

PATIENT NAME	PATIENT ID	SEX	DOB	REPORT TYPE
GCR, SampleReport_A	SampleReport_A	Male	01-01-2000	Genomic Clinical Report



PATIENT INFORMATION		
PATIENT NAME: GCR, SampleReport_A		
PATIENT ID SampleReport_A	SEX Male	DOB 01-01-2000
CASE ACCESSION GCR9652A383	SPECIMEN ID SPC837B974B	
TEST REQUESTED Genomic Clinical Report	COLLECTION DATE 08-21-2026	ORDERING PROVIDER Test Doc
SPECIMEN TYPE Whole Blood EDTA	INDICATION Healthy Adult Screening	SAMPLE ID SAM3329E1BA

Genomic Clinical Report

REVIEW STATUS: FINAL

Approvals and Comments

LABORATORY DIRECTOR	APPROVAL		
Henry Tsai, MD, PhD	Report electronically reviewed and signed out by: Henry Tsai	Location: SG-001	Date Reported: 09/10/2026 18:44:34 PDT

Hereditary Disease Risk

The scope of this section includes monogenic variants associated with high or moderate genetic risk for developing a disease. Variant zygosity and disease inheritance determine whether you or your children have an increased risk of disease. The results in this section should not be used to guide medical decisions without consulting with your physician beforehand. Any results which warrant a change in treatment should be confirmed by an accredited clinical laboratory's diagnostic test prior to making the change. Genetic counseling is recommended.

FINDINGS SUMMARY

GENOME SUMMARY

3.2 Billion	Base pairs analyzed
5.2 Million	Total variants detected
2011	Total genes assessed
2240	Total diseases assessed

YOUR RISK

YOUR DISEASE RISK

VARIANTS IDENTIFIED

Musculoskeletal Disorder

1

YOUR CARRIER STATUS

VARIANTS IDENTIFIED

Metabolic Disorder

2

Neurologic Disorder

1

Skin Disorder

1

Variant Summary

HEALTH CATEGORY	GENE	VARIANT	ZYGOSITY	CLASSIFICATION	DISEASE	INHERITANCE
Musculoskeletal Disorder	CLCN1	c.854G>A (p.Gly285Glu) NM_000083.2	Heterozygous	Pathogenic	Myotonia congenita	Autosomal Dominant; Autosomal Recessive
Metabolic Disorder (CARRIER)	PAH	c.1241A>G (p.Tyr414Cys) NM_000277.1	Heterozygous	Pathogenic	Phenylketonuria	Autosomal Recessive
Metabolic Disorder (CARRIER)	HFE	c.187C>G (p.His63Asp) NM_000410.3	Heterozygous	Risk Factor	Hemochromatosis	Autosomal Recessive

LABORATORY NAME	ADDRESS	CONTACT	CLIA	CAP	VERSION	PAGE
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HEALTH CATEGORY	GENE	VARIANT	ZYGOSITY	CLASSIFICATION	DISEASE	INHERITANCE
Neurologic Disorder (CARRIER)	TPP1	c.509-1G>A NM_000391.4	Heterozygous	Pathogenic	Ceroid lipofuscinosis, neuronal, 2	Autosomal Recessive
Skin Disorder (CARRIER)	FLG	c.7339C>T (p.Arg2447*) NM_002016.1	Heterozygous	Pathogenic	Ichthyosis vulgaris	Autosomal Recessive

Variant Details

Variant Associated with Musculoskeletal Disorder

	CLCN1 pathogenic variant, c.854G>A (p.Gly285Glu)	Allele Frequency: 0.0114% (gnomAD, European (Non-Finnish))
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Patient was found to have a pathogenic variant associated with an increased risk for Musculoskeletal Disorder.

The c.854G>A missense variant has been identified in several individuals affected with myotonia congenita in either heterozygous, compound heterozygous or homozygous state (PMID 9736777, PMID 21387378, PMID 12390967, PMID 18337730, PMID 24037712).

The CLCN1 gene codes for a protein called chloride channel voltage sensitive 1 that transports negatively charged chlorine atoms and plays a key role in a cell's ability to generate and transmit electrical signals. Pathogenic CLCN1 variants are associated with autosomal recessive and dominant forms of myotonia congenita (MIM 255700, MIM 160800). Beginning in childhood, individuals with this condition experience bouts of sustained muscle tensing that prevent muscles from relaxing normally. Although myotonia can affect any skeletal muscles, including muscles of the face and tongue, it occurs most often in the legs. Myotonia causes muscle stiffness that can interfere with movement. In some individuals the stiffness is very mild, while in other cases it may be severe enough to interfere with walking, running, and other activities of daily life. The autosomal recessive form of myotonia congenita (Becker syndrome) is often associated with more severe symptoms than the autosomal dominant form (Thomsen syndrome). Individuals with the autosomal recessive form may have progressive, minor distal weakness and attacks of transient weakness brought on by movement after rest. The age of onset is variable and for autosomal dominant myotonia congenita the onset of symptoms is usually during infancy or early childhood, whereas for the autosomal recessive form, the average age of onset is slightly older. The prevalence of myotonia congenita ranges from 1 to 10 in 100,000 individuals (ORPHA 614).

Variant Associated with Metabolic Disorder

	PAH pathogenic variant, c.1241A>G (p.Tyr414Cys)	Allele Frequency: 0.0692% (gnomAD, Other)
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Patient is a carrier for a pathogenic variant associated with a Metabolic Disorder. Reproductive partner and/or first-degree relatives may benefit from screening.

The c.1241A>G missense variant is the most common pathogenic variant associated with mild phenylketonuria (PKU) in Europe, especially among Scandinavians, and has been identified in a homozygous state in individuals affected with mild PKU or non-PKU hyperphenylalaninemia (PMID 8556304, PMID 9399896, PMID 23764561). Results from functional studies indicate that the c.1241A>G variant results in a mild decrease of the PAH enzymatic activity (PMID 18538294, PMID 19036622).

The PAH gene codes for phenylalanine-4-hydroxylase, an enzyme that catalyzes the hydroxylation of phenylalanine to tyrosine. Pathogenic PAH variants result in intolerance to dietary intake of phenylalanine and are associated with an autosomal recessive inborn error of metabolism disorder called phenylketonuria (MIM 261600). Phenylketonuria can be diagnosed by newborn screening in nearly 100% of the cases and treated successfully. However, if left untreated, affected individuals will have profound and irreversible intellectual disability, microcephaly, epilepsy, and behavioral problems (PMID 20301677). Phenylketonuria is primarily treated with a phenylalanine-restricted dietary regimen including monitoring of phenylalanine levels in the blood, however, neuropsychological symptoms may still persist in the form of decreased cognitive function and psychological problems (PMID 23266195). The estimated prevalence of phenylketonuria is 1 in 10,000 individuals (PMID 18184144, PMID 22552820).

Variant Associated with Metabolic Disorder

	HFE risk factor variant, c.187C>G (p.His63Asp)	Allele Frequency: 14.4269% (gnomAD, European (Non-Finnish))
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Patient is a carrier for a risk factor variant associated with a Metabolic Disorder. Reproductive partner and/or first-degree relatives may benefit from screening.

The c.187C>G missense variant is a low-penetrance variant observed frequently in general populations. The c.187C>G variant is considered to confer an increased risk for hemochromatosis only in individuals, who are compound heterozygous for the variant and a well-known pathogenic HFE variant, c.845G>A (PMID 26365338). Individuals homozygous for the c.187C>G variant are commonly asymptomatic without iron overload (PMID 8696333, PMID 11874997). The penetrance of the c.187C>G variant is estimated between 0.3% and 1.4% depending on the genotype and gender (PMID 11399207).

The HFE gene codes for a protein called homeostatic iron regulator, also known as hereditary hemochromatosis protein, involved in iron sensing and absorption. Defective HFE protein impairs the ability to limit iron uptake via the transferrin receptor leading to excessive iron absorption in the gastrointestinal mucosa and accumulation of iron in organs. Pathogenic HFE variants are associated with autosomal recessive hereditary hemochromatosis (MIM 235200) characterized by increased serum ferritin and iron storage in organs, leading to organ failure and high risk of cirrhosis, arthritis, cardiomyopathy, and hepatomas (PMID 18061062). Hemochromatosis presents with symptoms related to iron overload between 40 and 60 years of age, and after menopause in women. Individuals with hemochromatosis have a normal life expectancy if diagnosed before the development of liver cirrhosis (PMID 20301613). The prevalence of hemochromatosis ranges from 1 in 200 to 1 in 400 Caucasians and is less frequent in African Americans with a prevalence of 1 in 7,000 individuals (PMID 15858186).

Variant Associated with Neurologic Disorder

	TPP1 pathogenic variant, c.509-1G>A	Allele Frequency: 0.0026% (gnomAD, European (Non-Finnish))
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Patient is a carrier for a pathogenic variant associated with a Neurologic Disorder. Reproductive partner and/or first-degree relatives may benefit from screening.

The TPP1 gene codes for a protein called tripeptidyl-peptidase 1, a lysosomal serine protease that breaks down peptides into amino acids, especially into groups of three amino acids. Impaired function of the TPP1 protein result in accumulation of proteins in the lysosome leading to neurological dysfunction. Pathogenic TPP1 variants are associated with autosomal recessive late infantile neuronal ceroid lipofuscinosis (CLN2, MIM 204500). Late infantile neuronal ceroid lipofuscinosis is characterized by early visual impairment, behavioral problems and seizures (PMID 9295267, PMID 20340139). The onset of late infantile neuronal ceroid lipofuscinosis is typically between 2 and 4 years of age and is characterized by progressive seizures, dementia and retinal degeneration along with ataxia, ultimately leading to cortical and cerebellar degeneration with a fatal outcome (PMID 23374165, PMID 23266810). The overall prevalence of late infantile neuronal ceroid lipofuscinosis is less than 1 in 1,000,000 individuals (ORPHA 284324), however, incidence of 1 in 128,200 births in Italy and 1 in 11,161 births in Newfoundland has been reported (PMID 23374165, PMID 18684116).

Variant Associated with Skin Disorder

	FLG pathogenic variant, c.7339C>T (p.Arg2447*)	Allele Frequency: 0.6488% (gnomAD, European (Finnish))
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Patient is a carrier for a pathogenic variant associated with a Skin Disorder. Reproductive partner and/or first-degree relatives may benefit from screening.

The c.7339C>T nonsense variant results in truncated FLG protein and deficient function (PMID 17417636). The c.7339C>T variant has been frequently identified in a homozygous or compound heterozygous state in individuals affected with ichthyosis vulgaris or atopic dermatitis (PMID 19874431, PMID 27363669, PMID 26451970).

The FLG gene codes for profilaggrin, a protein found in the outermost layer of the skin called epidermis. Profilaggrin is processed to filaggrin, which is important for the structure of the epidermis, and plays an important role in the barrier function and hydration of the skin. Pathogenic FLG variants are associated with autosomal recessive ichthyosis vulgaris (MIM 146700) and autosomal dominant susceptibility to atopic dermatitis 2 (MIM 605803). Ichthyosis vulgaris is characterized by palmar hyperlinearity, keratosis pilaris, and a fine scale that is most prominent over the lower abdomen, arms, and legs. Impairment of the skin's barrier function can predispose to allergic conditions and infections. Atopic dermatitis is characterized by inflammation of the skin, which begins in early infancy and often disappears before adolescence. However, in some affected individuals, the condition continues into adulthood and in others, it does not manifest until adulthood. Hallmarks of atopic dermatitis include dry, itchy skin and red rashes that come and go. Hereditary ichthyosis vulgaris is a common disease in the United States, with a prevalence of approximately 1 in 300 individuals (PMID 12708996).

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Alzheimer's Disease Risk

Alzheimer's disease is a progressive disorder that causes a slow decline in an individual's memory, judgment, cognition, learning, and ability to live independently. Alzheimer's disease starts as a mild cognitive impairment, with an increase in forgetfulness and slight difficulty with focus or concentration. Alzheimer's disease is a prevalent condition; one in 10 people 65 years or older will develop the disease. Risk factors for Alzheimer's disease that you cannot change include age, past head traumas, family history, and genetic background (genetic factors contribute about 60 - 80% to the variability in risk between individuals of developing Alzheimer's disease). Risk factors that you can change are lack of exercise, obesity, smoking, unhealthy diet, heart disease, lack of lifelong learning, and social engagement. Some medicines may help delay and reduce the severity of symptoms. Note that this section only reports risk based on common risk variants in the APOE gene, and based on polygenic risk models. Other rare variants that are implicated in the development of Alzheimer's are reported in the Hereditary Risk Section of this report.

FINDINGS SUMMARY

APOE Status

E3/E3



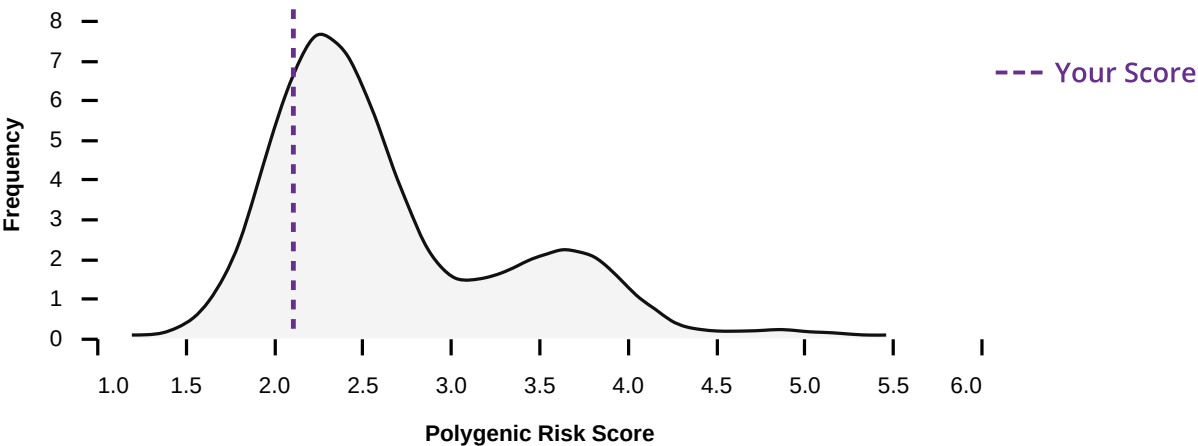
The 'neutral' E3/E3 genotype with two E3 alleles. The E3 allele is the most common APOE allele and does not have any genetic impact on the disease risk (PMID 17234815).

Polygenic Risk

Percentile: 12, Relative Risk: 0.9



Given the variants you carry, your genetic predisposition to Alzheimer's disease is greater than 12% of research participants of European descent. Your estimated genetic risk is 0.9 times that of an average person in the reference population.



