

Report Description

The ACMG Test is based on Germline DNA mutation analysis. Actionable Insights will test 77 genes associated with medically actionable conditions allowing you to better understand your inherited health risks for cancer, heart disease, and more conditions. By knowing whether you carry any of these genetic factors, you will be able to be more proactive about your health.

In our analysis, we found pathogenic or likely pathogenic variants related to:

- Breast-ovarian cancer, familial 1

Variants analyzed

DSP 1

NF2 1

TTN 1

APOB 1

LDLR 1

RYR2 1

TP53 1

BRCA1 1

PCSK9 3

TNNI3 2

TMEM43 1

Summary Table

Pathogenic/Likely pathogenic variant(s) detected.

Gene	Coordinates	Nucleotide Change	rsID	Clinvar class.	Zygosity	Disease
BRCA1	17:41199722	NM_007294.4(BRCA1):c.5407-2A>G	rs80358002	Pathogenic	HOM	Breast-ovarian cancer, familial 1, Breast and/or ovarian cancer

## Clinical Variants Found

**BRCA1**

PATHOGENIC

HGMD

**17 41199722 T>C**

rs80358002 - NM\_007294.4(BRCA1):c.5407-2A&gt;G

## Phenotypes

Breast-ovarian cancer, familial 1, Breast and/or ovarian cancer

ZYG HOM

MAF -

ACMG -

CLIN. SIG Pathogenic [★★]

HGMD Rankscore 0.69

HGMD Variant Class DM

**APOB**

CONFLICTING

HGMD

**2 21231592 G>A**

rs6413458 - NM\_000384.3(APOB):c.8148C&gt;T (p.Ile2716=)

## Phenotypes

Familial hypercholesterolemia, Familial hypercholesterolemia 1, Familial hypercholesterolemia 2, Hypobetalipoproteinemia, familial, 1, Hypercholesterolaemia

ZYG HET

MAF 0.01438

ACMG Benign

CLIN. SIG Conflicting interpretations of pathogenicity [★]

HGMD Variant Class DM?

**DSP**

CONFLICTING

RARE

**6 7584173 T>A**

rs149070106 - NM\_004415.4(DSP):c.6678T&gt;A (p.Gly2226=)

## Phenotypes

Cardiomyopathy, Dilated cardiomyopathy with woolly hair and keratoderma, Arrhythmogenic right ventricular dysplasia 8, Skin fragility-woolly hair-palmoplantar keratoderma syndrome, Lethal acantholytic epidermolysis bullosa, Cardiovascular phenotype

ZYG HET

MAF 0.0004

ACMG Benign

CLIN. SIG Conflicting interpretations of pathogenicity [★]

**LDLR**

CONFLICTING

**19 11221454 T>C**

NM\_000527.5(LDLR):c.1060+7=

## Phenotype

Familial hypercholesterolemia 1

ZYG HOM

MAF -

ACMG -

CLIN. SIG Conflicting interpretations of pathogenicity [★]

PCSK9 CONFLICTING

1 55518093 G>A

rs11800243 - NM\_174936.4(PCSK9):c.657+9G>A

Phenotypes

Familial hypercholesterolemia 1, Familial hypercholesterolemia 3, Hypobetalipoproteinemia

ZYG HET  
MAF 0.03914  
ACMG -  
CLIN. SIG Conflicting  
interpretations of pathogenicity  
[★]

PCSK9 CONFLICTING HGMD

1 55523033 A>G

rs509504 - NM\_174936.4(PCSK9):c.1026A>G (p.Gln342\_Asp343=)

Phenotypes

Familial hypercholesterolemia 1, Familial hypercholesterolemia 3, Hypobetalipoproteinemia, Hypercholesterolaemia

ZYG HOM  
MAF 0.98183  
ACMG Benign  
CLIN. SIG Conflicting  
interpretations of pathogenicity  
[★]  
HGMD Variant Class DM?

