Rice, Millets, Whole wheat flour), Green leafy vegetables.**	
Concern- Cholesterol Disorders Several benign variants, structural variants for cholesterol disorders- Moderate chances.	• **GENES SEEN- APOB, PCSK9, LDLR** • **Monitor lipid profile every 6 months. Consume only cold pressed oils. Monitor TSH levels.**	

CANCER RISKS

COLON CANCER- MILD RISK	• Recommend colonoscopy, within the next 2 years. • **If you have symptoms like blood in the stools, weight loss, abdominal pain, fatigue, please let your doctor know.**	
BREAST CANCER- MILD RISK Positive for multiple structural variants.	• Recommend yearly mammogram. • **Include foods like green leafy vegetables, buttermilk, sprouts.** • **If you have symptoms like lump in the breast, please let your doctor know.**	
Risk of other cancers- solid or blood, low.		

FITNESS RECOMMENDATIONS

Below is a snapshot of your fitness genomics -

1. Genes for Glycogen Storage Disorders seen- **Need a pre workout snack rich in complex carbohydrates as glucose may not be readily available during work outs.**
2. **Medium chain acyl coa dehydrogenase deficiency-** Can cause muscle aches, decreased exercise tolerance and fatigue. **Avoid high fat diets and prolonged periods of fasting. Include riboflavin supplementation or riboflavin rich foods like dairy, green vegetables.**

NUTRITION RECOMMENDATIONS

a. Nutrigenomics	❖ **Avoid cold foods like ice creams- Positive for a gene, NLRP3,** Excessive cold exposure, ingestion of cold foods, stress can lead to joint dysfunction, muscle aches, fatigue. ❖ **Genes for HMG CoA Lyase deficiency seen- Avoid fasting. Advise Low protein diet** ❖ You have **genes for 3 MCC deficiency- can cause hair loss and aging skin. Include biotin rich foods like soy bean, lentils.** ❖ **Mutations seen in anemia related genes (Megaloblastic)- Can cause symptoms of tingling and numbness. Include dark green leafy vegetables, Vitamin B12 supplementation.**

IMMUNITY PROFILE

You have homozygous mutations in the following genes, which are clinically pertinent-

FAS- Gene is responsible for pathway of programmed cell death. Mutations can lead to autoimmune disorders and solid tumors. **Screening for solid tumors as per guidelines. Yearly physical exam and regular follow up with your physician.**

BTK – This gene is crucial for B cell development and immunoglobulin activity. Mutations can predispose to recurrent respiratory infections, esp upper respiratory tract and infectious diarrhea. **Breathing exercise, proper hand hygiene, avoid eating outside.**

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PHARMACOGENOMIC ANALYSIS AND DRUG RESPONSE STATUS

(FDA, CPIC & PharmGkb Approved Biomarker evaluation)

1. G6PD STATUS

No risk of predisposition to G6PD deficiency.

Gene name & rsid	Zygosity	Condition	Clinical Significance
G6PD rs2230037	Heterozygous	Anemia, nonspherocytic hemolytic, due to G6PD deficiency	Benign
G6PD rs2071429	Heterozygous	none provided	Benign

2. RESPONSE TO ANTIPLATELET AGENTS

Good Response	Intermediate Response	Poor Response
Aspirin, Aspirin+Prasugrel, Clopidogrel, Prasugrel	--	Aspirin+Clopidogrel, Ticagrelor

CPIC Guidelines for Antiplatelet therapy recommendations

(When considering clopidogrel for ACS patients undergoing PCI based on CYP2C19 status)

CPIC Guideline- Recommended dosing of simvastatin based on SLCO1B1 phenotype.

Phenotype	Examples Of Diplotypes	Genotype At rs4149056	Implications For Simvastatin	Dosing Recommendations For Simvastatin	Classification Of Recommendations
Normal function, Homozygous wild-type (two normal function alleles)	*1a/*1a, *1a/*1b, *1b/*1b	TT	Normal myopathy risk	Prescribe desired starting dose and adjust doses of simvastatin based on disease-specific guidelines.	Strong

METABOLISM STATUS

Increased Metabolism	Intermediate Metabolism	Decreased Metabolism
Anticoagulants - Warfarin Calcium Channel Blockers – Amlodipine, Verapamil Angiotensin II Receptor Blockers (ARBS) - Losartan,	Antiarrhythmic Drugs - Propafenone Calcium Channel Blockers - Nifedipine Beta Blockers - Metoprolol Gastrointestinal Drugs (Proton Pump Inhibitors) - Rabeprazole	Glinides - Repaglinide Gastrointestinal Drugs (Proton Pump Inhibitors) - Dexlansoprazole Cough Medicine - Codeine Antibiotics - Erythromycin