The distribution of polygenic risk scores for research participants is shown in the figure along with the polygenic risk score computed from your genome (Your Score). The APOE E4 variant (rs429358) is a well-known genetic risk factor for Alzheimer's disease. On average, people without the APOE e4 variant have an approximately 10-15% chance of developing Alzheimer's disease during their lifetime. Having one copy of the variant increases lifetime risk of Alzheimer's disease to 20-25% and having two copies - up to 55%. The polygenic risk score for Alzheimer's disease includes 20 risk variants. One risk variant is the APOE e4 variant itself. The other 19 variants are a set of non-APOE variants. Each variant has a smaller effect than the APOE e4 variant, but together they make an important contribution to risk. The contribution of the E4 variant is evident as 3 separate modes in the distribution, corresponding to 0, 1, or 2 copies of the APOE E4 variant.

Pharmacogenomic Findings

The results of this section may help your doctor better understand how you process certain medications. The way you respond to drugs depends on genetics as well as other factors. Your doctor will take these factors into account when deciding which drug or what drug dose is the best for you. Do not stop taking or alter the dosage of any prescribed medications without consulting with your doctor beforehand. Only variants with an established drug association are included in the PGx reportable scope. Differences may be observed between the PGx and Hereditary Disease results.

FINDINGS SUMMARY

REPORTING SCOPE

27

Total genes assessed

224

Total drugs assessed

YOUR RISK



YOUR PHARMACOGENOMIC RESULTS

121 Drugs Potentially Impacted

Drugs Potentially Impacted

DRUG CATEGORY	GENE	GENOTYPE	PHENOTYPE	DRUG	COMMENTS
ADHD treatment	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Viloxazine (Qelbree®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).
ADHD treatment	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Atomoxetine (Strattera®)	Increased risk of side effects (e.g., blurred vision, dry mouth, constipation, decreased appetite, tremor, insomnia, erectile dysfunction) due to higher systemic concentration of atomoxetine. Dose reduction is recommended. Refer to FDA labeling for specific dosing recommendations (FDA drug label, CPIC guideline).
ADHD treatment	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Amphetamine (Adderall®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).

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Anesthetic	CACNA1S	No Pharmacogenomic Reportable Variants Found	Uncertain Susceptibility	Sevoflurane (Ultane®)	These results do not eliminate the possibility that this individual would be susceptible to malignant hyperthermia (MH). The genetic cause of approximately half of all malignant hyperthermia survivors, with MH susceptibility confirmed by contracture test, remains unknown (FDA drug label).	
Anesthetic	CACNA1S	No Pharmacogenomic Reportable Variants Found	Uncertain Susceptibility	Isoflurane (Forane®)	These results do not eliminate the possibility that this individual would be susceptible to malignant hyperthermia (MH). The genetic cause of approximately half of all malignant hyperthermia survivors, with MH susceptibility confirmed by contracture test, remains unknown (FDA drug label, CPIC guideline).	
Anesthetic	CACNA1S	No Pharmacogenomic Reportable Variants Found	Uncertain Susceptibility	Desflurane (Suprane®)	These results do not eliminate the possibility that this individual would be susceptible to malignant hyperthermia (MH). The genetic cause of approximately half of all malignant hyperthermia survivors, with MH susceptibility confirmed by contracture test, remains unknown (FDA drug label, CPIC guideline).	
Anesthetic	RYR1	No Pharmacogenomic Reportable Variants Found	Uncertain Susceptibility to Malignant Hyperthermia	Sevoflurane (Ultane®)	These results do not eliminate the possibility that this individual would be susceptible to malignant hyperthermia (MH). The genetic cause of approximately half of all malignant hyperthermia survivors, with MH susceptibility confirmed by contracture test, remains unknown (FDA drug label).	
Anesthetic	RYR1	No Pharmacogenomic Reportable Variants Found	Uncertain Susceptibility to Malignant Hyperthermia	Isoflurane (Forane®)	These results do not eliminate the possibility that this individual would be susceptible to malignant hyperthermia (MH). The genetic cause of approximately half of all malignant hyperthermia survivors, with MH susceptibility confirmed by contracture test, remains unknown (FDA drug label, CPIC guideline).	

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Anesthetic	RYR1	No Pharmacogenomic Reportable Variants Found	Uncertain Susceptibility to Malignant Hyperthermia	Enflurane (Ethrane®)	These results do not eliminate the possibility that this individual would be susceptible to malignant hyperthermia (MH). The genetic cause of approximately half of all malignant hyperthermia survivors, with MH susceptibility confirmed by contracture test, remains unknown (FDA drug label, CPIC guideline).	
Anesthetic	RYR1	No Pharmacogenomic Reportable Variants Found	Uncertain Susceptibility to Malignant Hyperthermia	Desflurane (Suprane®)	These results do not eliminate the possibility that this individual would be susceptible to malignant hyperthermia (MH). The genetic cause of approximately half of all malignant hyperthermia survivors, with MH susceptibility confirmed by contracture test, remains unknown (FDA drug label, CPIC guideline).	
Antiarrhythmic agent	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Quinidine (Cardioquin®)	Quinidine is not metabolized by the CYP2D6 enzyme, however therapeutic serum levels of quinidine inhibit the action of this enzyme. Caution must be exercised whenever quinidine is prescribed together with drugs metabolized by the CYP2D6 enzyme. Refer to FDA labeling for specific dosing recommendations (FDA drug label).	
Antiarrhythmic agent	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Propafenone (Rythmol®)	Increased risk of side effects (cardiac arrhythmias and exaggerated beta-adrenergic blocking activity) due to higher systemic concentration of propafenone. Dose reduction and drug monitoring are recommended. Refer to FDA labeling for specific dosing recommendations (FDA drug label, DPWG guideline).	
Anticonvulsant	CYP2C19	*2 *2	Poor Metabolizer	Phenytoin (Dilantin®)	Phenytoin is primarily metabolized by the CYP2C9 enzyme and to a lesser degree by the CYP2C19 enzyme. Poor CYP2C9 and/or CYP2C19 metabolizers may have significantly increased circulating levels of phenytoin enhancing the risk of drug toxicity. Refer to FDA labeling for specific dosing recommendations (FDA drug label).	

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Anticonvulsant	CYP2C19	*2 *2	Poor Metabolizer	Lacosamide (Vimpat®)	Reduction of plasma concentrations of the lacosamide O-desmethyl metabolite have been observed in individuals who are CYP2C19 poor metabolizers as compared to normal metabolizers. However, there are no clinically relevant differences in lacosamide pharmacokinetics between poor metabolizers and normal metabolizers. Refer to FDA labeling for specific dosing recommendations (FDA drug label).
Anticonvulsant	CYP2C19	*2 *2	Poor Metabolizer	Brivaracetam (Briviact®)	Increased risk of side effects due to higher systemic concentration of brivaracetam. Dose reduction is recommended. Refer to FDA labeling for specific dosing recommendations (FDA drug label, FDA's Table of Pharmacogenetic Associations).
Antidepressant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Vortioxetine (Trintellix®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label, CPIC guideline).
Antidepressant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Venlafaxine (Effexor®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label, DPWG guideline).
Antidepressant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Trimipramine (Surmontil®)	Increased risk of side effects due to higher systemic concentration of trimipramine. Dose reduction and drug monitoring are recommended. Refer to FDA labeling for specific dosing recommendations (FDA drug label, CPIC guideline).
Antidepressant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Protriptyline (Vivactil®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).
Antidepressant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Paroxetine (Paxil®)	Increased risk of side effects due to higher systemic concentration of paroxetine. Refer to FDA labeling for specific dosing recommendations (FDA drug label, CPIC guideline).

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Antidepressant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Nortriptyline (Pamelor®)	Increased risk of side effects due to higher systemic concentration of nortriptyline. Dose reduction and drug monitoring are recommended. Refer to FDA labeling for specific dosing recommendations (FDA drug label, CPIC guideline).
Antidepressant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Imipramine (Tofranil®)	Increased risk of side effects due to higher systemic concentration of imipramine. Dose reduction and drug monitoring are recommended. Refer to FDA labeling for specific dosing recommendations (FDA drug label, CPIC guideline).
Antidepressant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Fluvoxamine (Luvox®)	Increased risk of side effects due to higher systemic concentration of fluvoxamine. While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label, CPIC guideline).
Antidepressant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Fluoxetine (Prozac®)	While the gene affecting the drug's metabolism is altered, no changes to the FDA label-recommended drug dosage are recommended (FDA drug label).
Antidepressant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Duloxetine (Cymbalta®)	While the gene affecting the drug's metabolism is altered, no changes to the FDA label-recommended drug dosage are recommended (FDA drug label).
Antidepressant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Doxepin (Silenor®)	Increased risk of side effects due to higher systemic concentration of doxepin. Dose reduction and drug monitoring are recommended. Refer to FDA labeling for specific dosing recommendations (FDA drug label, CPIC guideline).
Antidepressant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Desipramine (Norpramin®)	Increased risk of side effects due to higher systemic concentration of desipramine. Dose reduction and drug monitoring are recommended. Refer to FDA labeling for specific dosing recommendations (FDA drug label, CPIC guideline).

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Antidepressant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Clomipramine (Anafranil®)	Increased risk of side effects due to higher systemic concentration of clomipramine. Dose reduction and drug monitoring are recommended. Refer to FDA labeling for specific dosing recommendations (FDA drug label, CPIC guideline).	
Antidepressant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Bupropion (Wellbutrin®)	Bupropion and its metabolites are CYP2D6 inhibitors. Coadministration of wellbutrin with drugs that are metabolized by CYP2D6 can increase the exposures of drugs that are substrates of the CYP2D6 enzyme. Refer to FDA labeling for specific dosing recommendations (FDA drug label).	
Antidepressant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Amoxapine (Asendin®)	May alter systemic concentrations of amoxapine. Refer to FDA labeling for specific dosing recommendations (FDA drug label).	
Antidepressant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Amitriptyline (Elavil®)	Increased risk of side effects due to higher systemic concentration of amitriptyline. Dose reduction and drug monitoring are recommended. Refer to FDA labeling for specific dosing recommendations (FDA drug label, CPIC guideline).	
Antidepressant	CYP2C19	*2 *2	Poor Metabolizer	Sertraline (Zoloft®)	Increased risk of side effects due to higher systemic concentration of sertraline. Dose reduction and dose titration are recommended. Refer to FDA labeling for specific dosing recommendations. Medications that are not predominantly metabolized by CYP2C19 should be considered (FDA drug label, CPIC guideline).	
Antidepressant	CYP2C19	*2 *2	Poor Metabolizer	Escitalopram (Lexapro®)	Increased risk of side effects due to higher systemic concentration of escitalopram. Dose reduction and dose titration are recommended. Medications that are not predominantly metabolized by the CYP2C19 enzyme should be considered. Refer to FDA labeling for specific dosing recommendation (FDA drug label, CPIC guideline).	

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Antidepressant	CYP2C19	*2 *2	Poor Metabolizer	Citalopram (Celexa®)	Results in higher systemic concentrations and adverse reaction risk (QT prolongation). Medications that are not predominantly metabolized by the CYP2C19 enzyme should be considered. Refer to FDA labeling for specific dosing recommendations (FDA drug label, FDA's Table of Pharmacogenetic Associations, CPIC guideline).
Antiemetic and antinauseant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Tropisetron (Navoban®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label, CPIC guideline).
Antiemetic and antinauseant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Palonosetron (Posfrea®)	While the gene affecting the drug's metabolism is altered, no changes to the FDA label-recommended drug dosage are recommended (FDA drug label).
Antiemetic and antinauseant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Ondansetron (Zofran®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label, CPIC guideline).
Antiemetic and antinauseant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Metoclopramide (Reglan®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).
Antiemetic and antinauseant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Meclizine (Antivert®)	May affect systemic concentrations. Monitor for adverse reactions and clinical effect. Refer to FDA labeling for specific dosing recommendations (FDA drug label, FDA's Table of Pharmacogenetic Associations).
Antifungal	CYP2C19	*2 *2	Poor Metabolizer	Voriconazole (Vfend®)	Increased risk of side effects due to higher systemic concentration of voriconazole. Dose reduction and dose titration are recommended. Refer to FDA labeling for specific dosing recommendations. Medications that are not predominantly metabolized by CYP2C19 should be considered (FDA drug label, CPIC guideline).

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Antineoplastic agent	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Tamoxifen (Soltamox®)	Increased risk of reduced efficacy due to lower systemic concentration of endoxifen, a potent metabolite of tamoxifen. Dose increase is recommended. Refer to FDA labeling for specific dosing recommendations. Alternative hormonal therapy should also be considered (FDA drug label, CPIC guideline).	
Antineoplastic agent	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Gefitinib (Iressa®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).	
Antineoplastic agent	CYP3A5	*3 *3	Poor Metabolizer	Axitinib (Inlyta®)	Axitinib is primarily metabolized by the CYP3A4 and CYP3A5 enzymes. Take into consideration the metabolizer status of both of these enzymes when planning for treatment. Refer to FDA labeling for specific dosing recommendations (FDA drug label).	
Antineoplastic agent	UGT1A1	*1 *80+*28	Intermediate Metabolizer	Sacituzumab Govitecan-Hziy (Trodelyv®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label, CPIC guideline).	
Antineoplastic agent	UGT1A1	*1 *80+*28	Intermediate Metabolizer	Pazopanib (Votrient®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label, CPIC guideline).	
Antineoplastic agent	UGT1A1	*1 *80+*28	Intermediate Metabolizer	Nilotinib (Tasigna®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label, CPIC guideline).	
Antineoplastic agent	UGT1A1	*1 *80+*28	Intermediate Metabolizer	Irinotecan (Onivyde®)	Results in higher systemic concentrations of the active metabolite and higher adverse reaction risk (severe or life-threatening neutropenia). Monitoring for neutropenia during and after treatment is recommended. Refer to FDA labeling for specific dosing recommendations (FDA's Table of Pharmacogenetic Associations, FDA drug label, CPIC guideline).	