RYR2 CONFLICTING RARE

1 237664060 T>G

rs762905211 - NM\_001035.3(RYR2):c.2253T>G (p.Thr751=)

Phenotypes

Cardiomyopathy, Arrhythmogenic right ventricular dysplasia, familial, 2, Catecholaminergic polymorphic ventricular tachycardia type 1, Catecholaminergic polymorphic ventricular tachycardia

ZYG HET  
MAF 0.00015  
ACMG Likely benign  
CLIN. SIG Conflicting  
interpretations of pathogenicity  
[★]

TNNI3 CONFLICTING

19 55665410 C>T

rs3729841 - NM\_000363.5(TNNI3):c.537G>A (p.Glu179=)

Phenotypes

Cardiomyopathy, Hypertrophic cardiomyopathy, Primary ciliary dyskinesia, Familial restrictive cardiomyopathy 1, Dilated cardiomyopathy 2A, Familial hypertrophic cardiomyopathy 7, Cardiovascular phenotype, Familial Hypertrophic Cardiomyopathy with Wolff-Parkinson-White Syndrome

ZYG HET  
MAF 0.04772  
ACMG Benign  
CLIN. SIG Conflicting  
interpretations of pathogenicity  
[★]

TNNI3 CONFLICTING

19 55665584 A>C

rs7252610 - NM\_000363.5(TNNI3):c.373-10=

Phenotypes

Cardiomyopathy, Hypertrophic cardiomyopathy, Primary ciliary dyskinesia, Familial restrictive cardiomyopathy 1, Dilated cardiomyopathy 2A, Familial hypertrophic cardiomyopathy 7, Primary familial hypertrophic cardiomyopathy, Familial Hypertrophic Cardiomyopathy with Wolff-Parkinson-White Syndrome, Nemaline Myopathy, Recessive

ZYG HOM  
MAF -  
ACMG -  
CLIN. SIG Conflicting  
interpretations of pathogenicity  
[★]

NF2

22 30092078 T>C

NM\_000268.4(NF2):c.\*1287T>C

Phenotypes

Neurofibromatosis, type 2

ZYG HET  
MAF -  
ACMG -  
CLIN. SIG Uncertain significance  
[★]

PCSK9

1 55518287 G>A

rs11800265 - NM\_174936.4(PCSK9):c.658-36G>A

Phenotype

Familial hypercholesterolemia 1

ZYG HET  
MAF 0.03914  
ACMG -  
CLIN. SIG Uncertain significance  
[★]

TTN RARE HGMD

2 179590654 G>A

rs751534449 - NM\_001267550.2(TTN):c.20395C>T (p.Arg6799Trp)

Phenotypes

Hypertrophic cardiomyopathy, Skeletal myopathy

ZYG HET  
MAF 0.00003  
ACMG Uncertain significance  
CLIN. SIG Uncertain significance  
[★★]  
HGMD Rankscore 0.27  
HGMD Variant Class DM

Informational Variants Found

TMEM43

HGMD

3 14187449 G>T

rs2228001 - NM\_004628.5(XPC):c.2815C>A (p.Gln939Lys)

Phenotypes

Xeroderma pigmentosum, group C, Arrhythmogenic right ventricular cardiomyopathy, Xeroderma pigmentosum, cisplatin response - Toxicity/ADR, DNA repair rate: association with

**ZYG** HET  
**MAF** 0.6847  
**ACMG** Benign  
**CLIN. SIG** Drug response [★★★]  
**HGMD Rankscore** 0.1  
**HGMD Variant Class** DFP

TP53

HGMD

17 7579472 G>C

rs1042522 - NM\_000546.6(TP53):c.215C>G (p.Pro72Arg)

Phenotypes

CODON 72 POLYMORPHISM, Li-Fraumeni syndrome 1, Hereditary cancer-predisposing syndrome, Li-Fraumeni syndrome, Lip and oral cavity carcinoma, antineoplastic agents response - Efficacy, Toxicity/ADR, cisplatin response - Efficacy, Toxicity/ADR, cyclophosphamide response - Efficacy, Toxicity/ADR, fluorouracil response - Efficacy, Toxicity/ADR, paclitaxel response - Efficacy, Toxicity/ADR, Lung cancer: association with

