HK LONGEVITY MEDICAL CENTRE

Genetic Risk Carriers Screening and Analysis Report

PATIENT NAME
John Doe
GENDER
Male
DATE OF BIRTH
01/11/1990
SAMPLE TYPE
Whole Blood
COLLECTION DATE
01/01/2023
SAMPLE ID
A123456
ACCESSION #
4316546
REPORT DATE
07/08/2023

Overview

Your genetic blueprint, steeped in your DNA, is the most critical factor in determining who you are. From the beginning of life to your golden years, it is these unique genetic variants that set you apart from your relatives and acquaintances. As you navigate through the later stages of life, an interplay of these inherent genetic traits, your lifestyle choices, and environmental factors, collectively contribute to the pace at which you age. This complex interaction also influences your susceptibility to various age-related health conditions and consequently how long you live.

Here at HK Longevity Medical Centre, our expertise lies in conducting comprehensive Genetic Risk Carriers Screening and Analysis. Our principal objective is to deliver personalized genomic data that can illuminate your genetic predisposition towards hereditary health conditions and diseases and provide insights into your potential physical fitness.

In our pursuit of this mission, we employ Whole Genome Sequencing (WGS), a state-of-the-art technology that deciphers an individual's DNA sequence, comprising approximately three billion base pairs. WGS grants us a panoramic view of the entire genome, enabling the detection of genetic variants that could potentially influence your health and disease susceptibility.

Armed with this knowledge, you gain the power to make well-informed decisions concerning your health, lifestyle, and preventive care. Our services aim to demystify the intricate realm of genomics, forging a clear path from raw genetic information to actionable health insights. At HK Longevity Medical Centre, we are your trusted partner in navigating the complex life journey from genetic understanding to your life goal Healthy Aging and Longevity.

Finding Summary

This is a brief summary of the WGS screening and analysis.

Category	Test Results	Your Risk
Genome sequenced	3.2 Billion base pairs analyzed	nan
Variants detected	5.3 millions	nan
Total genes assessed	1519	Carrying 5 disease-causing variants
Total hereditary diseases assessed	1652	1 hereditary cancer, 2 metabolic disorders, 1 endocrine disorder, and 1 respiratory disorder
Total pharmacogenetic genes assessed	1234	nan
Total drugs assessed	120	51 drugs potentially impacted
Total age-related phenotypes/ traits assessed	25	High risk of developing muscle degeneration condition, one neurological condition

Total physical fitness traits assessed	12	Physically active, risk in developing cardiovascular conditions

Section 1: Hereditary Disease Risk

This section includes variants that, when found by themselves, are associated with high and moderate genetic risk of developing a disease. Depending on a variant zygosity and disease inheritance, the disease can affect you or represent a risk for the next generation (carrier variants).

Subsection 1.1: Variant Summary

HEALTH CATEGORY	GENE	VARIANT	ZYGOSITY	CLASSIFICATION	DISEASE ASSOCIATED	INHERITANCE
Hereditary Cancer	ATM	rsxxxxxx c. 1564_1565delGA (p.Glu522fs) NM_000051.3	Heterozygous	Pathogenic	Breast cancer	Autosomal dominant
xxxxxx	xxxxx	xxxxx	xxxxxx	xxxxxx	xxxxxx	xxxxx
xxxxxx	xxxxx	xxxxx	xxxxxx	xxxxxx	xxxxxx	xxxxx
xxxxxx	xxxxx	xxxxx	xxxxxx	xxxxxx	xxxxxx	xxxxx
xxxxxx	xxxxx	xxxxx	xxxxxx	xxxxxx	xxxxxx	xxxxx

Subsection 1.2: Variant Details

Variants Associated with Hereditary Cancer

Patient was found to have a pathogenic variant associated with an increased risk for Hereditary Cancer

Variant ID	Gene	VARIANT	Effect allele	Effect allele frequency
rsxxxxx	ATM	c.1564_1565delGA (p.Glu522fs)	C>delGA	nan

