23andMe

23andMe Genetic Health Overview

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What this overview includes

This overview includes brief summaries of your 23andMe results for:

- diseases for which you are at greater than average genetic risk,
- heritable diseases for which you carry one or more genetic variants (carrier status),
- and drugs to which you are likely to have an atypical response based on genetics.

These results are based on your genetic data and any sex and ancestry information you have provided along with population-level risk data for specified age ranges. They do not take into account non-genetic factors, family history, or additional genetic factors that may influence these conditions. Only results for genetic associations that are scientifically well established are included. This overview does not provide details regarding diseases for which you are at typical or lower than average genetic risk, heritable diseases for which you aren't known to carry a variant, or drugs to which you are likely to have a typical response. If you would like more information on any of your 23andMe results, please go to that topic's individual report page on our website at https://www.23andme.com/you/health/.

Overview of Genetic Health

Brian Davies
Year of Birth: 1976

Disease risk results are included in this overview only if your risk based on genetics is greater than 1%. Note that certain conditions may have genetic information applicable only to specific populations.

Components of this test were performed in a clinical laboratory regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) to perform high-complexity testing. The data provided are intended for informational and educational use and are not for diagnostic use.

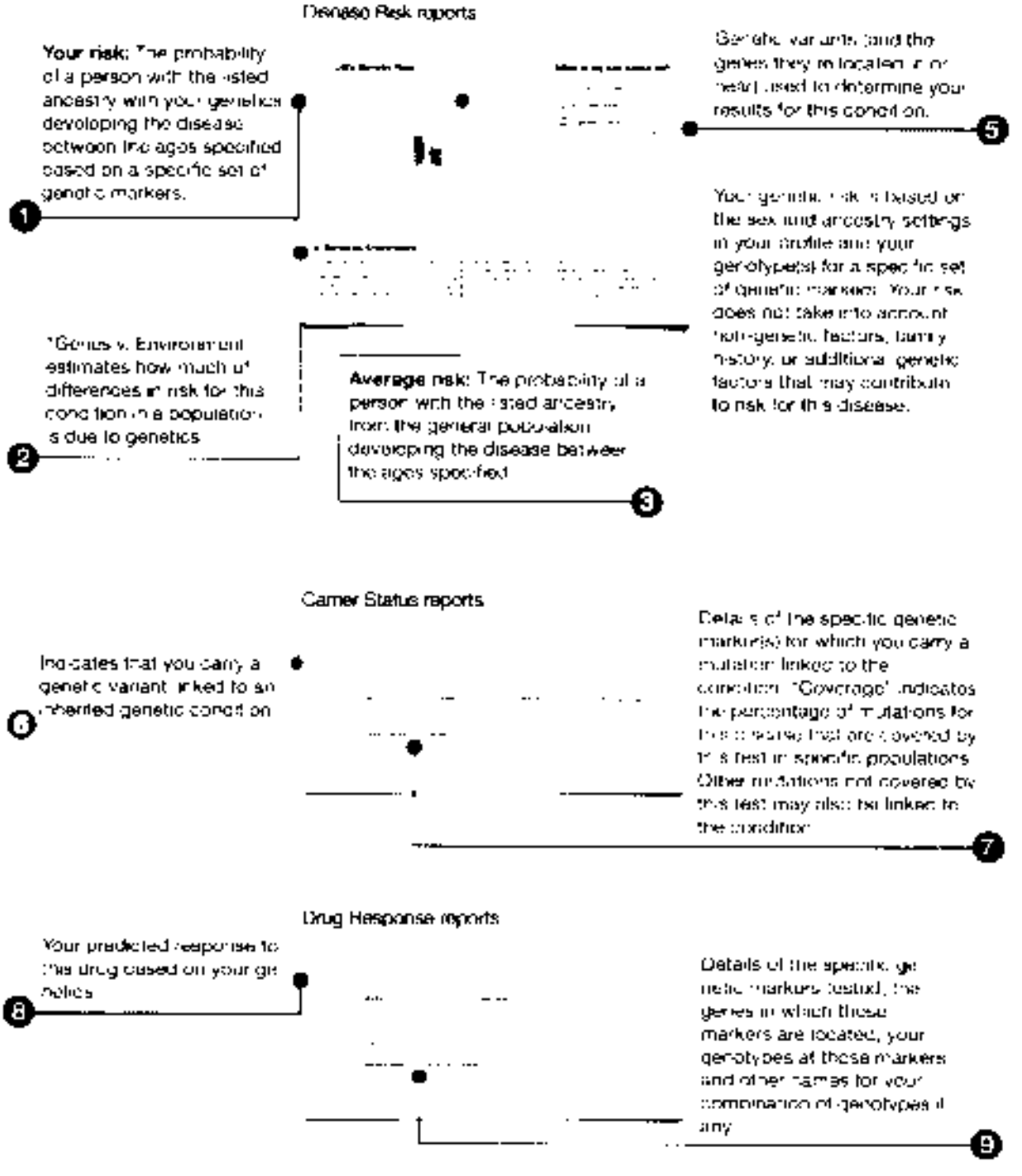
**All conditions tested are listed at the end of the report. You may not have data for every report*

