Interpreting Your Incite Health™

Pharmacogenomics Reports

incite health™

What is Pharmacogenomic Testing?

The Incite Health Pharmacogenomic Tests

evaluate your DNA to determine how your genetic profile influences your response to certain medications. These tests help healthcare professionals make informed medication selection and dosing decisions that are optimal for you, all while reducing the risks of side-effects.

The Incite Health Pharmacogenomic VeriDose Core Test

provides pharmacogenomic information for a range of drugs targeting...

- Mental Health
- Cardiovascular Disease
- Neurology
- Autoimmunity
- Pain Management
- Gastroenterology
- Cancers
- Infections

How Does Pharmacogenomic Testing Work?

Pharmacogenomic testing is a cutting-edge advancement in medical science that allows us to personalize medication plans based on an individual's genetic profile. This revolutionary approach helps to ensure safer, more effective treatments with fewer, potentially dangerous side-effects.

01

Once we receive your buccal swab sample at the Incite Health Laboratories, **we extract your DNA.**

02

We then use a technique known as Polymerase Chain Reaction (PCR) to amplify around 20 of your genes that are associated with drug absorption, metabolism, and excretion.

03

By looking at the variations that you have for each of these genes, **we apply a combinatorial approach to build your genetic profile** and use this to make recommendations for prescription drug selection and dosing.

04

These recommendations are based on guidelines published by the Clinical Pharmacogenetics Implementation Consortium (CPIC) and the Dutch Pharmacogenetics Working Group (DPWG), as well as in studies reviewed by the Food and Drug Administration (FDA).

05

All of this ensures the clinical validity of your data and enables Incite Health to provide up to date reporting based on the very latest published clinical studies.

06

Our Short Report provides you with a summary of your genetic profile based on this test. **Our Long Report provides your doctor with a comprehensive breakdown of your metabolic profile** across a range of widely prescribed medications.

Interpreting Your Short Report

You can see that there are several sections to your Short Pharmacogenomics Report.

1 The *Summary of Genetic Lab Data & Phenotypes* lists all of the genes examined along with your specific gene variants also known as alleles; we refer to this as your *'genotype'*.

Summary of Genetic Lab Data & Phenotypes

Attention

Clinically significant alleles were detected in the HLA genes which are associated with increased risk for severe drug-induced cutaneous adverse reactions (SCAR), including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and maculopapular exanthema (MPE).

Allopurinol: See FDA product monograph and CPIC guideline(doi:10.1038/clpt.2012.209)
Carbamazepine: See FDA product monograph and CPIC guideline(Tegretol Product Monograph, 2018)
Fosphenytoin: See FDA product monograph and CPIC guideline(Cerebyx Product Monograph, 2020)
Oxcarbazepine: See FDA product monograph and CPIC guideline(Trileptal Product Monograph, 2015)
Phenytoin: See FDA product monograph and CPIC guideline(Dilantin Product Monograph, 2018)

Gene	Allele Result	Phenotype Result
CYP2A6	*1/*9	Normal Metabolizer
CYP2D6	(*1/*1)3N	Ultrarapid Metabolizer
CYP2C9	*3/*3	Poor Metabolizer
CYP2C19	*1/*1	Normal Metabolizer
SLCO1B1	*1/*1	Normal Function
CYP2B6	*1/*1	Normal Metabolizer
CYP3A4	*1/*1	Normal Metabolizer
CYP3A5	*3/*3	Poor Metabolizer
UGT1A1	*1/*80	Intermediate Metabolizer

Descriptions of the three categories of drug-gene interactions based on your unique genotype:

1 Mild or no known interaction

The left column in **green** lists the drugs that are optimal for your treatment based on your genotype and have no to mild known gene-drug interactions. In most cases your healthcare provider will select one of these medications for your treatment unless there are other considerations.

2 Moderate gene-drug interaction

The central columns in **blue** lists all of the drugs that may not be optimal for you to be medicated with based on your genotype. These drugs have been shown to have moderate gene-drug interactions at 'Use As Directed' doses. Your healthcare provider may either recommend avoiding these drugs completely, or adjusting the dose at which you are prescribed these drugs, coupled with monitoring.

3 Serious gene-drug interaction

The right column in **navy blue** lists all of the drugs that you should avoid. These drugs have been shown to display serious gene-drug interactions based on your genotype.