**ZYG** HET  
**MAF** 0.54293  
**ACMG** Benign  
**CLIN. SIG** Drug response [★★★]  
**HGMD Rankscore** 0.1  
**HGMD Variant Class** DFP

TP53 Description

Ara et al. (1990) reported that the pro72-to-arg (P72R) change in p53 is caused by polymorphism rather than mutation. Olschwang et al. (1991) assessed the frequency of the pro72-to-arg (P72R) polymorphism and, from its frequency in colon cancer patients and control subjects, concluded that there was no strong association with colon cancer. In both the cancer group and the control group, the frequencies of the pro72 and arg72 alleles were about 31 and 69%, respectively.

[PubMed 1975675](#) | [1999338](#)

The E6 oncoprotein derived from tumor-associated human papillomaviruses (HPVs) binds to and induces degradation of p53. Storey et al. (1998) investigated the effect of the P72R polymorphism on susceptibility of p53 to E6-mediated degradation and found that the arg72 form of p53 was significantly more susceptible than the pro72 form. Moreover, allelic analysis of patients with HPV-associated tumors revealed a striking overrepresentation of homozygous arg72 p53 compared with the normal population, indicating that individuals homozygous for arg72 are about 7 times more susceptible to HPV-associated tumorigenesis than heterozygotes.

[PubMed 9607760](#)

Using immunoprecipitation followed by SDS-PAGE, Thomas et al. (1999) found that the arg72 and pro72 p53 variants did not differ in their ability

to bind DNA in a sequence-specific manner. They concluded that arg72 and pro72 are conformationally indistinguishable and that both can be considered wildtype. However, Thomas et al. (1999) noted that p53(pro) was a stronger inducer of transcription than p53(arg), whereas p53(arg) induced apoptosis faster and was a more potent suppressor of transformation than p53(pro).

[PubMed 9891044](#)

Marin et al. (2000) found that some tumor-derived p53 mutants bound and inactivated p73 (601990). The binding of such mutants was influenced by whether TP53 codon 72 encoded arginine or proline. The ability of p53 to bind p73, neutralize p73-induced apoptosis, and transform cells in cooperation with EJ-Ras (see 190020) was enhanced when codon 72 encoded arg. Marin et al. (2000) found that the arg-containing allele was preferentially mutated and retained in squamous cell tumors arising in arg/pro germline heterozygotes. They concluded that inactivation of p53 family members may contribute to the biologic properties of a subset of p53 mutants, and that a polymorphic residue within p53 affects mutant behavior.

[PubMed 10802655](#)

Laryngeal papillomatosis is caused by human papillomavirus and is associated with malignant transformation in 3 to 7% of cases. Aaltonen et

al. (2001) found no difference in the prevalence of the P72R polymorphism between a group of patients with laryngeal papillomas and a control group.

[PubMed 11403041](#)

The pro72-to-arg polymorphism occurs in the proline-rich domain of p53, which is necessary for the protein to fully induce apoptosis. Dumont et al. (2003) found that in cell lines containing inducible versions of alleles encoding the pro72 and arg72 variants, and in cells with endogenous p53, the arg72 variant induced apoptosis markedly better than the pro72 variant. They suggested that at least 1 source of this enhanced apoptotic potential is the greater ability of the arg72 variant to localize to mitochondria; this localization was accompanied by release of cytochrome c into the cytosol.

[PubMed 12567188](#)

In 92 Caucasian MLH1 (120436) or MSH2 (609309) mutation carriers, including 47 with colorectal cancer, Jones et al. (2004) analyzed the p53 codon 72 genotype and found that arg/pro heterozygotes were 1.94 times more likely to get colorectal cancer during any age interval and developed it 13 years earlier than arg/arg homozygotes. The number of pro/pro homozygotes was too small to provide meaningful results.