The c.1564_1565delGA frameshift variant is predicted to truncate the ATM protein, resulting in a loss or deficient function. The variant has been identified in a homozygous or compound heterozygous state in individuals affected with ataxia-telangiectasia (PMID 9463314, PMID 10817650, PMID 9000145, PMID 12497634, PMID 21965147), as well as in an individual diagnosed with breast cancer (PMID 27083775). The ATM gene codes for an enzyme called serine-protein kinase. This enzyme plays a key role in DNA damage response by transducing checkpoint signaling, cell cycle regulation, and tumor suppression. Pathogenic ATM variants result in impaired response to DNA damage, cell death, and formation of cancerous tumors and are associated with autosomal dominant susceptibility to breast cancer (MIM 114480) and autosomal recessive ataxia-telangiectasia (AT, MIM 208900). Women with a pathogenic ATM variant have a 5-to 9-fold increased risk of breast cancer (PMID 1961222, PMID 15928302). There is also some evidence supporting an association with autosomal dominant pancreatic, colorectal, prostate, and possibly other cancers (PMID 26483394, PMID 15928302, PMID 26662178). Ataxia-telangiectasia a childhood-onset disease characterized by progressive cerebellar ataxia, neurologic degeneration, conjunctival telangiectasias, immunodeficiency and increased risk of leukemia and lymphoma as well as other cancers (PMID 20301790). The worldwide prevalence of ataxiatelangiectasia is unknown, however, the estimated prevalence in the US ranges from 1 in 40,000 to 1 in 100,000 live births (PMID 20301790).

Variants Associated with Endocrine Disorder

Patient is a carrier for a pathogenic variant associated with a Endocrine Disorder. Reproductive partner and/or first-degree relatives may benefit from screening

Variant ID	Gene	VARIANT	Effect allele	Effect allele frequency
rsxxxxx	ATM	c.1564_1565delGA (p.Glu522fs)	C>delGA	nan

The c.1564_1565delGA frameshift variant is predicted to truncate the ATM protein, resulting in a loss or deficient function. The variant has been identified in a homozygous or compound heterozygous state in individuals affected with ataxia-telangiectasia (PMID 9463314, PMID 10817650, PMID 9000145, PMID 12497634, PMID 21965147), as well as in an individual diagnosed with breast cancer (PMID 27083775). The ATM gene codes for an enzyme called serine-protein kinase. This enzyme plays a key role in DNA damage response by transducing checkpoint signaling, cell cycle regulation, and tumor suppression. Pathogenic ATM variants result in impaired response to DNA damage, cell death, and formation of cancerous tumors and are associated with autosomal dominant susceptibility to breast cancer (MIM 114480) and autosomal recessive ataxia-telangiectasia (AT, MIM 208900). Women with a pathogenic ATM variant have a 5-to 9-fold increased risk of breast cancer (PMID 1961222, PMID 15928302). There is also some evidence supporting an association with autosomal dominant pancreatic, colorectal, prostate, and possibly other cancers (PMID 26483394, PMID 15928302, PMID 26662178). Ataxia-telangiectasia a childhood-onset disease characterized by progressive cerebellar ataxia, neurologic degeneration, conjunctival telangiectasias, immunodeficiency and increased risk of leukemia and lymphoma as well as other cancers (PMID 20301790). The worldwide prevalence of ataxiatelangiectasia is unknown, however, the estimated prevalence in the US ranges from 1 in 40,000 to 1 in 100,000 live births (PMID 20301790).

Section 2: Pharmacogenomic Findings

Unnamed: 0	REPORTING SCOPE	YOUR RISK
Total genes assessed	12	YOUR PHARMACOGENOMIC RESULTS
Total drugs assessed	96	14 Drugs Potentially Impacted

The way you respond to therapeutic drugs depends on your genes as well as other factors. This analysis found all your genetic alterations (genotypes) that may have a impact on how your body processing or metabolizing drugs (phenotypes). It helps your doctor better understand your personal situation, and 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.