2 The Medication Review compartmentalizes medications into these categories based on your unique genotype.

	1 Mild or no known interaction	2 Moderate gene-drug interaction: Consider alternative medications	2 Moderate gene-drug interaction: May require an increased dose	2 Moderate gene-drug interaction: May require a reduced dose	2 Moderate gene-drug interaction: Efficacy may be affected by genetics	2 Moderate gene-drug interaction: Increased risk of adverse events	2 Moderate gene-drug interaction: See TreatGx for dose calculations	3 Medication with serious gene-drug interaction should be evaluated carefully and alternative medications should be given
Analgesia	Alfentanil Carisoprodol Fentanyl Hydrocodone Morphine	Meloxicam Piroxicam Tenoxicam		Celecoxib Flurbiprofen Ibuprofen	Celecoxib Flurbiprofen Ibuprofen Meloxicam Piroxicam Tenoxicam	Acetylsalicylic acid Celecoxib Flurbiprofen Ibuprofen Meloxicam Piroxicam Tenoxicam		Codeine Imipramine Tramadol
Anesthesia	Desflurane Isoflurane Methoxyflurane Sevoflurane Succinylcholine							
Autoimmune	Azathioprine Cevimeline Cyclosporine Mercaptopurine Tacrolimus Thioguanine				Etanercept			Siponimod

Mild or no known interaction

May be used as directed under the drug label. These have no or low risks of adverse reaction with your specific genetic profile, based on published clinical data.

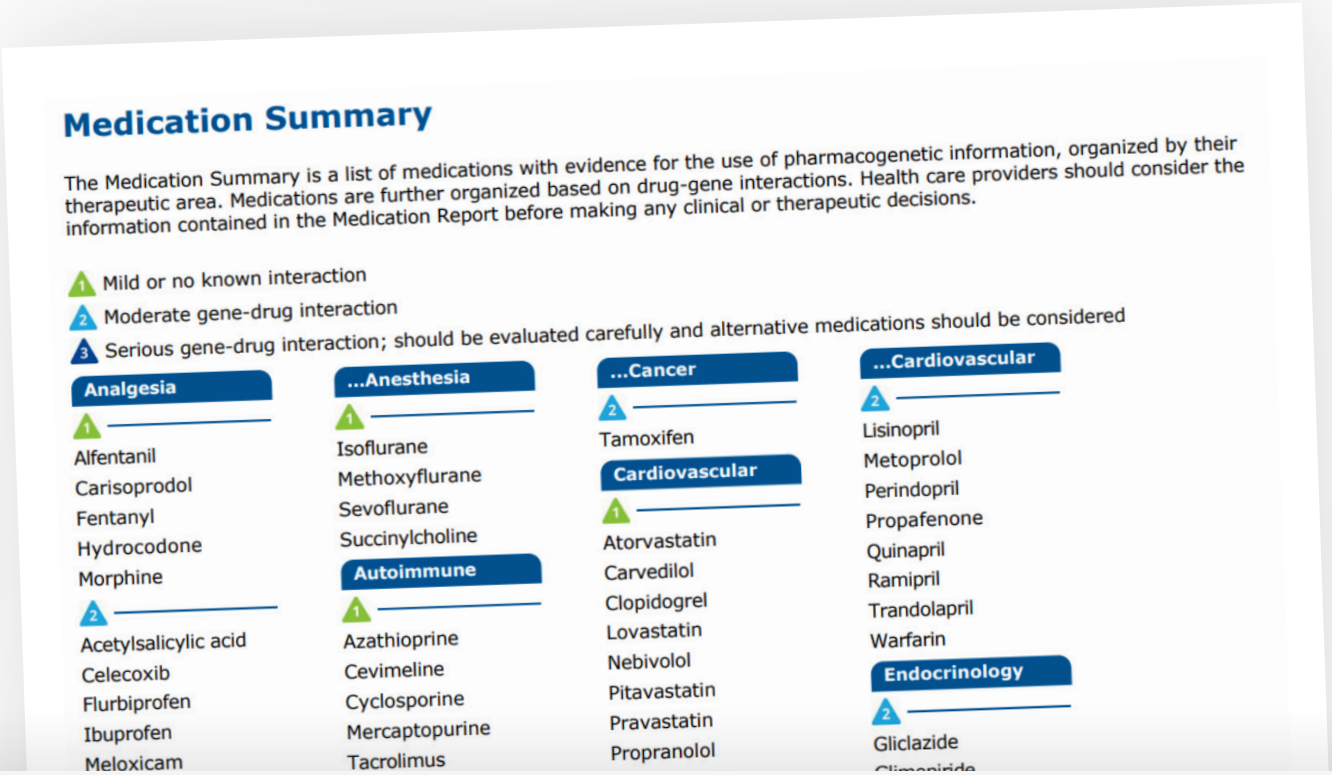
Moderate gene-drug interaction

May have reduced efficacy, or an increased risk of side effect when Used As Directed under the drug label. This is because your genetic profile is not optimal for that drug's performance. You can find a more detailed description of what this means under the Medication Report Listing under that drug name. There you will find a summary of your genotype and phenotype and the Implication they have on your response to that drug. For some drugs this is based on a single gene profile, but for others you will see more than one gene is influencing your phenotype to this drug. Your Healthcare Provider will use this information to assess if this drug is right for you at a modified dose, or if there are other alternative drugs for you based on this profile.

