HUMAN LONGEVITY

Genomic Report

PATIENT INFORMATION		
NAME: [redacted]		
[redacted]	SEX: Female	[redacted]
ACCESSION #: TM736UJ6	REPORT DATE: 2026-06-08	STATUS: FINAL
COLLECTION DATE: 2026-04-18		

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. These results should be considered for research only. While these results may have medical significance, they have not been validated for clinical use. The results in this section should not be used to guide medical decisions without consulting your clinician beforehand. Any results that warrant a change in treatment should be confirmed by a diagnostic test from a CLIA-accredited clinical laboratory, and you should consult a clinician before making any changes. Genetic counseling is recommended.

FINDINGS SUMMARY

GENOME SUMMARY	
3.2 Billion	Base pairs analyzed
5.4 Million	Total variants detected
3900	Total genes assessed
5494	Total diseases assessed

YOUR RISK		
	Monogenic dominant inheritance	VARIANTS IDENTIFIED
	Neurodegenerative Disorder	1
	Monogenic recessive inheritance	VARIANTS IDENTIFIED
	Skin Disorder	1
	Vision Disorder	1

Variant Summary

HEALTH CATEGORY	GENE	VARIANT	ZYGOSITY	CLASSIFICATION	DISEASE ASSOCIATED	INHERITANCE
Neurodegenerative Disorder	APOE	c.388T>C (p.Cys130Arg) NM_000041.3	Heterozygous	risk factor	Alzheimer's disease; Coronary artery disease, severe, susceptibility to	Autosomal dominant

HUMAN LONGEVITY

Genomic GeneByGene Report

PATIENT INFORMATION

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[redacted] | SEX: Female | [redacted]

HEALTH CATEGORY	GENE	VARIANT	ZYGOSITY	CLASSIFICATION	DISEASE ASSOCIATED	INHERITANCE
Skin Disorder(Carrier)	FLG	c.2282_2285delCAGT (p.Ser761fs) NM_002016.1	Heterozygous	Pathogenic	Ichthyosis vulgaris	Autosomal recessive
Vision Disorder(Carrier)	USH2A	c.2276G>T (p.Cys759Phe) NM_206933.2	Heterozygous	Likely pathogenic	Retinitis pigmentosa 39 Usher syndrome, type 2A	Autosomal recessive

APOE Summary

GENE	SUBTYPE	RS429358	RS7412
APOE	ε3/ε4	T/C	C/C

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Variant Details

Variants Associated with Neurodegenerative Disorder

+	APOE risk factor variant, c.388T>C(p.Cys130Arg)	37.8788% (1000 Genomes, African)

Client was found to have a risk factor variant associated with an increased risk for Neurodegenerative Disorder

The c.388T>C variant, also known as APOE e4, increases the risk for early-onset and late-onset Alzheimer's disease but is not sufficient to cause disease. On average, people without the APOE e4 variant have an approximately 10-15% chance of developing Alzheimer's disease during their lifetime and an average age of disease onset of 84 years (PMID:28323826,23296339). Individuals with the APOE e4 variant in heterozygous state are estimated to have a 3-fold increased risk of developing Alzheimer's disease compared to people without the variant. They have an approximately 20-25% chance of developing Alzheimer's disease during their lifetime (PMID:28323826). Individuals with the APOE e4 variant in homozygous state have a 15-fold increased risk of developing Alzheimer's disease compared to people without the variant, resulting in an approximately 30-55% chance of developing Alzheimer's disease during their lifetime. The average age of disease onset is 76 and 68 years of age for people with the APOE e4 variant in heterozygous and in homozygous state, respectively (PMID:23296339). Additionally, the APOE e4 variant is associated with an increased risk of developing coronary artery disease. The APOE e4 variant in heterozygous state confers a 1.22-fold increased risk compared to people without the variant (in other words, a 22% increased risk) and the APOE e4 variant in homozygous state a 1.45-fold increased risk compared to people without the variant (or 45% increased risk) (PMID:27868062).

The APOE gene codes for apolipoprotein E, a protein responsible for packaging cholesterol and other fats and carrying them through the bloodstream. Some variants in the APOE gene are associated with both an increased and decreased risk for various disorders including autosomal dominant early-and late-onset Alzheimer's disease (MIM:104310) and coronary artery disease (MIM:617347). 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 begins as mild cognitive impairment, at which time individuals can experience increased forgetfulness as well as slight difficulty with focus or concentration. The signs and symptoms of the early-onset form of Alzheimer's disease appear before age 65, while the late-onset form appears after age 65. Coronary artery disease develops when the major blood vessels that supply blood to the heart muscle become hardened and narrowed. This happens due to the buildup of plaque inside the arteries (also called atherosclerosis). As a result, the heart muscle is unable to get enough oxygen-rich blood. Over time, the heart muscle weakens, which can lead to heart failure, arrhythmias, and heart attack. Chest discomfort is the most common symptom of coronary artery disease. Coronary artery disease is very common; one in two men and one in three women of 40 years or older will develop the condition during their lifetime. Many other risk factors besides the variants in the APOE gene contribute to the development of Alzheimer's disease and coronary artery disease, including variants in other genes, lifestyle and environmental factors. Lifestyle and environmental factors are often modifiable and may help reduce the risk for developing these diseases.

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Variants Associated with Skin Disorder

+	FLG Pathogenic variant, c.2282_2285delCAGT(p.Ser761fs)	2.3256% (1000 Genomes, South Asian)

Client 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.2282_2285delCAGT frameshift variant has been reported to result in abolished FLG protein (PMID:16444271). The c.2282_2285delCAGT deletion is a common pathogenic FLG variant and has been identified in a homozygous or compound heterozygous state in several individuals affected with ichthyosis vulgaris, with incomplete penetrance and seasonal variation of the phenotype (PMID:29444371,29068602,21777221).

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 is 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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Variants Associated with Vision Disorder

+	USH2A Likely pathogenic variant, c.2276G>T(p.Cys759Phe)	0.4808% (1000 Genomes, Admixed American)

Client is a carrier for a likely pathogenic variant associated with a Vision Disorder , Reproductive partner and/or first-degree relatives may benefit from screening

The c.2276G>T missense variant has been identified in a homozygous or compound heterozygous state in several individuals affected with retinitis pigmentosa or Usher syndrome with considerable phenotypic heterogeneity (PMID:16098008,18273898,25472526). Furthermore, co-segregation of the c.2276G>T variant with the disease has been established in two families (PMID:10775529,12525556).