Subsection 2.1: Drugs Potentially Impacted

Gene	Genotype	Phenotype	Drugs
CYP2B6	*9/*9	Poor Metabolizer	Efavirenz
CYP2C19	*38/*38	Normal Metabolizer	Abrocitinib, Brivaracetam, Citalopram, Clobazam, Clopidogrel, Flibanserin, Pantoprazole, Mavacamten, Voriconazole, Carisoprodol, Dexlansoprazole, Diazepam, Doxepin, Escitalopram, Esomeprazole, Lansoprazole, Omeprazole, Rabeprazole
CYP2C9	*3/*3	Poor Metabolizer	Celecoxib, Dronabinol, Erdafitinib, Flurbiprofen, Meloxicam, Nateglinide, Piroxicam, Siponimod, Warfarin, Avatrombopag, Ibuprofen
CYP2D6	*1/*1	Normal Metabolizer	Amphetamine, Aripiprazole, Aripiprazole Lauroxil, Atomoxetine, Brexpiprazole, Clozapine, Codeine, Deutetrabenazine, Eliglustat, Gefitinib, Iloperidone, Lofexidine, Meclizine, Metoclopramide, Oliceridine, Pimozide, Pitolisant, Propafenone, Tetrabenazine, Thioridazine, Tramadol, Valbenazine, Venlafaxine, Vortioxetine, Carvedilol, Cevimeline, Codeine, Perphenazine, Tolterodine, Tramadol, Amitriptyline, Amoxapine, Clomipramine, Darifenacin, Desipramine, Donepezil, Doxepin, Fesoterodine, Fluvoxamine, Galantamine, Imipramine, Metoprolol, Mirabegron, Nebivolol, Nortriptyline, Paroxetine, Propranolol, Protriptyline, Risperidone, Tamoxifen, Tamsulosin, Trimipramine, Viloxazine

CYP3A5	*3/*3	Poor Metabolizer	Tacrolimus
CYP4F2	*1/*4	V433M variant carriers	Warfarin
DPYD	c.1627A>G (*5)/c. 1627A>G (*5)	Normal Function	Capecitabine, Fluorouracil
NUDT15	*1/*1	Normal Metabolizer	Azathioprine, Mercaptopurine, Thioguanine
SLCO1B1	*37/*37	Normal Function	Simvastatin, Atorvastatin, Elagolix, Rosuvastatin
TPMT	*1/*1	Normal Metabolizer	Azathioprine, Mercaptopurine, Thioguanine
UGT1A1	*1/*6	Intermediate Metabolizer	Belinostat, Irinotecan, Sacituzumab Govitecan-hziy, Nilotinib, Pazopanib, Dolutegravir, Raltegravir
VKORC1	rs9923231 variant (T)/ rs9923231 variant (T)	1639G>A variant carriers	Warfarin

Subsection 2.2: Gene and Phenotype Findings

Drug	USP.Category	USP.Class	Indication	Gene	Genotype	Phenotype	Recommendation
Avatrombopag	Blood Products and Modifiers	Platelet Modifying Agents	Thrombocytopenia in Chronic Liver Disease;	CYP2C9	*3/*3	Poor Metabolizer	Results in higher systemic concentrations.
Celecoxib	Cardiovascular Agents	Cardiovascular Agents	Osteoarthritis; Rheumatoid Arthritis; Ankylosing Spondylitis; Acute Pain; Dysmenorrhea	CYP2C9	*3/*3	Poor Metabolizer	Results in higher systemic concentrations. Reduce starting dose to half of the lowest recommended dose in poor metabolizers. Consider alternative therapy in poor metabolizers with juvenile rheumatoid arthritis.
Dronabinol	Antiemetics	Emetogenic Therapy Adjuncts	Antiemetic for Chemotherapy-Induced Nausea and Vomiting (CINV); Appetite Stimulation in AIDS-Related Anorexia; Synthetic Cannabinoid;	CYP2C9	*3/*3	Poor Metabolizer	May result in higher systemic concentrations and higher adverse reaction risk. Monitor for adverse reactions.
Efavirenz	Antivirals	Anti-HIV Agents, Non-nucleoside Reverse Transcriptase Inhibitors (NNRTI)	HIV Treatment; Prevention of Mother-to-Child Transmission (PMTCT);	CYP2B6	*9/*9	Poor Metabolizer	Results in higher systemic concentrations and higher adverse reaction risk (QT prolongation).
Eliglustat	Genetic, Enzyme, or Protein Disorder:	nan	Gaucher Disease Type 1;	CYP2D6	*1/*1	Normal Metabolizer	Alters systemic concentrations, effectiveness, and adverse reaction risk