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DRUG CATEGORY	GENE	GENOTYPE	PHENOTYPE	DRUG	COMMENTS			
Antineoplastic agent	UGT1A1	*1 *80+*28	Intermediate Metabolizer	Binimetinib (Mektovi®)	Binimetinib is used in combination with encorafenib to treat BRAF V600 mutation-positive unresectable or metastatic melanoma and non-small cell lung cancer. Refer to FDA labeling for specific dosing recommendations (FDA drug label).			
Antineoplastic agent	UGT1A1	*1 *80+*28	Intermediate Metabolizer	Belinostat (Beleodaq®)	May result in higher systemic concentrations and higher adverse reaction risk. Reduce starting dose, and refer to FDA labeling for specific dosing recommendations (FDA's Table of Pharmacogenetic Associations, FDA drug label, CPIC guideline).			
Antineoplastic agent	CYP2C19	*2 *2	Poor Metabolizer	Belzutifan (Welireg®)	Results in higher systemic concentrations of belzutifan and may result in increased risk of side effects (anemia, hypoxia). Monitor patients who are poor metabolizers for adverse reactions. Refer to FDA labeling for specific dosing recommendations (FDA's Table of Pharmacogenetic Associations, FDA drug label).			
Antipsychotic	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Xanomeline (Cobenfy®)	COBENFY is a combination of two muscarinic antagonists, xanomeline and trospium chloride, and indicated for the treatment of schizophrenia in adults. The CYP2D6 enzyme is a significant contributor to the metabolism of xanomeline, and the CYP2D6 polymorphism impacts pharmacokinetic parameters of xanomeline. Refer to FDA labeling for specific dosing recommendations (FDA drug label).			
Antipsychotic	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Thioridazine (Mellaril®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).			
Antipsychotic	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Risperidone (Risperdal®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).			
Antipsychotic	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Pimozide (Orap®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).			
LABORATORY NAME		ADDRESS		CONTACT	CLIA	CAP	VERSION	PAGE
Simplify Genomics Clinical Laboratory, LLC		440 Stevens Avenue, Suite 200, CA 94040		support@simplifygenomics.com	05D2094189	9013965	10.0.0	16 of 62

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GCR, SampleReport_A		SampleReport_A	Male	01-01-2000	Genomic Clinical Report			
DRUG CATEGORY	GENE	GENOTYPE	PHENOTYPE	DRUG	COMMENTS			
Antipsychotic	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Perphenazine (Trilafon®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).			
Antipsychotic	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Paliperidone (Invega®)	While the gene affecting the drug's metabolism is altered, no changes to the FDA label-recommended drug dosage are recommended (FDA drug label).			
Antipsychotic	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Olanzapine (Zyprexa®)	Olanzapine is primarily metabolized by the CYP1A2 enzyme and to a lesser degree by the CYP2D6 enzyme. Refer to FDA labeling for specific dosing recommendations (FDA drug label).			
Antipsychotic	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Iloperidone (Fanapt®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).			
Antipsychotic	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Clozapine (Clozaril®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label, DPWG guideline).			
Antipsychotic	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Brexpiprazole (Rexulti®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).			
Antipsychotic	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Aripiprazole Lauroxil (Aristada®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).			
Antipsychotic	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Aripiprazole (Abilify®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label, DPWG guideline).			
Antipsychotic	CYP1A2	*30 *30	Ultrarapid Metabolizer	Olanzapine (Zyprexa®)	Increased function of the CYP1A2 enzyme has been observed in individuals harboring the rs762551 A/A genotype, especially in association with smoking, heavy coffee consumption, or omeprazole treatment. Refer to FDA labeling for specific dosing recommendations (FDA drug label).			
LABORATORY NAME		ADDRESS		CONTACT	CLIA	CAP	VERSION	PAGE
Simplify Genomics Clinical Laboratory, LLC		440 Stevens Avenue, Suite 200, CA 94040		support@simplifygenomics.com	05D2094189	9013965	10.0.0	17 of 62

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DRUG CATEGORY	GENE	GENOTYPE	PHENOTYPE	DRUG	COMMENTS
Antipsychotic	CYP1A2	*30 *30	Ultrarapid Metabolizer	Clozapine (Clozaril®)	Increased function of the CYP1A2 enzyme has been observed in individuals harboring the rs762551 A/A genotype, especially in association with smoking, heavy coffee consumption, or omeprazole treatment. Refer to FDA labeling for specific dosing recommendations (FDA drug label).

Antipsychotic	CYP1A2	*30 *30	Ultrarapid Metabolizer	Chlorpromazine (Thorazine®)	Increased function of the CYP1A2 enzyme has been observed in individuals harboring the rs762551 A/A genotype, especially in association with smoking, heavy coffee consumption, or omeprazole treatment. Refer to FDA labeling for specific dosing recommendations (FDA drug label).
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Antiviral therapy	IFNL3	rs12979860	Heterozygous Variant Found	Ribavirin (Rebetol®)	Ribavirin is used in combination with PEG-interferon-alpha. A genetic variant, IL28B rs12979860, is a strong predictor of response to peginterferon alfa and ribavirin. Individuals with the rs12979860 C/T or T/T genotype and hepatitis C infection may have decreased response to PEG-interferon-alpha-containing treatment regimens compared to individuals with IFNL3 genotype rs12979860 C/C. Other genetic and clinical factors may also influence the response to this therapy. Refer to FDA labeling for specific dosage and administration recommendations (FDA drug label).
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Antiviral therapy	IFNL3	rs12979860	Heterozygous Variant Found	Peginterferon Alfa-2B (Pegintron®)	Individuals with the IFNL3 rs12979860 C/T genotype and hepatitis C infection may have decreased response to PEG-interferon-alpha-containing treatment regimen as compared to individuals with IFNL3 genotype rs12979860 C/C. Other genetic and clinical factors may also influence the response to this therapy. Refer to FDA labeling for specific dosage and administration recommendations (FDA drug label).
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DRUG CATEGORY	GENE	GENOTYPE	PHENOTYPE	DRUG	COMMENTS	
Antiviral therapy	IFNL3	rs12979860	Heterozygous Variant Found	Peginterferon Alfa-2A (Pegasys®)	Individuals with the IFNL3 rs12979860 C/T genotype and hepatitis C infection may have decreased response to PEG-interferon-alpha-containing treatment regimen as compared to individuals with IFNL3 genotype rs12979860 C/C. Other genetic and clinical factors may also influence the response to this therapy. Refer to FDA labeling for specific dosage and administration recommendations (FDA drug label).	
Antiviral therapy	UGT1A1	*1 *80+*28	Intermediate Metabolizer	Rilpivirine (Edurant®)	While the gene affecting the drug's metabolism is altered, no changes to the FDA label-recommended drug dosage are recommended (FDA drug label).	
Antiviral therapy	UGT1A1	*1 *80+*28	Intermediate Metabolizer	Raltegravir (Isentress®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label, CPIC guideline).	
Antiviral therapy	UGT1A1	*1 *80+*28	Intermediate Metabolizer	Dolutegravir (Tivicay®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label, CPIC guideline).	
Antiviral therapy	UGT1A1	*1 *80+*28	Intermediate Metabolizer	Cabotegravir (Apretude®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug dosage are recommended (FDA drug label).	
Antiviral therapy	UGT1A1	*1 *80+*28	Intermediate Metabolizer	Atazanavir (Reyataz®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label, CPIC guideline).	
Antiviral therapy	CYP2C19	*2 *2	Poor Metabolizer	Nelfinavir (Viracept®)	Coadministration of nelfinavir and drugs that induce CYP3A4 or CYP2C19, may decrease nelfinavir plasma concentrations and reduce its therapeutic efficacy. Refer to FDA labeling for specific dosing recommendations (FDA drug label).	

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DRUG CATEGORY	GENE	GENOTYPE	PHENOTYPE	DRUG	COMMENTS	
Beta Blocker	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Propranolol (Hemangeol®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).	
Beta Blocker	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Nebivolol (Bystolic®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).	
Beta Blocker	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Metoprolol (Lopressor®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).	
Beta Blocker	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Carvedilol (Coreg®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label, DPWG guideline).	
Bladder relaxant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Tolterodine (Detrol®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).	
Bladder relaxant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Mirabegron (Myrbetriq®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).	
Bladder relaxant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Fesoterodine (Toviaz®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).	
Bladder relaxant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Darifenacin (Enablex®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).	
Blood thinner	CYP2C9	*1 *1	Normal Metabolizer	Warfarin (Coumadin®)	Calculation of warfarin dose based on the combination of CYP2C9, VKORC1, CYP4F2, and rs12777823 genotypes is recommended. Monitor and adjust dosages based on INR (FDA drug label, CPIC guideline).	

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DRUG CATEGORY	GENE	GENOTYPE	PHENOTYPE	DRUG	COMMENTS
Blood thinner	VKORC1	No Pharmacogenomic Reportable Variants Found	Normal Function	Warfarin (Coumadin®)	Individuals with rs9923231:CC generally have normal sensitivity to warfarin. Calculation of warfarin dose based on the combination of CYP2C9, VKORC1, CYP4F2, and rs12777823 genotypes is recommended. Monitor and adjust doses based on INR (FDA drug label, CPIC guideline).
Blood thinner	CYP2C19	*2 *2	Poor Metabolizer	Clopidogrel (Plavix®)	Results in lower systemic active metabolite concentrations, lower antiplatelet response, and higher cardiovascular risk. Alternative antiplatelet medications are recommended (FDA drug label, FDA's Table of Pharmacogenetic Associations, CPIC guideline).
Blood thinner	RS12777823	rs12777823:AA	Increased Warfarin Sensitivity	Warfarin (Coumadin®)	Calculation of warfarin dose based on the combination of CYP2C9, VKORC1, CYP4F2, and rs12777823 genotypes is recommended. Monitor and adjust doses based on INR (FDA drug label, CPIC guideline).
Bronchodilator	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Umeclidinium (Incruse Ellipta®)	While the gene affecting the drug's metabolism is altered, no changes to the FDA label-recommended drug dosage are recommended (FDA drug label).
Bronchodilator	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Tiotropium (Spiriva®)	While the gene affecting the drug's metabolism is altered, no changes to the FDA label-recommended drug dosage are recommended (FDA label).
Bronchodilator	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Formoterol (Foradil®)	Formoterol is primarily metabolized by UGT1A1-mediated glucuronidation, followed by O-demethylation by the CYP2D6 enzyme and other cytochrome P450 isozymes, including CYP2C9, CYP2C19 and CYP2A6. When planning treatment, it is important to consider the UGT1A1 metabolizer status, as well. Refer to FDA labeling for specific dosing recommendations (FDA drug label).

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DRUG CATEGORY	GENE	GENOTYPE	PHENOTYPE	DRUG	COMMENTS	
Bronchodilator	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Arformoterol (Brovana®)	Arformoterol is primarily metabolized by UGT-mediated glucuronidation, followed by O-demethylation by the CYP2D6 and CYP2C19 enzymes. When planning treatment, it is important to consider the UGT1A1 metabolizer status, as well. Refer to FDA labeling for specific dosing recommendations (FDA drug label).	
Bronchodilator	UGT1A1	*1 *80+*28	Intermediate Metabolizer	Indacaterol (Arcapta Neohaler®)	While the gene affecting the drug's metabolism is altered, no changes to the FDA label-recommended drug dosage are recommended (FDA drug label).	
Bronchodilator	UGT1A1	*1 *80+*28	Intermediate Metabolizer	Formoterol (Foradil®)	Formoterol is metabolized primarily by UGT1A1-mediated glucuronidation, followed by O-demethylation by four cytochrome P450 isozymes, CYP2D6, CYP2C19, CYP2C9 and CYP2A6. Refer to FDA labeling for specific dosing recommendations (FDA drug label).	
Bronchodilator	UGT1A1	*1 *80+*28	Intermediate Metabolizer	Arformoterol (Brovana®)	While the gene affecting the drug's metabolism is altered, no changes to the FDA label-recommended drug dosage are recommended (FDA drug label).	
Bronchodilator	CYP2C19	*2 *2	Poor Metabolizer	Formoterol (Foradil®)	Formoterol is primarily metabolized by UGT1A1-mediated glucuronidation, followed by O-demethylation by the CYP2C19 enzyme and other cytochrome P450 isozymes, including CYP2C9, CYP2D6 and CYP2A6. When planning treatment, it is important to consider the UGT1A1 metabolizer status, as well. Refer to FDA labeling for specific dosing recommendations (FDA drug label).	
Bronchodilator	CYP2C19	*2 *2	Poor Metabolizer	Arformoterol (Brovana®)	Arformoterol is primarily metabolized by UGT-mediated glucuronidation, followed by O-demethylation by the CYP2C19 and CYP2D6 enzymes. When planning treatment, it is important to consider the UGT1A1 metabolizer status, as well. Refer to FDA labeling for specific dosing recommendations (FDA drug label).	

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Cardiac myosin inhibitor	CYP2C19	*2 *2	Poor Metabolizer	Mavacamten (Camzyos®)	Results in higher systemic concentrations of mavacamten and potentially increased adverse reaction risk (heart failure). Adjust dosage based on individual response. Refer to FDA labeling for specific dosing recommendations and monitoring (FDA drug label).
Central nervous system stimulant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Modafinil (Provigil®)	While the gene affecting the drug's metabolism is altered, no changes to the FDA label-recommended drug dosage are recommended (FDA drug label).
Cognition-enhancing therapy	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Galantamine (Razadyne®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).
Cognition-enhancing therapy	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Donepezil (Aricept®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).
Contraceptive	CYP2C19	*2 *2	Poor Metabolizer	Drospirenone (Slynd®)	Drospirenone is commonly paired with ethinyl estradiol in combination birth control pills like Yaz and others. While the gene affecting the drug's metabolism is altered, no changes to the FDA label-recommended drug dosage are recommended (FDA drug label).
Cough suppressant	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Dextromethorphan (Robitussin®)	While the gene affecting the drug's metabolism is altered, no changes to the FDA label-recommended drug dosage are recommended (FDA drug label).
Dry mouth treatment	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Cevimeline (Evoxac®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).
Enzyme Inhibitor	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Eliglustat (Cerdelga®)	Coadministration with strong CYP3A inhibitors is contraindicated. Dose adjustment may be required for use with other CYP2D6 and CYP3A inhibitors to avoid side effects, QT prolongation. Refer to FDA labeling for specific dosing recommendations (FDA drug label, FDA's Table of Pharmacogenetic Associations).

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Enzyme Inhibitor	CYP2C19	*2 *2	Poor Metabolizer	Abrocitinib (Cibinqo®)	Results in higher systemic concentrations of abrocitinib and may result in increased risk of side effects. Dosage adjustment is recommended. Refer to FDA labeling for specific dosing recommendations (FDA's Table of Pharmacogenetic Associations, FDA drug label).	
Female sexual dysfunction treatment	CYP2C19	*2 *2	Poor Metabolizer	Flibanserin (Addyi®)	Increased risk of side effects due to higher systemic concentration of flibanserin. Monitor patients for adverse reactions. Refer to FDA labeling for specific dosing recommendations (FDA drug label, FDA's Table of Pharmacogenetic Associations).	
Immunosuppressant	CYP3A4	*1 *1	Normal Metabolizer	Tacrolimus (Prograf®)	May result in lower systemic concentration of the drug and decreased efficacy. It is recommended to adjust dosage based on whole blood tacrolimus concentrations. Refer to FDA labeling for specific dosing recommendations (FDA drug label, CPIC guidelines).	
Immunosuppressant	CYP3A5	*3 *3	Poor Metabolizer	Tacrolimus (Prograf®)	When co-administering tacrolimus with strong CYP3A4 inhibitors and/or strong inducers, adjustments in the dosing regimen of tacrolimus and subsequent frequent monitoring of tacrolimus blood concentrations and tacrolimus-associated adverse reactions are recommended. Refer to FDA labeling for specific dosing recommendations (FDA drug label, CPIC guideline).	
Involuntary movement reducer	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Valbenazine (Ingrezza®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).	
Involuntary movement reducer	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Tetrabenazine (Xenazine®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).	