Disease risk	Your risk	Average risk
Rheumatoid Arthritis	↑ 4.3%	2.4%
Chronic Kidney Disease	↑ 4.2%	3.4%
Exfoliation Glaucoma	↑ 2.2%	0.7%
27 conditions*	↓ Typical or decreased risk	

Carrier status	Status
Hemochromatosis (HFE-related)	Variant Present
48 heritable conditions*	Variant Absent

Drug response	Response
Thiopurine Methyltransferase Deficiency	Increased
Warfarin (Coumadin®) Sensitivity	Increased
7 other drugs*	Typical Response

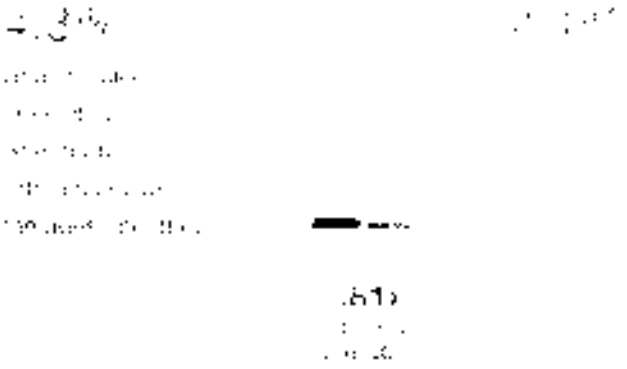
How to read your reports



Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a chronic autoimmune disease that affects the joints. Early symptoms of RA include swelling, pain, and stiffness. As the disease progresses, more debilitating symptoms can arise: in particular, joints lose their shape and ability to flex. RA affects about two million people in the United States. It can strike at any age, but onset is usually between the ages of 30 and 50. Like many autoimmune diseases, RA is more prevalent in women—two to three times more women than men have this disease. Medical research is focused on understanding how RA develops and finding new ways to treat it.

Brian's Genetic Risk



What is my risk based on?

- 18 - 79
- Men
- European ancestry
- 9 genetic markers

rs849617 (HLA region), rs11203366 (PADI4), rs2476601 (PTPN22), rs2280749 (MMEL1), rs2327832 (8q23 region), rs3761847 (TRAF1/C5), rs7574865 (STAT4), rs1569723 (CD40), rs13031237 (REL)

Genes vs. Environment

The heritability of rheumatoid arthritis is estimated to be 53-65%. This means that genetic factors contribute slightly more to differences in risk for this condition than environmental factors do. Genetic factors that play a role in rheumatoid arthritis include both unknown factors and known factors such as one's sex and the SNPs we describe here. Environmental factors that may increase your risk include smoking cigarettes and exposure to infections. Rheumatoid arthritis is extremely rare in Africans.

Additional Information

Screening and Risk Assessment

Talk to your health care provider early if you think you have rheumatoid arthritis. It is often possible to prevent further damage to the joints with proper early treatment.

Lifestyle Factors

Don't smoke: Research shows that smoking increases the risk of rheumatoid arthritis. The effect seems to be strongest in men.

View the full report online for links to resources, references, and more detailed genetic results and information.

