


# PERSONAL GENETIC REPORT

 PATHWAY GENOMICS™

FULL HEALTH  
REPORT

## Personal Details

[REDACTED]  
[REDACTED]  
[REDACTED]

Ethnicity: Caucasian

Indication: Population Screening

Specimen Source: Saliva

Report Date: 02/25/2010

## Ordering Healthcare Professional

[REDACTED]  
[REDACTED]  
[REDACTED]

877-505-7374

NPI: 1033265780

## Test Performed / Method

Genotyping by array-based evaluation of multiple molecular probes

## Laboratory Info

Accession # A0000172

## Lab Director

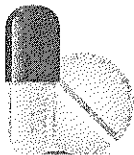
*James R. Nickel, M.D.*  
James R. Nickel, M.D.



## Carrier Status

You are a carrier for 1 conditions  
Hearing loss, nonsyndromic hereditary

We tested your DNA for  
**37 single gene conditions.**



## Drug Responses

You have an atypical response to 3 drugs tested:

Caffeine: Metabolism  
Methotrexate: Toxicity  
Tamoxifen: Metabolism

We tested your response to  
**9 Drugs.**



Updated 17MAR2010 - See Appendix For Details

## Health Conditions

- Take Action(1)
- Be Proactive(3)
- Learn More(16)
- Live A Healthy Lifestyle(3)

\*Number of conditions tested will vary depending on ethnicity and gender.

\*We tested your DNA for  
**23 complex health conditions.**

## Introduction

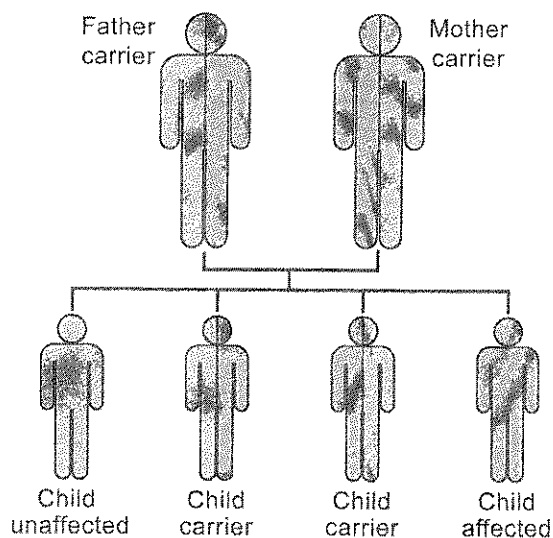
Recessive genetic conditions are caused by mutations that can be carried silently in a family for generations, only to be discovered when two carriers have a child with the condition. They are usually single-gene disorders (also known as monogenic disorders), meaning that mutations in a single gene are responsible for the disease. Most recessive disorders are rare because a person must have a disease-causing variation in their DNA on each copy of the gene inherited from both parents, which requires that both parents are carriers and that the child inherits the disease-causing variant from each.

The most well-known of these are diseases like cystic fibrosis, nonsyndromic hereditary hearing loss, Tay-Sachs disease, and beta-thalassemia, although there are thousands more. Pathway Genomics tests for hundreds of mutations for recessive genetic disorders, which can tell you whether you are a carrier and if you may pass on a disease-causing variant to your children. If your partner is also tested, this test will let you know whether your children could inherit a disease-causing variant from both of you and potentially be affected by the condition.

## What it means to be a carrier

Some diseases have a recessive inheritance pattern, meaning that in order to develop the disease a person must have two disease-causing mutations (also called alleles, or variants), one on each copy of the gene involved in the condition. Since we inherit two copies of each gene (one from each of our parents), usually a recessive disease occurs when a person inherits one disease-causing variant from each parent.

In a very small percentage of cases, a person inherits a disease-causing allele from one parent and has a spontaneous mutation in the normal copy of the gene inherited from the other parent, thus giving rise to two disease-causing alleles.



A person who has only one disease-causing allele is a carrier, but does not develop the disease. Carriers can pass the disease-causing variant on to their children, who will also be carriers if they inherit a variant from one parent.

If both parents are carriers, then each child from the couple has a 25% chance of inheriting two copies of the disease-causing variant and developing the disease, a 25% chance of inheriting no disease alleles and being free of the condition, and a 50% chance of being a carrier. If only one parent is a carrier, then each child has a 50% chance of inheriting one copy of the variant and being carriers themselves.

People affected with the disease will pass on one of their disease-causing alleles to each child.

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## Condition List

Condition Name	Present	Not Present
3-Methylcrotonyl-CoA carboxylase deficiency		✓
Alpha-1 antitrypsin deficiency		✓
Amyotrophic lateral sclerosis		✓
Beta-thalassemia		✓
Biotinidase deficiency		✓
Bloom syndrome		✓
Canavan disease		✓
Cystic fibrosis		✓
Diabetes, permanent neonatal		✓
Factor XI deficiency		✓
Familial dysautonomia		✓
Familial Mediterranean fever		✓
Fanconi anemia		✓
Galactosemia		✓
Gaucher disease		✓
Glutaric acidemia, type 1		✓
Glycogen storage disease, type 1A		✓
Hearing loss, nonsyndromic hereditary	✓	
Hemochromatosis		✓
Hemoglobin C		✓
Hemoglobin E		✓
HMG-CoA lyase deficiency		✓
Maple syrup urine disease		✓
Medium-chain acyl-CoA dehydrogenase deficiency		✓
Methylmalonic acidemia		✓
Mucopolipidosis		✓
Multiple carboxylase deficiency		✓
Niemann-Pick disease		✓
Phenylketonuria		✓
Polycystic kidney disease		✓
Pompe disease		✓
Propionic acidemia		✓
Sick sinus syndrome		✓
Tay-Sachs disease		✓
Tay-Sachs pseudodeficiency		✓
Tyrosinemia		✓
Very long-chain acyl-CoA dehydrogenase deficiency		✓

## Hearing Loss, Nonsyndromic Hereditary

### Your Results

We scanned your DNA for 6 variants related to hearing loss, nonsyndromic hereditary. Your DNA gave positive results for one:

L90P in GJB2

This means that you are a carrier for this condition, but you are not likely to develop the disease yourself. To find out more about carrier status and what this means for your children, please contact our genetic counselors.

Residual risk: Since there are many rare mutations, it is possible to carry a mutation that is not on our test in addition to the variant that we found in your DNA. If you have a family history or are concerned about your status for this disease and wish to find out more, please contact our genetic counselors.

Pathway Genomics has scanned your DNA for markers related to hearing loss, nonsyndromic hereditary and found that you carry the following:

L90P	Present
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### About the genes

Our knowledge about the genetic causes of hearing impairment has improved significantly in recent years. Scientists believe that changes in more than 100 genes can lead to NSHL. About half of the genes responsible have already been identified. Proteins encoded by these genes perform a variety of functions in the development of ear structures or in the hearing process. Both autosomal recessive and autosomal dominant mutations have been found, although autosomal recessive mutations are more common and account for about 80% of NSHL cases. Each genetic locus of autosomal recessive NSHL is designated with a name composed of "DFNB" and a number. Generally, autosomal recessive NSHL is congenital, severe-to-profound, and non-progressive. GJB2 encodes a protein called connexin 26, a member of the connexin protein family. Connexins form gap junctions, which are channels between neighboring cells for exchanging small molecules. Gap junctions in the inner ear are involved in the maintenance of the normal ionic environment, which is essential for the auditory hair cells to survive and function. Recessive mutations in GJB2 cause the DFNB1 type of NSHL.

OTOF encodes a protein called otoferlin, a membrane-anchored cytosolic protein. Otoferlin is believed to play a role in neurotransmitter release from nerve cells in the ear. Hearing loss caused by recessive mutations in OTOF is designated DFNB9, which is typically congenital, severe-to-profound, and bilateral.

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## Disease description

Hearing loss is the most common sensory disorder and it is categorized in many ways. The severity of hearing loss is graded as mild, moderate, severe or profound. The sound frequencies affected can be low (<500 Hz), middle (500-2000 Hz), or high (>2000 Hz), and the impairment can be in only one ear (unilateral) or both ears (bilateral). The defects can be found in the inner ear (sensorineural hearing loss), in the outer or middle ear (conductive hearing loss), or a combination of the two. The symptoms can be progressive (worsening over time) or stable. Hearing loss can begin during any period of life. The impact of hearing loss is most significant if it is prelingual, which refers to hearing loss that begins before the critical period of language acquisition. Most prelingual hearing loss is congenital, which can now be detected by newborn hearing screening programs.

Hearing loss can be caused by both external and internal factors. Environmental factors like exposure to loud noises, viral infection, premature birth, use of certain medications, and physical trauma can all contribute to this condition. More than half of hearing loss cases have genetic causes and are considered hereditary. About 1% of genes in the human genome are believed to function in the hearing process. Hereditary hearing loss can be syndromic, meaning that the hearing loss is associated with additional clinical features in other tissues or organs. There are more than 400 syndromes in which hearing loss is a recognized finding, and these make up about 30% of hereditary hearing loss cases. Nonsyndromic hearing loss (NSHL) accounts for the remaining 70% of hereditary hearing loss cases and is predominantly sensorineural. NSHL is usually caused by mutations in a single gene (monogenic), which may be autosomal dominant (a defect in one of a person's two copies of a gene is enough to cause the condition) or autosomal recessive (both copies of the gene must have a mutation in order for the person to exhibit the condition). In some rare cases, mutations are found on the X chromosome (X-linked) or in mitochondrial DNA ([PMID 18804553](#)).

Genetic hearing loss is highly heterogeneous, meaning that symptoms vary substantially among people with the condition, and the gene variant(s) found are not the only factors that determine the course or severity of the condition. The individual's family history, genetic background and environmental factors play a major role. It is important to consult with the appropriate physicians including audiologists and otolaryngologists if you suspect you have hearing loss. Your genotype may provide important information for your diagnosticians.

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## Mutations tested

Pathway Genomics tests for 6 recurrent autosomal recessive mutations (5 in GJB2 and 1 in OTOF) that are found in people with NSHL.

In people of European descent, the most common autosomal recessive deafness-causing mutation is 35delG (sometimes also called 30delG) in GJB2. Mutations in GJB2 account for more than a half of autosomal recessive NSHL in Caucasian populations, and about 70% of these mutations are 35delG. The combined carrier rate of all recessive deafness-causing GJB2 mutations has been estimated at 3% in the general population of the Midwestern United States. The prevalence of GJB2 mutations as a cause of deafness varies in other ethnic groups, and other GJB2 mutations may be found more often than 35delG. For example, 167delT is the most common GJB2 mutation in the Ashkenazi Jewish population with a carrier rate of about 4%. In the Japanese and Chinese populations, 235delC is the most common deafness-causing GJB2 mutation. V37I is also common in the Chinese population (carrier rate 11.5%) and causes mild to moderate hearing loss.

The Q829X mutation in OTOF accounts for 3% (the third most frequent) of mutations causing recessive prelingual deafness in Spain. The majority of Spanish Q829X carriers are likely to be descended from a single ancestor in whom the mutation first took place.

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### **Ethnic prevalence and frequency**

In developed countries, hearing loss is the most common birth defect, with one in 500 newborns affected. Because some types of hearing loss are progressive, the prevalence figure gradually reaches 3.5 per 1,000 by adolescence. According to a recent survey in the United States ([PMID 18663164](#)), 16.1% of adults have hearing loss in speech frequencies. Men are 5.5 times more likely to have impaired hearing than women. Risk of hearing loss is 70% lower in African-Americans compared to people of European ancestry, whereas Mexican-Americans have the highest odds of both high-frequency hearing loss and bilateral hearing loss. The risk of hearing loss also increases with age.

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This section lists the common names of all the individual markers that were tested. Markers are listed by disease, with gene name in parentheses. **Orange:** If you carry any of these markers, they will be highlighted in orange and you will have a corresponding Condition Detail page preceding this one that describes the condition and your results.

**Black:** For markers you do not carry, these are listed below in black.

**Strikethrough:** We make every effort to provide you with accurate genotypes at all the markers we test. Infrequently, our lab is unable to determine a genotype at a marker. This means that we are not able to determine the status of your DNA for this mutation. Any mutations that give no results are indicated by strike-through of that mutation. If you are concerned about your status for the variant we were unable to determine, other methods are available to test your DNA.

**Residual risk:** Since there are many rare mutations, it is possible to carry a mutation that is not on our test. If you have a family history or are concerned about your status for this disease and wish to find out more, please contact your physician or a genetic counselor.

You should know that it is not usually possible to determine health prognosis solely from genotype information. There is a great deal of variability in how diseases are expressed among individuals, which depends on many other factors including environment and lifestyle. To find out more about what your genotype means for your health and for your offspring, please contact our genetic counselors and consult your physician.

### 3-Methylcrotonyl-CoA carboxylase deficiency

D532H (MCCC1), L437P (MCCC1), R385S (MCCC1), A289V (MCCC1), E99Q (MCCC2), S173L (MCCC2), R193C (MCCC2), V339M (MCCC2), I437V (MCCC2)

### Alpha-1 antitrypsin deficiency (SERPINA1)

S allele, Z allele

### Amyotrophic lateral sclerosis (ALS2)

1867delCT

### Beta-thalassemia (HBB)

IVS2-1G>A, cd39C>T, IVS1-110G>A, IVS1-6T>C, IVS1-1G>A, cd24T>A, Hb Malay, 17A>T, cd8/9+G, cd8-AA, 29A>G, cd44-C, 41/42-TTCT

### Biotinidase deficiency (BTD)

C33FfsX36, A171T, D444H, Q456H, R538C

### Bloom syndrome (BLM)

S186X, W428X, W567X, Q645X, blmAsh, W803fsX, R836fsX, R899X, Q975fsX, C1055S

### Canavan disease (ASPA)

245insA, Y109X, 433-2A>G, M195R, C218X, G274R, 827delGT, P280S, F295S, E285A

### Cystic fibrosis (CFTR)

394delTT, 405+1G>A, 405+3A>C, 444delA, Y122X, 574delA, 621+1G>T, 663delT, G178R, 712-1G>T, P205S, L206W, V232D, 846delT, 935delA, 936delTA, deltaF311, 1078delT, G330X, R334W, R352Q, Q359K/T360K, S364P, Q493X, deltaF508, 1677delTA, C524X, 1717-1G>A, S549R (T>G), L558S, 1812-1G>A, A561E, P574H, 2043delG, 2055del9>A, 2105del13ins5, 2108delA, 2184delA, R709X, K710X, 2307insA, P750L, 2869insG, 3120G>A, 3171delC, 3272-26A>G, W1089X, Q1100P, D1152H, R1158X, R1162X, 3659delC, 3667ins4, S1196X, W1204X, 3791delC, Q1238X, 3876delA, S1251N, 3905insT, N1303K, G1349D, R347P, G622D, S549N, S549R (A>C), 2789+5G>A, R117H, G85E, 3849+10kbC>T, 711+1G>T, 1949del84, V520F/I, 1898+1G>A, A455E, G551D, W1282X, I148T, M1101K

### Diabetes, permanent neonatal

E382K (ABCC8), N72S (ABCC8), P45L (ABCC8), R397L (GCK), IVS8+2T>G (GCK)

### Factor XI deficiency (F11)

IVS14+1G>A, E117X, C128X

### Familial dysautonomia (IKBKAP)

IVS20+6T>C, R696P

### Familial Mediterranean fever (MEFV)

R761H, A744S, V726A, K695R, M694I, M694V, M680I, R653H, R408Q

### Fanconi anemia (FANCC)

L554P, R548X, R185X, IVS4+4A>T, 322delG, Q13X

### Galactosemia (GALT)

IVS2-2A>G, S135L, F171S, Q188R, L195P, E203K, Y209C, K285N, N314D, L218L (c.652C>T)

### Gaucher disease (GBA)

R463C, D409H, N370S, V394L

### Glutaric acidemia, type 1 (GCDH)

R227P, A293T, V400M, R402W, A421V

### Glycogen storage disease, type 1A (G6PC)

c.79delC, R83C, c.378\_379dupTA, G188R, Q242X, G270V, deltaF327, Q347X

### Hearing loss, nonsyndromic hereditary

L90P (GJB2), 235delC (GJB2), 167delT (GJB2), V37I (GJB2), 35delG (GJB2), Q829X (OTOF)

### Hemochromatosis

G320V (HFE2), H63D (HFE), S65C (HFE), Y250X (TFR2), M172K (TFR2), C282Y (HFE)

### Hemoglobin C (HBB)

Hemoglobin C

### Hemoglobin E (HBB)

Hemoglobin E

### HMG-CoA lyase deficiency (HMGCL)

c.504\_505delCT, E37X, R41Q

### Maple syrup urine disease

Y438N (BCKDHA), G278S (BCKDHB), E372X (BCKDHB), R183P (BCKDHB)

### Medium-chain acyl-CoA dehydrogenase deficiency (ACADM)

Y42H, K304E



Methylmalonic acidemia

R145X (MMAA), 503delC (MMAA), G717V (MUT), N219Y (MUT),  
E117X (MUT), R108C (MUT)

Mucopolidosis (MCOLN1)

IVS3-2A>G

Multiple carboxylase deficiency (HLCS)

R665X, G581S, D571N, V550M, R508W, 780delG, L237P

Niemann-Pick disease

L302P (SMPD1), P330SfsX382 (SMPD1), H421Y (SMPD1), R496L  
(SMPD1), deltaR608 (SMPD1), E20X (NPC2), I1061T (NPC1),  
G992W (NPC1)

Phenylketonuria (PAH)

Y414C, R408Q, R408W, A403V, IVS10-11G>A, P281L, E280K,  
R261Q, V245A, R243X, R158Q, I65T, L48S, F39L

Polycystic kidney disease (PKHD1)

R3482C, V3471G, Q3392X, D3230fs, I3177T, I2957T, I2944fs,  
P805L, R496X, I222V, T36M

Pompe disease (GAA)

2741AG>CAGG, G309R, D645E

Propionic acidemia

R399Q (PCCA), 1172\_1173insT (PCCB), 1218del14ins12 (PCCB),  
R410W (PCCB), T428I (PCCB)

Sick sinus syndrome (SCN5A)

R1632H, G1408R, P1298L, T220I

Tay-Sachs disease (HEXA)

R504C, R499H, IVS12+1G>C, C458Y, 1278insTATC, IVS9+1G>A,  
I335F, W329X, deltaTTC910-912, G269S, S210F, 613delC,  
IVS5-1G>T, V192L, R178H/L, R178H/L, R170Q, R170W,  
IVS2+1G>C, IVS9-1G>T

Tay-Sachs pseudodeficiency (HEXA)

R247W, R249W

Tyrosinemia (FAH)

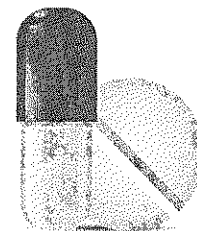
Q64H, P261L, W262X, G337S

Very long-chain acyl-CoA dehydrogenase deficiency (ACADVL)

V283A

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One of the great promises of genetic testing is personalized medicine - allowing caregivers to prescribe the medication that is optimal for you based on your genotype. Your genetics can cause some medications to be more or less effective, suggest optimal dosing levels, or in some cases lead to personal harm with the wrong medication. The Pathway Genomics Drug Response Report indicates which medications are optimal for you based on your genotype. Even if you are not currently taking any of these medications, this information could be critical in an emergency situation.



