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Your genetic guide to

PERSONALIZED MEDICINE

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Introduction

Pharmacogenetics identifies the variations in genes that encode drug-metabolizing enzymes, drug transporters, and drug targets, as well as other specific genes related to the action of drugs. Any variations in the deoxyribonucleic acid (DNA) sequence can change the protein structure, which translates into major differences in how the protein functions. The study of these variations in DNA sequence related to drug response is referred to as pharmacogenomics, and its testing requires genotyping to detect specific variants.

A Pharmacogenomics test provides information about a person's genetic makeup to help the physician decide which medications and doses might work best. It also helps to reduce the cost and time associated with a trial-and-error approach to treatment. The results of this test should be used as a supplement to the clinical decision-making process and should not replace or override appropriate clinical judgment.

This panel is based on relevant literature sources that may provide clinical insights to help inform the physicians about a patient's genetic changes to optimize patient treatment considerations and outcomes. This panel can be used to optimize therapy for listed ~200 commonly prescribed drugs ranging in multiple categories, including statins, platelet aggregation inhibitors, biguanides, sulfonylureas, anticoagulants, beta-blockers, antihypertensives, proton pump inhibitors, non-steroidal anti-inflammatory drugs, and antiarrhythmics. Based on the SNP-drug interaction, the drug metabolic status and evidence levels are reported.

Some interesting facts about genes and your medications-

- **Adverse Drug Reactions (ADRs) are estimated to be between the 4th and 6th leading cause of death in the US.**
- **75% of patients have detectable changes in their DNA that impact drug metabolism**
- **100+ drugs carry product label FDA guidance on pharmacogenetic testing**
- **The CYP2D6 gene processes 25% of all cytochrome-metabolized drugs.**
- **Research on the benefits of pharmacogenomic recommendations in the long term care of patients showed that nearly 50% of the patients had to change one to three drugs, with significant estimated savings annually.**
- **Codeine, a commonly used pain medication, is poorly metabolized by CYP2D6 ultra-rapid metabolizers. These individuals may experience symptoms of extreme sleepiness, shallow breathing, and even confusion. They may not have sufficient relief from pain as they will be unable to convert codeine into its active form.**
- **In a recent review conducted by King's College London, thirty-three economic evaluations (75%) supported PGx-guided treatment, 11 studies (25%) found PGx cost-effective, and 22 studies (50%) showed that it was dominant and cost-saving.**
- **In a study conducted by the Medical University of Vienna, the fraction of patients with an actionable genetic profile was 69% for warfarin, 28.5% for clopidogrel, 23% for tacrolimus, 25.7% for simvastatin, and 9.1% for thiopurines.**

In this report, we profile gene variants associated with your metabolic responses to various drug therapies. This report can help your physician prescribe for you-

The Right Medication at The Right Dose!

Introduction

Human health is a complex interplay between genetics and the environment (lifestyle, diet, activity, stress, and other factors). Your genes, diet, and lifestyle all play a vital role in your well-being.

This report is presented in a user-friendly language and format. The following tips will help you get the best information value out of the report.

- **What are the various metabolizer phenotypes?**

Ultra Rapid metabolizers (UM) are individuals with variants associated with elevated drug metabolism.

Extensive metabolizers (EM) are individuals with variants associated with fast drug metabolism.

Poor metabolizers (PM) are individuals with variants associated with poor drug metabolism.

Intermediate metabolizers (IM) are individuals with variants associated with moderate drug metabolism.

Normal metabolizers (NM) are individuals with variants associated with normal drug metabolism.

Indeterminate (IN) means that your metabolizer status could not be determined.

- **Where did the information contained in the report come from?**

The information presented in this report is curated by our team of scientists from various high authority sources such as the Clinical Pharmacogenetics Implementation Consortium (CPIC), the Royal Dutch Association for the Advancement of Pharmacy - Pharmacogenetics Working Group (DPWG), the Canadian Pharmacogenomics Network for Drug Safety (CPNDS) and other professional societies and sources.

- **How do I understand the information in the report?**

The report is organized by the drug names and areas of use. For example, you will find "ANALGESICTRAMADOL," which means that the drug is Tramadol, and it's used as an analgesic. Right underneath, you will find your "diplotype" (genetic type) and your Metabolizer status, indicated as NM, PM, EM, etc.,

(please see question 1 above).