Chronic Kidney Disease

Chronic kidney disease (CKD) develops when damage to the kidneys decreases their ability to perform their many jobs, leading to waste build-up in the body and chemical imbalances. CKD ranges in severity from nearly normal kidney function to complete kidney failure requiring dialysis or kidney transplantation for survival. CKD affects about 26 million adults in the United States and this number is increasing as rates of diabetes and hypertension—the two most common causes of CKD—continue to rise.

Brian's Genetic Risk

What is my risk based on?

20 - 79 Men

European ancestry

2 genetic markers
rs4293393 (UMOD), rs7805747 (PRKAG2)

Genes vs. Environment

Although the relative contributions of genetic and non-genetic risk factors for CKD have not been definitively established, there is a clear familial component as having a family member with CKD increases a person's risk of getting the disease. Markers of kidney function—which are used to diagnose CKD—are estimated to be 27-33% heritable, suggesting that environmental risk factors may play a larger role than genetics in determining a person's risk for declining kidney function. The most common causes of CKD are diabetes and high blood pressure, which are responsible for up to two-thirds of CKD cases. Environmental risk factors for CKD include smoking and exposure to certain medications or environmental toxins. However, diabetes and high blood pressure are responsible for up to two-thirds of CKD cases. Other risk factors for CKD include heart disease, high cholesterol, obesity, older age, male gender, and ethnicity.

Additional Information

Other Medical Conditions

Diabetes and hypertension are the most common causes of CKD. If you have diabetes or high blood pressure, your health care provider may work with you to manage these conditions and lower your risk of CKD.

Screening and Risk Assessment

The National Kidney Foundation recommends CKD screening if you have any of the following risk factors:

- Diabetes
- High blood pressure
- A family history of CKD
- Older age

Lifestyle Factors

- **Maintain a healthy weight:** Obesity is associated with increased risk for CKD.

- **Don't smoke:** Smoking increases the risk of getting CKD and the risk for progression once you have it.

Environmental Factors

Repeated exposure to certain toxins such as lead, some drugs such as non-steroidal anti-inflammatory pain medications, and certain classes of antibiotics can cause damage to the kidneys that can lead to CKD. If you are concerned about CKD, talk with your health care provider about your usage of these pain medications and antibiotics.

View the full report online for links to resources, references, and more detailed genetic results and information.

Exfoliation Glaucoma

Glaucoma is one of the most common causes of blindness in the United States and globally, accounting for about 12% of the world's cases. It is caused by a buildup of fluid pressure inside the eye, which eventually damages the optic nerve and causes sight to deteriorate. Exfoliation glaucoma (sometimes called pseudo-exfoliation glaucoma) is a subtype of the disease that often results from exfoliation syndrome, a disorder which causes an accumulation of flaky, white material inside the eye that blocks fluid drainage. Exfoliation syndrome affects about 10% of the population over 50, though some populations — especially Scandinavians — have much higher rates of the condition.

Brian's Genetic Risk

2.29%

2.90x

What is my risk based on?

- 40 - 79
- Men
- European ancestry
- 1 genetic markers
  rs2165241 (LOXL1)

Genes vs. Environment

The heritability of exfoliation glaucoma has not been studied. However, the heritability of open-angle glaucoma, a broad category of the disease that includes many cases of exfoliation glaucoma, has been estimated to be 13%. This means that environmental factors contribute more to differences in risk for this condition than genetic factors. Environmental factors that may increase the risk for glaucoma include diabetes, high blood pressure, heart disease, eye injury or disease and prolonged corticosteroid use.

Additional Information

Screening and Risk Assessment

See the Glaucoma Research Foundation recommendations for screening. Anyone at high risk for glaucoma should be tested every year or two after the age of 35.

Family History

Having an immediate family member with glaucoma increases your risk substantially. Use 23andMe's Family Health History tool to collect this important information.

View the full report online for links to resources, references, and more detailed genetic results and information.

Carrier status: Hemochromatosis (HFE-related)

Iron, an essential mineral, is absorbed via the intestines from food and is important for many bodily functions including red blood cell formation and proper brain function. The iron absorption process must be tightly regulated or else iron can accumulate in the body, possibly causing organ damage. Inherited forms of iron overload, known as hereditary hemochromatosis (HH), are caused by mutations in genes that normally play important roles in regulating iron levels. This report includes three mutations in the HFE gene that are typically found in people with European ancestry and are responsible for most cases of HH. HFE-related HH is inherited in a recessive manner, meaning that a person must receive a mutated copy of the HFE gene from each parent to have the condition. In Europeans, roughly one in 300 individuals has HFE-related HH and at least one in 10 carries a mutation for the condition. Rates are even higher in certain European populations including Irish, Norwegian and Australian. HFE-related HH is much rarer in Asian and African populations.