Atypical Response

Drug Name	Drug Response
Abacavir	Hypersensitivity
Caffeine	Metabolism
Carbamazepine	Hypersensitivity
Clopidogrel	Metabolism
Methotrexate	Toxicity
Statins	Protection against myocardial infarction
Statins	Myopathy
Tamoxifen	Metabolism
Warfarin	Sensitivity

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## Abacavir : Hypersensitivity

### Your Results

Your genotype suggests that you are not likely to have a hypersensitive reaction to abacavir. However, this does not guarantee you will not have a hypersensitive reaction to abacavir. Patients with your genotype do develop hypersensitive reactions to abacavir, but much less frequently than patients who have the HLA-B\*5701 allele.

### About this medication

Abacavir is an antiviral medication that is used to treat people infected with HIV and patients with AIDS. Although it is well tolerated by most people, some individuals become hypersensitive with symptoms that include fever, skin rash, fatigue, gastrointestinal problems, and respiratory problems. Hypersensitivity can be severe, and in rare cases, fatal. The FDA approved labeling for abacavir suggests genetic screening for HLA-B\*5701 prior to therapy.

Your genetic result	x/x
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### We evaluated the following markers

Gene <sup>1</sup>	Marker <sup>1</sup>	Your Genotype <sup>2</sup>
HLA	rs3828917	G/G

See glossary at the back of the document for definitions of these terms

### Genetics of this response

Several observations led scientists to hypothesize that genetic factors are primarily responsible for abacavir hypersensitivity. The first clue was that only a subset of individuals exposed to abacavir developed hypersensitivity. A meta-analysis of 25 clinical studies involving 5248 participants showed that ethnic origin might influence abacavir hypersensitivity and familial predisposition was also reported ([PMID 11675863](#)). Evidence from the pathogenesis of other similar multi-system drug hypersensitivity reactions pointed to genetic variants that lie within the Major Histocompatibility Complex (MHC) region, and the HLA-B\*5701 allele was implicated in abacavir hypersensitivity by two studies published back-to-back in Lancet in 2002, one in Australia and another in the U.S. ([PMID 11888582](#), [PMID 11943262](#)). A later study assessing the HLA region more closely, in a larger Australian population confirmed that the HLA-B\*5701 allele is the risk allele ([PMID 15024131](#)). Population studies have since been conducted and have confirmed the HLA-B\*5701 allele association (see Research Details section). The mechanism of the adverse reaction is not known, but clinical symptoms suggest an immunological reaction influenced by genetic factors.

There is a strong correlation between abacavir hypersensitivity in world populations and the prevalence of the HLA-B\*5701 allele. Abacavir hypersensitivity is observed in about 10% of individuals of western European ancestry ([PMID 18256392](#), [PMID 16758424](#)), but is much less in East Asian populations ([PMID 19115972](#)). Correspondingly, the prevalence of HLA-B\*5701 is about 5-7% in western Europe, 8% in U.S. Caucasians and in the U.K., but very rare (<1%) in East Asian (Korean, Chinese, Japanese, Taiwanese) and African populations. The prevalence of the risk allele is higher in South and Southeast Asian populations; the frequency is about 5% to 20% in Asian Indian populations and 4% to 10% among people from Thailand ([PMID 16758425](#)).

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## Caffeine : Metabolism

### Your Results

Your genotype indicates that you metabolize caffeine at a slow rate, and that caffeine consumption may increase your risk of heart attack. If your genetic profile, family history, or lifestyle indicates a higher risk for cardiovascular disease, please discuss with your doctor how you can reduce your caffeine intake.

### About this medication

Caffeine is the most widely consumed stimulant in the world and it is often added to many foods such as tea, coffee, chocolate, many soft drinks, as well as pain relievers and other over-the-counter medications. Caffeine is metabolized by a liver enzyme called cytochrome P450 1A2 which is encoded by the CYP1A2 gene. Individuals differ in CYP1A2 enzyme activity, and thus, in their ability to metabolize caffeine.

Your genetic result	CYP1A2*1F
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### We evaluated the following markers

Gene <sup>1</sup>	Marker <sup>1</sup>	Your Genotype <sup>2</sup>
CYP1A2	rs762551	A/C

See glossary at the back of the document for definitions of these terms

### Genetics of this response

Caffeine is metabolized by a liver enzyme called cytochrome P450 1A2 which is encoded by the CYP1A2 gene. Individuals differ in CYP1A2 enzyme activity, and thus, in their ability to metabolize caffeine. An A>C substitution at position 734 (CYP1A2\*1F) in the CYP1A2 gene results in decreased levels of the enzyme activity and impaired caffeine metabolism ([PMID 18089957](#), [PMID 10233211](#)). Carriers of the variant CYP1A2\*1F allele are "slow" caffeine metabolizers, whereas individuals who are homozygous for the CYP1A2\*1 allele are "fast" caffeine metabolizers. Approximately 55% to 65% of people are carriers of the slow CYP1A2\*1F allele.

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## Carbamazepine : Hypersensitivity

### Your Results

You are not likely to have a hypersensitive reaction to carbamazepine. However, it is also known that the risk allele we have checked, HLA-B\*1502, does not account for all forms of carbamazepine-induced hypersensitivity, especially in Caucasians. There is a small chance that individuals may develop a reaction even if they are negative for the allele.

### About this medication

Carbamazepine is a widely prescribed anticonvulsant, commonly used in the treatment of epilepsy. It is also prescribed for the treatment of bipolar depression and trigeminal neuralgia. Most people tolerate carbamazepine; however, in a small fraction of the population, carbamazepine can cause idiosyncratic hypersensitivity reactions which include fatal skin reactions (Stevens-Johnson syndrome, SJS; toxic epidermal necrolysis, TEN) accompanied with fever, lymphadenopathy, and multi-organ abnormalities. In December 2007, the United States Food and Drug Administration (FDA) issued an alert that dangerous and fatal skin reactions to carbamazepine are significantly more common in patients who carry a particular human leukocyte antigen (HLA) allele, HLA-B\*1502, which occurs most frequently in people with Asian ancestry. The FDA recommends that patients with Asian ancestry should be screened for the HLA-B\*1502 allele before starting treatment with carbamazepine.

Your genetic result	x/x
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### We evaluated the following markers

Gene <sup>1</sup>	Marker <sup>1</sup>	Your Genotype <sup>2</sup>
HLA Region	rs2844682	C/T
HLA Region	rs3909184	G/G

See glossary at the back of the document for definitions of these terms

## Genetics of this response

Studies indicate that the risk of Stevens Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) due to carbamazepine therapy is significantly increased in patients positive for the HLA-B\*1502 allele. The human leukocyte antigen system (HLA) is a region on chromosome 6 that contains a large number of genes related to immune system function in humans. The proteins encoded by HLA genes are found on the outer part of the body's cells. HLA proteins form paired molecules which bind to protein fragments processed within the cell and display them for the immune system cells (called T cells) to recognize as either "self" or "non-self" derived. HLA-B\*1502 is the type of HLA which displays "self" proteins. Normally, cells displaying an individual's "self"-derived proteins are not targeted as an invader by the individual's T cells. The strong genetic association of HLA-B\*1502 allele with carbamazepine hypersensitivity suggests a direct involvement of HLA in the pathogenesis of carbamazepine hypersensitivity, but the exact mechanism is still unknown. The HLA-B\*1502 allele is more prevalent in individuals of Asian ancestry. The HLA-B\*1502 allele has been observed in about 10-15% of people in parts of China, Thailand, Malaysia, Indonesia, the Philippines, and Taiwan. South Asians, such as Indians, have about 2 to 4% frequency of this allele, but the frequency may be higher in some groups. The prevalence of HLA-B\*1502 is much lower (<1%) in Japan and Korea. The prevalence of this allele is also low in Caucasians (1–2%).

Corresponding to allele prevalence, the incidence of SJS in Han Chinese is much higher than in Caucasians with about 8 cases per million people per year in Han Chinese compared with 2–3 cases in Caucasians. Based on data from the '90s, carbamazepine therapy accounts for 25–33% of cases of the syndrome in Asians ([PMID 8781718](#), [PMID 9679693](#)), whereas only 5–6% of SJS cases in Caucasians are caused by it ([PMID 7477195](#), [PMID 10392983](#)). Other studies suggest that the HLA-B\*1502 allele may not be a good marker for major forms of carbamazepine hypersensitivity in the Caucasian population and ethnicity should be considered when using the HLA-B\*1502 as a marker to predict hypersensitivity to carbamazepine prior to treatment ([PMID 16981842](#), [PMID 16415921](#)).

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## Clopidogrel : Metabolism

### Your Results

You do not have the variations in CYP2C19 that decrease the metabolism of clopidogrel and should expect a typical response to clopidogrel therapy at typical doses. We encourage you to share this information with your physician.

### About this medication

Clopidogrel (marketed under brand names such as Plavix, Clopilet and Ceruvin) is an oral anti-platelet agent used to inhibit blood clots in patients with coronary artery disease, peripheral vascular disease, and cerebrovascular disease. Genetics plays important roles in determining how effectively clopidogrel is processed, contributing to the significant variability in the therapeutic response to clopidogrel. Pathway Genomics tests for variations in the CYP2C19 gene, which encodes an essential enzyme for metabolizing clopidogrel into an active form. In 2009, information about the effects of these CYP2C19 variations on clopidogrel response was included by the United States Food and Drug Administration (FDA) in its updated label for clopidogrel.

Your genetic result	*1/*1
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### We evaluated the following markers

Gene <sup>1</sup>	Marker <sup>1</sup>	Your Genotype <sup>2</sup>
CYP2C19	rs4244285	G/G
CYP2C19	rs4986893	G/G

See glossary at the back of the document for definitions of these terms

## Genetics of this response

Two loss-of-function variants in the CYP2C19 gene (\*2 and \*3), which codes for the cytochrome P450 2C19 enzyme, are the most important determinants of inter-individual variability in the response to clopidogrel.

First, the defective CYP2C19 \*2 allele results from a G-to-A mutation at nucleotide 681 in exon 5 that creates an aberrant splice site. This change alters the reading frame of the mRNA starting with amino acid 215 and produces a premature stop codon 20 amino acids further downstream, resulting in a truncated, nonfunctional protein ([PMID 8195181](#)). Second, the CYP2C19\*3 allele results from a G-to-A mutation at nucleotide 636 in exon 4 of the CYP2C19 gene that creates a premature termination codon (Trp212TER) and results in a truncated protein ([PMID 7969038](#)). The \*2 and \*3 alleles account for 85 percent of the reduced function alleles in Caucasians and 99 percent in Asians.

The cytochrome P450 2C19 enzyme, which is produced in the liver, is responsible for metabolizing a variety of structurally diverse drugs, including the anticonvulsant S-mephenytoin, omeprazole, proguanil, certain barbiturates, diazepam, propranolol, citalopram and imipramine. Upon ingestion, clopidogrel is absorbed in the intestine and transported to the liver where it is converted to its active form by the 2C19 enzyme. In individuals with the \*2 or \*3 alleles of CYP2C19, there is less active 2C19 enzyme and consequently, a diminished response to clopidogrel because less active drug is produced. Patients are classified into CYP2C19 metabolizer phenotypes according to their CYP2C19 enzyme function: "Poor" (no or low enzyme levels), "Intermediate" (reduced enzyme levels) and "Extensive" (normal enzyme levels). The frequency of each group varies with ethnic population, but poor and intermediate metabolizers are more frequently found in Asian and African-American populations. CYP2C19 poor or intermediate metabolizer status is associated with diminished response to clopidogrel. Individuals carrying one copy of the \*2 or \*3 allele fall into the intermediate metabolizer category, and those with two copies of the \*2 and/or \*3 allele are poor metabolizers ([PMID 11264478](#)). The evidence that CYP2C19 metabolizer status is associated with CYP2C19 alleles led the FDA in 2009 to update the label for Plavix to include pharmacogenetic data about the diminished response to Plavix and the increased risk of heart attack in patients with reduced CYP2C19 function due to genetic polymorphism. However, the FDA has not specified guided dosing nor does it explicitly require or recommend genetic testing prior to administration of the Plavix. The updated Plavix label states that the CYP2C19\*2 (rs4244285) and CYP2C19\*3 (rs4986893) alleles are associated with reduced metabolism of clopidogrel.

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## Methotrexate : Toxicity

### Your Results

People with your genotype are twice as likely to have Methotrexate-induced toxicity and adverse effects. Share your genetic information with your physician if you are currently taking or considering Methotrexate. Your physician may suggest other treatment options.

### About this medication

Methotrexate (MTX) is a low-cost anticancer drug (chemotherapeutic agent) used in the treatment of lymphoma, leukemia, uterus, breast, skin, ovary and other cancers. MTX is also used to treat very severe and disabling psoriasis or in haemopoietic stem cell transplantation to prevent graft-versus-host disease. Some people taking MTX may experience many and/or severe side effects, which are often referred to as MTX toxicity.

### We evaluated the following markers

Gene <sup>1</sup>	Marker <sup>1</sup>	Your Genotype <sup>2</sup>
MTHFR	rs1801133	C/T

See glossary at the back of the document for definitions of these terms

### Genetics of this response

Studies in patients with rheumatoid arthritis treated with MTX have suggested that genetic variation within genes involved in MTX transport, folic acid metabolism and nucleotide synthesis may influence the efficacy and toxicity of the drug ([PMID 19208607](#)). While many markers in these genes have shown association in small studies, the results have been difficult to replicate. However, the rs1801133 marker in the MTHFR gene was recently shown to have significant association with MTX toxicity in a meta-analysis of eight small studies in patients with rheumatoid arthritis ([PMID 19208607](#)). As large pharmacogenetic studies are completed, it is expected that more markers associated with MTX toxicity and efficacy will be identified.

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## Statins : Protection Against Myocardial Infarction

### Your Results

The effectiveness of pravastatin (Pravachol) for cardiovascular disease is typical for your genotype. Please follow your physician's instructions when statin therapy is indicated. Please also see your test result on susceptibility to statin-induced myopathy.

### About this medication

Statins (atorvastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, simvastatin) are a type of widely prescribed cholesterol-lowering medicines. They block the production of cholesterol in cells by inhibiting a certain enzyme that is critical in the synthesis of cholesterol.

### We evaluated the following markers

Gene <sup>1</sup>	Marker <sup>1</sup>	Your Genotype <sup>2</sup>
KIF6	rs20455	T/T

See glossary at the back of the document for definitions of these terms

### Genetics of this response

An association of the single nucleotide polymorphism (SNP) rs20455 with coronary heart disease (CHD) has been demonstrated by several studies involving Caucasian subjects ([PMID 17443022](#), [PMID 18222353](#), [PMID 18222354](#)). The SNP is located in the KIF6 gene, which encodes the kinesin-like protein 6, a member of a large family of kinesin motor proteins involved in the transport of other molecules and vesicles within cells. The rs20455 SNP translates to a variation at amino acid position 719 of the KIF6 protein, with the major allele (T) encoding a tryptophan and the minor allele (C) encoding an arginine (Trp719Arg). The 719Arg allele is associated with higher risks for CHD events including myocardial infarction, need for revascularization procedures, or cardiovascular death. Interestingly, in both a primary and a secondary prevention trial, carriers of the same allele benefited more from pravastatin treatment than non-carriers ([PMID 18222353](#)). As a result, although 719Arg confers more CHD risk, carriers and non-carriers of the allele have similar levels of CHD risk when on standard pravastatin therapy. This suggested that statin therapy is more effective in 719Arg carriers. Consistently, for 719Arg carriers (but not for non-carriers), intensive statin therapy (80 mg/day atorvastatin) was shown to bring benefits additional to standard pravastatin therapy (40mg/day) ([PMID 18222355](#)). It is currently not known if these findings extend to other statins.

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## Statins : Myopathy

### Your Results

Your genotype does not have a marker that is known to increase the risk of statin-induced myopathy (muscular pain and damage). About 5-10% of patients taking statins experience myopathy. While your risk is significantly lower than those who have the risk marker, many other factors involved in statin-induced myopathy are still unknown. Therefore, individuals with your genotype still have a risk, although a significantly reduced one, for myopathy when treated with statins.

### About this medication

Statins (atorvastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, simvastatin) are a type of widely prescribed cholesterol-lowering medicines. They block the production of cholesterol in cells by inhibiting a certain enzyme that is critical in the synthesis of cholesterol.

### We evaluated the following markers

Gene <sup>1</sup>	Marker <sup>1</sup>	Your Genotype <sup>2</sup>
SLCO1B1	rs4149056	T/T

See glossary at the back of the document for definitions of these terms

### Genetics of this response

The major adverse effect of statins is pain and damage in the skeletal muscles (myopathy). About 5-10% of patients taking statins experience muscle pain (myalgia) (PMID 19528564). A small portion of patients may develop more severe symptoms including muscle weakness, muscle cramps, myositis (inflammation of muscles, may be accompanied by increased creatine kinase levels in the blood), and the rare but potentially lethal rhabdomyolysis. In rare cases, myalgia and creatine kinase elevations persist after statin withdrawal (PMID 12672737). When rhabdomyolysis occurs, skeletal muscles rapidly break down, releasing large quantities of muscle cell contents into the blood. Some of those contents, such as myoglobin, cannot be properly processed by the kidneys and may lead to acute renal failure and death. In randomized, controlled trials, reported incidence of statin-induced myopathy ranges from 1.5% to 5.0%. The rate of statin-induced rhabdomyolysis is approximately 0.1 to 0.2 cases per 1000 person-years (PMID 19528564). The risk of myopathy varies with the type of statin and is dose-related. The incidence of myopathy while taking 80 mg simvastatin daily is more than 25 times the incidence of a daily dose of 20 mg. Drug-drug interactions can also increase the risk of myopathy when simvastatin, lovastatin or atorvastatin are administered in combination with medicines that share the same metabolic pathway as these statins. Erythromycin, cyclosporine, amiodarone, verapamil, protease inhibitors and fibrates are a few examples of medicines that can inhibit the metabolism of those statins, which may in turn accumulate in the blood to a harmful level. The mechanism of statin-induced myopathy may involve inefficient uptake of the drug by the liver, decreased cholesterol content in the plasma membrane of muscle cells, and reduced availability of coenzyme Q10, whose synthesis is also inhibited by statins. According to a recent report by the Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine (SEARCH) group published in the New England Journal of Medicine (PMID 18650507), about 60% of myopathy cases in a simvastatin (80 mg/day) clinic trial can be attributed to the C allele of the common variation rs4149056 in the SLCO1B1 gene. SLCO1B1 encodes the organic anion-transporting polypeptide 1B1 (OATP1B1, also known as OATP-C or OATP2), which had been shown to regulate the transport of statins and other drugs from the bloodstream into the liver cells. The rs4149056-C allele encodes an alanine, instead of a valine by the more common T allele, at amino acid position 174. This change reduces the activity of the OATP1B1 transporter, leading to increased blood simvastatin levels and the potential for increased toxicity to the muscles.

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## Tamoxifen : Metabolism

### Your Results

Your genetic profile shows you have one good copy and one non-functional copy of the CYP2D6 gene. This means tamoxifen is less effective for you because your body has a reduced ability to convert tamoxifen to its active form. If you are currently taking, or considering taking, tamoxifen, please share this information with your physician.

### About this medication

Tamoxifen (Nolvadex) is the most widely used drug for the treatment of breast cancer and works by blocking the action of estrogen which is necessary for the growth of estrogen-sensitive breast cancers. Since a cytochrome P450 enzyme called CYP2D6 converts tamoxifen to its active form, individuals with defective or reduced CYP2D6 protein function have a reduced response to standard tamoxifen therapy and an increased risk of breast cancer recurrence.