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Involuntary movement reducer	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Deutetrabenazine (Austedo®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).	
Muscle relaxant	CACNA1S	No Pharmacogenomic Reportable Variants Found	Uncertain Susceptibility	Succinylcholine (Quelcin®)	These results do not eliminate the possibility that this individual would be susceptible to malignant hyperthermia (MH). The genetic cause of approximately half of all malignant hyperthermia survivors, with MH susceptibility confirmed by contracture test, remains unknown (FDA drug label, CPIC guideline).	
Muscle relaxant	CYP1A2	*30 *30	Ultrarapid Metabolizer	Tizanidine (Zanaflex®)	Increased function of the CYP1A2 enzyme has been observed in individuals harboring the rs762551 A/A genotype, especially in association with smoking, heavy coffee consumption, or omeprazole treatment. Refer to FDA labeling for specific dosing recommendations (FDA drug label).	
Muscle relaxant	RYR1	No Pharmacogenomic Reportable Variants Found	Uncertain Susceptibility to Malignant Hyperthermia	Succinylcholine (Quelcin®)	These results do not eliminate the possibility that this individual would be susceptible to malignant hyperthermia (MH). The genetic cause of approximately half of all malignant hyperthermia survivors, with MH susceptibility confirmed by contracture test, remains unknown (FDA drug label, CPIC guideline).	
Muscle relaxant	CYP2C19	*2 *2	Poor Metabolizer	Carisoprodol (Soma®)	Results in higher systemic concentrations and should be used with caution. Refer to FDA labeling for specific dosing recommendations (FDA drug label).	
Narcolepsy	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Pitolisant (Wakix®)	Increased risk of side effects due to higher systemic concentration of pitolisant. Refer to FDA labeling for specific dosing recommendations (FDA drug label).	

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DRUG CATEGORY	GENE	GENOTYPE	PHENOTYPE	DRUG	COMMENTS	
Non-opioid analgesic	RYP1	No Pharmacogenomic Reportable Variants Found	Uncertain Susceptibility to Malignant Hyperthermia	Methoxyflurane (Pentrox [®])	These results do not eliminate the possibility that this individual would be susceptible to malignant hyperthermia (MH). The genetic cause of approximately half of all malignant hyperthermia survivors, with MH susceptibility confirmed by contracture test, remains unknown (FDA drug label, CPIC guideline).	
Opioid	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Tramadol (Ultram [®])	Increased risk of reduced efficacy due to lower systemic concentration of active metabolites of tramadol. Dose increase is recommended. Refer to FDA labeling for specific dosing recommendations. Medications that are not predominantly metabolized by CYP2D6 should be considered (FDA drug label, CPIC guideline, DPWG guideline).	
Opioid	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Oxycodone (Oxaydo [®])	Increased risk of reduced efficacy due to lower systemic concentration of active metabolites of oxycodone. Medications that are not predominantly metabolized by CYP2D6 (not tramadol or codeine) should be considered. Refer to FDA labeling for specific dosing recommendations (FDA drug label, CPIC guideline, DPWG guideline).	
Opioid	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Oliceridine (Olinvyk [®])	Increased risk of side effects due to higher systemic concentration of oliceridine. Refer to FDA labeling for specific dosing recommendations (FDA drug label).	
Opioid	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Hydrocodone (Norco [®])	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label, CPIC guideline, DPWG guideline).	

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DRUG CATEGORY	GENE	GENOTYPE	PHENOTYPE	DRUG	COMMENTS	
Opioid	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Codeine (Codeine Sulfate [®])	Increased risk of reduced efficacy due to lower systemic concentration of morphine, an active metabolite of codeine. Refer to FDA labeling for specific dosing recommendations. Medications that are not predominantly metabolized by CYP2D6 (e.g., acetaminophen, NSAID, morphine not tramadol or oxycodone) should be considered (FDA drug label, CPIC guideline).	
Opioid withdrawal treatment	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Lofexidine (Lucemyra [®])	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).	
PARP inhibitor	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Rucaparib (Rubraca [®])	While the gene affecting the drug's metabolism is altered, no changes to the FDA label-recommended drug dosage are recommended (FDA drug label).	
Potassium-competitive acid blocker	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Vonoprazan (Voquezna [®])	While the gene affecting the drug's metabolism is altered, no changes to the FDA label-recommended drug dosage are recommended (FDA drug label).	
Potassium-competitive acid blocker	CYP2C19	*2 *2	Poor Metabolizer	Vonoprazan (Voquezna [®])	While the gene affecting the drug's metabolism is altered, no changes to the FDA label-recommended drug dosage are recommended (FDA drug label).	
Proton-pump inhibitor	CYP2C19	*2 *2	Poor Metabolizer	Rabeprazole (Aciphex [®])	Results in higher systemic concentrations. However, while the gene affecting the drug's metabolism is altered, no changes to the label- recommended drug dosage are recommended (FDA drug label, DPWG guideline).	
Proton-pump inhibitor	CYP2C19	*2 *2	Poor Metabolizer	Pantoprazole (Protonix [®])	Increased risk of potential toxicity due to higher systemic concentration of pantoprazole. Consider dosage reduction in children. Refer to FDA labeling for specific dosing recommendations (FDA drug label, FDA's Table of Pharmacogenetic Associations, CPIC guideline, DPWG guideline).	

PATIENT NAME		PATIENT ID	SEX	DOB	REPORT TYPE	
GCR, SampleReport_A		SampleReport_A	Male	01-01-2000	Genomic Clinical Report	
DRUG CATEGORY	GENE	GENOTYPE	PHENOTYPE	DRUG	COMMENTS	
Proton-pump inhibitor	CYP2C19	*2 *2	Poor Metabolizer	Omeprazole (Prilosec®)	Increased risk of potential toxicity due to higher systemic concentration of omeprazole. Drug monitoring is recommended. Refer to FDA labeling for specific dosing recommendations (FDA drug label, CPIC guideline, DPWG guideline).	
Proton-pump inhibitor	CYP2C19	*2 *2	Poor Metabolizer	Lansoprazole (Prevacid®)	Increased risk of potential toxicity due to higher systemic concentration of lansoprazole. Drug monitoring is recommended. Refer to FDA labeling for specific dosing recommendations (FDA drug label, CPIC guideline, DPWG guideline).	
Proton-pump inhibitor	CYP2C19	*2 *2	Poor Metabolizer	Esomeprazole (Nexium®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label, DPWG guideline).	
Proton-pump inhibitor	CYP2C19	*2 *2	Poor Metabolizer	Dexlansoprazole (Dexilant®)	Increased risk of side effects due to higher systemic concentration of dexlansoprazole. Refer to FDA labeling for specific dosing recommendations (FDA drug label, CPIC guideline).	
Sedative	CYP2C19	*2 *2	Poor Metabolizer	Diazepam (Valium®)	May affect systemic concentrations. While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).	
Sedative	CYP2C19	*2 *2	Poor Metabolizer	Clobazam (Onfi®)	Increased risk of side effects due to higher systemic concentration of an active metabolite of clobazam. Dose reduction and dose titration are recommended. Refer to FDA labeling for specific dosing recommendations (FDA drug label, FDA's Table of Pharmacogenetic Associations).	

PATIENT NAME		PATIENT ID	SEX	DOB	REPORT TYPE	
GCR, SampleReport_A		SampleReport_A	Male	01-01-2000	Genomic Clinical Report	
DRUG CATEGORY	GENE	GENOTYPE	PHENOTYPE	DRUG	COMMENTS	
Statin	ABCG2	rs2231142	Decreased Function	Rosuvastatin (Crestor®)	Increased rosuvastatin exposure and lipid lowering effects as compared to normal function. The risk for myopathy is unknown. Use desired starting dose and adjust doses of rosuvastatin based on disease-specific guidelines and specific population guidelines. Refer to FDA labeling for specific dosing recommendations (FDA drug label, CPIC guidelines).	
Urological agent	CYP2D6	*41 *68+*4	Intermediate Metabolizer	Tamsulosin (Flomax®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).	

PATIENT NAME	PATIENT ID	SEX	DOB	REPORT TYPE
GCR, SampleReport_A	SampleReport_A	Male	01-01-2000	Genomic Clinical Report

Gene and Phenotype Findings

GENE	GENOTYPE	PHENOTYPE	DRUG
ABCG2	rs2231142	Decreased Function	Rosuvastatin (Crestor®)
BCHE	No Pharmacogenomic Reportable Variants Found	Normal Function	Mivacurium (Mivacron®), Succinylcholine (Quelicin®), Tetracaine (Tetcaine®)
CACNA1S	No Pharmacogenomic Reportable Variants Found	Uncertain Susceptibility	Desflurane (Suprane®), Isoflurane (Forane®), Sevoflurane (Ultane®), Succinylcholine (Quelicin®)
CFTR	No Pharmacogenomic Reportable Variants Found	Normal Function	Ivacaftor (Kalydeco®)
CYP1A2	*30 *30	Ultrarapid Metabolizer	Chlorpromazine (Thorazine®), Clozapine (Clozaril®), Olanzapine (Zyprexa®), Tizanidine (Zanaflex®)
CYP2C19	*2 *2	Poor Metabolizer	Abrocitinib (Cibinqo®), Arformoterol (Brovana®), Belzutifan (Welireg®), Brivaracetam (Briviact®), Carisoprodol (Soma®), Citalopram (Celexa®), Clobazam (Onfi®), Clopidogrel (Plavix®), Dexlansoprazole (Dexilant®), Diazepam (Valium®), Drospirenone (Slynd®), Escitalopram (Lexapro®), Esomeprazole (Nexium®), Flibanserin (Addyi®), Formoterol (Foradil®), Lacosamide (Vimpat®), Lansoprazole (Prevacid®), Mavacamten (Camzyos®), Nelfinavir (Viracept®), Omeprazole (Prilosec®), Pantoprazole (Protonix®), Phenytoin (Dilantin®), Rabeprazole (Aciphex®), Sertraline (Zoloft®), Vonoprazan (Voquezna®), Voriconazole (Vfend®)
CYP2C9	*1 *1	Normal Metabolizer	Avatrombopag (Doptelet®), Celecoxib (Celebrex®), Deuruxolitinib (Leqselvi®), Dronabinol (Marinol®), Erdafitinib (Balversa®), Etrasimod (Velsipity®), Flurbiprofen (Ansaid®), Fluvastatin (Lescol®), Formoterol (Foradil®), Fosphenytoin (Cerebyx®), Ibuprofen (Advil®), Lesinurad (Zurampic®), Lornoxicam (Xefo®), Meloxicam (Vivlodex®), Nateglinide (Starlix®), Ospemifene (Osphena®), Phenytoin (Phenytek®), Piroxicam (Feldene®), Rimegepant (Nurtec Odt®), Seladelpar (Livdelzi®), Siponimod (Mayzent®), Tenoxicam (Mobiflex®), Vonoprazan (Voquezna®), Warfarin (Coumadin®)

PATIENT NAME	PATIENT ID	SEX	DOB	REPORT TYPE
GCR, SampleReport_A	SampleReport_A	Male	01-01-2000	Genomic Clinical Report

GENE	GENOTYPE	PHENOTYPE	DRUG
CYP2D6	*41 *68+*4	Intermediate Metabolizer	Amitriptyline (Elavil®), Amoxapine (Asendin®), Amphetamine (Adderall®), Arformoterol (Brovana®), Aripiprazole (Abilify®), Aripiprazole Lauroxil (Aristada®), Atomoxetine (Strattera®), Brexpiprazole (Rexulti®), Bupropion (Wellbutrin®), Carvedilol (Coreg®), Cevimeline (Evoxac®), Clomipramine (Anafranil®), Clozapine (Clozaril®), Codeine (Codeine Sulfate®), Darifenacin (Enablex®), Desipramine (Norpramin®), Deutetrabenazine (Austedo®), Dextromethorphan (Robitussin®), Donepezil (Aricept®), Doxepin (Silenor®), Duloxetine (Cymbalta®), Eliglustat (Cerdelga®), Fesoterodine (Toviaz®), Fluoxetine (Prozac®), Fluvoxamine (Luvox®), Formoterol (Foradil®), Galantamine (Razadyne®), Gefitinib (Iressa®), Hydrocodone (Norco®), Iloperidone (Fanapt®), Imipramine (Tofranil®), Lofexidine (Lucemyra®), Meclizine (Antivert®), Metoclopramide (Reglan®), Metoprolol (Lopressor®), Mirabegron (Myrbetriq®), Modafinil (Provigil®), Nebivolol (Bystolic®), Nortriptyline (Pamelor®), Olanzapine (Zyprexa®), Oliceridine (Olinvyk®), Ondansetron (Zofran®), Oxycodone (Oxaydo®), Paliperidone (Invega®), Palonosetron (Posfrea®), Paroxetine (Paxil®), Perphenazine (Trilafon®), Pimozide (Orap®), Pitolisant (Wakix®), Propafenone (Rythmol®), Propranolol (Hemangeol®), Protriptyline (Vivactil®), Quinidine (Cardioquin®), Risperidone (Risperdal®), Rucaparib (Rubraca®), Tamoxifen (Soltamox®), Tamsulosin (Flomax®), Tetrabenazine (Xenazine®), Thioridazine (Mellaril®), Tiotropium (Spiriva®), Tolterodine (Detrol®), Tramadol (Ultram®), Trimipramine (Surmontil®), Tropisetron (Navoban®), Umeclidinium (Incruse Ellipta®), Valbenazine (Ingrezza®), Venlafaxine (Effexor®), Viloxazine (Qelbree®), Vonoprazan (Voquezna®), Vortioxetine (Trintellix®), Xanomeline (Cobenfy®)
CYP3A4	*1 *1	Normal Metabolizer	Alprazolam (Xanax®), Amlodipine (Norvasc®), Atorvastatin (Lipitor®), Axitinib (Inlyta®), Buspirone (Buspar®), Cariprazine (Vraylar®), Clarithromycin (Biaxin®), Cyclosporine (Neoral®), Diltiazem (Cardizem®), Erythromycin (Erythrocine®), Felodipine (Plendil®), Fentanyl (Sublimaze®), Flibanserin (Addyi®), Imatinib (Gleevec®), Indinavir (Crixivan®), Itraconazole (Sporanox®), Ketoconazole (Nizoral®), Loratadine (Claritin®), Lovastatin (Mevacor®), Midazolam (Versed®), Nefazodone (Serzone®), Nifedipine (Adalat®), Prasugrel (Effient®), Remibrutinib (Rhapsido®), Rimegepant (Nurtec Odt®), Ritonavir (Norvir®), Saquinavir (Invirase®), Sildenafil (Viagra®), Simvastatin (Zocor®), Sirolimus (Rapamune®), Tacrolimus (Prograf®), Terbinafine (Lamisil®), Ticagrelor (Brilinta®), Triazolam (Halcion®), Upadacitinib (Rinvoq®), Verapamil (Calan®), Vonoprazan (Voquezna®)
CYP3A5	*3 *3	Poor Metabolizer	Axitinib (Inlyta®), Tacrolimus (Prograf®)
CYP4F2	*1 *5	Unable to Determine	Warfarin (Coumadin®)
DPYD	*1 *4	Normal Metabolizer	Capecitabine (Xeloda®), Fluorouracil (Efudex®), Tegafur (Uft®)
F2	No Pharmacogenomic Reportable Variants Found	Normal Function	Avatrombopag (Doptelet®), Lusutrombopag (Mulpleta®)
F5	No Pharmacogenomic Reportable Variants Found	Normal Function	Avatrombopag (Doptelet®), Eltrombopag (Promacta®), Lusutrombopag (Mulpleta®), Norelgestromin (Ortho Evra®), Relugolix (Myfembree®)