Brian's Genetic Results

Variant Present

[illegible] mutations is not typically prone to higher levels of iron in the body, but can pass the mutation [illegible]. May have other mutations in the HFE gene not reported here.

Gene	Variant	DNA change	Brian's genotype
HFE	C282Y	G to A	AG

Markers tested: 3 **Coverage:** Up to 90%

What does this test cover?

There are several forms of hereditary hemochromatosis (HH). The most common form is caused by mutations in the HFE gene, of which more than 20 have been documented. 23andMe reports data for the three HFE mutations most commonly linked to hereditary hemochromatosis: the severe C282Y mutation and the milder H63D and S65C mutations.

How is Hemochromatosis (HFE-related) inherited?

HFE-related hemochromatosis is inherited in a recessive manner, meaning that only a child who receives two mutated copies of the HFE gene (one from each parent) is at risk of developing the disease.

How common is this condition?

HFE-related hereditary hemochromatosis is fairly common. Roughly 10-30% of people with European ancestry carry one of the three HFE mutations reported here. About one in 300 individuals has two HFE mutations and is at risk for iron overload; however, only a small fraction of individuals with two mutations go on to develop symptoms.

Additional Information

Other Risk Factors

Men with two mutated copies of the HFE gene are more likely to develop symptoms than pre-menopausal women due to the fact that women eliminate iron through menstruation, pregnancy, and childbirth.

Advancing age also raises the likelihood of developing symptoms in those with two mutations. Experts recommend avoiding iron supplements and advise against taking vitamin C supplements or consuming

vitamin C-rich juices with meals, as vitamin C aids in the absorption of iron. Alcohol can worsen liver damage in people with hemochromatosis.

Other Medical Conditions

Hemochromatosis can lead to liver disease, arthritis, heart problems, and diabetes. Alcohol can worsen liver damage in people with hemochromatosis.

Medications and Treatment

Hemochromatosis is treatable and health complications can be avoided if caught early and managed properly through lifestyle modifications. Blood removal on a regular basis (just like donating blood) is the standard treatment. If you are concerned about hereditary hemochromatosis, please consult your health care provider or a genetic counselor.

View the full report online for links to resources, references, and more detailed genetic results and information.

Drug response: Thiopurine Methyltransferase Deficiency

Thiopurines are a family of drugs used to treat acute lymphoblastic leukemia, inflammatory bowel disease and autoimmune diseases, and to prevent the rejection of transplanted organs. Thiopurine methyltransferase (TPMT) is one of the enzymes that converts these drugs into less toxic compounds. Deficiency of TPMT causes drug hypersensitivity with toxic effects on the bone marrow such as low blood count and bleeding. Although many factors can affect TPMT enzyme activity, several mutations in the TPMT gene result in low or no activity and increase a person's risk of thiopurine toxicity. About one in ten people with European ancestry has reduced TPMT enzyme activity due to having inherited one mutated copy of TPMT and one out of 300 has no TPMT enzyme activity at all due to having inherited two mutant copies.

Brian's Genetic Results

[redacted] has one *3B mutation and one *3C mutation. A person with these mutations typically has [redacted] TPMT function and [redacted] risk of toxic reaction when treated with thiopurine drugs.

See the technical report for more details. May have other mutations in the TPMT gene that [redacted]

[redacted]

Gene	Marker	DNA change	Brian's genotype
TPMT	*2	C to G	CC
TPMT	*3B	C to T	CT
TPMT	*3C	T to C	CT

Markers tested: 3

What does this test cover?

Additional Information

View the full report online for links to resources, references, and more detailed genetic results and information.