[PubMed 15355915](#)

Kruger et al. (2005) studied the p53 genotype of 167 unrelated patients with hereditary nonpolyposis colon cancer (HNPCC; see 120435) with germline mutations in either MSH2 or MLH1 and found that the median age of onset was 41 years for arg/arg, 36 years for arg/pro, and 32 years for pro/pro individuals (p less than 0.0001). There was no difference in age of onset in 126 patients with microsatellite stable colorectal cancers. Kruger et al. (2005) concluded that in a mismatch repair-deficient background, p53 codon 72 genotypes are associated with the age of onset of colorectal carcinoma in a dose-dependent manner.

[PubMed 16199549](#)

Bougeard et al. (2006) studied the effect of the MDM2 SNP309 polymorphism (164785.0001) and the arg72-to-pro polymorphism of the p53 gene on cancer risk in 61 French carriers of the p53 germline mutation. The mean age of tumor onset in p53 codon 72 polymorphism arg allele carriers (21.8 years) was different from that of pro/pro patients (34.4 years, p less than 0.05). Bougeard et al. (2006) also observed a cumulative effect of both polymorphisms because the mean ages of tumor onset in carriers of MDM2 G and p53 arg alleles (16.9 years) and those with the MDM2 T/T and p53 pro/pro genotypes (43 years) were clearly different (p less than 0.02). The results confirmed the impact of the MDM2 SNP309 G allele on the age

of tumor onset in germline p53 mutation carriers, and suggested that this effect may be amplified by the p53 arg72 allele.

[PubMed 16258005](#)

IASPP (607463) is among the most evolutionarily conserved inhibitors of p53, whereas ASPP1 (606455) and ASPP2 (602143) are activators of p53. Bergamaschi et al. (2006) showed that, in addition to the DNA-binding domain, the ASPP family members also bound to the proline-rich region of p53 containing the codon 72 polymorphism. Furthermore, the ASPP family members, particularly IASPP, bound to and regulated the activity of p53 pro72 more efficiently than that of p53 arg72.

[PubMed 16964264](#)

Orsted et al. (2007) stated that arg72 increases the ability of p53 to locate to mitochondria and induce cell death, whereas pro72 exhibits lower apoptotic potential but increases cellular arrest in G1 of the cell cycle. In a study of 9,219 Danish individuals, they found that overall 12-year survival was increased in p53 arg/pro heterozygotes by 3% (P of 0.003) and in pro/pro homozygotes by 6% (P of 0.002) compared with arg/arg homozygotes, corresponding to an increase in median survival of 3 years for pro/pro versus arg/arg homozygotes. Pro/pro homozygotes also showed increased survival after development of cancer, or even after development of other life-threatening diseases, compared with arg/arg homozygotes. The arg72-to-pro change was not associated with decreased risk of cancer.

[PubMed 17535973](#)

Among 254 patients with glioblastoma multiforme (see 137800), El Hallani et al. (2009) found an association between the pro72 allele and earlier age at onset. The pro/pro genotype was present in 20.6% of patients with onset before age 45 years, compared to in 6.5% of those with onset after age 45 years (p = 0.002) and 5.9% among 238 controls (p = 0.001). The findings were confirmed in an additional cohort of 29 patients. The variant did not have any impact on overall patient survival. Analysis of tumor DNA from 73 cases showed an association between the pro allele and a higher rate of somatic TP53 mutations.

[PubMed 8242752](#)

In a study of 863 individuals with European grandparents from an unselected New Zealand birth cohort, Hancox et al. (2009) analyzed lung function (FEV1 and FEV1/FVC) between ages 18 and 32 in relation to cumulative history of cigarette smoking and the rs1042522 SNP, and found that the G allele was associated with smoking-related accelerated rate of decline in lung function (see 608852) (FEV1, p = 0.020; FEV1/FVC, p = 0.037).