The USH2A gene codes for usherin, an important component of the basement membrane protein that plays a role in the development and homeostasis of the inner ear and retina. Pathogenic USH2A variants are associated with autosomal recessive retinitis pigmentosa-39 (RP39, MIM:613809) and Usher syndrome type 2A (USH2A, MIM:276901). Retinitis pigmentosa is characterized by night blindness during the third decade of life, progressing to loss of central vision in later years of life (PMID:12427073). Usher syndrome type 2A is characterized by sensorineural hearing loss at birth and later development of progressive retinitis pigmentosa (PMID:9624053). Pathogenic USH2A variants account for 10-15% of the retinitis pigmentosa cases (PMID:20301590) and 57-79% of the Usher syndrome cases (PMID:20301515,18273898). The prevalence is between 1 in 3,000 and 1 in 5,000 individuals for all forms of retinitis pigmentosa (PMID:18376416,11921605) and 6 in 100,000 individuals for Usher syndrome (PMID:12107518).

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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.

FINDINGS SUMMARY

REPORTING SCOPE	
18	Total genes assessed
135	Total drugs assessed

YOUR RISK	
	YOUR PHARMACOGENOMIC RESULTS
	79 Drugs Potentially Impacted

Drugs Potentially Impacted

THERAPEUTIC	GENE	GENOTYPE	PHENOTYPE	DRUG	COMMENTS
ANTIARRHYTHMIC AGENT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Propafenone (Rythmol®)	Increased risk of reduced efficacy due to lower systemic concentration of propafenone. Dose increase and drug monitoring are recommended. Refer to FDA labeling for specific dosing recommendations. Medications that are not predominantly metabolized by CYP2D6 should be considered (FDA drug label, DPWG guideline).
BETA BLOCKER	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid 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).
BETA BLOCKER	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid 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).

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THERAPEUTIC	GENE	GENOTYPE	PHENOTYPE	DRUG	COMMENTS
BETA BLOCKER	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid 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	*34x2|*39;*1|*2 x2	Ultrarapid 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).
BLOOD THINNER	VKORC1	rs9923231:CT	Increased Warfarin Sensitivity	Warfarin (Coumadin®)	Individuals with rs9923231:CT or rs9923231:TT have increased 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, FDA's Table of Pharmacogenetic Associations, CPIC guideline).
BLOOD THINNER	CYP4F2	*1|*3	Decreased 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, FDA's Table of Pharmacogenetic Associations, CPIC guideline).
BLOOD THINNER	CYP2C19	*1|*17	Rapid Metabolizer	Clopidogrel (Plavix®)	Normal or increased clopidogrel active metabolite formation. Normal or lower on-treatment platelet reactivity, however, no association with higher bleeding risk (FDA drug label, CPIC guideline).
CARDIAC MYOSIN INHIBITOR	CYP2C19	*1|*17	Rapid Metabolizer	Mavacamten (Camzyos®)	May have an increased risk of reduced efficacy due to lower systemic concentration of mavacamten. Refer to FDA labeling for specific dosing recommendations (FDA drug label).

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THERAPEUTIC	GENE	GENOTYPE	PHENOTYPE	DRUG	COMMENTS
UROLOGICAL AGENT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid 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).
UROLOGICAL AGENT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid 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).
PROTON-PUMP INHIBITOR	CYP2C19	*1|*17	Rapid Metabolizer	Dexlansoprazole (Dexilant®)	Increased risk of reduced efficacy due to lower systemic concentration of dexlansoprazole. Dose increase and drug monitoring are recommended. Refer to FDA labeling for specific dosing recommendations (FDA drug label, CPIC guideline).
PROTON-PUMP INHIBITOR	CYP2C19	*1|*17	Rapid Metabolizer	Omeprazole (Prilosec®)	Increased risk of reduced efficacy due to lower plasma concentration of omeprazole. Dose increase and drug monitoring are recommended (FDA drug label, CPIC guideline, DPWG guideline).
PROTON-PUMP INHIBITOR	CYP2C19	*1|*17	Rapid Metabolizer	Rabeprazole (AcipHex®)	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	*1|*17	Rapid Metabolizer	Pantoprazole (Protonix®)	Increased risk of reduced efficacy due to lower plasma concentration of pantoprazole. Dose increase and drug monitoring are recommended (FDA drug label, CPIC guideline, DPWG guideline).
PROTON-PUMP INHIBITOR	CYP2C19	*1|*17	Rapid Metabolizer	Lansoprazole (Prevacid®)	Increased risk of reduced efficacy due to lower plasma concentration of lansoprazole. Dose increase and drug monitoring are recommended (FDA drug label, CPIC guideline, DPWG guideline).

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PROTON-PUMP INHIBITOR	CYP2C19	*1|*17	Rapid Metabolizer	Esomeprazole (Nexium®)	Increased risk of reduced efficacy due to lower plasma concentration of esomeprazole. Dose increase is recommended (FDA drug label, DPWG guideline).
ANTIFUNGAL	CYP2C19	*1|*17	Rapid Metabolizer	Voriconazole (Vfend®)	Increased risk of reduced efficacy due to lower plasma concentration of voriconazole. Medications that are not predominantly metabolized by CYP2C19 should be considered (FDA drug label, CPIC guideline).
BLADDER RELAXANT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid 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	*34x2|*39;*1|*2 x2	Ultrarapid 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	*34x2|*39;*1|*2 x2	Ultrarapid 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).
ANESTHETIC	CACNA1S	*1|*1	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).

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THERAPEUTIC	GENE	GENOTYPE	PHENOTYPE	DRUG	COMMENTS
ANESTHETIC	CACNA1S	*1|*1	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).
OPIOID	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid 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).
OPIOID	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Codeine (Codeine Sulfate®)	Results in higher systemic active metabolite concentrations and higher adverse reaction risk (life-threatening respiratory depression and death). Medications that are not predominantly metabolized by CYP2D6 should be considered. Codeine is contraindicated in children under 12 years of age (FDA drug label, FDA's Table of Pharmacogenetic Associations, CPIC guideline).
OPIOID	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Tramadol (Ultram®)	Results in higher systemic and breast milk concentration of active metabolites, which may lead to increased risk of side effects, including respiratory depression and death. Dose reduction is recommended, refer to FDA labeling for specific dosing recommendations. Tramadol is contraindicated in children under 12 and not recommended during breastfeeding (FDA drug label, FDA's Table of Pharmacogenetic Associations, CPIC guideline, DPWG guideline).