Drug response: Warfarin (Coumadin®) Sensitivity

Each time a doctor writes a prescription for warfarin (Coumadin ®), a blood thinner given to about two million people each year in the United States, it's a guessing game. There is no "right" dose of the drug. Everyone is different and it can take weeks of adjustment to find a patient's optimal amount of the medication. Too much puts the patient at risk for bleeding. Too little can lead to clots and in turn, heart attack, stroke or even death. A patient's optimal dose depends not only on age, size, other medications and even diet, but also to a large extent on genetics.

Brian's Genetic Results

Increased Slightly increased warfarin sensitivity. May require decreased warfarin dose.

Marker	Brian's Genotype
rs1799853	CT
rs1057910	AA
rs9923231	CC

Markers tested: 3 **Genotype combination:** CYP2C9 *1/*2, VKORC1 -1639/3673 GG

What does this test cover?

Several genes involved in warfarin metabolism play prominent roles in the variable response to warfarin. 23andMe tests for two variants in the CYP2C9 gene (*2, defined using rs1799853, and *3, defined using rs1057910) that are associated with reduced ability to break down warfarin. 23andMe also tests for a variant near the VKORC1 gene (rs9923231) that is associated with increased sensitivity to the drug. Read more about the genetics

Additional Information

Other Risk Factors

Many other clinical and demographic factors affect the optimal warfarin dose for an individual, including age, sex, weight, alcohol consumption, smoking status, ethnicity, vitamin K intake, and other medications. Other genetic variations in other genes (not reported here) can also impact a person's response to warfarin. Only a medical professional can determine the optimal dose for an individual.

Medications and Treatment

Warfarin can interact with other medications, including some antibiotics, non-steroidal anti-inflammatory drugs, some antidepressants, cholesterol medications, and chemotherapy drugs. If you are taking one of these drugs, your health care provider can help devise appropriate treatment plans.

View the full report online for links to resources, references, and more detailed genetic results and information

Brian Davies's results for all conditions tested by 23andMe

Conditions and diseases tested by 23andMe: This list is continually expanding as new genetic associations are discovered and reported. Please visit our website at https://www.23andme.com/about/health/ to view the most up-to-date list of conditions tested by 23andMe.

About Risk Estimates:
23andMe reports results as genotype-specific incidence, which is an estimate of how many individuals in a population composed of people with a customer's genotype are expected to be diagnosed with a condition given a specified ancestry and age range. These estimates are based on well-established genetic associations reported in the biomedical literature and do not account for non-genetic factors, family history, or additional genetic factors that may modify a customer's risk. The genotype-specific incidence estimate combines the odds for a condition for a customer's genotypes at a set of SNPs with data about disease incidence. For more information on how 23andMe calculates these estimates, please see our technical papers available at https://www.23andme.com/publications/.

Disease risk (30)	Your risk	Average risk
Rheumatoid Arthritis	↑ 4.3%	2.4%
Chronic Kidney Disease	↑ 4.2%	3.4%
Exfoliation Glaucoma	↑ 2.2%	0.7%
Primary Biliary Cirrhosis	↑ 0.14%	0.06%
Atrial Fibrillation	Typical risk	
Bipolar Disorder	Typical risk	
Breast Cancer	Typical risk	
Colorectal Cancer	Typical risk	
Coronary Heart Disease	Typical risk	
Crohn's Disease	Typical risk	
Gallstones	Typical risk	
Lung Cancer	Typical risk	
Lupus (Systemic Lupus Erythematosus)	Typical risk	
Melanoma	Typical risk	
Obesity	Typical risk	
Parkinson's Disease	Typical risk	
Scleroderma (Limited Cutaneous Type)	Typical risk	
Type 2 Diabetes	Typical risk	
Ulcerative Colitis	Typical risk	
Venous Thromboembolism	Typical risk	
Age-related Macular Degeneration	↓ Decreased risk	
Alzheimer's Disease	↓ Decreased risk	
Celiac Disease	↓ Decreased risk	

Esophageal Squamous Cell Carcinoma (ESCC)	↓ Decreased risk
Multiple Sclerosis	↓ Decreased risk
Prostate Cancer	↓ Decreased risk
Psoriasis	↓ Decreased risk
Restless Legs Syndrome	↓ Decreased risk
Stomach Cancer (Gastric Cardia Adenocarcinoma)	↓ Decreased risk
Type 1 Diabetes	↓ Decreased risk

About Carrier Status:
23andMe tests for specific genetic variants that are strongly linked to a number of inherited genetic conditions. These variants are typically the most common ones linked to the condition. Certain variants may be more common in certain populations than others. The absence of specific variants does not rule out the possibility that a customer may carry another variant linked to the condition.