### We evaluated the following markers

Gene <sup>1</sup>	Marker <sup>1</sup>	Your Genotype <sup>2</sup>
CYP2D6	rs3892097	G/A

See glossary at the back of the document for definitions of these terms

### Genetics of this response

CYP2D6 is involved in the metabolism of approximately 30% of all medications, including tamoxifen. The CYP2D6 gene is highly polymorphic, with at least 46 major polymorphic alleles (<http://www.cypalleles.ki.se/cyp2d6.htm>) resulting in four phenotypes: poor, intermediate, extensive, and ultra-rapid metabolizers. Pharmacokinetic studies have demonstrated common CYP2D6 genetic variants that abolish (e.g., \*3, \*4, \*5) or decrease (\*10) CYP2D6 enzyme activity significantly decrease plasma endoxifen concentrations in Tamoxifen-treated women. It has been estimated that 3-10% of Caucasians are poor metabolizers due to inheritance of two defective CYP2D6 alleles, whereas 1 to 2% of Caucasians are ultrarapid metabolizers due to amplification (more than one copy) of the CYP2D6 gene. The CYP2D6\*4 allele is found at about 20% frequency in Caucasian populations and is most studied in relation to population variation in Tamoxifen therapy response. This allele results from a change of a G to A at the first nucleotide of exon 4 in the CYP2D6 gene. The change results in a shift of the splice site and introduction of a premature stop codon resulting in a mutant protein with no residual activity.

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## Warfarin : Sensitivity

### Your Results

Your genetic profile suggests you have a normal sensitivity to warfarin for the mutations that we tested. If you are currently taking, or considering taking, warfarin, please share these genetic results with your physician. Nevertheless, be aware that nongenetic factors such as food, medication, age, alcohol consumption and other medical conditions may also affect your sensitivity to warfarin.

### About this medication

Warfarin (Coumadin) is a drug that is widely prescribed for the treatment or prevention of blood clots in conditions such as arterial and venous thrombosis, pulmonary embolism and before surgical procedures such as heart valve replacement. Warfarin is a difficult drug to manage because the correct dosage is highly variable in the population.

Both genetic and nongenetic factors, such as food and other medications, can affect an individual's sensitivity to warfarin.

Determining the correct dosage is critical because too much warfarin can cause bleeding and hemorrhage and too little warfarin can lead to stroke or other complications. Pathway Genomics tests for common mutations in two different genes that make individuals more sensitive to warfarin.

Your genetic result	*1/*1; GG
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### We evaluated the following markers

Gene <sup>1</sup>	Marker <sup>1</sup>	Your Genotype <sup>2</sup>
CYP2C9	rs1057910	A/A
CYP2C9	rs1799853	C/C
VKORC1	rs9923231	G/G

See glossary at the back of the document for definitions of these terms

## Genetics of this response

Genetic differences can alter warfarin-dosing requirements, and since 2007 the FDA has encouraged the use of pre-therapy genetic testing to help determine the initial dose of warfarin. Research on warfarin sensitivity has focused on genes encoding two proteins: cytochrome P450 2C9 (CYP2C9 gene), and vitamin K epoxide reductase complex 1 (VKORC1 gene). Knowing the genotypes at these two genes may reduce the time required to achieve the effective dose of warfarin and may also lower the risk of bleeding complications ([PMID 17906972](#)).

### CYP2C9

The liver enzyme cytochrome P450 2C9 is involved in the metabolism and subsequent elimination of warfarin from the blood. Patients can be categorized as "normal", "intermediate" or "poor" metabolizers based on their enzyme activity and thus their ability to eliminate warfarin. The two most important variants of the CYP2C9 gene that effect warfarin sensitivity are CYP2C9\*2, which can reduce warfarin elimination by 30-50%, and CYP2C9\*3, which can reduce warfarin elimination by 80-90%. Decreased warfarin elimination means that higher doses of warfarin are in the blood, leading to an increased risk of bleeding complications ([PMID 15714076](#)). Studies have shown that people with two variant alleles in any combination of \*2 and \*3, needed less than half the dose of warfarin for effective treatment, as compared to people with one or no variant alleles ([PMID 15714076](#), [PMID 15947090](#)). Ethnicity can affect whether or not a person is likely to have a variant allele. Around 28% of Caucasians have one \*2 or one \*3 allele, and 21% have two alleles. Far fewer African Americans have one \*2 or \*3 allele, around 4% and 2.5% respectively, and having two variant alleles is very rare. Similarly, only around 7% of Asian people have one or more of these alleles (more often \*3); and in the few studies of Hispanic people almost all are \*1/\*1 ([PMID 19139476](#)).

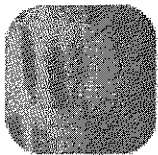
### VKORC1

Vitamin K is necessary for the production of active blood coagulation proteins, such as clotting factors II (prothrombin), VII, IX and X. Warfarin decreases blood coagulation by inhibiting vitamin K epoxide reductase, an enzyme that recycles oxidized vitamin K to its active form. The VKORC1 gene, codes for vitamin K epoxide reductase complex subunit 1 ([PMID 15930419](#)). The variant allele occurs when a G nucleotide (GG) is replaced by an A nucleotide (GA or AA) at position -1639. When this occurs there is a decreased amount of active vitamin K, thus decreased blood coagulation and a reduction in the necessary effective dose of warfarin. Studies show that those with variant AA alleles required only half, and in one study 4.5 times less, the dose of warfarin compared to people with non-variant GG alleles ([PMID 17510308](#), [PMID 1597090](#), [PMID 15888487](#)). VKORC1 allele frequency also varies by ethnicity. In one study the occurrence of AA, AG and GG alleles was 80%, 17% and 3% in Chinese subjects, but 14%, 47% and 39% for Caucasians ([PMID 15888487](#)). However, the lower dose requirements for individuals who have AA alleles was observed despite ethnic group ([PMID 15930419](#), [PMID 18252229](#), [PMID 15888487](#)).

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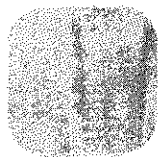
## Risk Levels

To assist you in understanding the implications of your genetic report and of your lifestyle choices, we have created five categories that summarize your risk and recommendations. For clarity, color-coded symbols representing your genetic and lifestyle risk are at the beginning of each health condition. Your genetic score is derived from a proprietary algorithm that correlates your genetic profile with published scientific research. Your lifestyle score is derived from your responses to our health survey as well as your reported personal factors of age, gender and ethnicity.



### Immediate Attention (Lifestyle Only)

Your health survey responses indicated that you have lifestyle or personal factors which put you at significant risk of developing this condition. There are many factors affecting your overall risk, but we encourage you to discuss these conditions with your doctor to determine what preventive actions you can take to reduce your risk.



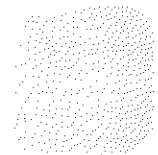
### Take Action

**Genetic:** You have genetic markers that are highly correlated with these conditions. **Lifestyle:** Your lifestyle choices and/or your age, gender and ethnicity have indicated factors that are associated with a significant increase in risk of developing these conditions and possible opportunities for improving your health. There are many factors affecting your overall risk, and we encourage you to discuss these conditions with your doctor to determine what preventive actions you can take.



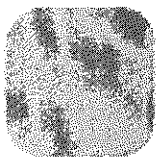
### Be Proactive

**Genetic:** Your genetic profile shows slightly increased susceptibility for these health conditions. **Lifestyle:** Your responses to the health survey and/or your age, gender and ethnicity showed some factors associated with increased risk of developing these conditions and possible opportunities for improving your health. It would be appropriate to discuss these conditions with your doctor to determine what preventive actions you can take.



### Learn More

**Genetic:** Your genetic profile did not indicate that you are at a significantly higher or lower risk for getting these conditions; most people fall into this category. **Lifestyle:** Your health survey did not raise any flags, but we still encourage you to learn more about these conditions and find out if there are any additional preventive actions that you can take.



### Live A Healthy Lifestyle

**Genetic:** Your genetics do not show a strong susceptibility for these conditions. **Lifestyle:** You are generally making smart choices that may lower your overall risk for these conditions. As with all health conditions, you should strive to continually make health lifestyle choices.

## Validated / Preliminary



Conditions that are reported as "Validated" meet our most stringent criteria for inclusion in your report, and use markers that have shown statistically significant results in published studies with a minimum of 1,000 cases and 1,000 controls. Additionally, the results of that study have been replicated in other studies showing similar results in the same ethnicity.



Conditions that are reported as "Preliminary" use markers that have shown statistically significant results in published studies with a minimum of 1,000 cases and 1,000 controls, but those results have not been replicated in other studies. We feel these results meet our minimum threshold for reporting to you, but would need further studies to demonstrate similar results before reporting them as "Validated".

Each condition is placed into one of four risk categories. Your placement in these categories is determined by our proprietary algorithm using knowledge of your genotype together with published research about the risk associated with individual genotypes for that condition. Where possible we have used research in individuals of your stated ethnicity. Where there is no research concerning your ethnic group, we have used the best available research (usually Caucasian). The four categories are intended to represent the appropriate level of reaction based upon your genotype for the markers we have tested.

Condition Name	Condition Risk	Population Risk *
Age-related macular degeneration Updated 17MAR2010	Learn More	12%
Amyotrophic lateral sclerosis	Learn More	0.3%
Asthma	Learn More	11.2%
Atrial fibrillation	Learn More	25%
Colorectal cancer	Learn More	5.2%
Coronary artery disease Updated 17MAR2010	Be Proactive	40%
Diabetes, type 1	Learn More	1.8%
Diabetes, type 2	Learn More	33.9%
Exfoliation glaucoma	Take Action	2.3%
Hypertension	Be Proactive	90%
Leukemia, chronic lymphocytic	Learn More	0.5%
Lung cancer Updated 17MAR2010	Learn More	7%
Melanoma	Learn More	1.9%
Multiple sclerosis	Learn More	0.2%
Myocardial infarction Updated 17MAR2010	Be Proactive	19%
Obesity	Learn More	29%
Osteoarthritis	Learn More	44.7%
Peripheral arterial disease Updated 17MAR2010	Learn More	Unknown
Prostate cancer	Learn More	15.9%
Psoriasis	Live A Healthy Lifestyle	4%
Rheumatoid arthritis	Live A Healthy Lifestyle	Unknown
Systemic lupus erythematosus	Live A Healthy Lifestyle	Unknown
Ulcerative colitis	Learn More	Unknown

\* Population risk is defined here as an estimate of the percentage of people in the general population who will develop the condition in their remaining lifetime. These estimates are taken from published research for individuals free of the condition in a specific population at a particular age and are not adjusted for individual results.

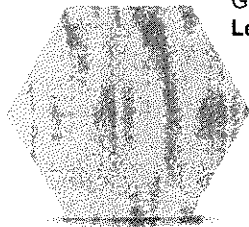
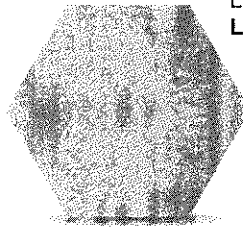
This report has been reviewed and approved for release to authorized persons by Linda Wasserman, MD, PhD.



## Age-related macular degeneration

Content Provided By: Pathway Genomics

Updated 17MAR2010 - See Appendix For Details


 Genetics:  
[Learn More](#)

 Lifestyle:  
[Learn More](#)

 Population Risk:  
**12/100**  
 Will get this disease  
 within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
ARMS2	rs10490924	G/T	2.69	T	20%	Validated	16174643
C2	rs547154	G/G	1.00	T	6%	Validated	16518403
C3	rs1047286	C/C	1.00	T	20%	Validated	19168221
CFH	rs1061147	C/C	1.00	A	37%	Validated	15870199

See glossary at the back of the document for definitions of these terms

## What Should I Do?

Your genetic profile gives you an average predisposition for this condition, and most people fall into this category. Because aging and cigarette smoking increase your chance of developing this disease independent of genetics ([PMID 19027484](#), [PMID 15234127](#)), quitting smoking and getting routine eye exams as you age will help reduce your chance of this disease.

## Genetics Overview

There is a strong hereditary component to AMD. In studies with twins, it was estimated that 46% to 71% of the variation in the overall severity of AMD is genetically determined. AMD is a complex disease that results from the cumulative effect of changes in many genes. In the last five years, variants in the two most important genes that increase the risk of developing AMD have been identified and characterized. These two genes are the complement factor H gene (CFH) on chromosome 1 and the HTRA1 gene on chromosome 10. The study of these genes will give scientists clues to the defects that lead to the development of AMD. Unlike AMD, early-onset macular dystrophies are usually caused by mutations in single genes. For example, Stargardt disease, which is the most common form of inherited juvenile macular degeneration, is caused by an autosomal recessive mutation in the ABCA4 gene.

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## What Is It?

Macular degeneration is a common cause of blindness and vision problems among older people. Macular degeneration is also called age-related macular degeneration, or AMD.

AMD damages the macula. The macula is a part of the eye that is responsible for seeing sharp details directly in the center of the field of vision. Damage caused by AMD can interfere with:

- The ability to see straight ahead. This is necessary for driving and viewing distances, such as when recognizing faces or watching television.
- Fine, detailed vision. This is necessary for reading newsprint, sewing, working with crafts and making repairs.

Most people with AMD have fluffy, yellow-white spots on the macula. These spots are called drusen. Not everyone who gets AMD has these spots.

There are two forms of AMD:

- **Dry AMD:** The vast majority of people who lose significant vision from AMD have dry AMD. In dry AMD, the cells of the macula slowly break down. This produces blurring then blank spots in the eye's central vision. The symptoms are subtle at first then become more noticeable over time.
- **Wet AMD:** In wet AMD, delicate new blood vessels begin to grow beneath the retina. They leak blood and fluid into the macula, causing scarring. Wet AMD can cause rapid loss of vision over days to weeks and continued loss of vision over time. Wet AMD is much less common than the dry form. But it generally progresses much more rapidly and is therefore more serious.

Age is the most important risk factor for AMD. Cigarette smoking and cardiovascular risk factors, such as high cholesterol levels, may also increase risk.

## Prevention

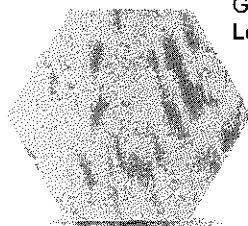
There is no proven way to prevent AMD.

However, evidence suggests that people with a history of smoking are more likely to develop AMD. If you don't smoke, don't start. If you do smoke, try to quit.

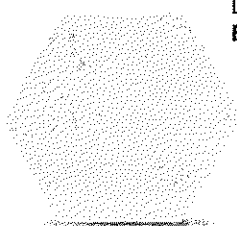
People who take cholesterol-lowering medications are less likely to develop AMD. So are people who eat a diet rich in leafy vegetables and nuts. Some evidence suggests that a diet rich in omega-3 fatty acids reduces the risk of macular degeneration.

## Amyotrophic lateral sclerosis

Content Provided By: Pathway Genomics



Genetics:  
Learn More



Lifestyle:  
Be Proactive



Population Risk:  
**0.3/100**  
Will get this disease  
within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
DPP6	rs10260404	C/T	1.20	C	44%	Preliminary	18084291

See glossary at the back of the document for definitions of these terms

### What Should I Do?

Your genetic profile indicates a typical chance of developing ALS, meaning your genetics do not give you a greater or lesser predisposition for developing this disease compared to the average person. Stay healthy with a smart diet and exercise program, and visit your doctor for routine checkups.

### Genetics Overview

Most cases of amyotrophic lateral sclerosis (ALS) do not have a family history (sporadic ALS or SALS). However, about 10% of ALS patients have another affected family member (familial ALS or FALS). The clinical features of SALS and FALS are very similar. At least seven genes connected to FALS have been identified. Less progress has been made in uncovering the main genetic causes of SALS. More than 38 candidate genes have been examined in at least 76 studies, but the results have been inconclusive or could not be replicated. Genome-wide association studies have identified three genes with possible association to SALS. Unfortunately, it has also been difficult to replicate these results. We do present one gene, DPP6, as a possible candidate gene connected to SALS because there was a second study showing association ([PMID 18057069](#)) even though there was an overlap of data with the first study ([PMID 18084291](#)).

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## What Is It?

Amyotrophic lateral sclerosis (ALS) causes a slow degeneration of nerve cells that control muscle movements. As a result, people with ALS gradually lose the ability to control their muscles. Fortunately, their capacity to think and remember things usually is not affected. ALS is also known as Lou Gehrig's disease, after the famous U.S. baseball player who developed the disease.

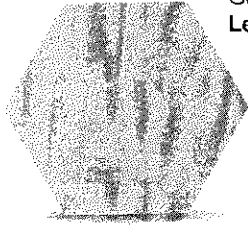
The cause of ALS remains unknown. Risk factors include advancing age and family history. ALS generally strikes patients between the ages of 50 and 70. It affects men slightly more often than women. Some cases appear to be inherited. Certain genes may increase the risk of developing the illness.

## Prevention

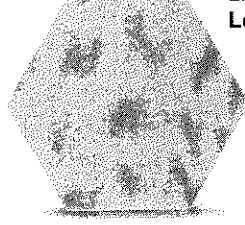
There is no way to prevent ALS.

# Asthma

Content Provided By: Pathway Genomics



Genetics:  
[Learn More](#)



Lifestyle:  
[Learn More](#)



Population Risk:  
**11.2/100**  
 Will get this disease  
 within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
ORMDL3	rs7216389	C/T	1.50	T	49%	Validated	18395550
IL1RL1	rs1420101	A/A	1.35	A	35%	Preliminary	19198610

See glossary at the back of the document for definitions of these terms

## What Should I Do?

Your genetic profile is typical of the general population for asthma. This does not mean you will or will not develop asthma. Since most asthma is caused by allergies ([PMID 19726699](#), [PMID 17889931](#), [PMID 10852847](#)), in addition to maintaining a healthy diet and exercise plan, reducing your exposure to certain allergens such as dust mites or mold can reduce your chances of asthma.

## Genetics Overview

Asthma is known to run in families, a fact best shown by studies in twins. A 1995 study showed that, if the first child had asthma, there was a 60 in 100 chance the twin would have asthma if they were identical compared to a 24 in 100 chance if the twins were fraternal ([PMID 7574852](#)). On the island of Tristan da Cunha in the South Atlantic Ocean, more than half of the inhabitants have some form of asthma. No environmental factors unique to the island have been identified to account for such a high prevalence of asthma. A convincing explanation lies in the fact that the whole population is descended from only a few dozen people (founders). In such a small gene pool, asthma-predisposing genetic factors carried by some of those founders have been passed on to many members of the subsequent generations ([PMID 8665053](#)).

There may also be common genetic links between asthma and related conditions such as allergies, hay fever and chronic-obstructive pulmonary disease (COPD). However, a universal genetic factor has not yet been found for these conditions.

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## What Is It?

Asthma is a chronic (long-term) lung condition that causes breathing difficulties and wheezing when air passages narrow and become inflamed. The condition ranges from mild to severe. Some people have only occasional, mild symptoms, while others have nearly constant symptoms with severe, life-threatening flare-ups.

During an asthma attack, the airways become inflamed and narrower as the muscles surrounding them constrict. The flow of air is blocked partially or completely as mucus produced by the inflammation fills a narrower passageway. Asthma affects both the lung's larger airways, called the bronchi, and the lung's smaller airways, called the bronchioles. Treatment focuses on preventing or stopping the inflammation, and relaxing the muscles that line the airways.