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OPIOID	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Oliceridine (Olinvyk®)	Increased risk of reduced efficacy due to lower systemic concentration of oliceridine. Refer to FDA labeling for specific dosing recommendations (FDA drug label).
OPIOID	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Oxycodone (Oxaydo®)	Increased risk of side effects (e.g., nausea, vomiting, constipation, respiratory depression, confusion, urinary retention) due to higher systemic concentration of oxycodone. 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 WITHDRAWAL TREATMENT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid 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).
ANTINEOPLASTIC AGENT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid 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	CYP2C19	*1|*17	Rapid Metabolizer	Belzutifan (Welireg®)	May have an increased risk of reduced efficacy due to lower systemic concentration of belzutifan. Refer to FDA labeling for specific dosing recommendations (FDA drug label).
ANTINEOPLASTIC AGENT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Tamoxifen (Soltamox®)	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).

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ENZYME INHIBITOR	CYP2C19	*1|*17	Rapid Metabolizer	Abrocitinib (Cibinqo®)	May result in reduced efficacy due to lower systemic concentration of abrocitinib. Refer to FDA labeling for specific dosing recommendations (FDA drug label).
IMMUNOSUPPRESSANT	CYP3A5	*3|*3	Poor Metabolizer	Tacrolimus (Prograf®)	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	*34x2|*39;*1|*2 x2	Ultrarapid 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	*34x2|*39;*1|*2 x2	Ultrarapid 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).
ANTIEMETIC AND ANTINAUSEANT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Ondansetron (Zofran®)	Increased risk of reduced efficacy due to lower plasma concentration of ondansetron. Medications that are not predominantly metabolized by CYP2D6 should be considered (FDA drug label, CPIC guideline).
ANTIEMETIC AND ANTINAUSEANT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Tropisetron (Navoban®)	Increased risk of reduced efficacy due to lower plasma concentration of tropisetron. Medications that are not predominantly metabolized by CYP2D6 should be considered (FDA drug label, CPIC guideline).
ADHD TREATMENT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid 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).

HUMAN LONGEVITY

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ADHD TREATMENT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid 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).
ANTICONVULSANT	CYP2C19	*1|*17	Rapid Metabolizer	Brivaracetam (Briviact®)	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	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Amoxapine (Asendin®)	May alter systemic concentrations of amoxapine. Refer to FDA labeling for specific dosing recommendations (FDA drug label).
ANTIDEPRESSANT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Paroxetine (Paxil®)	Increased risk of reduced efficacy due to lower systemic concentration of paroxetine. Refer to FDA labeling for specific dosing recommendations. Medications that are not predominantly metabolized by CYP2D6 should be considered (FDA drug label, CPIC guideline).
ANTIDEPRESSANT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid 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	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Vortioxetine (Trintellix®)	Increased risk of reduced efficacy due to lower systemic concentration of vortioxetine. Select alternative drug not predominantly metabolized by the CYP2D6 enzyme. Refer to FDA labeling for specific dosing recommendations for dose increase (FDA drug label, CPIC guideline).

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ANTIDEPRESSANT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Trimipramine (Surmontil®)	Increased risk of reduced efficacy due to lower systemic concentration of trimipramine. Dose increase, dose titration and drug monitoring are 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).
ANTIDEPRESSANT	CYP2C19	*1|*17	Rapid Metabolizer	Escitalopram (Lexapro®)	Increased risk of reduced efficacy due to lower plasma concentration of escitalopram. Medications that are not predominantly metabolized by CYP2C19 should be considered (FDA drug label, CPIC guideline).
ANTIDEPRESSANT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Imipramine (Tofranil®)	Increased risk of reduced efficacy due to lower systemic concentration of imipramine. Dose increase, dose titration and drug monitoring are 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).
ANTIDEPRESSANT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Fluvoxamine (Luvox®)	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).

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ANTIDEPRESSANT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Desipramine (Norpramin®)	Increased risk of reduced efficacy due to lower systemic concentration of desipramine. Dose increase and drug monitoring are 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).
ANTIDEPRESSANT	CYP2C19	*1|*17	Rapid Metabolizer	Sertraline (Zoloft®)	Increased risk of reduced efficacy due to lower plasma concentration of sertraline. While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended. Medications that are not predominantly metabolized by CYP2C19 could be considered (FDA drug label, CPIC guideline).
ANTIDEPRESSANT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Amitriptyline (Elavil®)	Increased risk of reduced efficacy due to lower plasma concentration of amitriptyline. Dose increase, dose titration and drug monitoring are recommended. Medications that are not predominantly metabolized by CYP2D6 should be considered (FDA drug label, CPIC guideline).
ANTIDEPRESSANT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Clomipramine (Anafranil®)	Increased risk of reduced efficacy due to lower systemic concentration of clomipramine. Dose increase, dose titration and drug monitoring are 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).

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THERAPEUTIC	GENE	GENOTYPE	PHENOTYPE	DRUG	COMMENTS
ANTIDEPRESSANT	CYP2C19	*1|*17	Rapid Metabolizer	Citalopram (Celexa®)	Increased risk of reduced efficacy due to lower systemic concentration of citalopram. Medications that are not predominantly metabolized by the CYP2C19 enzyme should be considered. Refer to FDA labeling for specific dosing recommendations (FDA drug label, CPIC guideline).
ANTIDEPRESSANT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Doxepin (Silenor®)	Increased risk of reduced efficacy due to lower plasma concentration of doxepin. Dose increase and drug monitoring are recommended. Medications that are not predominantly metabolized by CYP2D6 should be considered (FDA drug label, FDA's Table of Pharmacogenetic Associations, CPIC guideline).
ANTIDEPRESSANT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Nortriptyline (Pamelor®)	Increased risk of reduced efficacy due to lower plasma concentration of nortriptyline. Dose increase, dose titration and drug monitoring are recommended. Medications that are not predominantly metabolized by CYP2D6 should be considered (FDA drug label, FDA's Table of Pharmacogenetic Associations, CPIC guideline).
ANTIDEPRESSANT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Venlafaxine (Effexor®)	Increased risk of reduced efficacy due to lower plasma concentration of venlafaxine. Dose increase is recommended. Alternative medications (e.g., citalopram, sertraline) could be considered (FDA drug label, DPWG guideline).
ANTIPSYCHOTIC	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid 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).