Carrier status (49)	Status
Hemochromatosis (HFE-related)	Variant Present
ARSACS	Variant Absent
Agenesis of the Corpus Callosum with Peripheral Neuropathy (ACCPN)	Variant Absent
Alpha-1 Antitrypsin Deficiency	Variant Absent
Autosomal Recessive Polycystic Kidney Disease	Variant Absent
BRCA Cancer Mutations (Selected)	Variant Absent
Beta Thalassemia	Variant Absent
Bloom's Syndrome	Variant Absent
Canavan Disease	Variant Absent
Congenital Disorder of Glycosylation Type 1a (PMM2-CDG)	Variant Absent
Connexin 26-Related Sensorineural Hearing Loss	Variant Absent
Cystic Fibrosis	Variant Absent
D-Bifunctional Protein Deficiency	Variant Absent
DPD Deficiency	Variant Absent
Dihydrolipoamide Dehydrogenase Deficiency	Variant Absent
Factor XI Deficiency	Variant Absent
Familial Dysautonomia	Variant Absent
Familial Hypercholesterolemia Type B	Variant Absent
Familial Hyperinsulinism (ABCC8-related)	Variant Absent
Familial Mediterranean Fever	Variant Absent
Fanconi Anemia (FANCC-related)	Variant Absent
G6PD Deficiency	Variant Absent

GRACILE Syndrome	Variant Absent
Gaucher Disease	Variant Absent
Glycogen Storage Disease Type 1a	Variant Absent
Glycogen Storage Disease Type 1b	Variant Absent
Hereditary Fructose Intolerance	Variant Absent
Hypertrophic Cardiomyopathy (MYBPC3 25bp-deletion)	Variant Absent
LAMB3-related Junctional Epidermolysis Bullosa	Variant Absent
Leigh Syndrome, French Canadian Type (LSFC)	Variant Absent
Limb-girdle Muscular Dystrophy	Variant Absent
Maple Syrup Urine Disease Type 1B	Variant Absent
Medium-Chain Acyl-CoA Dehydrogenase (MCAD) Deficiency	Variant Absent
Mucolipidosis IV	Variant Absent
Neuronal Ceroid Lipofuscinosis (CLN5-related)	Variant Absent
Neuronal Ceroid Lipofuscinosis (PPT1-related)	Variant Absent
Niemann-Pick Disease Type A	Variant Absent
Nijmegen Breakage Syndrome	Variant Absent
Pendred Syndrome	Variant Absent
Phenylketonuria	Variant Absent
Primary Hyperoxaluria Type 2 (PH2)	Variant Absent
Rhizomelic Chondrodysplasia Punctata Type 1 (RCDP1)	Variant Absent
Salla Disease	Variant Absent
Sickle Cell Anemia & Malaria Resistance	Variant Absent
TTR-Related Cardiac Amyloidosis	Variant Absent
Tay-Sachs Disease	Variant Absent
Torsion Dystonia	Variant Absent
Tyrosinemia Type I	Variant Absent
Zellweger Syndrome Spectrum	Variant Absent

About Drug Response:
23andMe displays your likely response to a number of drugs based on genetic variants associated with differences in response. These may be differences in sensitivity, in the likelihood or severity of side effects, or differences in disease risk tied to use of a drug. Only a medical

Drug response (8)	**Response**
Thiopurine Methyltransferase Deficiency	Increased
Warfarin (Coumadin®) Sensitivity	Increased
Abacavir Hypersensitivity	Typical

professional can determine whether a drug is right for a particular patient. The information contained in this report should not be used to independently establish a drug regimen, or abolish or adjust an existing course of treatment.

Alcohol Consumption, Smoking and Risk of Esophageal Cancer	Typical
Clopidogrel (Plavix®) Efficacy	Typical
Fluorouracil Toxicity	**Typical**
Oral Contraceptives, Hormone Replacement Therapy and Risk of Venous Thromboembolism	Not Applicable
Pseudocholinesterase Deficiency	**Typical**
Response to Hepatitis C Treatment	Typical