[PubMed 19521721](#)

## Related Conditions:

- Breast-ovarian cancer, familial 1

## Genes Analyzed

This report analyzed the following genes:

PKP2, PALB2, BMPR1A, COL3A1, FLNC, NF2, DES, STK11, MLH1, MUTYH, SDHD, GLA, TP53, LDLR, MYL2, DSC2, PMS2, TSC2, MSH2, RB1, KCNQ1, SDHAF2, ACTC1, HNF1A, CACNA1S, TMEM127, MYH7, DSG2, MYH11, RPE65, TRDN, RBM20, MSH6, RET, TNNC1, HFE, PTEN, ACTA2, BRCA1, PCSK9, MAX, TPM1, LMNA, DSP, ATP7B, GAA, OTC, BRCA2, TSC1, SCN5A, RYR2, TGFB1, WT1, APOB, TMEM43, RYR1, VHL, APC, TGFB2, SMAD4, BTBD, MEN1, SDHC, ENG, MYBPC3, FBN1, TNNT2, KCNH2, TTR, TTN, BAG3, CASQ2, SDHB, MYL3, TNNT3, ACVRL1, SMAD3

## Terminology

Name	Symbol	Description
Zygosity	ZYG	Zygosity describes whether you inherited one copy of this variant from one of your parents (heterozygous), or you inherited two copies from both of your parents (homozygous). Typically for pathogenic variants homozygosity cause a more severe form of the condition. In many cases, heterozygous variants do not lead to the condition becoming apparent in the patient (also known as a recessive condition) but do mean that the next generation is at risk of inheriting the condition (or themselves becoming a carrier).
American College of Medical Genetics	ACMG	The American College of Medical Genetics is an organisation dedicated to the practice of medical genetics. Using a series of factors related to the variant and its context, they have identified the likelihood of a specific variant being causative for a disease. This score is based on a few factors, including allelic frequency (AF) and transcription consequence.
Allelic frequency	AF	Allelic frequency defines how often this variant has been observed in the general population. A very low allelic frequency could potentially be de novo (i.e. it wasn't inherited from either of your parents). Low allelic frequency variants are often considered more likely to be the cause of a negative phenotype or disease.
Autosomal dominant	AD	One mutated copy of the gene in each cell is sufficient for a person to be affected by an autosomal dominant disorder. In some cases, an affected person inherits the condition from an affected parent. In others, the condition may result from a new mutation in the gene and occur in people with no history of the disorder in their family.
Autosomal recessive	AR	In autosomal recessive inheritance, both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition. Autosomal recessive disorders are typically not seen in every generation of an affected family.
X-linked	X-linked dominant	Dominant X-linked dominant disorders are caused by mutations in genes on the X chromosome, one of the two sex chromosomes in each cell. In one of the two sex chromosomes in each cell. In females (who have two X chromosomes), a mutation in one of the two copies of the gene in each cell is sufficient to cause the disorder. In males (who have only one X chromosome), a mutation in the only copy of the gene in each cell causes the disorder. In most cases, males experience more severe symptoms of the disorder than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons (no male-to-male transmission).
Y-linked		A condition is considered Y-linked if the mutated gene that causes the disorder is located on the Y chromosome, one of the two sex chromosomes in each of a male's cells. Because only males have a Y chromosome, in Y-linked inheritance, a mutation can only be passed from father to son.
Mitochondrial		Mitochondrial inheritance, also known as maternal inheritance, applies to genes in mitochondrial DNA. Mitochondria, which are structures in each cell that convert molecules into energy, each contain a small amount of DNA. Because only egg cells contribute mitochondria to the developing embryo, only females can pass on mitochondrial mutations to their children. Conditions resulting from mutations in mitochondrial DNA can appear in every generation of a family and can affect both males and females, but fathers do not pass these disorders to their daughters or sons.
Pathogenic		This variant directly contributes to the development of disease. Some pathogenic variants may not be fully penetrant. In the case of recessive or X-linked conditions, a single pathogenic variant may not be sufficient to cause disease on its own. Additional evidence is not expected to alter the classification of this variant.
Likely Pathogenic		There is a high likelihood (greater than 90% certainty) that this variant is disease-causing. Additional evidence is expected to confirm this assertion of pathogenicity, but there is a small chance that new evidence may demonstrate that this variant does not have clinical significance.
Variant Uncertain significance	VUS	There is not enough information at this time to support a more definitive classification of this variant.
Phenotype Name		Phenotype represents the observable characteristics or traits of an organism that are produced by the interaction of the genotype and the environment : the physical expression of one or more genes. Multiple phenotypes can be associated with a single variant.