PATIENT NAME		PATIENT ID	SEX	DOB	REPORT TYPE		
GCR, SampleReport_A		SampleReport_A	Male	01-01-2000	Genomic Clinical Report		
GENE	GENOTYPE	PHENOTYPE	DRUG				
G6PD	B	Normal Function	Bupivacaine (Marcaine®), Chloroprocaine (Nesacaine®), Chlorpropamide (Diabinese®), Dabrafenib (Tafinlar®), Dapsone (Aczone®), Flutamide (Eulexin®), Glimepiride (Amaryl®), Glipizide (Glucotrol®), Glyburide (Diabeta®), Lidocaine (Xylocaine®), Mafenide (Sulfamylon®), Mepivacaine (Carbocaine®), Methylene Blue (Provayblue®), Nalidixic Acid (Neggram®), Nitrofurantoin (Macrobid®), Norfloxacin (Noroxin®), Pegloticase (Krystexxa®), Primaquine (Primaquine Phosphate®), Probenecid (Benemid®), Quinine (Qualaquin®), Rasburicase (Elitek®), Ropivacaine (Naropin®), Sulfadiazine (Lantrisol®), Sulfasalazine (Azulfidine®), Tafenoquine (Krintafel®), Tolazamide (Tolinase®), Toluidine Blue (Tbo®)				
IFNL3	rs12979860	Heterozygous Variant Found	Peginterferon Alfa-2A (Pegasys®), Peginterferon Alfa-2B (Pegintron®), Ribavirin (Rebetol®)				
NUDT15	*1 *1	Normal Metabolizer	Azathioprine (Imuran®), Mercaptopurine (Purinethol®), Thioguanine (Tabloid®)				
OPRM1	No Pharmacogenomic Reportable Variants Found	Normal Function	Morphine (Ms Contin®)				
PCSK9	No Pharmacogenomic Reportable Variants Found	Normal Function	Alirocumab (Praluent®), Evolocumab (Repatha®), Inclisiran (Leqvio®)				
POLG	No Pharmacogenomic Reportable Variants Found	Normal Function	Valproic Acid (Valproic®)				
RS113993960	No Pharmacogenomic Reportable Variants Found	Normal Function	Elexacaftor (Trikafta®), Lumacaftor (Orkambi®), Tezacaftor (Symdeko®)				
RS12777823	rs12777823:AA	Increased Warfarin Sensitivity	Warfarin (Coumadin®)				
RYR1	No Pharmacogenomic Reportable Variants Found	Uncertain Susceptibility to Malignant Hyperthermia	Desflurane (Suprane®), Enflurane (Ethrane®), Isoflurane (Forane®), Methoxyflurane (Penthrox®), Sevoflurane (Ultane®), Succinylcholine (Quelicin®)				
SLCO1B1	*1 *1	Normal Function	Atorvastatin (Lipitor®), Elagolix (Oriahnn®), Fluvastatin (Lescol®), Lovastatin (Mevacor®), Pitavastatin (Livalo®), Pravastatin (Pravachol®), Rosuvastatin (Crestor®), Simvastatin (Zocor®)				
TPMT	*1 *1	Normal Metabolizer	Azathioprine (Imuran®), Mercaptopurine (Purinethol®), Thioguanine (Tabloid®)				
LABORATORY NAME		ADDRESS	CONTACT	CLIA	CAP	VERSION	PAGE
Simplify Genomics Clinical Laboratory, LLC		440 Stevens Avenue, Suite 200, CA 94040	support@simplifygenomics.com	05D2094189	9013965	10.0.0	32 of 62

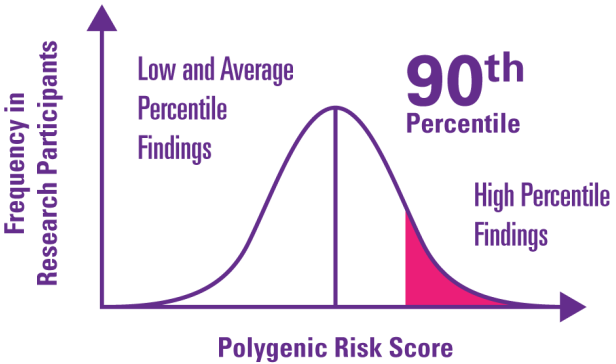
PATIENT NAME	PATIENT ID	SEX	DOB	REPORT TYPE
GCR, SampleReport_A	SampleReport_A	Male	01-01-2000	Genomic Clinical Report

GENE	GENOTYPE	PHENOTYPE	DRUG
UGT1A1	*1 *80+*28	Intermediate Metabolizer	Arformoterol (Brovana®), Atazanavir (Reyataz®), Belinostat (Beleodaq®), Binimetinib (Mektovi®), Cabotegravir (Apretude®), Dolutegravir (Tivicay®), Formoterol (Foradil®), Indacaterol (Arcapta Neohaler®), Irinotecan (Onivyde®), Nilotinib (Tasigna®), Pazopanib (Votrient®), Raltegravir (Isentress®), Rilpivirine (Edurant®), Sacituzumab Govitecan-Hziy (Trodelyv®)
VKORC1	No Pharmacogenomic Reportable Variants Found	Normal Function	Warfarin (Coumadin®)

Health Predisposition

This section describes your genetic predisposition to common diseases using an innovative approach called polygenic risk scores. This approach identifies common variants you have that are associated with low genetic risk. Having several low risk variants related to the same disease predisposes you to that disease. Learn more in [Your Results Guide](#).

Results use: The results in this section should not be used to guide medical care but rather to inform your lifestyle decisions. If you have a polygenic risk score that falls at or above the 90th percentile, it does not mean that you will develop the disease, rather it means that your genetic predisposition is increased. Lifestyle and environmental factors contribute more than genetics to the majority of common diseases. Polygenic risk scores in this report were developed using genomes of people of European descent and may be less accurate for people of other ethnicities.



High Percentile Findings (90th and above)

DISEASE	YOUR RESULT	ABOUT THE DISEASE	
Asthma	Given the variants you carry, your genetic predisposition to asthma is greater than 99% of research participants of European descent. Your estimated genetic risk is 1.6 times that of an average person in the reference population.	Asthma is a very common disease; one in 13 people currently have asthma.	Genetic factors contribute about 35 - 95% to the variability in risk between individuals for asthma.
Celiac Disease	Given the variants you carry, your genetic predisposition to celiac disease is greater than 96% of research participants of European descent. Your estimated genetic risk is 16.1 times that of an average person in the reference population.	Celiac disease is a common condition; one in 100 people is affected by the disease.	Genetic factors contribute up to 75% to the variability in risk between individuals for celiac disease.
Inflammatory Bowel Disease	Given the variants you carry, your genetic predisposition to inflammatory bowel disease is greater than 98% of research participants of European descent. Your estimated genetic risk is 2.8 times that of an average person in the reference population.	Inflammatory bowel disease is common; one in 80 adults will develop either ulcerative colitis or Crohn's disease in their lifetime.	Genetic factors contribute up to 70% to the variability in risk between individuals for inflammatory bowel disease.

Low and Average Percentile Findings (below 90th)

PATIENT NAME	PATIENT ID	SEX	DOB	REPORT TYPE
GCR, SampleReport_A	SampleReport_A	Male	01-01-2000	Genomic Clinical Report
HEALTH CATEGORY	DISEASES (YOUR PERCENTILE)			
Cancer Predisposition	Basal Cell Carcinoma (Percentile: 71, Relative Risk: 1.2), Bladder Cancer (Percentile: 52, Relative Risk: 1.0), Chronic Lymphocytic Leukemia (Percentile: 85, Relative Risk: 2.2), Colorectal Cancer (Percentile: 74, Relative Risk: 1.1), Melanoma (Percentile: 42, Relative Risk: 1.0), Pancreatic Cancer (Percentile: 79, Relative Risk: 1.4), Prostate Cancer (Percentile: 45 - 55, Relative Risk: 1.0), Thyroid Cancer (Percentile: 65, Relative Risk: 1.4)			
Heart and Vascular Health	Atrial Fibrillation (Percentile: 72, Relative Risk: 1.2), Coronary Artery Disease (Percentile: 68, Relative Risk: 1.1), Venous Thromboembolism (Percentile: 73, Relative Risk: 1.2)			
Mental Health	Schizophrenia (Percentile: 89, Relative Risk: 1.1)			
Metabolic Health	HDL Cholesterol (Percentile: 71, Relative Risk: 1.3), LDL Cholesterol (Percentile: 18, Relative Risk: 0.8), Total Cholesterol (Percentile: 35, Relative Risk: 0.9), Triglycerides (Percentile: 28, Relative Risk: 0.9), Type 2 Diabetes (Percentile: 85, Relative Risk: 1.4)			
Musculoskeletal Health	Dupuytren's disease (Percentile: 18, Relative Risk: 0.6), Gout (Percentile: 81, Relative Risk: 1.5), Rheumatoid Arthritis (Percentile: 85, Relative Risk: 1.4)			
Neurological Health	Alzheimer's Disease (Percentile: 12, Relative Risk: 0.9), Multiple Sclerosis (Percentile: 78, Relative Risk: 2.2), Parkinson's Disease (Percentile: 15, Relative Risk: 0.7)			
Respiratory Health	COPD (Percentile: 39, Relative Risk: 0.9)			
Sensory Health	Age-Related Macular Degeneration (Percentile: 19, Relative Risk: 1.0)			

Please refer to [Your Results Guide](#) for frequently asked questions, information on how each polygenic risk score was developed, and references supporting disease information in this section.

Nutrition and Wellness Traits

This section describes how your genes affect your body's response to certain foods, exercise, as well as your habits. The research into genetics of some traits is ongoing. You will see an icon describing the level of scientific evidence next to each prediction – from preliminary (one star) to established (four stars). The results in this section should not be used to guide medical care but rather to inform your lifestyle decisions. In some cases, the genotype result may be displayed as 'Unable to Determine' for any trait that includes a variant that could not be called confidently due to poor quality. Learn more about each trait in [Your Results Guide](#).

Food Reactions



Alcohol Flush Reaction



Your Result

Based on your genotype, you are unlikely to flush after consuming alcohol.

Your GENOTYPE

ALDH2, rs671, G/G

Description

The alcohol flush reaction is experienced by some people after consuming alcohol. In these individuals, a toxic substance called acetaldehyde builds up after drinking and causes tiny blood vessels in the face to temporarily expand and fill with more blood, which is similar to blushing. It can also cause dizziness, headaches, and nausea. Genetic variant, rs671, in the ALDH2 gene is associated with alcohol-related cutaneous flushing. Individuals, who have the G/A or A/A genotype, may be more prone to flushing after alcohol consumption.



Bitter Taste Perception



Your Result

Based on your genotype, you are likely to have an enhanced sensitivity to bitter taste

Your GENOTYPE

TAS2R38, rs713598, C/G

PATIENT NAME	PATIENT ID	SEX	DOB	REPORT TYPE
GCR, SampleReport_A	SampleReport_A	Male	01-01-2000	Genomic Clinical Report

Description

People have different sensitivities to taste. The rs713598 variant in the taste receptor gene TAS2R38 has been shown to influence the sensitivity to the bitter-tasting compound phenylthiocarbamide. This variant may partially explain the increased sensitivity to the bitter flavors found in some foods such as broccoli, brussels sprouts, grapefruit, cabbage, and coffee. Individuals, who have either the C/G or G/G genotype, may be more sensitive to bitter flavors. People with increased sensitivity to bitter taste tend to add salt to mask the bitter flavor in their foods.



Caffeine Metabolism



Your Result

Based on your genotype, you are likely to metabolize caffeine more quickly, causing shorter stimulant effects.

Your GENOTYPE

CYP1A2, rs762551, A/A

Description

Caffeine is one of the most widely consumed stimulants in the world. Caffeine can be found in coffee, tea, soft drinks as well as included in some pain relievers and other medications. The enzyme responsible for metabolism of caffeine is encoded by the CYP1A2 gene. The rs762551 genetic variant in the CYP1A2 gene has been associated with caffeine consumption. Individuals who are slow metabolizers may experience the stimulant effects of caffeine longer than individuals who are fast metabolizers. In addition to genetics, ability to metabolize caffeine can be affected by lifestyle choices such as smoking and overall caffeine consumption. Individuals with the A/A genotype are likely to metabolize caffeine more quickly, causing shorter stimulant effects. Whereas, individuals with the C/C genotype are likely to metabolize caffeine more slowly, causing longer lasting stimulant effects.



Sweet Taste



Your Result

Based on your genotype, you are likely to have a moderately reduced sensitivity to sweet foods.

Your GENOTYPE

TAS1R2, rs12033832, G/G

Your genotype is not associated with reduced sensitivity to sweet foods.

TAS1R3, rs307355, C/C

PATIENT NAME	PATIENT ID	SEX	DOB	REPORT TYPE
GCR, SampleReport_A	SampleReport_A	Male	01-01-2000	Genomic Clinical Report

Description

Sweetness is one of the basic tastes among sour, salty, bitter, and umami. Humans are able to taste food and other substances with the tongue papillae, each consisting of hundreds of taste buds. Sweet taste perception in humans is mediated by the TAS1R2 and TAS1R3 genes. Genetic variants, rs12033832 in the TAS1R2 gene and rs307355 in the TAS1R3 gene, are associated with reduced sensitivity to sweet foods. Depending on your genotype, you may have typical sensitivity, moderately reduced sensitivity, or reduced sensitivity to sweet foods. Individuals with either G/A or G/G genotype of the rs12033832 variant, as well as individuals with either T/C or T/T genotype of the rs307355 variant may have reduced sensitivity to sweet foods and may prefer foods with more sugar.

PATIENT NAME	PATIENT ID	SEX	DOB	REPORT TYPE
GCR, SampleReport_A	SampleReport_A	Male	01-01-2000	Genomic Clinical Report

Nutrition



OMEGA-6 and OMEGA-3 Levels



Scientific Strength

Your Result

Based on your genotype, you may have reduced levels of omega-3 and omega-6 fatty acids.