DOSAGE RECOMMENDATIONS

Increased Dose	Intermediate Dose	Decreased Dose
Antiplatelet Agents – Ticagrelor Anticoagulants – Acenocoumarol, Apixaban, Phenprocoumon Antiarrhythmic Drugs - Flecainide Angiotensin II Receptor Blockers (ARBS) – Telmisartan, Irbesartan Sulfonylureas - Tolbutamide HMG coa reductase inhibitors (Statins) – Simvastatin, Atorvastatin, Pitavastatin,	Antiplatelet Agents - Clopidogrel Painkillers (Analgesics, NSAIDs) – N-Desmethyltamoxifen	Anticoagulants - Warfarin Beta Blockers – Carvedilol, Metoprolol, Atenolol Biguanides - Metformin Glinides - Repaglinide HMG coa reductase inhibitors (Statins) - Pravastatin Painkillers (Analgesics, NSAIDs) - Fentanyl Antibiotics - Cyclosporine+Dicloxacillin (In cystic fibrosis), Dicloxacillin

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SIDE EFFECTS

To note: We recommend drugs listed as low side effect response (Low SE).
If you are on drugs listed as High SE (High side effect), consider an alternative.

Brief Report

Molecules	Side Effects Status	Likely Side effect
Antiplatelet Agents		
Aspirin	Low SE	Myocardial Infarction /Cardiovascular Events/ Peptic Ulcer Hemorrhage/ In-Stent Restenosis/ Chronic Urticaria / Asthma / Gastrointestinal Bleeding
Aspirin+Clopidogrel	Low SE	Cardiovascular Events (Cardiac Death and Recurrent Myocardial Infarction)
Clopidogrel	Low SE	Neurological Events/ Hemorrhage/ In-Stent Thrombosis / Transient Ischemic Attack

DETAILED REPORTS

Note: A small value for Chi square (Strength of the study) indicates a high correlation between Good and Poor response studies. Hence, drug molecules which have $P \leq 0.5$ or small Chi-square values are to be considered while drug decision making.

RESPONSE TO ANTIPLATELET AGENTS

No of variants analyzed: 71
No of gene markers evaluated: 40
Data validated on: 333935 individuals
No of studies evaluated /Supportive evidences (Publications): 358

Drug Molecule	% GOOD response studies	% POOR response studies	Response status	Chi square value	*P* value
Aspirin	62.50	37.50	Good	6.25	0.01
Aspirin+Clopidogrel	25.00	75.00	Poor	25.00	0.00
Aspirin+Prasugrel	100.00	0.00	Good	100.00	0.00
Clopidogrel	56.25	43.75	Good	1.56	0.21
Prasugrel	87.50	12.50	Good	56.25	0.00
Ticagrelor	0.00	100.00	Poor	100.00	0.00

DISCLAIMER

1.Genetic testing using the methods applied at K&H is expected to be highly accurate.

2. Normal findings do not rule out the diagnosis of a genetic disorder since some genetic abnormalities may be undetectable with this test.

3. This test cannot reliably detect mosaicism. Some genes have inherent sequence properties (for example: repeat, homology, or pseudogene regions, high GC content, rare polymorphisms) that may result in suboptimal data, and variants in those regions may not be reliably identified.

4. False negative results may also occur in the setting suboptimal DNA quality.

5. The chance of a false positive or false negative result due to laboratory errors incurred during any phase of testing cannot be completely excluded.

6. Interpretations are made with the assumption that any information provided on family relationships is accurate. Consultation with a genetics professional is recommended for better interpretation of results.

7. Collection, processing, use, storage and retention of the anonymized data, the sample collected and related anonymized reports from the tests conducted for ongoing test developments, educational, scientific research and/or other related activities.

Summary

We have stabled a strong data hub integrating disparate high-content data from databases as mentioned in figure 4. By applying advanced machine learning and deep learning model techniques, we have derived novel insights and helped drive data-driven decisions. Once the blood sample is collected, the first step is to extract DNA. The extracted DNA is then prepped and ready to be loaded for genomic analysis. The genomic analysis is conducted on a highly advanced platform called the "Next-Gen Sequencer" (NGS). The raw data from the NGS is then run thru a pipeline of open-source computer tools and in-house custom tools, including our proprietary database. The resultant genetic data is then cataloged based on the cumulative effect of the different gene variants for each condition. Finally, the report is generated keeping in mind your medical history, food habits, and lifestyle. The GenepoweRx® Comprehensive Test integrates meticulously curated information from literature and accredited professional communities. Data structures are designed for comprehensibility and easy incorporation into other systems. Phenotype and clinical elucidations are based on a procedure established to be clinically pertinent in explaining gene function, and also conform to phenotypic regulations published by a recognized pharmacogenetics association. The GenepoweRx® Comprehensive Genomic Test delivers translation of this information into a comprehensive, innate format for use by healthcare practitioners.

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