HUMAN LONGEVITY

Genomic Report

PATIENT INFORMATION

NAME: [redacted]

SEX: Female

THERAPEUTIC	GENE	GENOTYPE	PHENOTYPE	DRUG	COMMENTS
ANTIPSYCHOTIC	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid 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	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Eliglustat (Cerdelga®)	Increased risk of reduced efficacy due to lower systemic concentration of eliglustat. Refer to FDA labeling for specific dosing recommendations (FDA drug label, FDA's Table of Pharmacogenetic Associations).
ANTIPSYCHOTIC	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid 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	*34x2|*39;*1|*2 x2	Ultrarapid 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	*34x2|*39;*1|*2 x2	Ultrarapid 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).
ANTIPSYCHOTIC	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid 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	*34x2|*39;*1|*2 x2	Ultrarapid 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).

HUMAN LONGEVITY

Genomic Report

PATIENT INFORMATION

NAME: [redacted]

SEX: Female

THERAPEUTIC	GENE	GENOTYPE	PHENOTYPE	DRUG	COMMENTS
ANTIPSYCHOTIC	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid 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	*34x2|*39;*1|*2 x2	Ultrarapid 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).
FEMALE SEXUAL DYSFUNCTION TREATMENT	CYP2C19	*1|*17	Rapid Metabolizer	Flibanserin (Addyi®)	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	*34x2|*39;*1|*2 x2	Ultrarapid 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	*34x2|*39;*1|*2 x2	Ultrarapid 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).
INVOLUNTARY MOVEMENT REDUCER	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Tetrabenazine (Xenazine®)	Increased risk of reduced efficacy due to lower plasma concentration of active metabolites of tetrabenzine. Dose increase and dose titration are recommended (FDA drug label).
SEDATIVE	CYP2C19	*1|*17	Rapid Metabolizer	Diazepam (Valium®)	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	*1|*17	Rapid Metabolizer	Clobazam (Onfi®)	While the gene affecting the drug's metabolism is altered, no changes to the label-recommended drug use are recommended (FDA drug label).

HUMAN LONGEVITY

Genomic Report

PATIENT INFORMATION

NAME: [redacted]

SEX: Female

THERAPEUTIC	GENE	GENOTYPE	PHENOTYPE	DRUG	COMMENTS
SELECTIVE NOREPINEPHRINE REUPTAKE INHIBITOR	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Atomoxetine (Strattera®)	Ultrarapid metabolizers of atomoxetine have a lower likelihood of response as compared with poor metabolizers. This is due to not achieving adequate serum concentrations for the intended effect at standard dosing. Consult CPIC guidelines and FDA drug label for dosage recommendations. (FDA drug label, CPIC guideline).
DRY MOUTH TREATMENT	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid 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).
MUSCLE RELAXANT	CACNA1S	*1|*1	Uncertain Susceptibility	Succinylcholine (Quelicin®)	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	*1|*17	Rapid Metabolizer	Carisoprodol (Soma®)	May result in reduced efficacy due to lower systemic concentration of carisoprodol. Refer to FDA labeling for specific dosing recommendations (FDA drug label).
NARCOLEPSY	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Pitolisant (Wakix®)	Increased risk of reduced efficacy due to lower systemic concentration of pitolisant. Refer to FDA labeling for specific dosing recommendations (FDA drug label).
COGNITION-ENHANCING THERAPY	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid 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).

HUMAN LONGEVITY

Genomic Report

PATIENT INFORMATION

NAME: [redacted]

SEX: Female

THERAPEUTIC	GENE	GENOTYPE	PHENOTYPE	DRUG	COMMENTS
COGNITION-ENHANCING THERAPY	CYP2D6	*34x2|*39;*1|*2 x2	Ultrarapid Metabolizer	Donepezil (Aricept®)	May alter systemic concentrations of donepezil. Refer to FDA labeling for specific dosing recommendations (FDA drug label).

HUMAN LONGEVITY

Genomic Report

PATIENT INFORMATION

NAME: [redacted]

SEX: Female

Gene and Phenotype Findings

GENE	GENOTYPE	PHENOTYPE	DRUG
CYP2D6	*34x2|*39;*1|*2x2	Ultrarapid Metabolizer	Propafenone (Rythmol®), Carvedilol (Coreg®), Propranolol (Hemangeol®), Metoprolol (Lopressor®), Nebivolol (Bystolic®), Tolterodine (Detrol®), Tamsulosin (Flomax®), Fesoterodine (Toviaz®), Mirabegron (Myrbetriq®), Darifenacin (Enablex®), Hydrocodone (Norco®), Codeine (Codeine Sulfate®), Tramadol (Ultram®), Oliceridine (Olinvyk®), Oxycodone (Oxaydo®), Lofexidine (Lucemyra®), Gefitinib (Iressa®), Tamoxifen (Soltamox®), Metoclopramide (Reglan®), Meclizine (Antivert®), Ondansetron (Zofran®), Tropisetron (Navoban®), Viloxazine (Qelbree®), Amphetamine (Adderall®), Amoxapine (Asendin®), Paroxetine (Paxil®), Protriptyline (Vivactil®), Vortioxetine (Trintellix®), Trimipramine (Surmontil®), Imipramine (Tofranil®), Fluvoxamine (Luvox®), Desipramine (Norpramin®), Amitriptyline (Elavil®), Clomipramine (Anafranil®), Doxepin (Silenor®), Nortriptyline (Pamelor®), Venlafaxine (Effexor®), Risperidone (Risperdal®), Aripiprazole (Abilify®), Eliglustat (Cerdelga®), Aripiprazole Lauroxil (Aristada®), Clozapine (Clozaril®), Pimozide (Orap®), Thioridazine (Mellaril®), Perphenazine (Trilafon®), Brexpiprazole (Rexulti®), Iloperidone (Fanapt®), Valbenazine (Ingrezza®), Deutetrabenazine (Austedo®), Tetrabenazine (Xenazine®), Atomoxetine (Strattera®), Cevimeline (Evoxac®), Pitolisant (Wakix®), Galantamine (Razadyne®), Donepezil (Aricept®)
CYP2C9	*1|*1	Normal Metabolizer	Warfarin (Coumadin®), Fluvastatin (Lescol®), Nateglinide (Starlix®), Ibuprofen (Advil®), Meloxicam (Vivlodex®), Celecoxib (Celebrex®), Tenoxicam (Mobiflex®), Flurbiprofen (Ansaid®), Piroxicam (Feldene®), Lornoxicam (Xefo®), Erdafitinib (Balversa®), Dronabinol (Marinol®), Phenytoin (Phenytek®), Fosphenytoin (Cerebyx®), Siponimod (Mayzent®), Avatrombopag (Doptelet®)
VKORC1	rs9923231:CT	Increased Warfarin Sensitivity	Warfarin (Coumadin®)
CYP4F2	*1|*3	Decreased Warfarin Sensitivity	Warfarin (Coumadin®)
rs12777823	No Reportable Variants Found	Normal Function	Warfarin (Coumadin®)