	Replacement, Modifiers, Treatment						(QT prolongation). Indicated for normal, intermediate, and poor metabolizer patients. Ultrarapid metabolizers may not achieve adequate concentrations to achieve a therapeutic effect. The recommended dosages are based on CYP2D6 metabolizer status. Coadministration with strong CYP3A inhibitors is contraindicated in intermediate and poor CYP2D6 metabolizers. Refer to FDA labeling for specific dosing recommendations.
Erdafitinib	Antineoplastics	Molecular Target Inhibitors	Bladder Cancer Treatment; FGFR Alterations;	CYP2C9	*3/*3	Poor Metabolizer	May result in higher systemic concentrations and higher adverse reaction risk. Monitor for adverse reactions.
Flurbiprofen	Analgesics	Nonsteroidal Anti-inflammatory Drugs	Pain Relief; Inflammation; Postoperative Pain;	CYP2C9	*3/*3	Poor Metabolizer	Results in higher systemic concentrations. Use a reduced dosage in poor metabolizers.
Ibuprofen	Analgesics	Nonsteroidal Anti-inflammatory Drugs	Pain Relief; Anti-inflammatory; Fever Reduction;	CYP2C9	*3/*3	Poor Metabolizer	May result in higher systemic concentrations.
Irinotecan	Antineoplastics	Molecular Target Inhibitors	Colorectal Cancer; Gastrointestinal Cancers; Small Cell Lung Cancer;	UGT1A1	*1/*6	Intermediate Metabolizer	Results in higher systemic active metabolite concentrations and higher adverse reaction risk (severe or life-threatening neutropenia, severe diarrhea). Closely monitor for neutropenia during and after treatment. Consider reducing the starting dosage by at least one level in poor metabolizers and modify the dosage based on individual patient tolerance. Refer to FDA labeling for specific dosing recommendations.
Meloxicam	Analgesics	Nonsteroidal Anti-inflammatory Drugs	Osteoarthritis; Rheumatoid Arthritis; Ankylosing Spondylitis; Other Painful Inflammatory Conditions;	CYP2C9	*3/*3	Poor Metabolizer	Results in higher systemic concentrations. Consider dose reductions in poor metabolizers. Monitor patients for adverse reactions.
Nateglinide			Type 2 Diabetes;	CYP2C9	*3/*3		

	Blood Glucose Regulators	Antidiabetic Agents				Poor Metabolizer	Results in higher systemic concentrations and may result in higher adverse reaction risk (hypoglycemia). Dosage reduction is recommended. Increase monitoring frequency for adverse reactions. Refer to FDA labeling for specific dosing recommendations.
Piroxicam	Analgesics	Nonsteroidal Anti-inflammatory Drugs	Pain and Inflammation; Acute Gout; Post-Surgical Pain;	CYP2C9	*3/*3	Poor Metabolizer	Results in higher systemic concentrations. Consider reducing dosage in poor metabolizers.
Siponimod	Central Nervous System Agents	Multiple Sclerosis Agents	Relapsing Forms of Multiple Sclerosis; Active Secondary Progressive Multiple Sclerosis (SPMS) with Relapses;	CYP2C9	*3/*3	Poor Metabolizer	Results in higher systemic concentrations. Adjust dosage based on genotype. Do not use in patients with CYP2C9 *3/*3 genotype. Refer to FDA labeling for specific dosing recommendations.
Warfarin	Blood Products and Modifiers	Anticoagulants	Prevention and Treatment of Thrombosis; Stroke Prevention; Prosthetic Heart Valves; Hypercoagulable Conditions;	CYP2C9	*3/*3	Poor Metabolizer	Alters systemic concentrations and dosage requirements. Select initial dosage, taking into account clinical and genetic factors. Monitor and adjust dosages based on INR.
Warfarin	Blood Products and Modifiers	Anticoagulants	Prevention and Treatment of Thrombosis; Stroke Prevention; Prosthetic Heart Valves; Hypercoagulable Conditions;	CYP4F2	*1/*4	V433M variant carriers	May affect dosage requirements. Monitor and adjust doses based on INR.
Warfarin	Blood Products and Modifiers	Anticoagulants	Prevention and Treatment of Thrombosis; Stroke Prevention; Prosthetic Heart Valves; Hypercoagulable Conditions;	VKORC1	rs9923231 variant (T)/ rs9923231 variant (T)	1639G>A variant carriers	Alters dosage requirements. Select initial dosage, taking into account clinical and genetic factors. Monitor and adjust dosages based on INR.