HK LONGEVITY MEDICAL CENTRE

# Genetic Risk Carriers Screening and Analysis Report

| PATIENT NAME | GENDER |
|---|---|
| John Doe | Male |
| **DATE OF BIRTH** | **SAMPLE TYPE** |
| 01/11/1990 | Whole Blood |
| **COLLECTION DATE** | **SAMPLE ID** |
| 01/01/2023 | A123456 |
| **ACCESSION #** | **REPORT DATE** |
| 4316546 | 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** | 13 | YOUR PHARMACOGENOMIC RESULTS |
| **Total drugs assessed** | 88 | 51 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

| Symbol | Genotype | Phenotype | Drugs |
|---|---|---|---|
| **ABCG2** | rs2231142 reference (G)/rs2231142 variant (T) | Decreased Function | Rosuvastatin |
| **CACNA1S** | No CPIC variants found | Uncertain Susceptibility | Desflurane, Enflurane, Halothane, Isoflurane, Methoxyflurane, Sevoflurane, Succinylcholine |
| **CFTR** | No CPIC variants found | ivacaftor non-responsive in CF patients | Ivacaftor |
| **CYP2B6** | *9/*9 | Poor Metabolizer | Efavirenz, Sertraline |
| **CYP2C19** | *38/*38 | Normal Metabolizer | Amitriptyline, Citalopram, Clomipramine, Clopidogrel, Dexlansoprazole, Doxepin, Escitalopram, Imipramine, Lansoprazole, Omeprazole, Pantoprazole, Sertraline, Trimipramine, Voriconazole |
| **CYP2C9** | *3/*3 | Poor Metabolizer | Celecoxib, Flurbiprofen, Fluvastatin, Ibuprofen, Lornoxicam, Meloxicam, Piroxicam, Tenoxicam, Warfarin |
| **CYP2D6** | *1/*1 | Normal Metabolizer | Amitriptyline, Atomoxetine, Clomipramine, Codeine, Desipramine, Doxepin, Fluvoxamine, Hydrocodone, Imipramine, Nortriptyline, Ondansetron, Paroxetine, Tamoxifen, Tramadol, Trimipramine, Tropisetron, Venlafaxine, Vortioxetine |
| **CYP3A5** | *3/*3 | Poor Metabolizer | Tacrolimus |
| **CYP4F2** | *1/*4 | nan | Warfarin |
| **DPYD** | c.1627A>G (*5)/c.1627A>G (*5) | Normal Metabolizer | Capecitabine, Fluorouracil |

| | | | |
|---|---|---|---|
| **G6PD** | B (reference)/B (reference) | Normal | Aminosalicylic Acid, Aspirin, Chloramphenicol, Chloroquine, Ciprofloxacin, Dapsone, Dimercaprol, Doxorubicin, Furazolidone, Glyburide, Hydroxychloroquine, Mafenide, Methylene Blue, Nalidixic Acid, Nitrofurantoin, Norfloxacin, Ofloxacin, Pegloticase, Phenazopyridine, Primaquine, Quinine, Rasburicase, Sulfadiazine, Sulfadimidine, Sulfamethoxazole / Trimethoprim, Sulfanilamide, Sulfasalazine, Sulfisoxazole, Tafenoquine, Tolbutamide, Toluidine Blue, Vitamin C, Vitamin K |
| **IFNL3** | rs12979860 reference (C)/rs12979860 reference (C) | nan | Peginterferon Alfa-2a, Peginterferon Alfa-2b |
| **NUDT15** | *1/*1 | Normal Metabolizer | Azathioprine, Mercaptopurine, Thioguanine |
| **RYR1** | No CPIC variants found | Uncertain Susceptibility | Desflurane, Enflurane, Halothane, Isoflurane, Methoxyflurane, Sevoflurane, Succinylcholine |
| **SLCO1B1** | *37/*37 | Normal Function | Atorvastatin, Fluvastatin, Lovastatin, Pitavastatin, Pravastatin, Rosuvastatin, Simvastatin |
| **TPMT** | *1/*1 | Normal Metabolizer | Azathioprine, Mercaptopurine, Thioguanine |
| **UGT1A1** | *1/*6 | Intermediate Metabolizer | Atazanavir |
| **VKORC1** | rs9923231 variant (T)/rs9923231 variant (T) | nan | Warfarin |

## Subsection 2.2: Gene and Phenotype Findings

| Symbol | Genotype | Phenotype | Drugs |
|---|---|---|---|
| **ABCG2** | rs2231142 reference (G)/rs2231142 variant (T) | Decreased Function | Rosuvastatin |
| **CACNA1S** | No CPIC variants found | Uncertain Susceptibility | Desflurane, Enflurane, Halothane, Isoflurane, Methoxyflurane, Sevoflurane, Succinylcholine |
| **CFTR** | No CPIC variants found | ivacaftor non-responsive in CF patients | Ivacaftor |
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| **CYP3A5** | *3/*3 | Poor Metabolizer | Tacrolimus |
| **CYP4F2** | *1/*4 | nan | Warfarin |

| | | | |
|---|---|---|---|
| **DPYD** | c.1627A>G (*5)/c.1627A>G (*5) | Normal Metabolizer | Capecitabine, Fluorouracil |
| **G6PD** | B (reference)/B (reference) | Normal | Aminosalicylic Acid, Aspirin, Chloramphenicol, Chloroquine, Ciprofloxacin, Dapsone, Dimercaprol, Doxorubicin, Furazolidone, Glyburide, Hydroxychloroquine, Mafenide, Methylene Blue, Nalidixic Acid, Nitrofurantoin, Norfloxacin, Ofloxacin, Pegloticase, Phenazopyridine, Primaquine, Quinine, Rasburicase, Sulfadiazine, Sulfadimidine, Sulfamethoxazole / Trimethoprim, Sulfanilamide, Sulfasalazine, Sulfisoxazole, Tafenoquine, Tolbutamide, Toluidine Blue, Vitamin C, Vitamin K |
| **IFNL3** | rs12979860 reference (C)/rs12979860 reference (C) | nan | Peginterferon Alfa-2a, Peginterferon Alfa-2b |
| **NUDT15** | *1/*1 | Normal Metabolizer | Azathioprine, Mercaptopurine, Thioguanine |
| **RYR1** | No CPIC variants found | Uncertain Susceptibility | Desflurane, Enflurane, Halothane, Isoflurane, Methoxyflurane, Sevoflurane, Succinylcholine |
| **SLCO1B1** | *37/*37 | Normal Function | Atorvastatin, Fluvastatin, Lovastatin, Pitavastatin, Pravastatin, Rosuvastatin, Simvastatin |
| **TPMT** | *1/*1 | Normal Metabolizer | Azathioprine, Mercaptopurine, Thioguanine |
| **UGT1A1** | *1/*6 | Intermediate Metabolizer | Atazanavir |
| **VKORC1** | rs9923231 variant (T)/rs9923231 variant (T) | nan | Warfarin |