HUMAN LONGEVITY

Genomic Report

PATIENT INFORMATION

NAME: [redacted]

SEX: Female

GENE	GENOTYPE	PHENOTYPE	DRUG
CYP2C19	*1|*17	Rapid Metabolizer	Clopidogrel (Plavix®), Mavacamten (Camzyos®), Dexlansoprazole (Dexilant®), Omeprazole (Prilosec®), Rabeprazole (AcipHex®), Pantoprazole (Protonix®), Lansoprazole (Prevacid®), Esomeprazole (Nexium®), Voriconazole (Vfend®), Belzutifan (Welireg®), Abrocitinib (Cibinqo®), Brivaracetam (Briviact®), Escitalopram (Lexapro®), Sertraline (Zoloft®), Citalopram (Celexa®), Flibanserin (Addyi®), Diazepam (Valium®), Clobazam (Onfi®), Carisoprodol (Soma®)
SLCO1B1	Unable to Determine	Unable to Determine	Simvastatin (Zocor®), Rosuvastatin (Crestor®), Lovastatin (Mevacor®), Fluvastatin (Lescol®), Atorvastatin (Lipitor®), Pitavastatin (Livazo®), Pravastatin (Pravachol®), Elagolix (Oriahnn®)
ABCG2	No Reportable Variants Found	Normal Function	Rosuvastatin (Crestor®)
G6PD	WT|WT	Normal Function	Chlorpropamide (Diabinese®), Glimepiride (Amaryl®), Glipizide (Glucotrol®), Nitrofurantoin (Macrobid®), Norfloxacin (Noroxin®), Sulfadiazine (Azulfidine®), Nalidixic acid (NegGram®), Tafenoquine (Krintafel®), Primaquine (Primaquine Phosphate®), Quinine (Qualaquin®), Dapsone (Aczone®), Chloroquine (Aralen®), Pegloticase (Krystexxa®), Toluidine Blue (TBO®), Methylene blue (Provayblue®), Probenecid (Benemid®), Rasburicase (Elitek®)
UGT1A1	Unable to Determine	Unable to Determine	Atazanavir (Reyataz®), Raltegravir (Isentress®), Dolutegravir (Tivicay®), Nilotinib (Tasigna®), Belinostat (Beleodaq®), Sacituzumab Govitecan-hziy (Trodelvy®), Irinotecan (Onivyde®), Pazopanib (Votrient®)
RYR1	Unable to Determine	Unable to Determine	Desflurane (Suprane®), Isoflurane (Forane®), Succinylcholine (Quelicin®)
BCHE	*1|*1	Normal Function	Tetracaine (Tetcaine®), Mivacurium (Mivacron®), Succinylcholine (Quelicin®)
CACNA1S	*1|*1	Uncertain Susceptibility	Desflurane (Suprane®), Isoflurane (Forane®), Succinylcholine (Quelicin®)
TPMT	*1|*1	Normal Metabolizer	Thioguanine (Tabloid®), Mercaptopurine (Purinethol®), Azathioprine (Imuran®)
DPYD	*1|*1	Normal Metabolizer	Tegafur (UFT®), Capecitabine (Xeloda®), Fluorouracil (Efudex®)
NUDT15	*1|*1	Normal Metabolizer	Mercaptopurine (Purinethol®), Thioguanine (Tabloid®), Azathioprine (Imuran®)

HUMAN LONGEVITY

Genomic Report

PATIENT INFORMATION

NAME: [redacted]

SEX: Female

GENE	GENOTYPE	PHENOTYPE	DRUG
CYP3A5	*3|*3	Poor Metabolizer	Tacrolimus (Prograf®)
POLG	WT|WT	Normal Function	Valproic acid (Valproic®)

HUMAN LONGEVITY

Genomic Report

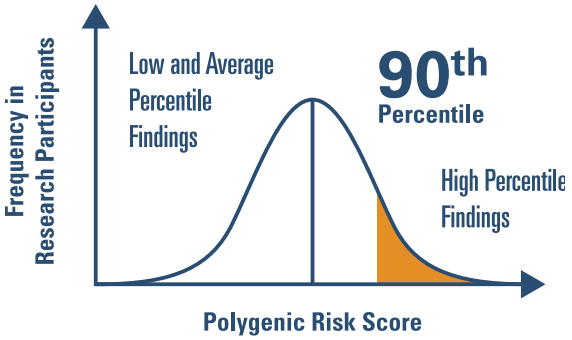
PATIENT INFORMATION		
NAME: [redacted]		
[redacted]	SEX: Female	[redacted]



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
BASAL CELL CARCINOMA	Given the variants you have, your genetic predisposition to Basal Cell Carcinoma is greater than 96-98% of the research participants of European descent. This suggests that your likelihood of developing the condition is 2.00 times that of an average person.	-Basal cell carcinoma is very common among people of some ethnicities; among Europeans, one in three men and one in four women will develop the condition during their lifetime. -Genes contribute over 40% to the risk of a nonmelanoma skin cancer.
HDL CHOLESTEROL	Given the variants you have, your genetic predisposition to HDL Cholesterol is greater than 92% of the research participants of European descent. This suggests that your likelihood of developing the condition is 2.40 times that of an average person.	-Having low levels of HDL cholesterol is very common; nearly one in three adults has low HDL cholesterol levels. -Genes contribute about 40 - 60% to the risk of developing low HDL cholesterol.

HUMAN LONGEVITY

Genomic Report

PATIENT INFORMATION

NAME: [redacted]

SEX: Female

DISEASE	YOUR RESULT	ABOUT THE DISEASE
UTERINE FIBROIDS	Given the variants you have, your genetic predisposition to Uterine Fibroids is greater than 96% of the research participants of European descent. This suggests that your likelihood of developing the condition is 1.60 times that of an average person.	-Uterine fibroids are a very common condition; one in two women will have fibroids by age 50. -Genes contribute up to 80% to the risk of uterine fibroids.