Serious gene-drug interaction

Should be avoided, if possible, based on available guidelines. This is because your genotype is associated with increased risk of adverse drug reaction with this drug. Your Healthcare Provider will use this information to make more informed and safer drug selections for your treatment.

Interpreting Your Long Report



Medication Summary

The Medication Summary is a list of medications with evidence for the use of pharmacogenetic information, organized by their therapeutic area. Medications are further organized based on drug-gene interactions. Health care providers should consider the information contained in the Medication Report before making any clinical or therapeutic decisions.

1 Mild or no known interaction
2 Moderate gene-drug interaction
3 Serious gene-drug interaction; should be evaluated carefully and alternative medications should be considered

Analgesia

1
Alfentanil
Carisoprodol
Fentanyl
Hydrocodone
Morphine

2
Acetylsalicylic acid
Celecoxib
Flurbiprofen
Ibuprofen
Meloxicam

...Anesthesia

1
Isoflurane
Methoxyflurane
Sevoflurane
Succinylcholine

Autoimmune

1
Azathioprine
Cevimeline
Cyclosporine
Mercaptopurine
Tacrolimus

...Cancer

2
Tamoxifen

Cardiovascular

1
Atorvastatin
Carvedilol
Clopidogrel
Lovastatin
Nebivolol
Pitavastatin
Pravastatin
Propranolol

...Cardiovascular

2
Lisinopril
Metoprolol
Perindopril
Propafenone
Quinapril
Ramipril
Trandolapril
Warfarin

Endocrinology

2
Gliclazide

1 **Within the *Medication Report* section, you'll see your phenotype listed for each drug. Your phenotype is your physiology or reaction to that drug based on your genotype. An example of how this information is presented is shown below:**

Example:

Generic name

Brand names

Potential Kidney interaction

Potential Liver interaction

Adalimumab	Phenotype	Genetic Test	Results	Source/Evidence
Amjevita Cyltezo Humira	Reduced response	TNS-alpha rs1800629	A/A	2B

Implication: TNF-alpha alleles may indicate a reduced response to Adalimumab

TreatGx
ReviewGx

These phenotype categories are based on a combined analysis of your variants or alleles across several genes. These genes are either Pharmacodynamic Genes or Pharmacokinetic Genes and are used to describe your drug metabolism profile for each medication.

Your Pharmacodynamic Genes provide a profile on how a given medication will work in your body, as well as highlight any risk for side effects. **Examples of these genes includes: ABCB1, ADRA2A, COMT, HTR2A, HTR2C/MTHFR, NAT2, OPRM1, SLC6A4.**

Your Pharmacokinetic Genes provide a profile on how your body will absorb and metabolize that drug, as well as excrete breakdown products. **Examples of these genes includes: CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP3A5.**

Ultrarapid Metabolizers breakdown certain medications rapidly, meaning that they may not get enough active drug in their bloodstream to be effective at the 'Use As Directed' doses.

At the other end of the spectrum, Poor Metabolizers breakdown certain medications very slowly, meaning they may not respond to these medications or may experience side effects at 'Use As Directed' doses.

2 The phenotype may include the following descriptions:

Typical risk of adverse drug reactions
means that your genetic profile is associated with the average level of risk associated with taking that drug at the 'Use As Directed' dose.

Increased risk of adverse drug reactions
means that your genetic profile is associated with an increased risk of adverse drug reactions when that drug is taken at the 'Use As Directed' dose. Your Healthcare Provider may either adjust the dose or switch to another medication.

Normal Metabolizer
means your phenotype displays normal rates of processing of this drug, and the drug is suitable for use at the 'Use As Directed' dose.

Intermediate Metabolizer
means your phenotype displays somewhat decreased rates at processing this drug, and therefore the use of this drug may require increased monitoring particularly early on or a dose adjustment.

Ultrarapid Metabolizer
means your phenotype displays very high rates of processing this drug. For some drugs, this means that they might be toxic at the 'Use As Directed' doses, for other drugs this means that they may be ineffective. The implication section of the report is used to guide your Healthcare Provider in next steps.

Poor Metabolizer
means your phenotype displays significantly decreased rates at processing this drug. There may be an impact on the effectiveness of this drug, or a dose adjustment might be required for efficacy. The implication section of the report is used to guide your Healthcare Provider in next steps.

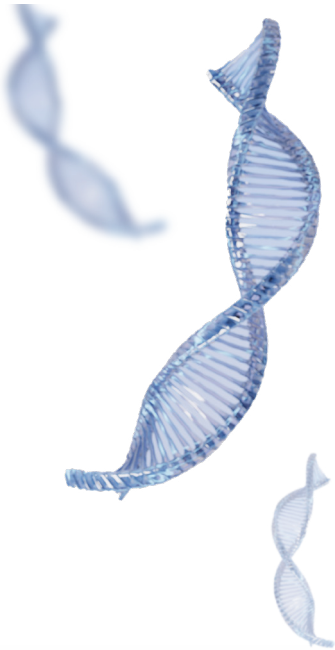
Normal Function means your phenotype does not require an adjustment of the 'Use As Directed' dose.