What causes asthma-related inflammation is not clear, but several environmental "triggers" have been identified. Many asthma triggers are allergens, substances that cause the immune system to overreact in some people. Common allergens include animal dander and saliva, pollens, molds, dust mites, cockroaches, some medications and certain foods. Also high on the list of asthma triggers are viral infections, such as colds and influenza; exercise; breathing cold, dry air; environmental pollutants, such as cigarette smoke, wood smoke, paint fumes and chemicals; strong odors; and emotional stress. For some people with severe asthma, no specific triggers can be identified.

Although asthma can develop early, often before age 5, its symptoms can begin at any age. The condition has a genetic (inherited) component and often affects people with a family history of allergies. The American Lung Association estimates that 25 million people in the United States will be diagnosed with asthma in their lifetime. One-third of Americans with asthma symptoms are children.

## Prevention

In some cases, asthma episodes can be prevented by avoiding or minimizing exposure to triggers. These include environmental triggers such as cigarette smoke, environmental pollutants (especially when pollution and ozone levels are high) and strong chemicals.

If exercise triggers your asthma, you can prevent an attack by breathing warm, humidified air before and during exercise or by using inhalers. Preventive medicine also can be used before an anticipated exposure to animals.

Eliminating allergens at home often can go a long way to control asthma symptoms. Some people may need to avoid animals entirely or to take special measures with their pets, such as keeping them out of bedrooms and bathing them regularly. If dust mites are a trigger, some household anti-mite measures include encasing mattresses in airtight enclosures, frequent household cleaning, washing bedding frequently in very hot water, and removing carpets and heavy draperies from sleeping areas.

Those who are affected by pollens might stay indoors whenever possible, use air conditioning and keep windows closed during high pollen season.

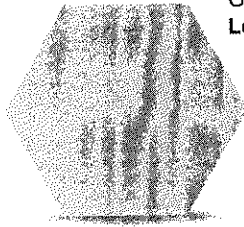
Monitoring your symptoms and peak-flow readings helps to identify a coming attack hours or even days before symptoms develop, which allows you to adjust your medications to prevent an attack.

Early signs or symptoms of an asthma flare-up include:

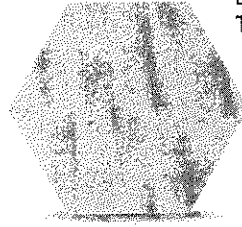
- Coughing more often
- Increased mucus or phlegm
- Becoming short of breath quickly with exertion or exercise
- Developing a sinus headache or fever
- Having symptoms that resemble a cold, such as a runny or congested nose, sneezing, or watery eyes

## Atrial fibrillation

Content Provided By: Pathway Genomics



Genetics:  
Learn More



Lifestyle:  
Take Action



Population Risk:  
25/100  
Will get this disease  
within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
PITX2	rs2200733	C/C	1.00	T	12%	Validated	17603472

See glossary at the back of the document for definitions of these terms

## What Should I Do?

Your genetic profile is typical of the general population for atrial fibrillation. This does not mean you will or will not develop atrial fibrillation. Learn more about this disease, and discuss your health history and lifestyle choices with your doctor.

## Genetics Overview

Recent studies have shown that atrial fibrillation (AF) has genetic causes ([PMID 16428254](#), [PMID 15199036](#), [PMID 16133178](#)). Ion channels in cell membranes control the voltage gradient within cells, and their activation and deactivation regulate the current that sets the heart rhythm. Mutations in ion channels have been associated with AF; these include potassium channels (KCNQ1, KCNE2, Kir2.1, Kv1.5, KCNH2) and sodium channels (eg. SCN5A) ([PMID 18929244](#)). However, these mutations only account for a small fraction of hereditary AF ([PMID 16887036](#), [PMID 18634977](#)). We test for 1 variant associated with increased risk of atrial fibrillation.

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## What Is It?

Atrial fibrillation is a type of cardiac arrhythmia, which is an abnormal heart rate or rhythm. Atrial fibrillation causes a rapid and irregular heartbeat, during which the upper two chambers of the heart that receive blood (the atria) quiver or "fibrillate" instead of beating normally.

During a normal heartbeat, the electrical impulses that cause the atria to contract come from a small area of the right atrium called the sinus node. During atrial fibrillation, however, these impulses come from all over the atria, triggering 300 to 500 contractions per minute in the heart's upper chambers. Normally, the atrioventricular node would receive these impulses and send them to the lower two chambers of the heart that do the pumping (the ventricles). During atrial fibrillation, however, the atrioventricular node becomes overwhelmed by all of the impulses it receives from the atria, and only lets a minority of the electrical impulses through to reach the ventricles. Still, there are so many impulses bombarding the atrioventricular node that the result is an irregular and rapid heartbeat, 80 to 160 beats per minute. A normal heartbeat is 60 to 100 beats per minute. The rapid and irregular heartbeat caused by atrial fibrillation cannot pump blood out of the heart efficiently. As a result, some people get short of breath and even faint when they first go into atrial fibrillation. A serious longer-term problem is that, because the walls of the atria are quivering instead of contracting, blood tends to pool along those walls, allowing formation of blood clots. These blood clots can travel from the heart into the bloodstream and circulate through the body. Ultimately, they may become lodged in an artery, causing pulmonary embolism, stroke and other disorders.

The major factors that increase the risk of atrial fibrillation are:

- Age
- Coronary artery disease
- Rheumatic heart disease (caused by rheumatic fever)
- High blood pressure (hypertension)
- Diabetes
- An excess of thyroid hormones (thyrotoxicosis)

In many people, the cause of atrial fibrillation is more serious than the arrhythmia itself.

## Prevention

Atrial fibrillation resulting from coronary artery disease can be prevented by taking these actions to modify your risk factors:

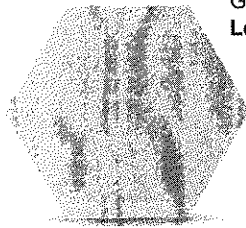
- Eat a low-fat diet.
- Control cholesterol and high blood pressure.
- Do not drink more than two alcoholic drinks per day.
- Quit smoking.
- Control your weight.
- Get regular exercise.

Some causes of atrial fibrillation cannot be prevented.

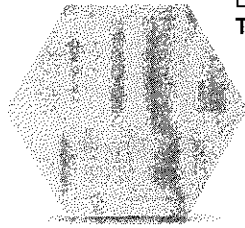


## Colorectal cancer

Content Provided By: Pathway Genomics



Genetics:  
Learn More



Lifestyle:  
Take Action



Population Risk:  
5.2/100  
Will get this disease  
within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
BMP4	rs4444235	C/T	1.13	T	56%	Validated	19011631
CDH1	rs9929218	G/G	1.00	A	28%	Validated	19011631
CRAC1	rs4779584	C/C	1.00	T	17%	Validated	18084292
EIF3H	rs16892766	A/A	1.00	C	11%	Validated	18372905
Intergenic_10p14	rs10795668	G/G	1.00	A	32%	Validated	18372905
Intergenic_20p12	rs961253	C/C	1.00	A	40%	Validated	19011631
Intergenic_8q24, region3	rs6983267	T/T	1.00	G	49%	Validated	17618284
LOC120376	rs3802842	A/A	1.00	C	23%	Validated	18753146
RHPN2	rs10411210	C/C	1.00	T	8%	Validated	19011631
SMAD7	rs4939827	T/T	1.44	T	47%	Validated	18372901

See glossary at the back of the document for definitions of these terms

### What Should I Do?

Your genetic profile is typical of the general population for colorectal cancer. It is recommended that you learn more about how your lifestyle choices can impact colorectal cancer. For example, a high level of physical activity may decrease your risk of colorectal cancer by as much as 50%.

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### Genetics Overview

From studies of twins, the genetic contribution to colorectal cancer has been estimated at 35% ([PMID 10891514](#)). Mutations in high penetrance genes have been shown to lead to hereditary colorectal cancer syndromes, such as familial adenomatous polyposis or Lynch syndrome (also called hereditary nonpolyposis colorectal cancer) ([PMID 16596323](#)). However, these high risk mutations only account for 5% of all colorectal cancers (see [www.cancer.gov](http://www.cancer.gov)). The remaining genetic risk is hypothesized to be due to multiple common low-risk susceptibility alleles, each contributing a small amount of risk. We test for 10 low risk susceptibility alleles for colorectal cancer.

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## What Is It?

Colorectal cancer is an uncontrolled growth of abnormal cells in the colon and/or rectum.

Together, the colon and rectum make up the large intestine. The large intestine carries waste from the small intestine and eliminates it through the anus.

Colorectal tumors often begin as small growths (polyps) on the inside of the large intestine. Polyps that are not removed eventually can become cancerous.

## Prevention

The best defense against colorectal cancer is regular screening. Screening tests are designed to find polyps so they can be removed before they become cancerous.

The American Cancer Society recommends that all adults begin screening at age 50. People at higher risk should begin screening earlier. You are at high risk if you:

- Have been diagnosed with polyps before age 50.
- Have inflammatory bowel disease, including ulcerative colitis and Crohn's disease.
- Have a genetic disorder that increases your likelihood of developing colorectal cancer.
- Have one or more first degree relatives (a parent or sibling) diagnosed with colon cancer before age 50.

Recommended screening methods include:

- **Digital rectal examination.** Your doctor inserts a gloved finger into your anus to check for abnormal lumps or masses. This should not be used as the only screening method.
- **Fecal occult blood test.** This test detects small amounts of blood in the stool. However, blood in the stool does not necessarily mean you have colon cancer.
- **Sigmoidoscopy.** The doctor uses a scope to examine the rectum and part of the colon.
- **Colonoscopy.** The doctor uses a scope to examine your entire colon and rectum.
- **Virtual colonoscopy.** Images of the colon are taken with computed tomography (CT) scans.

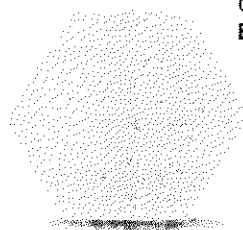
Daily exercise and a diet low in saturated fat may lower your risk of colorectal cancer.

Taking aspirin or folate every day may also reduce your risk. Talk to your doctor to see if this is appropriate for you.

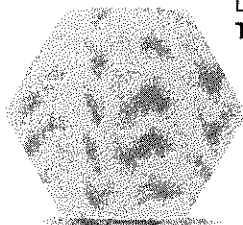
## Coronary artery disease

Content Provided By: Pathway Genomics

Updated 17MAR2010 - See Appendix For Details



Genetics:  
Be Proactive



Lifestyle:  
Take Action



Population Risk:  
**40/100**  
Will get this disease  
within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
HNF1A	rs2259816	C/C	1.00	A	38%	Validated	19198612
Intergenic_10q11	rs501120	C/T	1.11	T	83%	Validated	19164808
Intergenic_1q41	rs3008621	G/G	1.21	G	88%	Validated	19164808
Intergenic_9p21	rs1333049	C/C	1.67	C	46%	Validated	18362232
MRAS	rs9818870	C/C	1.00	T	17%	Validated	19198612
MTHFD1L	rs6922269	G/G	1.00	A	26%	Validated	17554300
CDH13	rs8055236	G/G	2.23	G	81%	Preliminary	17554300
Intergenic_2q36	rs2943634	A/C	1.22	C	65%	Preliminary	17634449
Intergenic_5q21	rs383830	A/T	1.60	A	79%	Preliminary	17554300
Intergenic_8p22	rs17411031	C/C	1.00	G	27%	Preliminary	17634449
SEZ6L	rs688034	C/C	1.00	T	33%	Preliminary	17554300
SMAD3	rs17228212	T/T	1.00	C	34%	Preliminary	17634449

See glossary at the back of the document for definitions of these terms

## What Should I Do?

Compared to the average person, your genetics indicate that you are somewhat more susceptible to coronary artery disease (CAD). It would be a good idea to discuss your genetics, personal health history and family history with your doctor to determine if a screening and prevention program is appropriate for you. Several lifestyle choices can reduce your chance of CAD. Maintaining a healthy body weight (BMI < 25), exercising routinely, quitting smoking, and watching your cholesterol can reduce your risk of CAD (PMID 17917527, PMID 16555862, PMID 19648392, PMID 16512042, PMID 19593318).

## Genetics Overview

Coronary artery disease (CAD; also called coronary heart disease), a major consequence of atherosclerosis, is a complex genetic disorder. It is estimated that the genetic risk of atherosclerosis involves variants in hundreds of genes. These genes have a variety of functions in regulating blood pressure, lipid and cholesterol metabolism, pro-inflammatory processes and cell adhesion and migration ([PMID 15485348](#)). These risk factors can act additively in causing the disease. In some patients, the cause of atherosclerosis can be attributed to single mutations in single genes. For example, the LDL receptor is mutated in familial hypercholesterolemia, which results in a decrease in LDL (bad cholesterol) uptake by the liver and elevated serum LDL levels. Within various populations, the heritability of atherosclerosis is generally high, often predicted to be greater than 50% ([PMID 15485348](#)). It is also known that African Americans are at higher risk than Caucasians, as are Mexican Americans, American Indians, native Hawaiians and some Asian Americans.

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## What Is It?

Coronary artery disease is the term commonly used to describe the buildup of fatty deposits and fibrous tissue (plaques) inside the arteries that supply blood to the heart (the coronary arteries). This buildup is called atherosclerosis. Coronary atherosclerosis eventually can cause the coronary arteries to become significantly narrower. This decreases the blood supply to parts of the heart muscle and triggers a type of chest pain called angina. Atherosclerosis also can cause a blood clot to form inside a narrowed coronary artery. This causes a heart attack, which can cause significant damage to the heart muscle. The factors that increase the risk of developing coronary artery disease are basically the same as those for atherosclerosis:

- A high blood cholesterol level
- A high level of LDL cholesterol, commonly called "bad cholesterol"
- A low level of HDL cholesterol, commonly called "good cholesterol"
- High blood pressure (hypertension)
- Diabetes
- A family history of coronary artery disease at a younger age
- Cigarette smoking
- Obesity
- Physical inactivity (too little regular exercise)

Coronary artery disease is the most common chronic, life-threatening illness in the United States. It affects 11 million Americans. Earlier in life, men have a greater risk of coronary artery disease than do women. However, after menopause, a woman's risk eventually equals that of a man.

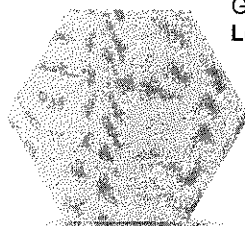
## Prevention

You can help to prevent coronary artery disease by controlling your risk factors for atherosclerosis. To do this:

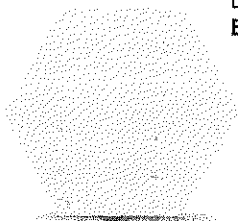
- Quit smoking.
- Eat a healthy diet.
- Reduce your high blood LDL cholesterol ("bad cholesterol").
- Reduce high blood pressure.
- Lose weight and exercise to prevent diabetes.

## Diabetes, type 1

Content Provided By: Pathway Genomics



Genetics:  
Learn More



Lifestyle:  
Be Proactive



Population Risk:  
1.8/100  
Will get this disease  
within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
CLEC16A	rs12708716	A/A	1.50	A	68%	Validated	17554260
CTLA4	rs3087243	A/G	1.18	G	54%	Validated	17554260
ERBB3	rs11171739	C/T	1.34	C	41%	Validated	17554300
HLA	rs2187668	A/G	3.64	A	8%	Validated	18252895
HLA	rs7454108	T/T	1.00	C	18%	Validated	18252895
IFIH1	rs1990760	C/T	1.18	T	62%	Validated	17554260
IL2RA	rs12251307	C/C	1.78	C	90%	Validated	18978792
INS	rs3741208	C/C	1.00	T	36%	Validated	17554260
Intergenic_4q27	rs2069763	G/G	1.00	T	33%	Validated	19073967
PTPN2	rs1893217	T/T	1.00	C	12%	Validated	17554260
PTPN22	rs2476601	G/G	1.00	A	12%	Validated	17554260
SH2B3	rs3184504	C/T	1.35	T	44%	Validated	19073967

See glossary at the back of the document for definitions of these terms

### What Should I Do?

You have a similar genetic predisposition for type 1 diabetes as the average person. Maintain health with routine exercise, a sensible low-fat diet, and visit the doctor regularly for checkups.

### Genetics Overview

It has been shown that type 1 diabetes (T1D) has both environmental (~20%) and heritable (~50-80%) components. The risk of T1D is higher in individuals with a family history of T1D, in particular among those who have parents (father 6% risk, mother 3% risk) or siblings (6-10% risk) with the disease. Identical twin studies have shown an overall risk of 50%. T1D is more common in those of Caucasian ancestry, where it has been the most studied, but it occurs in all ethnic groups.

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## What Is It?

Type 1 diabetes is a disease in which the body does not make enough insulin to control blood sugar levels. Type 1 diabetes was previously called insulin-dependent diabetes or juvenile diabetes.

Insulin is a hormone produced by the pancreas. It helps to regulate the body's blood sugar levels.

During digestion, food is broken down into basic components. The liver processes these nutrients into one type of sugar—glucose. Insulin helps move this sugar into the body's cells and tissues. The body later uses this stored sugar for energy.

Type 1 diabetes occurs when some or all of the pancreas's insulin-producing cells are destroyed. This leaves the patient with little or no insulin. Without insulin, sugar accumulates in the bloodstream rather than entering the cells. As a result, the body cannot use this glucose for energy.

When cells can't use glucose for energy, they have to use something else. As an alternative fuel, the liver produces acidic substances called ketones. These ketones build up in the blood. They make the blood abnormally acidic. This creates a severe, potentially life-threatening condition called ketoacidosis. Ketoacidosis can cause heart problems and affect the nervous system. Within hours, it may put a person at risk of coma or death.

Type 1 diabetes is an autoimmune disease. This means it begins when the body's immune system attacks cells in the body. In type 1 diabetes, the immune system destroys insulin-producing cells (beta cells) in the pancreas.

Why the immune system attacks the beta cells remains a mystery. Experts suspect that some people are genetically predisposed to the disease. And an environmental factor may act as a trigger. Viral infections and diet are two possible triggers.

Type 1 diabetes is not caused by the amount of sugar in a person's diet before the disease develops.

Type 1 diabetes is a chronic disease. It is diagnosed most commonly between ages 10 and 16. Type 1 diabetes equally affects males and females.

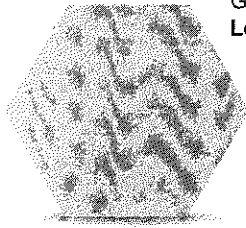
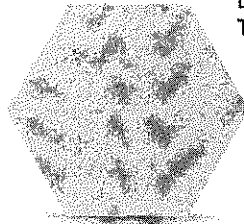
## Prevention

There is no proven way to prevent type 1 diabetes. Vitamin D deficiency, which is very common, may increase the risk of diabetes. However, correcting the deficiency has not been yet shown to prevent diabetes. Likewise, avoiding cow's milk during infancy may possibly prevent type 1 diabetes in genetically susceptible infants. But there is no definite proof that this prevents the disease.