HUMAN LONGEVITY

Genomic Report

PATIENT INFORMATION

NAME: [redacted]

SEX: Female

Low and Average Percentile Findings (below 90th)

HEALTH CATEGORY	DISEASES(YOUR PERCENTILE)
MENTAL HEALTH	Alzheimer's disease(74%), Multiple Sclerosis(62%), Parkinson's disease(36%), Schizophrenia(71%)
RESPIRATORY HEALTH	Asthma(80%), COPD(78%)
HEART AND VASCULAR HEALTH	Atrial Fibrillation(33%), Coronary artery disease(52%), Venous Thromboembolism(5%)
CANCER PREDISPOSITION	Bladder cancer(55%), Breast cancer(7%), Colorectal cancer(37%), Chronic Lymphocytic Leukemia(79%), Melanoma(22%), Pancreatic Cancer(17%), Thyroid Cancer(29%)
DIGESTIVE HEALTH	Celiac disease(85%), Inflammatory Bowel Disease(36%)
MUSCULOSKELETAL HEALTH	Dupuytren's disease(19%), Rheumatoid Arthritis(15%), Gout(49%)
WOMEN'S HEALTH	Endometriosis(76%)
METABOLIC HEALTH	LDL cholesterol(64%), Total Cholesterol(31%), Triglycerides(4%), Type 2 Diabetes(2%)
SENSORY HEALTH	Age-related Macular Degeneration(14%)

For frequently asked questions, information on how each polygenic risk score was developed, and references supporting disease information in this section, please refer to Your Results Guide.

HUMAN LONGEVITY

Genomic Report

PATIENT INFORMATION

NAME: [redacted]

SEX: Female



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. Learn more about each trait in https://www.humanlongevity.com/your-results-guide-5-0.pdf.

Vitamin A

★★☆☆ Scientific Strength

YOUR RESULT	YOUR GENOTYPE
You are not at higher risk of vitamin A deficiency	BCO1, rs7501331, C/C
You are not at higher risk of vitamin A deficiency	BCO1, rs12934922, A/A

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 in the BCO1 gene have been shown to be associated with an impaired conversion of beta-carotene into vitamin A. Certain genotypes are associated with a higher risk of vitamin A deficiency while other genotypes are not associated with higher risk. Preformed vitamin A supplements may help maintain healthy vitamin A levels in individuals who have a genetic predisposition to vitamin A deficiency.

PATIENT INFORMATION

NAME: [redacted]

SEX: Female

Vitamin B6

Scientific Strength

YOUR RESULT

You are likely to have a decreased vitamin B6 level

YOUR GENOTYPE

NBPF3, rs4654748, C/T

DESCRIPTION

Vitamin B6 helps support your body's nervous system, promotes red blood cell health and is involved in sugar metabolism. Certain genotypes are likely to have lower levels of vitamin B6 while other genotypes are associated with typical levels of vitamin B6. Getting vitamin B6 from dietary sources such as whole grains, beans, fish, meat, eggs, and some cereals can help maintain healthy vitamin B6 levels.

Vitamin B12

Scientific Strength

YOUR RESULT

Based on your genotype, you are likely to have reduced levels of vitamin B12

YOUR GENOTYPE

FUT2, rs601338, G/A

DESCRIPTION

Vitamin B12, also known as cobalamin, is an essential micronutrient for nervous system and red blood cell health. Deficiency of this vitamin has been linked to dietary, environmental, and genetic factors. Results from twin studies show an estimated heritability of 59%, indicating considerable genetic influence. The nutritional deficiency of vitamin B12 has been linked to many serious health complications, including neurological, cardiovascular, and various cancers. The genetic variant, rs601338, in the FUT2 gene is associated with lower plasma levels of vitamin B12. Individuals with either G/G or G/A genotypes may have reduced levels of vitamin B12. Vitamin B12 can be found in foods of animal origin such as eggs, milk, fish, and meat.

PATIENT INFORMATION

NAME: [redacted]

SEX: Female

[redacted]

Vitamin C

Scientific Strength

YOUR RESULT

Based on your genotype, you are likely to have typical levels of vitamin C

YOUR GENOTYPE

SLC23A1, rs33972313, C/C

DESCRIPTION

Vitamin C, or L-ascorbic acid, a water-soluble vitamin, must be obtained from dietary sources, as humans are unable to synthesize it. This vitamin is necessary for the biosynthesis of collagen, catecholamine, and L-carnitine and absorption of non-heme iron. Vitamin C also functions as a powerful antioxidant. While a severe deficiency of vitamin C ultimately leads to scurvy, variations in vitamin C levels have also been associated with a wide range of chronic complex diseases, such as atherosclerosis, type 2 diabetes, and cancer. Concentration of vitamin C in the body is regulated through interactions of intestinal absorption, cellular transport, and excretion. After ingestion, vitamin C gets transported across the cell membranes via transport proteins, one of which is 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 variant, rs33972313. Individuals harboring the A allele of this variant have been reported to have decreased levels of circulating vitamin C. Ascorbic acid is found in a variety of fruits and vegetables, including citrus fruits, green peppers, strawberries, tomatoes, broccoli, white potatoes, and sweet potatoes.

HUMAN LONGEVITY

Genomic Report

PATIENT INFORMATION

NAME: [redacted]

SEX: Female

Vitamin D

Scientific Strength

YOUR RESULT

YOUR GENOTYPE

You are more susceptible to developing vitamin D deficiency	GC, rs2282679, T/G
You are more susceptible to developing vitamin D deficiency	GC, rs1155563, T/C

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. Certain genotypes make you at higher risk for vitamin D deficiency while other genotypes are associated with the typical risk of 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 INFORMATION

NAME: [redacted]

SEX: Female

[redacted]

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.

PATIENT INFORMATION

NAME: [redacted]

[redacted]

SEX: Female

[redacted]

Food Reactions



Alcohol Flush Reaction

★★★★ Scientific Strength

YOUR RESULT

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, similar to blushing. It can also cause dizziness, headaches, and nausea. Certain genotypes may make you more prone to flushing after alcohol consumption while other genotypes carry a typical risk of flushing. Individuals who are more prone to flushing often avoid alcohol because the reaction is so unpleasant.



Caffeine Metabolism

★★★☆ Scientific Strength

YOUR RESULT

You are likely to metabolize caffeine more quickly

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. 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.

HUMAN LONGEVITY

Genomic Report

PATIENT INFORMATION

NAME: [redacted]

SEX: Female

Bitter Taste Perception

★★☆☆ Scientific Strength

YOUR RESULT

You may be unable to detect bitterness in some foods

YOUR GENOTYPE

TAS2R38, rs713598, C/C

DESCRIPTION

People have different sensitivities to taste. Genetic variants in the taste receptor gene TAS2R38 have been shown to influence the sensitivity to the bitter-tasting compound phenylthiocarbamide. The variants can partially explain the increased sensitivity to the bitter flavors found in some foods such as broccoli, brussels sprouts, grapefruit, cabbage, and coffee. Certain genotypes may make you more sensitive to bitter flavors, while other genotypes make you less sensitive to bitter flavors. People with increased sensitivity to bitter taste should be mindful of their salt intake since they tend to add excessive salt to mask the bitter flavor in their foods.