Typical Response
means your phenotype is associated with a normal response to the drug at the 'Use As Directed' dose.

Reduced Response
means your phenotype may indicate a reduced response to that drug.

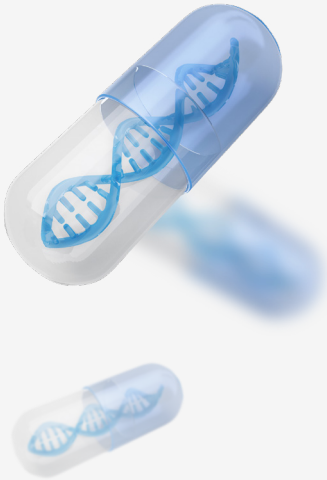
Increased Response
means your phenotype may have unpredictable effects on your response to the drug, and a dose adjustment may be required.

Frequently Asked Questions



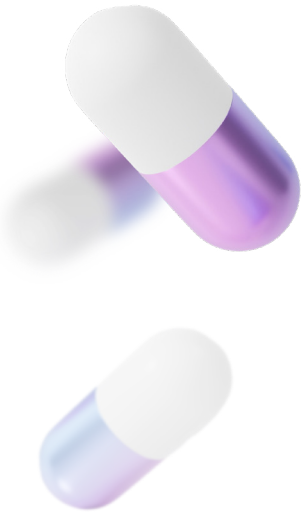
How will Incite Health's pharmacogenomic testing help me with my health goals?

Incite Health's Pharmacogenomic tests are designed to provide you with personalized medical solutions to manage your health and wellbeing most effectively. Sharing this information with your healthcare providers will help them select the optimal medications and doses of those medications as early on in your treatment plan as possible, and most importantly identify those medications that might cause you harm.



Will the drugs listed in the green column always work best for me?

Medications in the green column are expected to provide the best safety and efficacy profiles for you. That said, these medications may not necessarily work best for you. This is because the effectiveness of medication is based on a wide range of factors. Your genetics is an important part of this, but there are other factors also such as age, diet, drug-drug and drug-nutritional supplement interactions that can impact the effectiveness of some medications. What this test will do is let you know which drugs are most likely not to be effective for you, and which might even be dangerous for you to take. Think of this test as a tool in the toolkit for you and your healthcare provider.



Does my pharmacogenomic test result depend on the medications that I am taking?

No, your pharmacogenomic test results are based on your genetic profile (genotype) and not changed by medications.

Incite Health offers the ReviewGx report that enables your healthcare provider to review all of your current mediations and optimize these based on your sex, age, lifestyle, medical conditions, your blood test results and treatment regimes.

How often should I get the Incite Health pharmacogenomic test?

The pharmacogenomic test provided by Incite Health covers a significant portion of the genes involved in more than 70% of current medications on the market. So, this test will provide significant value to your personalized health journey throughout your lifetime. That said, the CPIC and DPWG guidelines are updated regularly and so if you are talking with your healthcare provider about starting a new medication, it is worth referencing our latest testing to see if you would benefit from the most up-to-date test available.

We hope this guide is helpful for you to understand your pharmacogenomic test reports more completely.

When it comes to your health, knowledge is power and the Incite Health Team strives to bring you the most powerful, state-of-the-art clinical testing solutions.

Incite Health also offers additional reporting solutions to healthcare providers:

ReviewGx

The ReviewPGx Report incorporates current medications into the patient's analysis to include drug-drug-gene interactions. This can be used in conjunction with Medication Therapy Management (MTM) and to develop Medication Action Plans (MAP). A ReviewPGx report may also consider patient demographics, allergies, medications, liver function, renal function, lab values. The report is then customized based on whether there is no change to a medication, medication change (with evidence, reason for change), or to adjust dose of a medication.

TreatGx

The TreatGx Report is targeted for specialized providers and specialist physicians as a core decision support engine for optimizing treatment options. The condition-based algorithm is multi-factorial, considering not only pharmacogenomic results, but existing drugs, previous drugs, liver function, kidney function, other conditions (diseases) the patient may have, and other lab tests. The report output summarizes the condition and treatment options based on these personalized factors.

For more information, please visit our website:

Search... **www.incitehealth.com**

Incite Health, Inc. is a CLIA-certified, CAP-accredited, high complexity clinical laboratory at the forefront of healthcare innovation by helping revolutionize clinical decision making.

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CLIA ID – 39D2176007

CAP Certificate of Accreditation – 9410964