## Diabetes, type 2

Content Provided By: Pathway Genomics


 Genetics:  
[Learn More](#)

 Lifestyle:  
[Take Action](#)

 Population Risk:  
**33.9/100**  
 Will get this disease  
 within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
CDKAL1	rs10946398	A/C	1.16	C	34%	Validated	17463249
CDKN2B	rs10811661	T/T	1.44	T	80%	Validated	17463246
FTO	rs8050136	A/C	1.27	A	46%	Validated	17463249
HHEX	rs1111875	A/A	1.00	G	57%	Validated	17463246
HNF1B	rs7501939	C/C	1.00	T	43%	Validated	17603484
IGF2BP2	rs1470579	A/A	1.00	C	30%	Validated	17463246
JAZF1	rs864745	C/T	1.10	T	49%	Validated	18372903
KCNJ11	rs5219	C/T	1.15	T	36%	Validated	17463246
KCNQ1	rs2237892	C/C	1.66	C	93%	Validated	18711367
MTNR1B	rs10830963	C/C	1.00	G	30%	Validated	19060907
NOTCH2	rs10923931	G/G	1.00	T	9%	Validated	18372903
PPARG	rs1801282	C/G	1.23	C	90%	Validated	17463249
SLC30A8	rs13266634	C/C	1.25	C	76%	Validated	17463249
TCF7L2	rs7903146	C/C	1.00	T	28%	Validated	17463246
WFS1	rs10010131	A/G	1.12	G	68%	Validated	18040659
ESR1	rs3020314	T/T	1.00	C	26%	Preliminary	18854778

See glossary at the back of the document for definitions of these terms

### What Should I Do?

Your genetic profile is typical of the general population for type 2 diabetes. Learn more about how your lifestyle choices affect your chance of type 2 diabetes. The two most important risk factors for T2D are obesity and lack of physical activity (PMID 19118286, PMID 19571786, PMID 17098085, PMID 18502303), so watch your weight and get plenty of exercise.

## Genetics Overview

Most of the variants found in or near type 2 diabetes (T2D) risk genes impact the development or function of pancreatic beta-cells, which produce, store and secrete the hormone insulin. Genetic factors associated with increased risk for obesity also contribute significantly to the development of T2D. It is estimated that up to 75% of T2D risk is caused by obesity. Hormones secreted by fat cells stimulate beta-cells to produce an excess amount of insulin. This abnormal demand by excess fat cells puts extra stress on beta-cells. Obesity also results in a state of insulin resistance whereby target organs for insulin action do not respond efficiently to take in glucose from the blood. Obesity is responsible for much of the increase in T2D that is seen world-wide.

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## What Is It?

Type 2 diabetes is a chronic disease. It is characterized by high levels of sugar in the blood. Type 2 diabetes is also called type 2 diabetes mellitus, adult-onset diabetes, non-insulin-dependent diabetes, or just diabetes.

Type 2 diabetes affects the way the body processes and uses carbohydrates, fats and proteins. During digestion, food is broken down into its basic components. The liver processes these nutrients into one type of sugar—glucose. Glucose is the most basic fuel for the body.

Glucose enters your body's cells with the help of insulin. Insulin is a hormone produced by the pancreas. Without insulin, glucose cannot pass through the cell wall.

Type 2 diabetes occurs when your body's cells do not react efficiently to insulin. This condition is called insulin resistance. In people with insulin resistance, the pancreas first makes extra insulin to maintain a normal blood sugar. Over time, the body's insulin resistance gets worse. The pancreas cannot keep up with the demand for more and more insulin. As a result, blood glucose levels rise.

Type 2 diabetes runs in families. It most often affects people who are older than 40. But type 2 diabetes is now being seen in more and more young people. Obesity greatly increases the risk of diabetes.

## Prevention

You can help to prevent type 2 diabetes by:

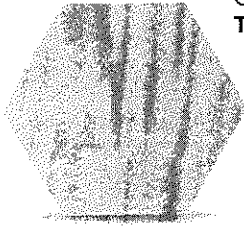
- Maintaining your ideal body weight. This is especially true if you have a family history of diabetes.
- Eating a healthy diet and getting regular exercise. These delay the onset of diabetes in people who are in the early stages of insulin resistance.
- Taking medication. The medication metformin (Glucophage) offers some additional protection for people with pre-diabetes. Pre-diabetes is defined as blood glucose levels between 100 and 125 mg/dL.

If you already have type 2 diabetes, you can still delay or prevent complications:

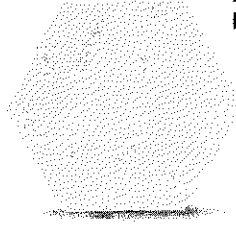
- Keep tight control of your blood sugar. This reduces the risk of most complications.
- Lower your risk of heart-related complications by:
  - Taking a daily aspirin.
  - Aggressively managing other risk factors for atherosclerosis, such as:
    - High blood pressure
    - High cholesterol and triglycerides
    - Cigarette smoking
    - Obesity
- Visit an eye doctor and a foot specialist every year to reduce eye and foot complications.

## Exfoliation glaucoma

Content Provided By: Pathway Genomics



Genetics:  
**Take Action**



Lifestyle:  
**Be Proactive**



Population Risk:  
**2.3/100**  
Will get this disease  
within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
LOXL1	rs2165241	T/T	13.10	T	44%	Preliminary	17690259

See glossary at the back of the document for definitions of these terms

### What Should I Do?

Your genetic profile suggests that you may be vulnerable to having glaucoma at some point in your life. Your results do not guarantee that you will develop glaucoma. The development of this disease is influenced by a complex interaction of genetics, lifestyle and other factors. Aside from genetics, advanced age, ethnicity, and nearsightedness (myopia) are all risk factors for glaucoma. African Americans, for example, are 6-8 times more likely than Caucasians to develop glaucoma ([PMID 2056646](#), [PMID 8002842](#), [PMID 12745004](#)). An elevated internal eye pressure (intraocular pressure, or IOP) poses greater risk for glaucoma. The good news is that there are both medical (drugs) and surgical treatments for glaucoma. ([PMID 19038621](#), [PMID 10519600](#), [PMID 8285897](#))

## Genetics Overview

Our knowledge about the genetic basis of glaucoma is still quite limited. Based on contemporary research, genetic causes underlying different forms of glaucoma are heterogeneous ([PMID 18936638](#)). In attempts to associate glaucoma with common genetic susceptibility factors, one particular type of glaucoma known as exfoliation glaucoma (XFG, alternatively known as pseudoexfoliation glaucoma) has stood out with compelling data. XFG mainly affects older people and accounts for about 12% cases of glaucoma. Clinically, XFG is considered a symptom of a systemic condition called exfoliation syndrome (XFS, also known as pseudoexfoliation syndrome). XFS is characterized by deposits of flaky material in the angle between the cornea and the iris. Similar deposits can be found in other tissues of XFS patients. In the eye, the deposited material can clog the drainage canal of the eye, leading to a rise of the inner eye pressure and, consequently, glaucoma. The risk of glaucoma is about 60% within 15 years of the initial diagnosis of XFS. Compared to other forms of glaucoma, XFG is considered a more severe form. It has been known for quite some time that relatives of XFS patients have increased risks for XFS ([PMID 9895242](#)), but no genetic susceptibility factors were identified until recently when genome-wide association studies were performed for this disorder.

The prevalence of XFS varies among different ethnic groups. It is especially prominent in Nordic countries, where more than 20% of people over age 65 are affected. In fact, common genetic variants associated with XFG were first identified in Icelandic and Swedish patients ([PMID 17690259](#)).

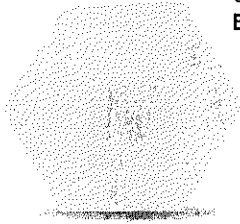
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## What is it?

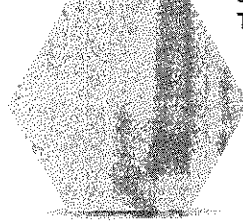
Glaucoma, a main cause of age-related blindness, is a disease of vision loss due to damage to the optic nerve. Glaucoma is often characterized by an elevation of fluid pressure inside the space between the cornea and the lens. However, in some patients, damage to the optic nerve can occur when the pressure is within the normal range. Based on clinical findings, there are two general types of glaucoma: open-angle glaucoma and angle-closure glaucoma. Exfoliation glaucoma (XFG, also known as pseudoexfoliation glaucoma) is a variant form of open-angle glaucoma. XFG is characterized by the accumulation of flaky materials in the anterior chamber, the front part of the eye defined by the inner surface of the cornea and the anterior surface of the iris. The scale-like exfoliative materials can clog the drainage system of the eye and cause the pressure in the chamber to rise. Deposits of exfoliative materials can also be found in many other parts of the body of an XFG patient. Therefore, XFG is considered secondary to a systemic condition called exfoliation syndrome (XFS). Not all XFS patients will suffer from glaucoma, but on average an XFS patient has six times the risk of developing glaucoma compared with the general population. XFG, like most other types of glaucoma, is a silent killer of sight because the onset of the disease is usually symptomless, but over time, if not treated, the vision loss can be profound and irreversible. People with XFS should have yearly eye examinations for early detection of glaucoma. Since XFG is distinct from other types of open-angle glaucoma in causes and prognosis, special considerations may be needed in choosing treatment options. The prevalence of XFG displays remarkable geographical variation. Particularly high incidences of XFG are seen in Nordic countries, where XFG accounts for more than half of open-angle glaucoma cases. In the United States, XFG has been reported to account for 12% of glaucoma cases ([PMID 7369310](#)). Age and genetics are the two main risk factors of XFG. The risks for XFS and XFG increase steadily with age. According to an Icelandic study, the risk of XFG increases by 10% every year in people 50 years and older ([PMID 12928689](#)). A role for genetics is suggested by strong geographical and familial clustering of XFG cases; indeed variation in the LOXL1 gene has been associated with risk of XFG ([PMID 17690259](#)). A variety of environmental factors have also been suspected, but a conclusive causal relationship is yet to be established.

## Hypertension

Content Provided By: Pathway Genomics



Genetics:  
Be Proactive



Lifestyle:  
Take Action



Population Risk:  
90/100  
Will get this disease  
within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
BCAT1	rs7961152	A/A	1.35	A	47%	Preliminary	17554300
PPARGC1A	rs8192678	A/G	0.70	A	35%	Preliminary	15738346

See glossary at the back of the document for definitions of these terms

## What Should I Do?

Your genetics indicate that you are somewhat more susceptible to hypertension compared to the average person. This does not mean you will develop hypertension, but you should be aware of your blood pressure and share these results with your physician. A low-fat, low-salt diet high in fruits and vegetables and regular exercise are the best preventive measures. (PMID 19583632, PMID 16434724, PMID 12570328) Limiting your consumption of alcohol will also help mitigate risk and, if you smoke, it is strongly recommended that you quit.

## Genetics Overview

Over 90% of hypertension cases are essential (primary) hypertension, meaning that no underlying medical cause for elevated blood pressure can be identified in the patient. Hypertension can also be secondary to existing medical problems, such as kidney disease. Some rare forms of hypertension are caused by mutations in single genes; these cases are usually familial and early-onset.

Our genetic tests focus on essential hypertension. Several genetic variations associated with essential hypertension have been successfully identified by studies of large populations. However, it is believed that many additional genetic factors, each contributing small effects to blood pressure variation, remain to be identified. The risk for hypertension also increases with obesity, excess salt intake, excess alcohol consumption, lack of physical activity, high levels of stress and advanced age.

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## What Is It?

Blood pressure has two components:

- **Systolic pressure**, the higher number, represents the pressure the heart generates to pump blood to the rest of the body.
- **Diastolic pressure**, the lower number, refers to the pressure in the blood vessels between heartbeats.

Usually, systolic pressure increases as we age. However, after age 60, diastolic pressure usually begins to decline because the body's blood vessels stiffen.

Blood pressure is measured in millimeters of mercury (mmHg). Normal blood pressure is defined as a systolic pressure of less than 120 and a diastolic pressure of less than 80. People with a systolic blood pressure between 120 and 139 or a diastolic blood pressure between 80 and 89 are said to have prehypertension. High blood pressure, or hypertension, is divided into two stages:

- Stage 1 hypertension — Systolic blood pressure between 140 and 159 and/or diastolic blood pressure between 90 and 99
- Stage 2 hypertension — Systolic blood pressure greater than 160 and/or diastolic blood pressure greater than 100.

High blood pressure can cause damage to many organs, including the brain, eyes, heart and kidneys, as well as to arteries throughout the body. If you have high blood pressure that has not been diagnosed, or that is not being treated adequately, you are at greater risk of having a heart attack, stroke, and kidney failure.

## Prevention

To prevent high blood pressure, you should:

- Get regular aerobic exercise
- Limit your intake of salt and alcoholic beverages
- Eat a diet rich in fruits and vegetables and low in saturated fats
- Avoid smoking
- Maintain a desirable body weight.

It is important to try to modify all the risk factors for coronary artery disease that are under your control. In addition to the above actions, you should:

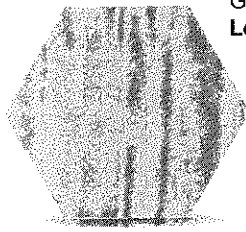
- Quit smoking
- Reduce your high LDL cholesterol (the "bad" cholesterol).

There is the real possibility that you can cure your high blood pressure just with lifestyle changes, and won't require blood pressure medicines.

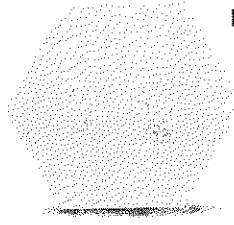


## Leukemia, chronic lymphocytic

Content Provided By: Pathway Genomics



Genetics:  
Learn More



Lifestyle:  
Be Proactive



Population Risk:  
**0.5/100**  
Will get this disease  
within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
Intergenic_11q24	rs735665	G/G	1.00	A	17%	Preliminary	18758461
IRF4	rs872071	A/G	1.54	G	51%	Preliminary	18758461
PRKD2	rs11083846	A/G	1.35	A	26%	Preliminary	18758461
SP140	rs13397985	T/T	1.00	G	20%	Preliminary	18758461

See glossary at the back of the document for definitions of these terms

## What Should I Do?

Your genetic profile is typical of the general population for chronic lymphocytic leukemia. This does not mean you will or will not develop chronic lymphocytic leukemia. Adopting a healthy diet and exercise plan, plus routine visits to your doctor, will help promote your well-being.

## Genetics Overview

Genetics may play a bigger role in the risk of chronic lymphocytic leukemia (CLL) compared to other types of leukemia. There is little evidence that environmental factors, such as chemical or radiation exposure, are associated with CLL ([PMID 19331210](#), [PMID 15269880](#)). While CLL incidence varies with geographical location, ethnic groups retain the risk associated with their country of origin rather than their new home ([PMID 15269880](#)). The importance of genetics in CLL is also illustrated by the increased risk (2-8 fold) associated with a family history ([PMID 19407315](#)). Even though there are many families with CLL, no high risk genes (such as BRCA1 for breast cancer) have been identified for CLL ([PMID 17687107](#)). Indeed, patients with a strong family history have similar symptoms and survival rates compared to patients with no family history. In addition, CLL often is preceded by monoclonal B-cell lymphocytosis, an asymptomatic condition which is fairly common, affecting 3% of adults in the general population ([PMID 18687638](#)). These data suggest that many common susceptibility alleles, each associated with a small amount of risk, account for the genetic risk of CLL. We test for 4 common low-risk alleles for CLL. More risk alleles are likely to be identified in future scientific investigations.

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## What is it?

Leukemia is a cancer that occurs in blood-forming tissue such as bone marrow and causes a buildup of cancerous cells in the bloodstream. Most leukemias can be grouped into 4 subtypes: chronic lymphocytic leukemia, chronic myeloid leukemia, acute lymphocytic leukemia, and acute myeloid leukemia. While acute leukemias can occur in adults and children, chronic leukemias occur primarily in adults.

Chronic lymphocytic leukemia (CLL) is the most common type of leukemia in Western countries, accounting for 30% of all leukemias ([PMID 18024649](#)). The National Cancer Institute ([www.seer.cancer.gov](http://www.seer.cancer.gov)) estimates that 1 in 212 men and women in the US will be diagnosed with CLL during their lifetime. CLL is characterized by an abnormally high number of mature-appearing white blood cells, called lymphocytes, in the blood, bone marrow and lymphoid tissues. The World Health Organization considers chronic lymphocytic leukemia identical to small lymphocytic lymphoma, a type of non-Hodgkin's lymphoma.

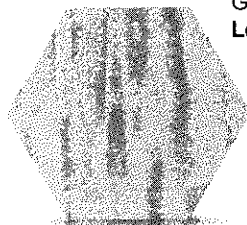
Risk factors for CLL include age, ethnicity, gender and family history. CLL is predominantly a disease of the elderly, with the median age of diagnosis in the US at 72 ([www.seer.cancer.gov](http://www.seer.cancer.gov)). The incidence of CLL is highest in Caucasians, followed closely by African-Americans, then Hispanics and Native Americans. Asians have the lowest risk of CLL. Roughly twice as many men as women are diagnosed with CLL. Finally, a family history of CLL is a risk factor for CLL ([PMID 18024649](#)). Unlike other cancers, there is no environmental factor that has been clearly associated with CLL. Compared to other leukemias, a role for genetics in CLL is well-established ([PMID 15269880](#)).

CLL is a progressive disease. In the early stages, there are often no symptoms and no treatment is necessary. In later stages, the disease is more aggressive and can spread to other parts of the body. Some patients who are diagnosed in the early stages may not need treatment for a long time, but others require treatment at the time of diagnosis. There is a large variation in survival among patients, ranging from several months to normal life expectancy. Treatment options include chemotherapy, allogeneic stem cell transplantation, and monoclonal antibody therapy.

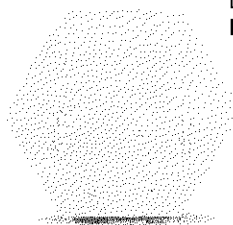
## Lung cancer

Content Provided By: Pathway Genomics

Updated 17MAR2010 - See Appendix For Details



Genetics:  
Learn More



Lifestyle:  
Be Proactive



Population Risk:  
7/100  
Will get this disease  
within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
BAT3	rs3117582	A/C	1.20	C	8%	Validated	18978787
CHRNA3	rs1051730	C/C	1.00	T	38%	Validated	18385676
TERT	rs2736100	A/C	1.07	C	53%	Validated	18978790

See glossary at the back of the document for definitions of these terms

### What Should I Do?

Your genetics indicates a typical predisposition for lung cancer. This does not mean you will or will not get lung cancer. The most potent lifestyle risk factor for lung cancer is tobacco smoke, so skip the cigarettes for optimal health (PMID: 17873159, PMID: 19107428).

### Genetics Overview

Lung cancer has long been described as a disease caused mostly by exposure to tobacco smoke (PMID 3826460). However, while 90% of lung cancers are in tobacco smokers, only 10-15% of smokers will develop lung cancer in their lifetime. In addition, never-smokers are estimated to account for 10-15% of all lung cancer deaths in the US (PMID 18788891). A role for genetics in lung cancer risk is suggested by studies of people with a family history of lung cancer. For both smokers and non-smokers, a family history of lung cancer has been shown to result in a 2-fold higher risk of being diagnosed with the disease (PMID 16160696). While this risk may reflect shared environmental as well as genetic influences, the risk of lung cancer was found to be higher for children, parents, and siblings compared to spouses, suggesting a genetic component. Lung cancer is also found in some rare, inherited cancer syndromes whereby tumors may develop in many other tissues (PMID 19005198, PMID 3568432, PMID 9438005, PMID 12802680). Finally, while no high-penetrance gene (like BRCA1 for breast cancer) has been identified for lung cancer, a study of 52 lung cancer families has identified a region on chromosome 6 which might contain such a gene (PMID 15272417, PMID 19351763).