Sweet Taste

★★☆☆ Scientific Strength

YOUR RESULT

You are likely to have typical sensitivity to sweet foods

YOUR GENOTYPE

TAS1R2, rs12033832, A/A

You are likely to have typical sensitivity to sweet foods

TAS1R3, rs307355, C/C

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. Depending on your genotype, you may have typical sensitivity, moderately reduced sensitivity, or reduced sensitivity to sweet foods. If you have moderately reduced or reduced sensitivity, you may prefer foods with more sugar.

PATIENT INFORMATION

NAME: [redacted]

[redacted]

SEX: Female

[redacted]

[redacted]

Fitness and Exercise



Achilles Tendinopathy



YOUR RESULT

You are unlikely at increased risk for an Achilles tendon injury or inflammation

YOUR GENOTYPE

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 jumping, can cause small breaks and tears (tendinopathy). Certain genotypes may make you more prone to injury while other genotypes have a typical risk of Achilles tendon injuries. You can help prevent Achilles tendon injuries by good stretching, maintaining a healthy weight, and avoiding certain medications like fluoroquinolones.

HUMAN LONGEVITY

Genomic Report

PATIENT INFORMATION

NAME: [redacted]

[redacted]

SEX: Female

[redacted]

Muscle Performance

★☆☆☆ Scientific Strength

YOUR RESULT

You are likely to have enhanced performance as an endurance athlete

YOUR GENOTYPE

ACTN3, rs1815739, T/T

DESCRIPTION

Athletic performance is influenced by a large number of genetic and environmental factors. A genetic variant influences how much of the ACTN3 protein our body can produce or whether it can produce the protein 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. You can increase your fast twitch muscle fibers by doing certain sprint exercises and plyometrics.

Endurance Training

★★☆☆ Scientific Strength

YOUR RESULT

You are likely to have enhanced performance as an endurance athlete

YOUR GENOTYPE

ACE, rs4343, A/A

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. Certain genotypes are associated with enhanced endurance performance while other genotypes are associated with typical endurance performance. Improving endurance potential and stamina can be achieved by introducing variety into your workout routines, eating a balanced diet, and improving sleep.

HUMAN LONGEVITY

Genomic Report

PATIENT INFORMATION

NAME: [redacted]

[redacted]

SEX: Female

[redacted]

Insulin Sensitivity

★★☆☆ Scientific Strength

YOUR RESULT

You are likely to have improved insulin sensitivity with exercise which allows your body to better process sugar

YOUR GENOTYPE

LIPC, rs1800588, C/C

DESCRIPTION

Insulin is a hormone that allows your cells to use glucose or sugar. 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. Certain genotypes are likely to have improved insulin sensitivity with exercise, while others don't have as much improvement. Other ways to improve your insulin sensitivity include eating less simple carbohydrates, intermittent fasting, getting better sleep, and certain prescription medications.

PATIENT INFORMATION

NAME: [redacted]

[redacted]

SEX: Female

[redacted]

Enhanced HDL Cholesterol Response to Exercise

Scientific Strength

YOUR RESULT

Based on your genotype you are unlikely to benefit from enhanced HDL cholesterol response to exercise

YOUR GENOTYPE

PPARD, rs2016520, T/T

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.

PATIENT INFORMATION

NAME: [redacted]

[redacted]

SEX: Female

[redacted]

Behavior and Mood

Risk Seeking Behavior

★★★☆ Scientific Strength

YOUR RESULT

You are likely to have typical risk seeking behavior

YOUR GENOTYPE

DRD4, rs1800955, T/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 sensation seeking is heritable, with few differences between males and females. The individual differences in risk taking behaviors can be partially explained by the variants in two genes, 5- HTTLPR and DRD4, that regulate dopamine and serotonin neurotransmission. These genes have been previously linked to emotional behavior, anxiety, and addiction. Certain genotypes are likely to have increased risk seeking behavior while other genotypes are associated with typical risk seeking behavior.

PATIENT INFORMATION

NAME: [redacted]

[redacted]

SEX: Female

[redacted]



Smoking Behavior



YOUR RESULT

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 shortens life on 7 - 8 years. Genetic background contributes about 50% to how much people smoke. For example, light smokers consume less than 10 cigarettes per day, while heavy smokers consume 20 or more. Certain genotypes are associated with smoking 1 cigarette per day more on average than the typical amount while other genotypes are associated with smoking 2 more per day on average.



Smoking Cessation



YOUR RESULT

If you smoke, you have a typical likelihood of success of quitting

YOUR GENOTYPE

ANKK1, rs1800497, G/G

DESCRIPTION

There are many benefits of stopping smoking. You will experience rapid normalization of blood pressure and heart rate, improvement in breathing and blood circulation. Over the long term, smoking cessation brings a much lower risk of developing many diseases as well as the chance to live longer years. Success of stopping smoking depends on the motivation to stop and the degree of dependence on cigarettes. It is estimated that genetic background contributes about 50% to the success of smoking cessation. Certain genotypes are associated with being more likely to successfully quit smoking, while other genotypes are associated with typical likelihood of success. 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 INFORMATION

NAME: [redacted]

[redacted]

SEX: Female

[redacted]

Disease Susceptibility

COVID-19 Severity

★☆☆☆ Scientific Strength

YOUR RESULT	YOUR GENOTYPE
Higher likelihood to develop respiratory failure in COVID-19	ABO, rs657152, A/C
Typical likelihood to develop respiratory failure in COVID-19	LZTFL1, rs11385942, G/G
Your genotype is not associated with increased risk for severe disease from COVID-19	LZTFL1, rs17713054, G/G

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 a 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.

HUMAN LONGEVITY

Genomic Report

PATIENT INFORMATION

NAME: [redacted]

SEX: Female

Histamine Intolerance

Scientific Strength

YOUR RESULT

Based on your genotype, Your histamine breakdown may be slowed, but histamine levels may not have significantly increased

YOUR GENOTYPE

HNMT, rs1050891, A/G

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.

HUMAN LONGEVITY

Genomic Report

PATIENT INFORMATION

NAME: [redacted]

SEX: Female

Lactose Intolerance

Scientific Strength

YOUR RESULT

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

YOUR GENOTYPE

MCM6, rs4988235, G/G

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.

HUMAN LONGEVITY

Genomic Report

PATIENT INFORMATION

NAME: [redacted]

[redacted]

SEX: Female

[redacted]



Obesity



YOUR RESULT

Based on your genotype, you may have typical risk for obesity

YOUR GENOTYPE

MC4R, rs17782313, T/T

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.