Explanation of terms used in the report-

Recommendations- Drug recommendations based on your genetics

Implications- Implications for your therapy

Evidence Level- Classification of the reliability of evidence, with 1 being the highest.

Evidence Strength- The strength of this recommendation is based on clinical evidence found in published literature.

Your Summary Results

Trait Name	Your Result	[illegible]
CYP2B6	*1/*6	[illegible]
CYP2C19	*1/*17	[illegible]
CYP2C9	*1/*1	[illegible]
CYP2D6	*2/*2	[illegible]
CYP3A5	*3/*3	[illegible]
NUDT15	*1/*1	[illegible]
SLCO1B1	*1/*15	[illegible]
TPMT	*1/*1	[illegible]
UGT1A1	*80+*28/*80+*28	[illegible]

3,4-Methylenedioxymethamphetamine|
SLC6A2 | rs2242446-TT|

Evidence Level: 3

Recommendations:

[illegible]

Genes Analyzed: SLC6A2

Antihypertensives|
ATP2B1 | rs12817819-CC|

Evidence Level: 3

Recommendations:

[illegible]

Genes Analyzed: ATP2B1

Antihypertensives|
PTPRD | rs324498-AG|

Evidence Level: 3

Recommendations:

Genes Analyzed: PTPRD

Antihypertensives|
| rs11749255-AA|

Evidence Level: 3

Recommendations:

Genes Analyzed:

Antihypertensives|
| rs6487504-TT|

Evidence Level: 3

Recommendations:

Genes Analyzed:

Beta Blocking Agents|
ADRB2 | rs1042713-AG|

Evidence Level: 4

Recommendations:

Genes Analyzed: ADRB2

Beta Blocking Agents|
GRK5 | rs11198893-AG|

Evidence Level: 3

Recommendations:

Genes Analyzed: GRK5

Dipeptidyl Peptidase 4 (Dpp-4) Inhibitors|
CDKAL1 | rs7754840-GG|

Evidence Level: 3

Recommendations:

Genes Analyzed: CDKAL1

Dipeptidyl Peptidase 4 (Dpp-4) Inhibitors|
CDKAL1 | rs7756992-AA|

Evidence Level: 3

Recommendations:

[redacted]

Genes Analyzed: CDKAL1

Drugs Used In Diabetes|
IRS1 | rs1801278-CC|

Evidence Level: 3

Recommendations:

[redacted]

Genes Analyzed: IRS1

Drugs Used In Nicotine Dependence;Nicotine|
CHRNA3 | rs1051730-AG|

Evidence Level: 3

Recommendations:

[redacted]

Genes Analyzed: CHRNA3

Drugs Used In Nicotine Dependence;Nicotine|
CHRNA3 | rs1051730-AG|

Evidence Level: 3

Recommendations:

[redacted]

Genes Analyzed: CHRNA3

Hepatitis Vaccines|
IL13 | rs1295686-CC|

Evidence Level: 3

Recommendations:

Genes Analyzed: IL13

Hepatitis Vaccines|
IL4R | rs1805015-TT|

Evidence Level: 3

Recommendations:

Genes Analyzed: IL4R

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Genetic information must always be considered in conjunction with other information about your health such as lifestyle, family history, risk factors, biomedical data, diet, nutrition, and physical activity, among several other factors. Gene mutation is not the only factor that influences health conditions or outcomes. There are several other factors, such as the environment and lifestyle, that may influence your health outcome. You are responsible for ascertaining that your Professional Practitioner is qualified to consider the genetic information indicated in this report in conjunction with all other information made available to him/her about you, including your family health history, lifestyle, bio-medical data, and any other information that you may provide to the Professional Practitioner. Xcode shall not be held responsible for any misinterpretation by your Professional Practitioner of this Report or for any matter arising out of this report.

Only full genome sequences are exhaustive. All other forms of genetic tests only provide a limited subset of genetic information that has been found to be relevant to specific conditions. Since this report is not generated by conducting a whole-genome sequence test, the results reported are limited to a specific set of mutations known to be associated with specific conditions. Genetic information is also subject to revisions based on the latest advances in scientific research. Therefore, it is possible that the interpretation of results reported herein may vary or be altered subject to ongoing research. Sometimes, the interpretations may vary from company to company based on which studies are being given a higher preference compared to others.

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