We test for 4 genetic variants which modify the overall risk of lung cancer by a small amount, and so they may be referred to as low susceptibility alleles.

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## What Is It?

One of the most common cancers, lung cancer usually occurs when a cancer-causing agent, or carcinogen, triggers the growth of abnormal cells in the lung. These cells multiply out of control and eventually form a tumor. As the tumor grows, it destroys nearby areas of the lung. Eventually, tumor cells can spread (metastasize) to nearby lymph nodes and other parts of the body. These include the

- liver
- bones
- adrenal glands
- brain.

In most cases, the carcinogens that trigger lung cancer are chemicals found in cigarette smoke. However, more and more lung cancers are being diagnosed in people who have never smoked.

Lung cancers are divided into two groups, based on how their cells look under the microscope: non-small cell lung cancer and small cell lung cancer. Non-small cell lung cancer may be localized. This means that it is limited to the lung or that it hasn't spread beyond the chest. As a result, it can usually be treated with surgery. Small cell lung cancer is rarely localized, even when it is detected early. It is rarely treated with surgery. Knowing whether the cancer has spread is critical, because it affects treatment decisions.

However, even when doctors think that the cancer is localized, it often comes back shortly after surgery. This means cancer cells had started to spread before surgery, but they couldn't yet be detected.

**Non-small cell lung cancer** Non-small cell lung cancer is more likely than small cell cancer to be localized at the time of diagnosis. It also is more likely than small cell cancer to be treatable with surgery. It often responds poorly to chemotherapy (anticancer drugs). However, sophisticated genetic tests can help predict which patients may show favorable responses to particular treatments, including chemotherapy.

Non-small cell lung cancer accounts for about 85% of all lung cancers. These cancers are divided into subgroups, based on how their cells look under a microscope:

- **Adenocarcinoma.** This is the most common type of lung cancer. Although it is related to smoking, it is the most common type of lung cancer in nonsmokers. It is also the most common form of lung cancer in women and in people younger than 45. It usually develops near the edge of the lung. It can also involve the pleura, the membrane covering the lung.
- **Squamous cell carcinoma.** This type of lung cancer tends to form a mass near the center of the lungs. As the mass gets larger, it can bulge into one of the larger air passages, or bronchi. In some cases, the tumor forms a cavity in the lungs.
- **Large cell carcinoma.** Like adenocarcinoma, large cell carcinoma tends to develop at the edge of the lungs and spread to the pleura. Like squamous cell carcinoma, it can form a cavity in the lungs.
- **Adenosquamous carcinoma, undifferentiated carcinoma, and bronchioloalveolar carcinoma.** These are relatively rare non-small cell lung cancers.

**Small cell lung cancer** At the time of diagnosis, small cell lung cancer is more likely than non-small cell cancer to have spread beyond the lung. This makes it almost impossible to cure with surgery. However, it can be managed with chemotherapy or radiation therapy. Small cell cancers account for about 15% of all lung cancers.

## Risk factors

Your risk of all types of lung cancer increase if you

- **smoke.** Smoking cigarettes is by far the leading risk factor for lung cancer. In fact, cigarette smokers are 13 times more likely to develop lung cancer than nonsmokers. Cigar and pipe smoking are almost as likely to cause lung cancer as cigarette smoking.
- **breathe tobacco smoke.** Nonsmokers who inhale fumes from cigarette, cigar, and pipe smoking have an increased risk of lung cancer.

- **are exposed to radon gas.** Radon is a colorless, odorless radioactive gas formed in the ground. It seeps into the lower floors of homes and other buildings and can contaminate drinking water. Radon exposure is the second leading cause of lung cancer. It's not clear whether elevated radon levels contribute to lung cancer in nonsmokers. But radon exposure does contribute to lung cancer in smokers and in people who regularly breathe high amounts of the gas at work (miners, for example). You can test radon levels in your home with a radon testing kit.
- **are exposed to asbestos.** Asbestos is a mineral used in insulation, fireproofing materials, floor and ceiling tiles, automobile brake linings, and other products. People exposed to asbestos on the job (miners, construction workers, shipyard workers, and some auto mechanics) have a higher-than-normal risk of lung cancer. People who live or work in buildings with asbestos-containing materials that are deteriorating also have an increased risk of lung cancer. The risk is even higher in people who also smoke. Asbestos exposure also increases the risk of developing mesothelioma, a relatively rare and usually fatal cancer. It usually starts in the chest and resembles lung cancer.
- **are exposed to other cancer-causing agents at work.** These include uranium, arsenic, vinyl chloride, nickel chromates, coal products, mustard gas, chloromethyl ethers, gasoline, and diesel exhaust.

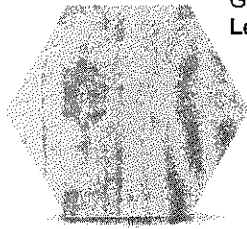
## Prevention

To reduce your risk of lung cancer,

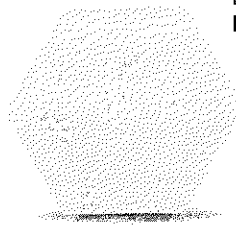
- **don't smoke.** If you already smoke, talk to your doctor about getting the help you need to quit.
- **avoid secondhand smoke.** Choose smoke-free restaurants and hotels. Ask guests to smoke outdoors, especially if there are children in your home.
- **reduce exposure to radon.** Have your home checked for radon gas. A radon level above 4 picocuries/liter is unsafe. If you have a private well, have your drinking water checked, too. Kits to test for radon are widely available.
- **reduce exposure to asbestos.** Because there is no safe level of asbestos exposure, any exposure is too much. If you have an older home, check to see if any insulation or other asbestos-containing material is exposed or deteriorating. The asbestos in these areas must be professionally removed or sealed up. If the removal isn't done properly, you may be exposed to more asbestos than you would have been if it had been left alone. People who work with asbestos-containing materials should use approved measures to limit their exposure and to prevent bringing asbestos dust home on their clothing.

## Melanoma

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Genetics:  
**Learn More**



Lifestyle:  
**Be Proactive**



Population Risk:  
**1.9/100**  
Will get this disease  
within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
MC1R	rs1805007	C/C	1.00	T	12%	Validated	18488027
TYR	rs1126809	G/G	1.00	A	22%	Validated	18488027
PIGU	rs910873	C/C	1.00	T	8%	Preliminary	18488026
TYRP1	rs1408799	C/T	1.15	C	69%	Preliminary	18488027

See glossary at the back of the document for definitions of these terms

## What Should I Do?

Your genetic profile is typical of the general population for melanoma. This does not mean you will or will not develop melanoma. Ultraviolet (UV) light exposure is the greatest environmental risk factor for melanoma (PMID: 15721476, PMID: 19254665). So be sun-smart: wear hats, sunscreen, and protective clothing when outside, and avoid sun exposure between 10 AM and 4PM.

## Genetics Overview

Genetic markers for melanoma fall into two categories – rare, high risk mutations and common, low risk susceptibility alleles (PMID 19095153, PMID 16297704). Rare mutations in high penetrance genes such as CDKN2A or CDK4 cause familial melanoma, a form of the disease that runs in families. However, known high risk mutations can explain only a small fraction of all melanoma cases. The genetic risk for most melanoma cases is hypothesized to be due to multiple common susceptibility alleles, each conferring a small amount of risk.

We test for 4 low risk susceptibility alleles for melanoma of the skin (also called cutaneous melanoma).

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## What is it?

Melanoma is cancer of the cells that give skin its color. It develops when these cells change and reproduce aggressively. The number of cases of melanoma, the deadliest form of skin cancer, is increasing faster than any other cancer.

Doctors aren't sure why melanoma rates are soaring. It could be from spending too much time in the sun during outdoor activities. It could also be due to global changes, such as the depletion of the ozone, which absorbs many of the sun's harmful rays.

Your pattern of sun exposure appears to affect your risk of developing melanoma more than the total amount of sun exposure in your lifetime. Short bursts of intense sun seem most dangerous, especially if you get sunburned. Being out in the sun can cause changes (mutations) in skin cells' genes. Researchers have recently found several gene mutations shared by many melanoma tumor cells. It is likely that one or more of these mutations starts the cancer.

The most common type of melanoma spreads on the skin's surface. It is called superficial spreading melanoma. It may stay on the surface or grow down into deeper tissues. Other types of melanoma can start anywhere on or inside the body.

Your risk of developing melanoma is higher if you have:

- Red or blond hair
- Green or blue eyes
- Fair skin
- Being in the sun a lot, especially as a child
- A mother, father, sister or brother with melanoma. If one of these relatives has melanoma, you are eight times more likely to develop it.

Features of freckles or moles that raise your risk of melanoma include:

- A new mole appearing after age 30
- A new mole at any age if it is in an area rarely exposed to the sun
- A change in an existing mole
- One or more atypical moles—moles that look like a fried egg or moles that are darker than others or have irregular borders or an irregular shape.
- 20 or more moles larger than 2 millimeters across
- or more moles larger than 5 millimeters across (larger than a pencil eraser)
- Freckles caused by being in the sun

## Prevention

To reduce your risk of melanoma, stay out of the sun. A bad sunburn is a major risk factor. Spending a lot of time in the sun as a child may pose the greatest risk. To be safe in the sun, take these steps:

- Apply plenty of sunscreen with a sun protection factor (SPF) of at least 15.
- Wear protective sunglasses, clothing (long sleeves and long pants) and wide-brimmed hats.
- Stay out of the sun when it is strongest (10 a.m. to 4 p.m.).
- Ask your doctor if any medications you take could make your skin more likely to be damaged by the sun.
- Avoid tanning salons. If you want to look tan, use sunless tanning creams. They are available in department and drug stores.

Melanoma is often easy to spot early, because it can be seen on your skin. If you are at risk of developing melanoma, ask your doctor to examine your skin. Also ask your doctor how often you should have your skin checked.

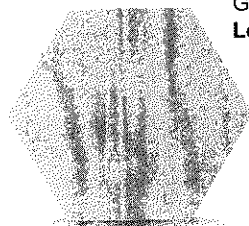
Your doctor will pay special attention to any atypical looking moles. Because some melanomas can arise from existing moles, your doctor may remove atypical moles. These moles may be more likely to become cancerous. Alternatively, your doctor may take pictures of your moles. He or she can compare the photos to your moles in the future to see if they have changed.

Examine your skin regularly, especially if you have risk factors for melanoma. Use a full-length and hand-held mirror. Have someone examine your scalp using a blow dryer to part your hair. That person can also examine your back and other areas that you can't easily see. Watch for new moles and changes in existing ones. Keep an eye on moles that you've had since birth; these moles may be more likely to turn into melanoma.

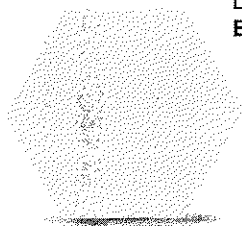


## Multiple sclerosis

Content Provided By: Pathway Genomics



Genetics:  
**Learn More**



Lifestyle:  
**Be Proactive**



Population Risk:  
**0.2/100**  
Will get this disease  
within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
HLA	rs3135388	C/T	1.99	T	19%	Validated	17660530
IL2RA	rs12722489	A/G	1.25	G	83%	Validated	17660530
IL7RA	rs6897932	T/T	1.00	C	76%	Validated	17660530
ANKRD15	rs10975200	A/A	1.00	G	16%	Preliminary	17660530
CBLB	rs12487066	C/T	1.09	T	68%	Preliminary	17660530
CD58	rs12044852	C/C	1.54	C	87%	Preliminary	17660530
EVI5	rs10735781	C/C	1.00	G	34%	Preliminary	17660530
FAM69A	rs11164838	T/T	1.00	C	57%	Preliminary	17660530
KIF1B	rs10492972	C/T	1.34	C	34%	Preliminary	18997785
KLRB1	rs4763655	A/G	1.10	A	33%	Preliminary	17660530
PDE4B	rs1321172	G/G	1.17	G	55%	Preliminary	17660530

See glossary at the back of the document for definitions of these terms

### What Should I Do?

Your genetics indicate you have a typical predisposition for multiple sclerosis, meaning you are similar to the average person. Adopting a healthy diet and exercise plan, plus routine visits to your doctor, will help promote your well-being.

## Genetics Overview

Multiple sclerosis (MS) often runs in families, suggesting a role of genetic factors. Genetic variations in the major histocompatibility complex (MHC) region of Chromosome 6 have long been known to play a role in susceptibility and we test some of these genetic markers in this region. Other genes are less well understood, but we examine both validated genetic markers as well as some newly identified genes representing the latest research on this condition. Intriguingly, MS is much more common in people of European descent, though this may be due to genetics or to shared environmental factors. Because the condition is rare in non-European populations, it has not been widely studied in people of African or Asian descent. As such, only data from studies using large cohorts of European descent are represented. Genetic risk factors found in Caucasians may well apply to people of other ethnicities, but this has not been proven. Also, only the most common relapsing-remitting form of MS has been well studied and all the information provided here relates to relapsing-remitting MS.

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## What Is It?

Multiple sclerosis (MS) is a disabling neurological illness. It affects the brain and spinal cord. The disease is usually progressive. This means it worsens over time.

An insulating sheath called myelin normally surrounds nerve cells. Myelin helps to transmit nerve impulses.

In MS, the myelin sheath becomes inflamed or damaged. This disrupts or slows nerve impulses. The inflammation leaves areas of scarring called sclerosis.

Multiple sclerosis may also damage nerve cells, not just their myelin lining.

The disruption of nerve signals causes a variety of symptoms. MS can affect a person's vision, ability to move parts of the body, and ability to feel sensations (such as pain and touch).

Symptoms usually come and go. Periods when symptoms suddenly get worse are called relapses. They alternate with periods when symptoms improve, called remissions.

Many people have a long history of MS attacks over several decades. In these cases, the disease may worsen in "steps," when the attacks occur. For others, the disease worsens steadily. In a minority of patients, MS causes relatively few problems.

Scientists believe MS is an autoimmune disease. This means the immune system mistakenly attacks its own body. In this case, the body attacks the myelin sheaths of the nerves.

In some cases, the trigger for an MS attack seems to be a viral infection. At other times, other physical or emotional stress may be to blame. The timing, duration and damage of MS attacks are unpredictable.

The symptoms of MS usually begin before age 40. But people between ages 40 and 60 sometimes are affected. Having a close relative with MS increases your chances of developing the disease.

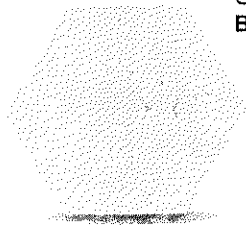
## Prevention

There is no way to prevent MS.

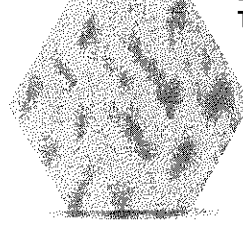
## Myocardial infarction

Content Provided By: Pathway Genomics

Updated 17MAR2010 - See Appendix For Details



Genetics:  
Be Proactive



Lifestyle:  
Take Action



Population Risk:  
19/100  
Will get this disease  
within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
CXCL12	rs1746048	C/T	1.17	C	85%	Validated	19198609
Intergenic_1p13	rs646776	C/T	1.19	T	75%	Validated	19198609
Intergenic_21q22	rs9982601	C/C	1.00	T	21%	Validated	19198609
Intergenic_9p21	rs10757278	G/G	1.64	G	50%	Validated	17478679
MIA3	rs17465637	C/C	1.30	C	27%	Validated	19198609
PCSK9	rs11206510	T/T	1.32	T	84%	Validated	19198609
PHACTR1	rs12526453	C/G	1.12	C	63%	Validated	19198609
SH2B3	rs3184504	C/T	1.13	T	44%	Validated	19198610
WDR12	rs6725887	C/C	1.37	C	16%	Validated	19198609
OR13G1	rs1151640	A/G	1.31	G	46%	Preliminary	16175505
PRR4	rs1376251	C/C	1.58	C	65%	Preliminary	16175505

See glossary at the back of the document for definitions of these terms

### What Should I Do?

Your genetics indicate that you are somewhat more susceptible to myocardial infarction (heart attack) compared to the average person. This does not mean you will have a myocardial infarction, but we encourage you to discuss your genetics and personal and family health histories with your physician to determine if a screening/prevention program is appropriate. Atherosclerosis is the main cause of heart attack. Reduce your risk of these conditions by eating a healthy diet with lots of fruits and vegetables ([PMID 12570328](#), [PMID 19720479](#)), watching your weight, and getting plenty of exercise.

---

## Genetics Overview

About 90% of myocardial infarction/heart attack cases are due to coronary atherosclerosis (see also coronary artery disease), which is a complex, multifactorial disease. Conventional risk factors include a history of cardiovascular disease (such as angina, stroke, coronary atherosclerosis), tobacco smoking, high cholesterol and triglyceride levels in the blood, diabetes, high blood pressure, obesity, excessive alcohol intake, chronic stress, lack of exercise, poor diet, and age. Genetic susceptibility factors also contribute to the risk of myocardial infarction and their importance is highlighted in about 15-20% of cases that lack any conventional risk factors ([PMID 12928466](#)). Recent studies suggest that many genetic variations associated with the disease are in genes involved in processes including endothelial function, inflammation, lipid metabolism, thrombosis and fibrinolysis ([PMID 18786860](#), [PMID 16770523](#)). Inflammation is now known to play a key role in the development of coronary atherosclerosis, which relies on the migration of immune cells and vascular smooth muscle cells on the artery wall to initiate atherosclerotic plaque formation ([PMID 12490960](#)). This is mediated by cellular attraction molecules such as cytokines, chemokines and their receptors. Subsequently, factors that aggravate progression of atherosclerotic lesions are released ([PMID 14751814](#)).

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## What Is It?

A heart attack occurs when one of the heart's coronary arteries is blocked suddenly, usually by a tiny blood clot (thrombus). The blood clot typically forms inside a coronary artery that already has been narrowed by atherosclerosis, a condition in which fatty deposits (plaques) build up along the inside walls of blood vessels. A heart attack also is called a myocardial infarction or coronary thrombosis.

Each coronary artery supplies blood to a specific part of the heart's muscular wall, so a blocked artery causes pain and malfunction in the area it supplies. Depending on the location and amount of heart muscle involved, this malfunction can seriously interfere with the heart's ability to pump blood. Also, some of the coronary arteries supply areas of the heart that regulate heartbeat, so a blockage sometimes causes potentially fatal abnormal heartbeats, called cardiac arrhythmias. The pattern of symptoms that develops with each heart attack and the chances of survival are linked to the location and extent of the coronary artery blockage.

In 25% of adults, the first sign of heart disease is sudden death from a heart attack. Heart attacks strike approximately 865,000 people in the United States each year, causing more than 179,000 deaths. Because most of these heart attacks result from atherosclerosis, the risk factors for heart attack and atherosclerosis are basically the same:

- An abnormally high level of blood cholesterol (hypercholesterolemia)
- An abnormally low level of HDL (high-density lipoprotein), commonly called "good cholesterol"
- High blood pressure (hypertension)
- Diabetes
- Family history of coronary artery disease at an early age
- Cigarette smoking
- Obesity
- Physical inactivity (too little regular exercise)

In early middle age, men have a greater risk of heart attack than women. However, a woman's risk increases once she begins menopause. This could be the result of a menopause-related decrease in levels of estrogen, a female sex hormone that may offer some protection against atherosclerosis.