PATIENT INFORMATION

NAME: [redacted]

[redacted]

SEX: Female

[redacted]

Protection Against Obesity

Scientific Strength

YOUR RESULT

Your genotype is unlikely to protect you from obesity

YOUR GENOTYPE

GPR75, rs148952285, G/G

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.

Protection Against Cardiovascular Disease

Scientific Strength

YOUR RESULT

Your genotype is not likely to protect you against cardiovascular

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.

PATIENT INFORMATION

NAME: [redacted]

SEX: Female

Longevity and Aging



Human Longevity

Scientific Strength

YOUR RESULT	YOUR GENOTYPE
Unable to determine your result due to sequencing quality of your sample affecting the variant(s) in the model	FOXO3, rs12206094, Unable to determine
Typical likelihood to live to the age of 90 years or older	FOXO3, rs4946935, G/G

DESCRIPTION

Longevity is impacted by many factors including a 25% contribution from genetics. 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. Variants rs12206094 (favorable allele - T) and rs4946935 (favorable allele - A) in the FOXO3 gene have been found more frequently in people who lived to 90 years and older. While some nutrients were shown to stimulate FOXO3 effects (green tea, curcumin, and resveratrol), lifestyle factors like maintaining a healthy diet, not smoking, exercising, and lowering stress are well-established contributors to longer lifespan.

Appendix

This test was developed and performed by Human Longevity US Clinic.

1.Intended Use

The Health Nucleus 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.

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 was performed by CLIA Number: 45D1102202 CAP Number: 7212851 Location: 1445 North Loop West, Suite 820, Houston, TX 77008.

Alignment and variant calling were performed by Human Longevity US Clinics (San Diego: 4570 Executive Drive, Suite 100, San Diego, CA 92121 ; San Francisco: 600 Gateway Blvd, Suite 101, South San Francisco, CA 94080) on GRCh38 using BWA version 0.7.12 implemented in Sentieion version 202503.03 and Sentieon Haplotype Caller version 202503.03, respectively. Sequencing and bioinformatics performed are able to assess the following three types of genetic alterations: single nucleotide variants (SNV), small insertions and deletions (<= 7bp) within the high-confidence region (93% of whole genome) based on the Illumina platinum genome for GRCh38.

Base pairs analyzed is the total number of base pairs that comprise the reference genome that was used for alignment and variant calling. Total variants detected is the total number of variants called prior to filtering for variant quality, reporting scope or removal of potential false positives.

3.Analytics

3.1. Hereditary Disease Risk

Variants included in this report have met the ACMG guidelines criteria for classification as pathogenic and likely pathogenic. The variants include alterations interpreted by Human Longevity Clinical Laboratories (85% of variants) and ClinVar submitters (15% of variants) according to the ACMG guidelines [1, 2]. To be included, variant classification in ClinVar should be provided without contradictions by selected expert panels or by at least 2 of Human Longevity's trusted submitters, i.e. leading laboratories that have demonstrated adherence of their variant interpretation protocols to ACMG guidelines and consistent quality of variant classification.

Several variants in the test (APOE c.388T>C, BTD c.1330G>C, BTD c.511G>A, HFE c.187C>G, HOXB13 c.251G>A, SERPINA1 c.863A>T, CHEK2 c.470T>C) are included with a classification category risk factor. These variants have an incomplete penetrance and are associated with a lower risk of disease. The variants are included as they either modify the impact of other variants or are often included in similar tests. Relative and absolute risk of disease are provided for each such variant where clinical significance is well-established.

3.2. Pharmacogenomic Findings

Pharmacogenomic reporting is based on the guidelines of the Clinical Pharmacogenetics Implementation Consortium (CPIC) [3], the Dutch Pharmacogenetics Working Group (DPWG) [4], and recommendations provided in the FDA drug labels [5]. 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. 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 1000 Genomes subpopulation [6].

Allele specific copy number is only reported for CYP2D6 as part of the star allele diplotype, e.g., *1 x 2|*2 x 1 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. The common variants are discovered in "Genome-Wide Association Studies" (termed GWAS) typically associated with a low genetic risk of developing a disease when considered independently and have been shown to play a greater role in common diseases than rare monogenic variants [7-9].

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

In addition to percentile, 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 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% descreased risk of developing a disease.

Please refer to https://www.humanlongevity.com/HN-Genomic-Clinical-White-Paper-Polygenic-1-0.pdf 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 comprise one or two common genetic variants contributing to development of a given trait. 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.

Results interpretation is provided for each variant separately. For example, "GDF5, rs143383 G/A". GDF5 is a name of the gene; rs143383 points to the location of the specific DNA base pair in the genome. G/A indicates the DNA basepair (or "genotype") at this location: there is guanine (G) in one copy of the GDF5 gene and adenine (A) in another copy. An interpretation of the result, for example, "You are likely at increased risk of Achilles tendon injury or inflammation", is provided next to the genotype.

4.Reporting Scope

4.1. Hereditary Disease Risk

The hereditary disease risk reporting scope includes 3,900 genes and 5,494 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	TOTAL GENES ASSESSED
Syndromic Disorder	1138
Neurologic Disorder	816
Metabolic Disorder	397
Musculoskeletal Disorder	347
Vision Disorder	226
Hereditary Cancer	153
Immunological Disorder	245
Endocrine Disorder	157
Cardiovascular Disorder	175
Hematologic Disorder	167

HEALTH CATEGORY	TOTAL GENES ASSESSED
Skin Disorder	133
Kidney Disorder	99
Hearing Disorder	127
Neurodegenerative Disorder	151
Respiratory Disorder	56
Liver Disorder	33
Gastrointestinal Disorder	23
Dental Disorder	27
Mitochondrial Disorder	109
Reproductive Disorder	27

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.

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.

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 genetic 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 variants included in the pre-defined list of variants described in section 4.1 are reported when identified. Other potentially pathogenic rare variants in the panel'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 the 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.

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 carbamazepine and abacavir.
- Not all variants relevant to known star alleles and not all known star alleles are included in this test due to the absence of functional characterization in the CPIC guidelines or star allele definition tables.
- 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.

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.

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 the section 4.3). Thus, apart from the Alzheimer's disease and the venous thromboembolism polygenic risk models, the results of the two tests are independed 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 the section 1.5.

- 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 https://www.humanlongevity.com/HN-Genomic-Clinical-White-Paper-Polygenic-1-0.pdf 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.
- 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.
- 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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