Your GENOTYPE

FADS1, rs174547, T/C

Description

Omega-3 and omega-6 fatty acids are polyunsaturated fats (PUFAs), essential fats that need to be obtained from your diet. Omega-3 fats (EPA, DHA, ALA) have important benefits for your heart, brain, and metabolism, and may help manage inflammation. Omega-6 fats (AA, GLA) mainly provide energy, but may also lower harmful LDL cholesterol and boost protective HDL. While EPA, DHA, and AA can be derived from diet, these long-chain PUFAs are also endogenously synthesized from the precursor fatty acids alpha-linolenic acid (ALA) and linoleic acid. Omega-3 and omega-6 fats are processed by enzymes called fatty acid desaturases, encoded by the FADS genes. Genome-wide association studies including over 10,000 subjects have shown that the variant, rs174547, in the FADS1 gene is associated with decreased blood levels of arachidonic acid (AA), as well as eicosapentaenoic acid (EPA). Individuals with either T/C or C/C genotype of the rs174547 variant may have decreased levels of omega-3 and omega-6 fatty acids. It is recommended that people monitor their intake of omega-6 fats while increasing their intake of omega-3 fats. Oily fish is the best source of omega-3 fats, EPA and DHA. Other marine sources include algal oils. ALA mainly comes from nuts and seeds.



Vitamin A



Scientific Strength

Your Result

Your genotype may increase susceptibility to vitamin A deficiency.

Your GENOTYPE

BCMO1, rs7501331, T/T

Your genotype is not associated with increased risk of vitamin A deficiency.

BCMO1, rs12934922, A/A

PATIENT NAME	PATIENT ID	SEX	DOB	REPORT TYPE
GCR, SampleReport_A	SampleReport_A	Male	01-01-2000	Genomic Clinical Report

Description

Vitamin A is a group of fat-soluble micronutrients that are important for multiple functions including the maintenance of the immune system and good vision. Vitamin A in the body is primarily derived from beta-carotene, a compound found in many vegetables including carrots, spinach, and sweet potatoes. Genetic variants, rs7501331 and rs12934922, in the BCMO1 gene have been shown to be associated with an impaired conversion of beta-carotene into vitamin A. Individuals with the T/T genotype of the rs12934922 variant, as well as individuals with the C/T or T/T genotypes of the rs7501331 variant are at higher risk of developing vitamin A deficiency. Vitamin A supplements may help maintain healthy vitamin A levels in individuals who have a genetic predisposition to vitamin A deficiency.



Vitamin B12



Your Result

Based on your genotype, your vitamin B12 levels are likely within typical range.

Your GENOTYPE

FUT2, rs601338, A/A

Description

Vitamin B12, also known as cobalamin, is an essential micronutrient required for maintaining normal nervous system function and red blood cell formation. Deficiency of this vitamin has been associated with a combination of dietary, environmental, and genetic factors. Evidence from twin studies suggests that vitamin B12 levels exhibit substantial heritability, estimated at approximately 59%, highlighting a significant genetic contribution to its regulation. Vitamin B12 is produced by microorganisms, and it accumulates in animal tissues, which is why foods of animal origin such as eggs, milk, fish, and meat are the primary natural dietary sources. The genetic variant, rs601338, in the FUT2 gene has been shown to influence circulating vitamin B12 levels. Individuals with either rs601338 G/G or G/A genotype may have reduced levels of vitamin B12. However, actual vitamin B12 status should be confirmed with laboratory testing, since non-genetic factors significantly influence circulating levels.



Vitamin B6



Your Result

Your genotype is associated with decreased levels of vitamin B6.

Your GENOTYPE

NBPF3, rs4654748, C/C

Description

Vitamin B6 (pyridoxine) plays a key role in nervous system function, red blood cell formation, and carbohydrate metabolism. Genetic variation at the rs4654748 locus within the NBPf3 gene has been associated with circulating vitamin B6 levels. Individuals carrying the C allele (C/T or C/C genotypes) have been reported to have lower vitamin B6 levels compared with individuals with the T/T genotype, likely due to differences in vitamin B6 metabolism and clearance. Despite this genetic association, dietary intake remains an important determinant of vitamin B6 status. Consuming vitamin B6-rich foods such as whole grains, legumes, fish, meat, eggs, and fortified cereals can help maintain healthy vitamin B6 levels.



Vitamin C



Your Result

Your GENOTYPE

Based on your genotype, you are likely to have adequate levels of vitamin C under normal dietary intake.

SLC23A1, rs33972313, C/C

Description

Vitamin C (L-ascorbic acid) is an essential water_soluble nutrient that must be obtained through diet, as humans lack the ability to synthesize it. This vitamin is necessary for the biosynthesis of collagen, catecholamine, and L-carnitine and it enhances the absorption of non_heme iron. In addition, vitamin C functions as a potent antioxidant. Severe deficiency results in scurvy, while suboptimal levels have been associated with increased risk of chronic conditions, including atherosclerosis, type 2 diabetes, and certain cancers. Vitamin C homeostasis is regulated by intestinal absorption, cellular transport, and renal excretion. Cellular uptake of vitamin C is mediated by sodium_dependent transporters, including sodium-dependent vitamin C transporter 1, encoded by the SLC23A1 gene. Recent studies have reported an association of reduced vitamin C levels with the SLC23A1 rs33972313 variant. Individuals harboring the rs33972313 A allele have been reported to have decreased levels of circulating vitamin C, likely due to decreased transporter efficiency. Good dietary sources of vitamin C include citrus fruits, green peppers, strawberries, tomatoes, broccoli, and both white and sweet potatoes.



Vitamin D



Your Result

Your GENOTYPE

Your genotype may increase susceptibility to vitamin D deficiency.

GC, rs2282679, G/G

Your genotype may increase susceptibility to vitamin D deficiency.

GC, rs1155563, C/C

PATIENT NAME	PATIENT ID	SEX	DOB	REPORT TYPE
GCR, SampleReport_A	SampleReport_A	Male	01-01-2000	Genomic Clinical Report

Description

Vitamin D is an important micronutrient that is necessary for building and maintaining healthy bones. Vitamin D is made primarily in the skin after exposure to sunlight. Insufficient vitamin D levels may lead to thin and brittle bones as well as certain types of cancer. Genetic variants, rs2282679 and rs1155563, in the GC gene have been reported to be associated with vitamin D deficiency. Individuals with either T/C or C/C genotype of the rs1155563 variant, as well as individuals with either T/G or G/G genotype of the rs2282679 variant may be at higher risk for developing vitamin D deficiency. Getting vitamin D from dietary sources such as fish oil, fatty fish, fortified cereals, milk, and certain supplements can help maintain healthy vitamin D levels.

PATIENT NAME	PATIENT ID	SEX	DOB	REPORT TYPE
GCR, SampleReport_A	SampleReport_A	Male	01-01-2000	Genomic Clinical Report

Fitness and Exercise



Achilles Tendinopathy



Scientific Strength

Your Result	Your GENOTYPE
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Based on your genotype you are not likely at increased risk for an Achilles tendon injury or inflammation.

GDF5, rs143383, G/A

Description

The Achilles tendon, the thickest tendon in the human body, connects the calf muscles to the heel bone. Continued intense stress on the Achilles tendon, especially activities that involve running and/or jumping, can cause small breaks and tears (tendinopathy). The genetic rs143383 variant in the GDF5 gene is associated with achilles tendinopathy. Individuals with A/A genotype may be more prone to Achilles tendon injuries. You can help prevent Achilles tendon injuries by good stretching, maintaining a healthy weight, and avoiding certain medications, such as fluoroquinolones.



Endurance Training



Scientific Strength

Your Result	Your GENOTYPE
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Based on your genotype, you are likely to have enhanced performance as an endurance athlete.

ACE, rs4343, A/A

Based on your genotype, you are likely to have enhanced performance as an endurance athlete.

ACTN3, rs1815739, T/T

Description

Endurance training refers to exercise done for medium to longer duration at moderate intensity. Endurance training has multiple health benefits including positive impact on cholesterol levels, body fat, and insulin sensitivity. Genetic variants, rs1815739 in the ACTN3 gene and rs4343 in the ACE gene, have been associated with enhanced endurance performance. The ACTN3 gene encodes for a type of actin that is expressed in type II muscle fibers (fast twitch). The ACE genotype influences bradykinin levels, and the high kinin activity has been associated with increased endurance performance. Individuals with the T/T genotype of the rs1815739 variant and/or the A/A genotype of the rs4343 variant may have enhanced performance as an endurance athlete. Improving endurance potential and stamina can be achieved by introducing variety into your workout routines, eating a balanced diet, and improving sleep.

PATIENT NAME	PATIENT ID	SEX	DOB	REPORT TYPE
GCR, SampleReport_A	SampleReport_A	Male	01-01-2000	Genomic Clinical Report



Enhanced HDL Cholesterol Response to Exercise



Your Result

Based on your genotype, you are likely to benefit from enhanced HDL cholesterol response to exercise.

Your GENOTYPE

PPARD, rs2016520, C/C

Description

One of the many health benefits of exercise can be the improvement of your cholesterol levels. High-density lipoprotein cholesterol (HDL) is known as the good cholesterol, since it helps remove other forms of cholesterol from your blood stream. Having higher levels of HDL is beneficial and may lower the risk for heart disease. Most individuals can improve their HDL levels by exercise, however, some have an enhanced benefit for having certain genetic variants in the PPARD gene. This gene encodes a nuclear transcriptional factor, a key regulator of energy metabolism due to its ability to enhance fatty acid catabolism, energy uncoupling, and insulin sensitivity in multiple tissues. Studies have shown that individuals with the C/T or C/C genotype of the rs2016520 variant were more likely to have an enhanced benefit on their HDL levels by exercising. Individuals, who do not have the aforementioned genotypes may also increase their HDL levels by exercising but may not experience an enhanced effect.



Insulin Sensitivity



Your Result

Based on your genotype, your insulin sensitivity and body's ability to process sugar may not greatly improve with exercise.

Your GENOTYPE

LIPC, rs1800588, C/T

Description

Insulin is a hormone that regulates blood sugar levels and allows glucose to enter the body's cells to provide energy. Individuals affected with type 2 diabetes do not respond well to insulin (insulin resistance) and, therefore, their sugar levels are high. Physical exercise is a beneficial way for affected individuals to increase sensitivity to insulin. The rs1800588 variant in the LIPC gene has been reported in association with higher hepatic lipase activity and better insulin sensitivity response to exercise. Individuals with the C/C genotype may have improved insulin sensitivity with exercise. Other ways to improve your insulin sensitivity include eating complex carbohydrates, intermittent fasting, getting better sleep, and certain prescription medications.



Muscle Performance



PATIENT NAME	PATIENT ID	SEX	DOB	REPORT TYPE
GCR, SampleReport_A	SampleReport_A	Male	01-01-2000	Genomic Clinical Report

Your Result	Your GENOTYPE
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Based on your genotype, you are likely to have enhanced performance as an endurance athlete.

ACTN3, rs1815739, T/T

Description

Athletic performance is influenced by several genetic and environmental factors. Genetic variation in the ACTN3 gene influences how much of the ACTN3 protein in our body can be produced or whether it can be produced at all. The ACTN3 protein is present in the fast twitch muscle fibers responsible for generating force at high velocity and is found in sprint and power-oriented athletes. Certain genotypes increase the likelihood of you having enhanced performance in power sports while individuals with mixed fast twitch/slow twitch fiber types have only a modest benefit in power sports. Genetic variant, rs1815739, in the ACTN3 gene has been associated with enhanced performance in power sports. Individuals with the T/T genotype may have enhanced performance as endurance athletes. Whereas, individuals with the C/C genotype may have enhanced performance in sprinting and other power sports. You can increase your fast twitch muscle fibers by doing certain sprint exercises and plyometrics.

PATIENT NAME	PATIENT ID	SEX	DOB	REPORT TYPE
GCR, SampleReport_A	SampleReport_A	Male	01-01-2000	Genomic Clinical Report

Behavior and Mood



Risk Seeking Behavior



Scientific Strength

Your Result

Based on your genotype, you are likely to have increased risk seeking behavior.

Your GENOTYPE

DRD4, rs1800955, C/C

Description

Human behavior is the result of a very complex interplay of environmental and biological factors. However, twin studies have shown that individual variation in risk seeking behaviors is substantially influenced by genetic background, with few differences between males and females. The individual differences in risk seeking behavior can be partially explained by variation in two genes, 5-HTTLPR and DRD4 (reported), that regulate dopamine and serotonin neurotransmission. These genes have been previously linked to emotional behavior, anxiety, and addiction. The C/C genotype of the DRD4 variant, rs1800955, has been associated with increased risk seeking behavior.



Smoking Behavior



Scientific Strength

Your Result

Based on your genotype, if you smoke, you are likely to smoke the typical number of cigarettes per day.

Your GENOTYPE

CHRNA3, rs1051730, G/G

Description

Cigarette smoking is the single largest cause of preventable death and disease. Smoking harms nearly every organ of the body, causes many diseases, and may shorten life by several years. Genetic background contributes about 50% to how much people smoke. The rs1051730 variant in the CHRNA3 gene has been reported in association with smoking behavior, and the genotypes G/A and A/A have been associated with smoking more than an average amount of cigarettes per day.



Smoking Cessation



Scientific Strength

Your Result

Based on your genotype, if you smoke, you have a typical likelihood of quitting successfully.

Your GENOTYPE

ANKK1, rs1800497, G/G

PATIENT NAME	PATIENT ID	SEX	DOB	REPORT TYPE
GCR, SampleReport_A	SampleReport_A	Male	01-01-2000	Genomic Clinical Report

Description

There are many benefits of quitting smoking. You will experience rapid normalization of blood pressure and heart rate, improvement in breathing and blood circulation. Over the long term, smoking cessation reduces the risk of developing many types of disease, as well as improves life expectancy. Success of stopping smoking depends on the motivation to quit and the degree of dependency on nicotine. Variation in genetic background may be a predictor for the success of smoking cessation. Genotypes G/A and A/A of the rs1800497 variant, in the ANKK1 gene have been associated with more successful quitting of smoking. Individuals who wish to quit smoking have various options for assistance including cognitive behavioral therapy, nicotine replacement patches and gum, as well as prescription medications.

PATIENT NAME	PATIENT ID	SEX	DOB	REPORT TYPE
GCR, SampleReport_A	SampleReport_A	Male	01-01-2000	Genomic Clinical Report

Disease Susceptibility



COVID-19 Severity



Scientific Strength

Your Result	Your GENOTYPE
Based on your genotype, you may have higher likelihood to develop respiratory failure from COVID-19.	ABO, rs657152, A/A
Based on your genotype, you may have higher likelihood to develop respiratory failure from COVID-19	SLC6A20, rs11385942, G/GA
Based on your genotype, you may have higher likelihood to develop respiratory failure from COVID-19.	LZTFL1, rs17713054, G/A

Description

COVID-19 is a disease caused by a virus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). While the majority of individuals who contract COVID-19 have mild symptoms and recover, others may develop serious medical complications such as respiratory failure, requiring mechanical ventilation. In a study of over 2,000 COVID-19 patients with severe respiratory failure from Italy and Spain, two genetic variants, rs11385942 in the SLC6A20 gene (risk allele - GA) and rs657152 (risk allele - A) in the ABO blood group locus, have been associated with an increased risk of developing respiratory failure. In addition, recent studies have discovered potential risk variants in the 3p21.31 locus associated with two-fold increased risk of respiratory failure from COVID-19. A specific genetic variant, rs17713054 (risk allele - A), affecting the LZTFL1 gene, has been reported to be associated with respiratory failure. Further studies are needed to establish these findings as strong scientific evidence. Please, talk to your doctor if you have concerns about your results.