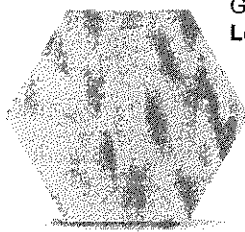
Although most heart attacks are caused by atherosclerosis, there are rarer cases in which heart attacks result from other medical conditions. These include congenital abnormalities of the coronary arteries, hypercoagulability (an abnormally increased tendency to form blood clots), a collagen vascular disease, such as rheumatoid arthritis or systemic lupus erythematosus (SLE, or lupus), cocaine abuse, a spasm of the coronary artery, or an embolus (small traveling blood clot), which floats into a coronary artery and lodges there.

## Prevention

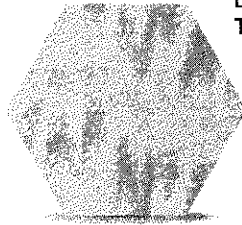
You can help to prevent a heart attack by controlling your risk factors for atherosclerosis, especially high blood cholesterol, high blood pressure, smoking and diabetes. If you have high cholesterol, follow your doctor's guidelines for a healthy diet low in fats and cholesterol, and, if necessary, take medication to decrease your blood cholesterol level. If you have high blood pressure, follow your doctor's recommendations for modifying your diet and taking your medication. If you smoke, quit. If you are diabetic, monitor your blood sugar level frequently, follow your diet, and take your insulin or oral medication as your doctor has prescribed. It is also wise to exercise regularly and to maintain an ideal weight.

## Obesity

Content Provided By: Pathway Genomics



Genetics:  
Learn More



Lifestyle:  
Take Action



Population Risk:  
29/100  
Will get this disease  
within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
FTO	rs9939609	A/T	1.31	A	46%	Validated	17434869
MC4R	rs17782313	T/T	1.00	C	26%	Validated	18454148
INSIG2	rs7566605	G/G	1.00	C	26%	Preliminary	17465681
PCSK1	rs6232	A/A	1.00	G	4%	Preliminary	18604207

See glossary at the back of the document for definitions of these terms

## What Should I Do?

You have a typical predisposition for obesity, according to your genetic profile. This does not mean you can not become obese, and it is important to prevent unhealthy weight gain by adopting a sensible diet and regular exercise plan.

## Genetics Overview

Family, twin and adoption studies suggest that approximately 40% to 70% of an individual's susceptibility to obesity is inherited. Some forms of obesity which show familial inheritance and a severe early onset in childhood are caused by a mutation in a single gene (monogenic obesity). About 7% of severe forms of obesity in children are monogenic in origin. The most common form of monogenic obesity is caused by mutations in the MC4R gene. Variations in multiple genes, each contributing a relatively small risk, are thought to be responsible for the common form of obesity. Small risk variants for obesity have been successfully identified by screening large numbers (20,000-50,000) of individuals in genome-wide association tests using gene chips containing 300,000 to 500,000 DNA markers. The first fruit of this approach was the identification of the FTO gene in four independent studies as a source of variants that increase the risk of common obesity. The importance of the MC4R gene, which was already implicated in monogenic obesity, was reconfirmed by the discovery of its association with common obesity.

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## What Is It?

Obesity is an excess of body fat.

It is difficult to directly measure body fat. Body mass index (BMI) is a popular method of defining a healthy weight. BMI should be used as a guide, along with waist size, to help estimate the amount of body fat.

BMI estimates a healthy weight based on your height. Because it considers height as well as weight, it is a more accurate guide than body weight alone.

To calculate your BMI:

- Multiply your weight in pounds by 703
- Divide that answer by your height in inches
- Divide that answer by your height in inches again

Then use the chart below to see what category your BMI falls into.

BMI	Category
Below 18.5	Underweight
18.5 – 24.9	Healthy
25.0 – 29.9	Overweight
30.0 – 39.9	Obese
Over 40	Morbidly obese

Obesity can shorten your life.

It can also put you at risk of developing a number of conditions. These include:

- High blood pressure
- Diabetes
- Heart disease
- Some forms of cancer

Many other health risks are higher for people who are obese. These risks may increase as the degree of obesity increases. Where you carry the extra weight is also important. People who carry extra weight around their waist may be more likely to experience health problems caused by obesity than those who carry it in their legs and thighs.

People become obese for a number of reasons. Often, several of these factors are involved.

Some of the most common reasons for obesity are:

- **Genetic influences:** Your genetic makeup plays a significant role in your chances of becoming obese. However, you still maintain most of the control when it comes to your weight. Some rare genetic diseases make it almost impossible to avoid obesity.
- **Physiological influences:** Some researchers believe that every person has a predetermined weight that the body resists moving away from. Also, people of the same age, sex and body size often have different metabolic rates. This means their bodies burn food differently. Someone with a low metabolic rate may require fewer calories to maintain approximately the same weight as someone whose metabolic rate is high.
- **Food intake and eating disorders:** If you eat a lot, especially foods that are high in fat and calories, you can become obese. Obesity also can result from eating disorders, such as a tendency to binge.
- **Lifestyle:** If you lead a sedentary lifestyle, you are at a higher risk of becoming obese.
  - **Your weight history:** If you were overweight as a child or adolescent, you are more likely to be obese as an adult.



- **Pregnancy:** Pregnancy can contribute to obesity. Many women weigh more after each pregnancy.
- **Drugs:** Some drugs can cause obesity. These include steroid hormones and many drugs used to treat psychiatric conditions.

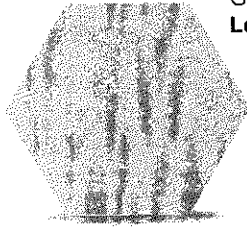
## Prevention

To prevent obesity and maintain a healthy body weight, eat a well-balanced diet and exercise regularly.

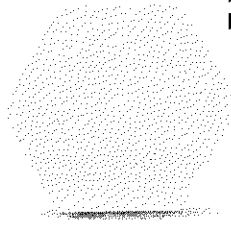
Preventing obesity is important. Once fat cells form, they remain in your body forever. Although you can reduce the size of fat cells, you cannot get rid of them.

## Osteoarthritis

Content Provided By: Pathway Genomics



Genetics:  
**Learn More**



Lifestyle:  
**Be Proactive**



Population Risk:  
**44.7/100**  
Will get this disease  
within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
GDF5	rs143383	C/T	1.13	T	67%	Preliminary	19479880
PTGS2	rs4140564	T/T	1.00	C	8%	Preliminary	18471798

See glossary at the back of the document for definitions of these terms

### What Should I Do?

Your genetic profile is typical of the general population for osteoarthritis. Learn more about this disease, and maintain a healthy lifestyle by adopting a sensible diet and exercise plan, plus routine checkups with your doctor.

### Genetics Overview

Genetics, age, estrogen use and bone density are all important systemic risk factors for osteoarthritis (OA). Obesity, joint injury, joint deformity, playing sports and muscle weakness affect the location and severity of OA. Family and twin studies suggest that approximately 40% to 80% of an individual's susceptibility to osteoarthritis is inherited. There are differences in the degree of heritability depending on the sex of the individual and on the location (i.e. hip or knee) of the affected joint. Some rare forms of early-onset OA are caused by mutations in single genes, but uncovering the genetic basis of the most common form of OA, which appears after age 45, has been more elusive. Researchers have identified more than 90 candidate genes, but follow-up studies have failed to convincingly confirm their association with OA. One problem is that the population size (<math>\geq 1000</math>) of most individual studies is too small to permit detection of mutations that have modest effects on disease risk. To get around this problem, fourteen teams of international OA researchers recently combined all their data (4000 individuals with OA and 6000 unaffected individuals) for the largest meta-analysis study to date of OA. They were able to find convincing evidence for the association of a variant in the GDF5 gene with OA of the knee (PMID 19479880).

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## What Is It?

Inside a joint, a tissue called cartilage cushions the joint and prevents the bones from rubbing against each other.

Osteoarthritis occurs when the cartilage of a joint erodes (breaks down). Bones begin to rub against each other, causing pain and difficulty moving the joint. Osteoarthritis also can affect nearby bones, which can become enlarged in places. These enlargements are called bone spurs or osteophytes.

Although the term arthritis means joint inflammation, there is relatively little inflammation in the joints of most people with osteoarthritis. For this reason, and because this type of arthritis seems to be caused by age-related degeneration of the joints, many experts and health care professionals prefer to call it degenerative joint disease.

Osteoarthritis can range from mild to severe. The pain associated with osteoarthritis can be significant and it usually is made worse by movement. Osteoarthritis can be limited to one joint or start in one joint usually the knee, hip, hand, foot or spine or it can involve a number of joints. If the hand is affected, usually many joints of the fingers become arthritic.

Osteoarthritis probably does not have a single cause, and, for most people, no cause can be identified. Age is a leading risk factor, because osteoarthritis usually occurs as people get older. However, research suggests that joints do not always deteriorate as people age. Other factors seem to contribute to osteoarthritis. Sports-related injuries or repeated small injuries caused by repeated movements on the job may increase the risk of developing osteoarthritis. Genetics also plays a role. Obesity seems to increase the risk of developing osteoarthritis of the knees.

Other factors that increase the risk of osteoarthritis include:

- Repeated episodes of bleeding into the joint, as may occur in hemophilia or other bleeding disorders
- Repeated episodes of gout or pseudogout, in which uric acid or calcium crystals in the joint cause episodes of inflammation
- Avascular necrosis, a condition in which the blood supply to the bone near the joint is interrupted, leading to bone death and eventually joint damage – The hip is affected most often.
- Chronic (long-lasting) inflammation caused by previous rheumatic illness, such as rheumatoid arthritis
- Osteoporosis, which can increase the risk of bone fractures, sometimes leading to osteoarthritis if the fracture is near a joint
- Metabolic disorders, such as hemochromatosis, in which a genetic abnormality leads to too much iron in the joints and other parts of the body
- Joint infection

One theory is that some people are born with defective cartilage or slight defects in the way joints fit, and as these people age, they are more likely to have cartilage in the joint break down.

Women are affected by osteoarthritis slightly more often than are men.

Osteoarthritis is one of the most common medical conditions, affecting an estimated 15.8 million people in the United States. In many people, it goes unrecognized. It is estimated that as many as half of all those who have osteoarthritis do not know that the pain and stiffness they are experiencing are symptoms of osteoarthritis.

## Prevention

There is no reliable way to prevent most cases of osteoarthritis. However, you may be able to control some factors that increase the risk of developing the disease. You can:

- Maintain an ideal body weight.
- Prevent osteoporosis by getting enough exercise and vitamin D and calcium, and possibly by taking additional prescription medication (such as alendronate/Fosamax or risedronate/Actonel).
- Prevent major accidents and injuries.

It may also help to prevent or treating any conditions that might contribute to joint damage, such as hemochromatosis, gout or infection.

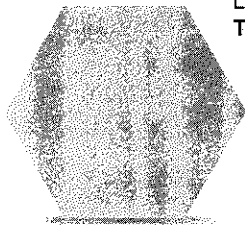
## Peripheral arterial disease

Content Provided By: Pathway Genomics

Updated 17MAR2010 - See Appendix For Details



Genetics:  
Learn More



Lifestyle:  
Take Action



Population Risk:  
**Unknown**  
Will get this disease  
within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
CHRNA3	rs1051730	C/C	1.00	T	38%	Validated	18385739

See glossary at the back of the document for definitions of these terms

### What Should I Do?

Your genetic predisposition for peripheral arterial disease is typical, meaning your genetics indicates a predisposition similar to the average person. Learn more about this disease, and promote your long-term health by incorporating a sensible diet and exercise plan plus routine visits to your doctor.

### Genetics Overview

Peripheral arterial disease (PAD), like coronary artery disease (CAD), is caused by atherosclerosis, a complex disorder involving both traditional and genetic risk factors. Traditional risk factors, such as age and smoking, play a large role in the development of the disease. The importance of genetics is suggested by the fact that PAD is more likely to affect those with a family history of cardiovascular diseases. Within various populations, genetics is often predicted to account for greater than 50% of the cause of atherosclerosis (PMID 15485348). It is estimated that hundreds of genes, both known and unknown, are involved and these factors can act additively. The involved genetic risk factors include those that alter blood pressure, lipid metabolism, pro-inflammatory processes, cell adhesion, and cell migration (PMID 15485348). Mutations known to cause Mendelian (monogenic) disorders can also act as genetic risk factors for atherosclerosis; for example, the LDL receptor is mutated in familial hypercholesterolemia, which results in decreased LDL uptake by the liver and elevated serum LDL levels.

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## What Is It?

In peripheral arterial disease (previously called peripheral vascular disease), not enough blood flows to the legs. The condition usually is caused by fatty deposits called plaques that build up along the walls of blood vessels. This buildup shrinks the size of the passageway and reduces the amount of blood that can flow through. This is a condition called atherosclerosis. The most common symptom is intermittent claudication, a cramping in the legs or buttocks when you exercise that goes away when you rest. The risk factors for getting peripheral arterial disease are similar to the risk factors for coronary heart disease, and include:

- Smoking cigarettes or using other forms of tobacco (such as snuff and chew)
- An abnormally high level of cholesterol (hypercholesterolemia)
- An abnormally low level of high-density lipoprotein (HDL, the good cholesterol)
- High blood pressure (hypertension)
- Diabetes
- Family history of cardiovascular disease
- Obesity
- Physical inactivity (too little regular exercise)
- Kidney disease
- Race (blacks appear to have a higher risk of developing the disease)

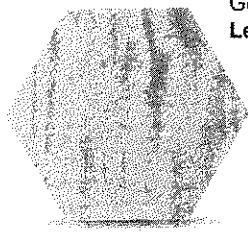
## Prevention

You can help to prevent peripheral arterial disease by modifying your risk factors:

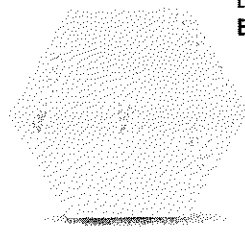
- **Don't smoke.** This a major risk factor that you can control.
- **Maintain a healthy weight.** Obesity, especially a concentration of body fat around the waist, has been linked to unhealthy blood levels of cholesterol and other fats, which can build up inside your arteries.
- **Eat a healthy diet.** Your diet should be loaded with vegetables and fruits, and it should be low in saturated fats.
- **Exercise regularly.** Ideally, you should exercise 45 minutes or more every day.
- **Lower your blood pressure.** Medications may be necessary if maintaining a healthy lifestyle is not enough.

## Prostate cancer

Content Provided By: Pathway Genomics



Genetics:  
[Learn More](#)



Lifestyle:  
[Be Proactive](#)



Population Risk:  
**15.9/100**  
 Will get this disease  
 within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds:Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
DAB21P	rs1571801	G/T	1.15	T	28%	Validated	19188186
EHBP1	rs721048	G/G	1.00	A	14%	Validated	18264098
HNF1B	rs7501939	C/C	1.42	C	56%	Validated	17603485
Intergenic_11q13	rs7931342	G/T	0.90	T	47%	Validated	18264097
Intergenic_17q24	rs1859962	G/T	1.17	G	47%	Validated	18199855
Intergenic_3p12	rs2660753	C/C	1.00	T	10%	Validated	19188186
Intergenic_8q24, region 1	rs1447295	A/C	1.43	A	7%	Validated	17401363
Intergenic_8q24, region 2	rs6983561	A/A	1.00	C	3%	Validated	18483343
Intergenic_8q24, region3	rs6983267	T/T	1.00	G	49%	Validated	18264096
JAZF1	rs10486567	C/C	1.25	C	75%	Validated	19188186
LMTK2	rs6465657	C/T	1.19	C	51%	Validated	18264097
MSMB	rs10993994	C/T	1.23	T	34%	Validated	19153072
NUDT11	rs5945572	A/A	1.51	A	38%	Validated	18264098
SLC22A3	rs9364554	C/T	1.20	T	27%	Validated	18708398
CLPTM1L	rs401681	C/T	1.07	C	56%	Preliminary	19151717
CTBP2	rs4962416	T/T	1.00	C	26%	Preliminary	18264096
TERT	rs2736098	G/G	1.00	A	37%	Preliminary	19151717
TNRC6B	rs9623117	C/T	1.11	C	22%	Preliminary	19117981

See glossary at the back of the document for definitions of these terms

## What Should I Do?

Compared to the average person, you have a typical predisposition towards developing prostate cancer. Learn how lifestyle factors might impact risk of prostate cancer, and see your doctor for routine physical exams.

## Genetics Overview

The identification of genetic markers for prostate cancer is the subject of ongoing research ([PMID 19104501](#)). Despite considerable effort, no high risk gene has yet been identified that is specific to prostate cancer ([PMID 19005198](#)). Many alleles, however, have been identified which confer small amounts of risk for or protection from prostate cancer; these may be referred to as low risk susceptibility alleles ([PMID 19104501](#)). We currently test 18 low risk susceptibility alleles to assess your genetic risk of developing prostate cancer. While most of the low-risk markers were identified from Caucasian populations, one study suggests that their presence in other ethnic populations is likely to predict similar risk or protection ([PMID 19318432](#)). On the other hand, some data suggest that there may be some markers that are specific for risk in African-Americans ([PMID 17978284](#)).

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## What Is It?

Prostate cancer results from the uncontrolled growth of abnormal cells in the prostate gland. This gland produces part of the fluid in semen. It is located below the bladder and in front of the rectum, near the base of the penis.

Prostate cancer is one of the most commonly diagnosed cancers in American men. Many other men have the disease, but have not been diagnosed. This is because prostate cancer has few symptoms early on.

Prostate cancer is common, but it is not always dangerous. This is because it usually grows very slowly. It affects older men; the average age at diagnosis is 70. And it's usually diagnosed before it causes any symptoms. Also, these men often have other illnesses which may be more important to treat than a cancer that doesn't cause symptoms.

When cells in the prostate become cancerous (malignant), they clump together, forming small "islands" of cancer in the prostate. In many cases, it takes years, even decades, for this localized cancer to spread beyond the prostate. And many of these cancers may never spread.

Researchers do not know the exact cause of prostate cancer. But they have identified several factors that raise a man's risk of the disease. These include:

- **Age.** Autopsy studies of men who died of other causes have found that about three-quarters or more of them have some degree of prostate cancer by age 80. These men didn't know they had prostate cancer.
- **Race.** African American men are more likely to get prostate cancer than other men—and to be diagnosed when the cancer is at a more advanced stage. They are also more than twice as likely to die of the disease as white men and about five times more likely to die of it than Asian Americans.
- **Family history.** If a man's father or brother has been diagnosed with prostate cancer, his cancer risk is two to three times higher than a man who doesn't have family members with the disease. Researchers have identified several genetic defects that may be more common in men who develop prostate cancer. But over all, most experts say that inherited defects cause a relatively small number of cancers.
- **Lifestyle.** Men who eat a lot of red meat or high-fat dairy products seem to have a higher risk of prostate cancer. There is little evidence that being overweight increases the risk of prostate cancer. However, obese men are more likely to die of the disease than men at a healthy weight.

## Prevention

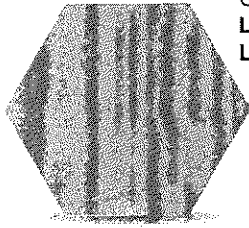
Although the evidence is mixed, men who eat a low-fat diet rich in fruits and vegetables may reduce their risk of prostate cancer. Older studies suggested that eating tomatoes, which contain the antioxidant lycopene, might reduce risk. Recent studies have questioned lycopene's value.

Some medications have been tested to see if they prevent prostate cancer. These include finasteride and dutasteride, drugs normally prescribed for benign prostate enlargement. One study showed that men who took finasteride reduced their prostate cancer risk by 25 percent. But it also found that the risk of aggressive cancer went up in some men. Later studies found that the drug doesn't increase aggressive tumors. Given the contradictory findings, experts don't agree about whether to offer finasteride to men with a higher risk of prostate cancer than normal.

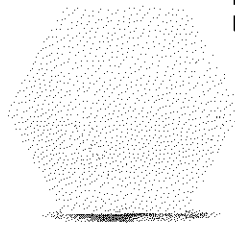


## Psoriasis

Content Provided By: Pathway Genomics



Genetics:  
**Live A Healthy Lifestyle**



Lifestyle:  
**Be Proactive**



Population Risk:  
**4/100**  
 Will get this disease  
 within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
HLA	rs10484554	C/C	1.00	T	13%	Validated	18369459
IL12B	rs3212227	A/C	1.62	A	81%	Validated	18219280
IL23R	rs11209026	G/G	1.96	G	96%	Validated	18219280
STAT2	rs2066808	A/A	1.80	A	93%	Validated	19169254
TNFAIP3	rs610604	T/T	1.00	G	43%	Validated	19169254
TNIP1	rs17728338	G/G	1.00	A	8%	Validated	19169254
Intergenic_1q21	rs4112788	C/C	1.99	C	60%	Preliminary	19169253
SPATA2	rs495337	C/T	1.25	C	56%	Preliminary	18364390

See glossary at the back of the document for definitions of these terms

## What Should I Do?

Your genetic profile does not show susceptibility for psoriasis. Adopting a healthy diet and exercise plan, plus routine visits to your doctor, will help promote your well-being.

## Genetics Overview

Psoriasis has long been known to have a heritable component, with the siblings of a psoriasis patient having a significantly greater likelihood of developing the condition than a random member of the population. For example, an Australian study on 4000 twins (PMID 8349859) found that if one twin had psoriasis, the chance of the second twin having the condition was 35% if they were identical (so sharing 100% of their DNA), but only 12% if they were fraternal twins (sharing half of their DNA). By comparison, the incidence of psoriasis was 2% in the general population, showing that genetics is a significant factor in psoriasis.

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## What Is It?

Psoriasis is a chronic skin disorder that causes scaling and inflammation.

Psoriasis may develop as a result of an abnormality in the body's immune system. The immune system normally fights infection and allergic reactions.

Psoriasis probably has a genetic component. Nearly half of patients have family members with psoriasis.

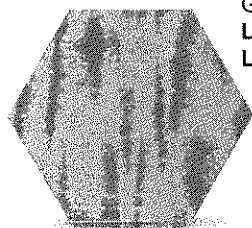
Certain medications may trigger psoriasis. Other medications seem to make psoriasis worse in people who have the disease.

## Prevention

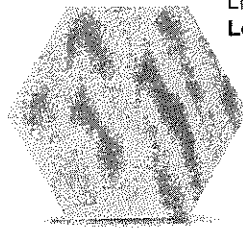
There is no way to prevent psoriasis.

## Rheumatoid arthritis

Content Provided By: Pathway Genomics



Genetics:  
**Live A Healthy Lifestyle**



Lifestyle:  
**Learn More**



Population Risk:  
**Unknown**  
Will get this disease within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
CD40	rs4810485	G/G	1.32	G	75%	Validated	18794853
CTLA4	rs3087243	A/G	1.11	G	54%	Validated	18794853
HLA	rs6457617	C/C	1.00	T	52%	Validated	17554300
Intergenic_4q27	rs6822844	G/T	1.28	G	85%	Validated	19404967
Intergenic_6q23	rs6920220	G/G	1.00	A	17%	Validated	18794853
MMEL1	rs3890745	T/T	1.26	T	67%	Validated	18794853
PTPN22	rs2476601	G/G	1.00	A	12%	Validated	17982455
STAT4	rs7574865	G/G	1.00	T	23%	Validated	19404967
TRAF1	rs3761847	A/G	1.32	G	48%	Validated	17804836
IL1B	rs16944	G/G	1.21	G	64%	Preliminary	18838388

See glossary at the back of the document for definitions of these terms

### What Should I Do?

You are not susceptible to rheumatoid arthritis, according to your genetic profile. Schedule routine checkups with your doctor, and maintain a sensible diet and exercise plan to enjoy optimal health.

## Genetics Overview

It is estimated that 2/3 of the risk for rheumatoid arthritis (RA) is genetic in origin. The risk in identical twins of RA patients is 12-15%, and in siblings of RA patients the risk is 2-4%. RA is two to three times more common in females and there is evidence for female hormone involvement. Immune system molecules responsible for "non-self" recognition called HLA Class II molecules are strongly associated with development of RA in all ethnic groups and account for 30-50% of the overall genetic risk in RA. Genetic factors associated with HLA Class II molecules define a common, distinct, and more severe form of RA that is characterized by the presence of anti-cyclic citrullinated peptide (anti-CCP) antibodies in the patient's body. These antibodies, produced by the patient's immune system, have an abnormal ability to mediate immune attacks against the patient's own normal proteins. Most importantly, anti-CCP antibodies are found in people sometimes years before the disease onset. Therefore, carriers of genetic risk alleles associated with the production of anti-CCP antibodies could benefit from anti-CCP antibody testing and monitoring for RA, enabling early intervention. The current goal of genetics is to determine an individual's genetic risk profile and tailor therapies accordingly. The future hope is that genetic understanding will allow vaccines to be developed and administered to genetically susceptible individuals to prevent RA.

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## What Is It?

Rheumatoid arthritis is a chronic (long-lasting) inflammatory disease that causes pain, stiffness, warmth, redness and swelling in joints. Over time, the affected joints may become misshapen, misaligned and damaged. Tissue lining the joint can become thick, and may wear away surrounding ligaments, cartilage and bone as it spreads. Rheumatoid arthritis usually occurs in a symmetrical pattern, meaning that if one knee or hand has it, the other usually does, too.

The cause of rheumatoid arthritis is unknown, although it appears to be an autoimmune disease. When the body's immune system does not operate as it should, white blood cells that normally attack bacteria or viruses attack healthy tissue instead — in this case, the synovium, or joint tissue. As the synovial membrane (the thin layer of cells lining the joint) becomes inflamed, enzymes are released. Over time, these enzymes and certain immune cells damage the cartilage, bone, tendons and ligaments near the joint.

Some research suggests that a virus triggers this faulty immune response. However, there is not yet convincing evidence that a single virus is the cause in all patients. At the same time, it appears that some people are more likely to get the disease because of their genetics.

Rheumatoid arthritis, the most disabling form of arthritis, generally affects more than one joint at a time. Commonly affected joints include those in the hands, wrists, feet, ankles, elbows, shoulders, hips, knees and neck. Rheumatoid arthritis can result in loose, deformed joints, loss of mobility and diminished strength. It also can cause painless lumps the size of a pea or acorn, called rheumatoid nodules. These develop under the skin, especially around the elbow or beneath the toes.

Generally, the pain of rheumatoid arthritis is described as a dull ache, similar to that of a headache or toothache. Pain is typically worse in the morning. It is not rare to have 30 minutes to an hour or more of morning stiffness. On days when the disease is more active, you may experience fatigue, loss of appetite, low-grade fever, sweats and difficulty sleeping.

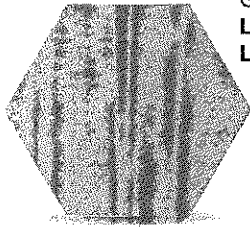
Because rheumatoid arthritis is a systemic disease (meaning it can affect the entire body), you also may have inflammation in other areas, including the heart, lungs or eyes. Symptoms vary between people and even in one person over time. People with mild forms of the disease are bothered by pain and stiffness, but they may not experience any joint damage. For other people, damage occurs early, requiring aggressive medical and surgical treatment. People with rheumatoid arthritis may notice worsening and improvement for no apparent reason. Although this disease most often afflicts people between the ages of 20 and 50, it may affect children and the elderly. Of the 2 million people with rheumatoid arthritis in the United States, at least 75 percent are women.

## Prevention

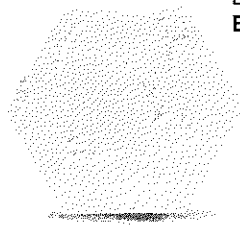
There is no way to prevent rheumatoid arthritis.

## Systemic lupus erythematosus

Content Provided By: Pathway Genomics



Genetics:  
**Live A Healthy Lifestyle**



Lifestyle:  
**Be Proactive**



Population Risk:  
**Unknown**  
 Will get this disease within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
BANK1	rs17266594	C/T	1.42	T	74%	Validated	18204447
BLK	rs13277113	G/G	1.00	A	23%	Validated	18204098
CTLA4	rs3087243	A/G	1.32	G	54%	Validated	15248219
FCGR2A	rs1801274	T/T	1.00	C	51%	Validated	12115187
HLA	rs2187668	A/G	1.76	A	8%	Validated	19493061
IRF5	rs2004640	G/T	1.40	T	51%	Validated	18288123
ITGAM	rs1143679	G/G	1.00	A	10%	Validated	18204448
MECP2	rs1734787	A/A	1.00	C	19%	Validated	19333917
PTPN22	rs2476601	G/G	1.00	A	12%	Validated	19493061
STAT4	rs7574865	G/G	1.00	T	23%	Validated	18516230
TNFAIP3	rs5029939	C/C	1.00	G	3%	Validated	19387456
TNFSF4	rs1234314	C/G	1.26	G	43%	Validated	19092840

See glossary at the back of the document for definitions of these terms

### What Should I Do?

You are not susceptible to developing systemic lupus erythematosus, according to your genetic profile. A healthy diet, routine exercise, and periodic checkups with your doctor will help you stay healthy.

---

## Genetics Overview

Systemic lupus erythematosus (SLE or lupus) has familial and sporadic forms. Genetics plays a role in the disease which shows shared inheritance of 35-50% in identical twins, and 2-5% in fraternal twins and siblings. Immune system molecules responsible for "non-self" recognition called HLA Class II molecules are strongly associated with the development of SLE, as are molecules involved in the complement system found in another region on chromosome 6. Environmental triggers are possibly due to bacterial or viral infections, exposure to sunlight, certain drugs or other toxins and workplace exposure to silica.

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## What Is It?

Lupus is thought to develop when your body's immune system mistakenly attack the body's own tissues rather than protecting them from outside invaders. Immune proteins called autoantibodies attack many different parts of the body, causing inflammation and tissue damage in many parts of the body, including the joints, skin, kidney, nervous system (brain, spinal cord and nerves), blood, heart, lungs, digestive system and eyes. Autoantibodies also can attach themselves to body chemicals, forming abnormal molecules called immune complexes that trigger additional inflammation and injury when they are deposited in various organs and tissues.

The exact cause of lupus remains a mystery, although scientists are investigating many different possibilities and believe several factors may play a role in the development of the disease. Since 90% of all lupus patients are women, usually of childbearing age, researchers think hormones may be involved. Lupus tends to run in families, so genetic factors may play a role. There is some evidence that the illness may be more common in people of African, Native American, West Indian and Chinese descent. Some researchers think lupus may be triggered by a virus or another type of infection in people who are genetically susceptible to the disease.

Lupus is relatively rare, affecting less than one in 2,000 people. The scientific name of the disease is systemic lupus erythematosus, or SLE.

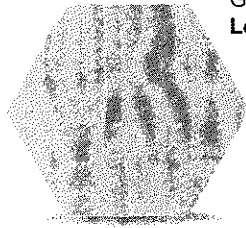
## Prevention

Since doctors haven't determined the cause of lupus, there's no way to prevent it. You may be able to prevent flare-ups of the illness by avoiding exposure to the sun as much as possible and using sunscreen when you are in the sun.

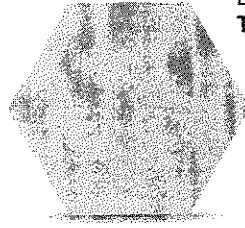


## Ulcerative colitis

Content Provided By: Pathway Genomics



Genetics:  
**Learn More**



Lifestyle:  
**Take Action**



Population Risk:  
**Unknown**  
Will get this disease  
within their lifetime

These results are based on your reported ethnicity of: Caucasian

## What We Tested and Your Results

Gene/Locus <sup>1</sup>	SNP <sup>1</sup>	Your Genotype <sup>2</sup>	Odds Ratio <sup>3</sup>	Associated Allele <sup>2</sup>	Population Frequency <sup>4</sup>	Validated Marker <sup>5</sup>	PMID <sup>6</sup>
BSN	rs9858542	G/G	1.00	A	26%	Validated	18438406
HLA	rs2395185	G/G	3.13	G	56%	Validated	19122664
IFNG	rs1558744	A/G	1.35	A	40%	Validated	19122664
IL10	rs3024505	C/C	1.00	T	18%	Validated	18836448
IL23R	rs11209026	G/G	3.28	G	96%	Validated	19122664
Intergenic_1p36	rs6426833	A/G	1.45	A	51%	Validated	19122664
MST1	rs3197999	C/C	1.00	T	26%	Validated	18438406
NKX2-3	rs10883365	A/A	1.00	G	46%	Validated	18438406
RNF186	rs3806308	A/G	1.37	G	60%	Validated	19122664

See glossary at the back of the document for definitions of these terms

## What Should I Do?

Your genetic profile is typical of the general population for ulcerative colitis. This means that your predisposition for this disease is similar to the average person. Schedule routine checkups with your doctor, and maintain a sensible diet and exercise plan to enjoy optimal health.

## Genetics Overview

Both genetics and environmental factors are known to contribute to the risk of developing ulcerative colitis (UC). A role for genetics is shown by the observation that people with a family history of UC have an increased risk of developing the disease. Up to 20% of UC cases occur in families, with a higher incidence in those of northern European and Jewish ancestry. Indeed, the Major Histocompatibility Complex (MHC) region on chromosome 6, which contains the gene encoding TNF-alpha is estimated to account for anywhere from 60-100% of the genetic risk for UC. There is hope going forward, for a personalized approach to therapy, as genetics is beginning to uncover more of the underlying mechanism involved in the UC inflammatory process.

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## What Is It?

A number of infections and other conditions can cause the rectum to become irritated and inflamed, but few of them cause lasting symptoms. Ulcerative colitis, however, is a lifelong condition that begins with rectal inflammation and can worsen to involve much or all of the large intestine. Ulcerative colitis most often begins to cause symptoms between the ages of 15 and 40.

Research suggests that ulcerative colitis is genetic (inherited). The illness may begin with a breakdown in the lining of the intestine. Normally, the lining of the intestines keeps bacteria that normally live in the colon carefully sealed within the digestive "pipeline." As long as the bacteria are perfectly contained, it remains invisible to your immune cells and does not provoke a reaction. When the intestine's lining fails, bacteria that usually are harmless can activate your immune system. Ulcerative colitis is an autoimmune disease, meaning that the immune system attacks part of the body. In ulcerative colitis, cells from the immune system collect in the bowel wall and cause inflammation, injuring the bowel. Once the bowel inflammation has started, it can continue, even if the immune system stops being exposed to the bowel bacteria. Ulcerative colitis affects the inner lining of the rectum and colon, causing it to wear away in spots (leaving ulcers), to bleed or to ooze cloudy mucus or pus. Sometimes, other parts of the body are affected by the inflammation, including the eyes, skin, liver, back and joints. One serious concern about ulcerative colitis is that it substantially increases the risk of colon cancer. The disease is not contagious, even within families, so contact with another person cannot spread the disease.

## Prevention

There is no way to prevent ulcerative colitis. However, some people are able to decrease the frequency of symptoms by avoiding certain foods, such as spicy foods or milk products. If you have ulcerative colitis, you can decrease the toll the condition takes on your body by eating a well-balanced, nutritious diet. By storing up vitamins and nutrients, even between episodes with symptoms, you can decrease complications from malnutrition, such as weight loss or a low blood count. It's important to know that ulcerative colitis increases your risk of colon cancer. People with extensive inflammation in the whole colon have the highest risk. When the entire colon is involved, the risk of cancer can be as much as 32 times normal. About 5 percent of people with ulcerative colitis will develop cancer in the colon. Because of the higher cancer risk, it is important to have your colon checked frequently for early signs of cancer. If you have had ulcerative colitis affecting the entire colon for eight years or more, or if you have had just the bottom half of the colon affected for 15 years, you should start being screened regularly for cancer. One good strategy is to have a colonoscopy every one to two years. Poor nutrition or the effect of colitis medicines can lead to osteoporosis, a disease that weakens bones and can cause bones to break. Osteoporosis can be prevented with specific medicines, as well as adequate exercise, calcium and vitamin D. If you have ulcerative colitis, you should discuss this issue with your doctor.

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## Glossary

1 - These are the gene and Single Nucleotide Polymorphism (SNP), also referred to as a marker, that were tested for this report. A SNP/Marker is a specific variation in an individual's DNA sequence.

2 - Your Genotype is the allele or base (A, T, G or C) composition found at the SNP/marker in your DNA and may contain the allele associated with the risk of the disease (Associated Allele). Two alleles (e.g. G/G) are shown because you inherit one copy from your mother and one copy from your father.

3 - The Odds Ratio is the statistical chance that a person who has the Associated Allele may have the disease compared to someone without the Associated Allele. An OR greater than 1 represents an increase in risk. An OR less than 1 represents a decrease in risk.

4 - Population Frequency is the percentage of people who have been found to have the Associated Allele in the Population Studied (Asian, Caucasian or African).

5 - Validated markers represent the highest quality genetic markers available, while Preliminary markers represent the latest in genetic research and have not met our high standards for validation.

6 - PubMed is a service managed by the National Library of Medicine that tracks more than 19 million citations for biomedical articles and scientific research. The Pubmed ID is used to identify each of those articles, and can be looked up at <http://www.ncbi.nlm.nih.gov/pubmed>

## Change History

Date	Action	Name	Description
17MAR2010	Updated	age-related macular degeneration	<b>Previous:</b> Your genetic risk score for Age-Related Macular Degeneration was reported as Live A Healthy Lifestyle. <b>Current:</b> We have updated the markers that are used to generate your report for Age-Related Macular Degeneration. Your new risk score for Age-Related Macular Degeneration is reported as Learn More.
17MAR2010	Updated	coronary artery disease	<b>Previous:</b> Your genetic risk score for Coronary Artery Disease was reported as Be Proactive. <b>Current:</b> We have updated the markers that are used to generate your report for this condition. Your risk score for Coronary Artery Disease did not change.
17MAR2010	Updated	lung cancer	<b>Previous:</b> Your genetic risk score for Lung Cancer was reported as Learn More. <b>Current:</b> We have updated the markers that are used to generate your report for this condition. Your risk score for Lung Cancer did not change.
17MAR2010	Updated	myocardial infarction	<b>Previous:</b> Your genetic risk score for Myocardial Infarction was reported as Be Proactive. <b>Current:</b> We have updated the markers that are used to generate your report for this condition. Your risk score for Myocardial Infarction did not change.
17MAR2010	Updated	peripheral arterial disease	<b>Previous:</b> Your genetic risk score for Peripheral Arterial Disease was reported as Learn More. <b>Current:</b> We have updated the markers that are used to generate your report for this condition. Your risk score for Peripheral Arterial Disease did not change.