Histamine Intolerance



Scientific Strength

Your Result	Your GENOTYPE
Based on your genotype, you are likely to have a reduced breakdown of histamine.	HNMT, rs1050891, A/G

PATIENT NAME	PATIENT ID	SEX	DOB	REPORT TYPE
GCR, SampleReport_A	SampleReport_A	Male	01-01-2000	Genomic Clinical Report

Description

Histamine regulates sleep, appetite, motivation, learning, and sexual behavior, and it also has some protective roles. Problems usually arise when histamine is not being broken down fast enough or if it's being produced in excess. Genetic variations in HDC, HNMT, DAO, H4R, and MS4A2 genes may affect histamine metabolism and response. Two enzymes, diamine oxidase (DAO), and N-methyltransferase (HNMT) are the major histamine metabolizers. DAO is the main histamine-degrading enzyme in the gut. Histamine N-methyltransferase is responsible for the elimination of the majority of histamine in the body. This enzyme plays a predominant role in brain histamine concentration and the regulation of the histaminergic nervous system. When your body has too much histamine, it can cause symptoms known as histamine intolerance, which can affect normal bodily functions. In individuals affected with histamine intolerance, food allergies, IBD, and IBS, the histamine system may become dysfunctional and trigger inflammatory reactions. Two genotypes of the rs1050891 variant in the HNMT gene have been reported in association with impaired function of histamine N-methyltransferase. Individuals with the A/A genotype may have elevated histamine levels, whereas the A/G genotype may result in reduced histamine breakdown without remarkable increase of histamine levels.



Lactose Intolerance



Your Result

Based on your genotype, you are likely to be lactose tolerant as an adult.

Your GENOTYPE

MCM6, rs4988235, A/A

Description

Lactose intolerance is an impaired ability to digest lactose, a sugar found in milk and other dairy products, caused by gradually decreasing activity of the LCT gene after infancy. Lactose intolerance is influenced by a genetic variation in a regulatory element in the MCM6 gene, which helps control the activity of a nearby gene called LCT. The ability to digest lactose into adulthood depends on which variations in the regulatory element individuals have inherited. The genetic variant rs4988235 has two alleles A and G. The allele A is associated with normal LCT activity, while the G allele is a marker for the gene being nonfunctional. Lactose intolerance is most prevalent in people of East Asian descent affecting more than 90% of adults. Lactose intolerance is also common in West Africa, Arab countries, Greece, Italy, and among people of Jewish descent. However, some populations have evolved to maintain high levels of lactase and be able to benefit from the consumption of dairy products through life.



Obesity



Your Result

Based on your genotype, you may be at increased risk for obesity.

Your GENOTYPE

MC4R, rs17782313, T/C

PATIENT NAME	PATIENT ID	SEX	DOB	REPORT TYPE
GCR, SampleReport_A	SampleReport_A	Male	01-01-2000	Genomic Clinical Report

Description

Obesity is defined as abnormal or excessive fat accumulation that presents a health risk. A body mass index over 30 is considered obese. Studies on family members, twins, and adoptees have shown that a portion of the variation in weight among adults is due to genetics. The heritability of obesity ranges between 40% and 70%, with some individuals still being obese despite a healthy lifestyle. Both lifestyle and genetic features contribute to obesity. The leptin-melanocortin pathway is commonly dysregulated in obesity. Melanocortin-4-receptor (MC4R) gene is one of the known hereditary factors of obesity. Studies have shown that the variant, rs17782313, downstream of the MC4R gene, has the strongest association with body mass index and obesity risk. Individuals, who have the genotype C/C of this variant would be more likely to experience excessive weight gain.



Protection Against Cardiovascular Disease



Your Result

Your genotype is not likely to protect you against cardiovascular disease.

Your GENOTYPE

B4GALT1, rs551564683, T/T

Description

Cardiovascular disease accounts for 1 in every 3 deaths in the USA and is the leading cause of morbidity and mortality worldwide. Cardiovascular risk factors, such as high low-density lipoprotein cholesterol (LDL-C) and fibrinogen blood levels are caused by both genetic and environmental factors. A new association between a missense variant (c.1055A>G) located in the B4GALT1 gene region that encodes a functional domain of beta-1,4-galactosyltransferase 1, and lower levels of LDL-C and plasma fibrinogen has been reported recently. Individuals who are carriers of this variant may have a decreased risk for cardiovascular disorders.



Protection Against Obesity



Your Result

Your genotype is unlikely to protect you from obesity.

Your GENOTYPE

GPR75, rs148952285, G/G

Your genotype is unlikely to protect you from obesity.

GPR75, c.329_335delCCAGTAG,
ACTACTGG/ACTACTGG

Description

Obesity is defined as abnormal or excessive fat accumulation that presents a risk to health. A body mass index over 30 is considered obese. Studies on family members, twins, and adoptees have produced scientific evidence that a portion of the variation in weight among adults is due to genetic factors. The heritability of obesity ranges between 40% and 70%. A recent study searching for genetic susceptibility loci for obesity discovered that variants in the brain-expressed gene, called GPR75 were associated with protection from obesity. The GPR75 gene encodes G protein-coupled receptor 75 that is highly expressed in hypothalamus, which is a center for neuroendocrine regulation of energy balance. Genetic variants in the GPR75 gene have been associated with lower BMI and 54% lower odds of obesity in heterozygous carriers compared with non-carriers. The results of this study suggest that individuals who are carriers of protein truncating variants in the GPR75 gene may have decreased risk of becoming obese. In addition to genetics, healthy lifestyle, diet and not being exposed to obesogenic environment can help to maintain healthy weight.



Response to GLP-1 receptor agonist treatment



Your Result

Based on your genotype you are likely to benefit from GLP-1 receptor agonist treatment.

Your GENOTYPE

GLP1R, rs6923761, G/G

Based on your genotype you are likely to have a typical response to GLP-1 receptor agonist treatment.

GLP1R, rs10305420, C/C

Description

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are medications that mimic the action of the naturally occurring GLP-1 hormone released from the intestine after meals. Activation of the GLP-1 receptor stimulates glucose-dependent insulin secretion, suppresses glucagon release, slows gastric emptying, and promotes satiety through effects on the central nervous system. Together, these actions help lower blood glucose levels and reduce food intake. GLP-1 receptor agonists have demonstrated efficacy in the treatment of type 2 diabetes, obesity, and certain cardiovascular conditions. However, treatment response varies substantially between individuals. While many patients experience significant improvements in glycemic control and weight loss, approximately 10-20% may fail to achieve clinically meaningful benefits. Ongoing pharmacogenetic research is investigating whether genetic variation contributes to this variability in treatment response. One gene of interest is GLP1R, which encodes the glucagon-like peptide-1 receptor. Several studies have evaluated the association between GLP1R variants and response to GLP-1 receptor agonist therapy. The GLP1R rs6923761 (G>A) variant has been associated with differential glycemic response. In some studies, individuals with the G/G genotype experienced a significantly greater reduction in glycated hemoglobin (HbA1c) following GLP-1 receptor agonist treatment compared with carriers of the A allele (G/A or A/A genotypes). Another GLP1R variant, rs10305420 (C>T), has been reported to influence weight-loss response to GLP-1 receptor agonists. Individuals with the T/T genotype have been observed in some studies to experience greater weight reduction during treatment compared with carriers of the C allele.

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SERPINE1 4G/5G Polymorphism-Associated Clotting Risk



Your Result	Your GENOTYPE
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This genotype may be associated with increased risk for VTE and MI, particularly when other thrombotic risk factors are present.

SERPINE1, rs1799762, T/TG

Description

The SERPINE1 gene encodes plasminogen activator inhibitor-1 (PAI-1), a key regulator of fibrinolysis, the process by which blood clots are broken down. PAI-1 inhibits tissue plasminogen activator (tPA) and urokinase plasminogen activator (uPA), thereby reducing clot dissolution and promoting clot stability. A common promoter polymorphism in SERPINE1, rs1799762, also known as the 4G/5G insertion/deletion variant, influences PAI-1 gene expression. The 4G allele is associated with higher transcriptional activity and increased circulating PAI-1 levels compared with the 5G allele. Individuals with the 5G/5G genotype typically have approximately 20-30% lower plasma PAI-1 concentrations than individuals with the 4G/4G genotype, while 4G/5G heterozygotes generally exhibit intermediate levels. Elevated PAI-1 levels can impair fibrinolysis, resulting in a reduced ability to break down blood clots. This hypofibrinolytic state has been associated with an increased risk of thrombotic disorders, including venous thromboembolism (VTE), myocardial infarction (MI), and other cardiovascular diseases. Elevated PAI-1 levels have also been implicated in certain pregnancy-related complications, such as recurrent pregnancy loss, preeclampsia, and placental vascular disorders. Individuals carrying one or two copies of the 4G allele may have an increased susceptibility to thrombotic and cardiovascular events, particularly when other inherited or acquired thrombophilic risk factors are present. However, the effect of the SERPINE1 4G/5G polymorphism alone is generally considered modest. Consequently, this variant is not currently regarded as a major independent thrombophilia marker, but rather as a genetic factor that may contribute to risk in combination with other genetic, metabolic, hormonal, or environmental risk factors.



Susceptibility to Non-Alcoholic Fatty Liver Disease



Your Result	Your GENOTYPE
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Based on your genotype, you are likely to have a typical risk for developing NAFLD.

PNPLA3, rs738409, C/C

Description

Non-alcoholic fatty liver disease (NAFLD) is a common liver disorder characterized by excessive fat accumulation in the liver in individuals who consume little or no alcohol. It is strongly associated with obesity, overweight status, insulin resistance, and other metabolic risk factors. NAFLD is currently the most common chronic liver disease worldwide. The disease spectrum ranges from simple hepatic steatosis (fatty liver) to the more severe form, non-alcoholic steatohepatitis (NASH), which can progress to fibrosis, cirrhosis, and liver cancer. A well-established genetic risk factor for NAFLD is the PNPLA3 rs738409 (C>G) variant. Studies have shown that individuals who are heterozygous (C/G) for this variant have approximately a 2.4-fold increased risk of developing NAFLD, while individuals who are homozygous (G/G) have approximately a 3.7-fold increased risk compared with individuals carrying the C/C genotype.

Longevity and Aging



Human Longevity



Your Result	Your GENOTYPE
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Based on your genotype, you are likely to live to the age of 90 years or older.	FOXO3, rs4946935, A/A
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Based on your genotype, you are likely to live to the age of 90 years or older.	FOXO3, rs12206094, C/T
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Description

Longevity is impacted by several factors, and it is estimated that about 25% is due to genetic variation. A protein encoded by the FOXO3 gene mobilizes an organism's response to stress - for example, as a result of shortage of nutrients, oxidative stress, or a reduction in key hormones. An increased activity of this protein has been linked to longevity. Genetic variants, rs12206094 and rs4946935, in the FOXO3 gene have been found more frequently in individuals who have lived to at least 90 years old. Individuals with the C/T or T/T genotype of the rs12206094 variant, as well as individuals with the A/A or A/G genotype of the rs4946935 variant are likely to live to 90 or longer. While some nutrients have been shown to stimulate FOXO3 effects (green tea, curcumin, and resveratrol), lifestyle factors such as maintaining a healthy diet, not smoking, exercising, and lowering stress are well-established contributors to longer lifespan.

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Appendix

This test was developed and performed by Simplify Genomics Clinical Laboratory. It has not been cleared or approved by the FDA. At this time, FDA approval is not required for clinical laboratory developed tests. The laboratory is regulated under the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high-complexity testing. This test is used for clinical purposes and should not be regarded as investigational or for research.

1. Intended Use

The Simplify Genomics Genomic Clinical Report is intended to be a screening test for apparently healthy individuals. The patient's health care provider will need to evaluate the patient's clinical status and will need to confirm the screening finding(s) which warrant a change in treatment via an appropriately licensed clinical laboratory's diagnostic test(s) before making such a change. These test results may have implications for family members. Genetic counseling is recommended for individuals who have questions or concerns about the genetic report.

1.1 Hereditary Disease Risk

This test is indicated for reporting genetic variants that are associated with high or medium genetic risk of developing hereditary (or monogenic) diseases. Findings of this test may warrant further evaluation. Such evaluations may include the use of appropriately validated diagnostic tests that are intended to diagnose the disease or condition related to a given genetic variant. If there are concerns regarding a particular genetic disease, or family history suggestive of a hereditary risk, a referral for a formal genetic consultation and discussion of appropriate diagnostic testing is recommended.

1.2 Pharmacogenomic Findings

This test is indicated for assessing how genetic variants may affect a person's response to prescribed medications. This test is not a substitute for clinical monitoring or other clinical evaluation. Only a health care provider should take action on the information contained in this test report. Do not stop taking or alter the dosage of any prescribed medications without consulting with your doctor beforehand.

1.3 Health Predisposition

This test is indicated for the reporting of combinations of genetic variants that are associated with genetic predisposition to common diseases. The variants included in the test are typically associated with a low genetic risk of developing a disease when considered independently, whereas the combined effects of multiple variants can contribute to increased risk of developing disease. The test results represent a percentile rank of the polygenic risk score as compared to research participants of European descent. The percentile rank is accompanied by the relative risk of developing a disease calculated using an independent cohort of affected and non-affected individuals of European descent. The test is expected to provide less accurate results to people of non-European background.

The results of this test should not be used to guide medical care but rather to inform patient's lifestyle decisions. This test does not describe a person's overall risk of developing a disease, which is dependent on lifestyle and environmental factors in addition to genetic background. Even the highest reported genetic risk should not be interpreted as indicating the certainty of developing a disease, nor should the lowest risk be interpreted as immunity. This test is not intended to diagnose a disease or determine current state of health.

1.4 Nutrition and Wellness Traits

This test is indicated for reporting of common genetic variants that affect nutrition and wellness traits. Some variants contribute to nutrient deficiency and food sensitivity; others have an effect on behavior and fitness. This test does not describe a person's overall chance of developing a trait, which is dependent on lifestyle and environmental factors in addition to genetic background. If two or more variants are associated with a trait, interpretation is provided for each variant separately.

LABORATORY NAME	ADDRESS	CONTACT	CLIA	CAP	VERSION	PAGE
Simplify Genomics Clinical Laboratory, LLC	440 Stevens Avenue, Suite 200, CA 94040	support@simplifygenomics.com	05D2094189	9013965	10.0.0	55 of 62

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The results of this test should not be used to guide medical care but rather to inform lifestyle decisions.

2. Sequencing Assay

Whole Genome Sequencing (WGS) on germline DNA was performed to ~30x mean depth using paired-end, 2 x 150 reads. Sequencing details for the specimen are provided below.

LABORATORY:	Sampled
ADDRESS:	30 Knightsbridge Road, Building 3, Piscataway, NJ 08854
CAP:	8981166
CLIA:	31D2077913

Alignment and variant calling were performed by the Simplify Genomics Clinical Laboratory (CAP #9013965; CLIA #05D2094189) using the GRCh38DH reference genome, based on the GRCh38 primary assembly (GCA_000001405.15) and incorporating alternate (ALT), decoy, and HLA sequences. Sequence alignment was performed using BWA v0.7.12, and variant calling was performed using Sentieon Genomics Haplotyper v202308.03. The sequencing and bioinformatics pipelines were validated for the detection of single nucleotide variants (SNVs), small insertions (≤7 bp), small deletions (≤7 bp), and copy number variants (CYP2D6 only) within the high-confidence regions (~93.25% of the genome) defined by the Simplify Genomics Clinical Laboratory using the Illumina Platinum Genomes benchmark for the GRCh38 reference assembly.

The overall performance characteristics of the assay (as compared to reference cell lines) are as follows:

Sensitivity: SNV>99%, Insertions>95%, Deletions>95%
Specificity: SNV>99%, Insertions>99%, Deletions>99%

3. Analytics

3.1 Hereditary Disease Risk

Variants included in this report have met the American College of Medical Genetics and Genomics (ACMG) and the Association for Molecular Pathology (AMP) variant classification guidelines criteria for classification as pathogenic and likely pathogenic [1-3]. In addition, risk factor and association variants are determined by laboratory established classification protocol. These variants include alterations interpreted manually in house by PhD-level Genomic Scientists as well as robust proprietary algorithm developed by Simplify Genomics Clinical Laboratory.

Several variants in the test are included with a classification category risk factor (e.g., APOEc.388T>C). The classification category "risk factor" is used for variants with incomplete penetrance that are associated with lower disease risk. In addition, some variants are included with the classification category, association. This applies when the suggested pathogenicity for a well-known variant (e.g., APC c.3920T>A) is solely based on evidence from association studies. These types of variants are included as they may modify the impact of other variants.

3.2 Pharmacogenomic Findings

Pharmacogenomic reporting is based on the guidelines of the Clinical Pharmacogenetics Implementation Consortium (CPIC) [4] and the Dutch Pharmacogenetics Working Group (DPWG) [5], as well as recommendations provided in the FDA drug labels [6], The FDA Table of Pharmacogenetic Associations [7], and ClinPGx [8]. Any deviations reflect edits for brevity or clarity. The assay covers star alleles and variants in genes impacting efficacy, dosage, and adverse effects of specific drugs.

Pharmacogenomic reporting evaluates variants and their zygosity to determine a genotype comprised of two star alleles. In addition, phenotypes (e.g., Intermediate metabolizer) are predicted following CPIC guidelines. Star allele *1 signifies a normal (wild type) genotype and is characterized by the absence of any tested variants in the given gene. All other star alleles are defined as combinations of variants, with definitions available from CPIC star allele definition tables.

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In the case of an incomplete match of variants to star allele definitions, the star allele provided is based only on the variants completely shared with the definition. A result of "unable to determine" is displayed when the sequencing data for common variant(s) of the star alleles is not of sufficient quality or the genotypes are not unambiguously resolvable as a combination of two known star alleles. A common variant is defined as a variant with allele frequency of more than 1% in any gnomAD subpopulation [9]. In some cases, an ambiguous result (separated by ;) will be reported for the genotype, phenotype, or both.

Allele-specific copy number is only reported for CYP2D6 as part of the star allele diplotype, e.g., *1x2|*2x1 corresponds to 2 copies of allele *1 and 1 copy of *2. The impact of multiple copies of an allele is accounted for when reporting the phenotype as per CPIC guidelines.

3.3 Health Predisposition

This test utilizes polygenic risk scores, an innovative approach that combines the impact of many common variants of small effect into a single score. These common variants are typically identified through genome-wide association studies (GWAS) and are often associated with a modest increase in disease risk or are in linkage disequilibrium with causal risk variants. Although individual common variants generally confer only a small effect on disease susceptibility, their cumulative impact can be substantial [10-12].

Polygenic risk models used in this test were defined based on findings of scientific studies called "Genome-Wide Association Studies" (termed GWAS). In these studies, scientists compare genomes of large groups of people, either with or without the disease, to find genetic variants that distinguish these two groups. The GWAS approach allows for the estimation of a variant-specific weight that is directly proportional to the strength of the association between the variant and the disease. A polygenic risk score is the sum of these weights for all variants that are shared between the polygenic risk model definition and the genome of the patient.

For each disease included in the test, available GWASs are reviewed to identify high-quality studies. Preference is given to studies that use a large number of genomes, are conducted by leading research groups, and that produce results corroborated by other studies. For each study selected, genetic variants associated with the disease and their weights are used as the basis of the polygenic risk model.

The test results include a percentile rank of the polygenic risk score that compares the score of a given patient to that of the scores of previous patients of European background ancestry. For example, the 65th percentile means that the polygenic risk score is greater than 65% of the previous patients of European descent. The European background ancestry of research participants was determined based on the ancestry computed from the individuals' genomes and is defined as the combined proportion of categories "Western European", "Eastern European" and "Southern European" ancestral groups being equal to or exceeding 60% from each included individual.

In addition to the percentile rank, the test results include a risk ratio (also called "relative risk") of developing a disorder as compared to the individuals with "most common" genetic profiles (individuals with percentile ranks between 40th and 60th). For example, a risk ratio of 2.80 means that the individual is at 2.8-fold increased risk for of developing a disease as compared to the individuals with "most common" genetic profiles; a risk ratio of 0.65 means that the individual is at 35% decreased risk for of developing a disease.

Please refer to [our whitepaper](#) for more details on the development and validation of the polygenic risk models included in the test, as well as calculation of risk ratios and other metrics of model performance.

3.4 Nutrition and Wellness Traits

This test includes a set of models, each of which comprises one or two common genetic variants contributing to the development of a given trait. The genetic variants used in models and the interpretation of their effects are identified by a comprehensive review of scientific literature for a specific trait. When selecting studies for inclusion, preference is given to ones that used a large number of people to study the trait, were conducted by leading research groups, and produced results that are corroborated by other studies. The research into genetics of some traits is ongoing. The level of current scientific evidence is ranked using a four-tier system - "preliminary" (one star), "moderate" (two stars), "strong" (three stars), "established" (four stars) - presented next to each trait.

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Results interpretation is provided for each variant separately. For example, 'GDF5, rs143383 G/A'. GDF5 is a name of the gene in which the variant occurs; rs143383 points to the location of the specific variant in the genome. G/A is the genotype at this location, where one copy of the gene has a G (guanine) at the variant location, and the other copy has an A (adenine). An interpretation of the result is provided alongside the genotype. For example, a statement such as 'Based on your genotype, you may have an increased risk of Achilles tendon injury or inflammation' explains the potential association between the identified genotype and the reported trait. In some cases, the genotype result may be displayed as 'Unable to Determine' for any trait that includes a variant that could not be called confidently due to poor quality.

4. Reporting Scope

4.1 Hereditary Disease Risk

The hereditary disease risk reporting scope includes 2011 genes and 2240 diseases. Please refer to the table below for the reportable genes and diseases.

For a full list of genes, please refer to the [Clinical Gene List](#).

	HEALTH CATEGORY	# GENES
	Cardiovascular Disorder	96
	Dental Disorder	9
	Endocrine Disorder	70
	Gastrointestinal Disorder	6
	Hearing Disorder	47
	Hematologic Disorder	70
	Hereditary Cancer	90
	Immunological Disorder	108

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	HEALTH CATEGORY	# GENES
	Kidney Disorder	49
	Liver Disorder	12
	Metabolic Disorder	228
	Musculoskeletal Disorder	125
	Neurodegenerative Disorder	51
	Neurologic Disorder	321
	Respiratory Disorder	34
	Skin Disorder	56
	Syndromic Disorder	512
	Vision Disorder	133

4.2 Pharmacogenomic Findings

For the list of genes and variants detected by this test, please refer to the [Clinical Gene List](#). A star allele *1 (normal or wild type genotype) signifies the absence of the targeted alleles and does not indicate the absence of other variants not covered by the assay. Only variants with an established drug association are included in the PGx reportable scope. Differences may be observed between the PGx and Hereditary Disease results.

4.3 Health Predisposition

For the list of variants included in each polygenic risk model, variants' weights characterizing the impact of each variant, as well as scientific studies, from which the variants were extracted, please refer to the [Clinical Gene List](#).

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There is a small overlap between variants included in the polygenic risk models and the scope of the "Hereditary Disease Risk" test. Specifically, the APOE e4 variant is included in the Alzheimer's disease polygenic risk model and the c.*97G>A variant in the F2 gene and the factor V Leiden variant in the F5 gene are included in the venous thromboembolism polygenic risk model. The polygenic risk scores for these diseases are expected to be higher when corresponding variants are identified by the "Hereditary Disease Risk" test.

4.4 Nutrition and Wellness Traits

For the list of variants included in trait models, please refer to the [Clinical Gene List](#).

5. Limitations

5.1 Hereditary Disease Risk

This test is validated to generate a high-quality consensus whole genome sequence, however, the following limitations need to be considered:

- Only likely pathogenic and pathogenic variants within the genes included in the reporting scope described in section 4.1 are reported when detected. Other potentially pathogenic rare variants in the reporting scope's genes as well as novel variants may be present in the patient's DNA and are not reported. A negative test result, therefore, does not completely rule out the possibility that the patient has other variants that could affect his or her health and does not rule out the possibility that the patient is a carrier.
- The "Hereditary Disease Risk" test excludes common variants included in the polygenic risk scores in the "Health Predisposition" assessment (with the exception of the three variants listed in section 4.3). Thus, apart from the Alzheimer's disease and the venous thromboembolism polygenic risk models, the results of the two tests are independent and a patient can be negative for one but positive for another assessment.
- The technology currently available for whole genome sequencing does not address the entire human genome: this assay assesses 90% - 93% of the human genome representing the high-confidence regions. The regions of the genome not reported in this test include regions where the human reference genome has not been completely resolved or where duplications of genetic regions impair accurate alignment. The presence of alterations outside the evaluated regions in the genome is not identified and therefore cannot be ruled out.
- Only single nucleotide variants, small insertions (<=7bp), and deletions (<=7bp) within the high-confidence regions are reported in this test.
- Variants included in the reporting scope but not meeting sufficient sequencing coverage in a given sample are not reported.
- It should be noted that blood limited acquired (somatic) variants may arise in the blood, particularly with advancing age, and may appear as germline variants.
- Copy number is only validated for use in the Pharmacogenomics Findings section, specifically for CYP2D6. Copy number results are not reported for Hereditary Disease Risk.
- Ability to align reads to the reference genome may be hindered by pseudogenes, regions of high homology, homopolymers, simple sequence repeats, tandem duplications, high or low-GC content, and repeat expansions.

5.2 Pharmacogenomic Findings

This test is validated to generate accurate star allele calls and associated phenotypes, however, the following limitations need to be considered:

- Other genetic and non-genetic factors such as drug-drug interactions are not considered in this test but may also impact drug response.
- This test does not cover HLA genes, although some of them are linked to significant adverse effects to certain drugs, including

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carbamazepine and abacavir.

- This test may not cover all known star alleles and variants due to updates in Pharmacogenomics guidelines or star allele definition tables that have occurred after the latest pharmacogenomics test revision.
- In some instances, CPIC guidelines provide variants comprising a star allele but do not provide a phenotype (e.g., SLCO1B1 *14). In these cases, only a genotype is reported.
- The methodology used in this test is unable to determine the allelic phase. In certain instances, this leads to ambiguity in genotype calling (e.g., SLCO1B1 *1 | *15 cannot be resolved from SLCO1B1 *1B | *5), leading to either an "unable to determine" output in cases where phenotypes are different, or output of two or more diplotypes in cases where all diplotypes are associated with the same phenotype.

5.3 Health Predisposition

This test is validated to generate accurate polygenic risk score calculations, however, the following caveats need to be considered:

- The polygenic risk models included in this report only describe the contribution of the genetic background. Other important contributors to disease risk are lifestyle and environmental factors that are not taken into account by the results provided in this report.
- This test provides genetic risk information based on assessment of specific genetic variants described in section 4.3. It does not report on the entire genetic profile and excludes rare variants included in scope of the "Hereditary Disease Risk" test (with the exception of the three variants listed in section 4.3). Thus, apart from the Alzheimer's disease and the venous thromboembolism polygenic risk models, the results of the two tests are independent and a patient can be negative for one but positive for another assessment
- This test does not detect all common variants related to a given disease. The absence of variants tested does not rule out the presence of other genetic variants that may be related to the disease. There are several reasons for some genetic variants to be excluded from this test:
 - This test reports on the genetic variants reported in published scientific studies at a single point in time and is considered current as of the report date. The list of articles that were consulted in preparing the report is not necessarily a comprehensive list, and other studies may exist that are relevant to the test results. New associations are discovered daily, some of which may relate to genes and variants that are included in this report or represent newly discovered genes and variants. A health care professional should reassess the results provided in this report as future relevant evidence becomes available
 - Only genetic variants meeting the validated parameters are included in this test, please review the sequencing limitation details provided in section 2 and section 5.1.
- Polygenic risk models used in this test were originally developed using genomes of people of European descent and may provide less accurate results to people of other ethnicities.
- Please refer to [White Paper](#) for limitations of the validation study, which evaluated predictive performance of the polygenic risk models.
- As polygenic risk models may include hundreds of variants, it may occur that one or more variants included into a model cannot be confidently identified for a given sample. Due to this uncertainty, a range of percentiles and/or relative risk are provided for the impacted models.

5.4 Nutrition and Wellness Traits

This test is validated to generate accurate genotype results, however, the following caveats need to be considered:

- The trait models included in this report only describe the contribution of the genetic background. Other important contributors to trait development are lifestyle and environmental factors that are not taken into account by the results provided in this report.

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- This test does not detect all common variants related to a given trait. See item 5.3 for additional details as polygenic risk models have a similar limitation.
- Models originally developed using genomes of a specific ethnicity cannot always be successfully used to predict physical traits for people of a different ethnicity. We recommend consulting [Your Results Guide](#) to learn for whom the models provide the most accurate result.
- The patient may get a different result using a test from a different company even if the test is for the same trait. Other companies offering genetic tests may be detecting different genetic variants for the traits. They could be using different sequencing technology or include evidence from different scientific studies.

6. References

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