Name	Symbol	Description
Significance		<p>Significance refers to the standard term used by ClinVar, the internationally recognized database on which this report is based, to classify the types of variants. As the database is a clinical database, the information is clinical and based on an authoritative source when available. The Significance section includes the following standard terms to classify the variants:</p> <ul style="list-style-type: none"> <li>• <b>Pathogenic:</b> A Pathogenic is classified as such if this variant directly contributes to the development of disease. Some pathogenic variants may not be fully penetrant. In the case of recessive or X-linked conditions, a single pathogenic variant may not be sufficient to cause disease on its own. Additional evidence is not expected to alter the classification of this variant.</li> <li>• <b>Likely Pathogenic:</b> A Likely Pathogenic variant is classified as such if there is a high likelihood (greater than 90% certainty) that this variant is disease-causing. Additional evidence is expected to confirm this assertion of pathogenicity, but there is a small chance that new evidence may demonstrate that this variant does not have clinical significance.</li> <li>• <b>Conflicting Interpretations of Pathogenicity:</b> A Conflicting Interpretations of Pathogenicity variant is classified as such if it is submitted from a scientific consortium, where groups within the consortium have conflicting interpretations of a variant but provide a single submission to ClinVar.</li> <li>• <b>Variant of Unknown Significance:</b> A Variant of Unknown Significance is classified as such if there is not enough information at this time to support a more definitive classification of this variant.</li> <li>• <b>Drug response:</b> A Drug response variant is classified as such if it represents a complex phenotype that emerges from the interplay of drug-specific genetics, human body, and environmental factors.</li> <li>• <b>Association:</b> An association variant is classified as such if there are one or more genotypes within a population co-occur with a phenotypic trait more often than would be expected by chance occurrence.</li> </ul>
Review Status		<p>ClinVar reports the level of review supporting the assertion of clinical significance for the variation as review status. Stars provide a graphical representation of the aggregate review status on web pages. Table 1 provides definitions of each review status and the corresponding number of stars. Review status is reported in text format in ClinVar's products available by FTP. A higher number of gold stars corresponds to higher review status. If you wish to get more information about that, please visit ClinVar at the following link: <a href="https://www.ncbi.nlm.nih.gov/clinvar/docs/review_status/">https://www.ncbi.nlm.nih.gov/clinvar/docs/review_status/</a></p>
HGMD Rankscore		<p>The HGMD computed rankscore is a probability of pathogenicity between 0 and 1, with 1 being most likely disease-causing compared to other HGMD entries. The score is computed using a machine learning approach, and is based upon multiple lines of evidence, including HGMD literature support for pathogenicity, evolutionary conservation (100 way vertebrate alignment), variant allele frequency and in-silico pathogenicity prediction.</p>
HGMD Variant Class		<p><b>DM:</b> Pathological mutation reported to be disease-causing in the corresponding literature report (majority of HGMD data).</p> <p><b>DM?:</b> Likely pathological mutation reported to be disease-causing in the corresponding report, but where the author has indicated that there may be some degree of doubt, or subsequent evidence has come to light in the literature, calling the deleterious nature of the variant into question.</p> <p><b>DF:</b> A polymorphism reported to be in significant association with a disease/phenotype (<math>p &lt; 0.05</math>) that is assumed to be functional (e.g. as a consequence of location, evolutionary conservation, replication studies etc.), although there may as yet be no direct evidence (e.g. from an expression study) of a functional effect.</p> <p><b>DFP:</b> A polymorphism reported to be in significant association with disease (<math>p &lt; 0.05</math>) that has evidence of being of direct functional importance (e.g. as a consequence of altered gene expression, mRNA studies etc).</p> <p><b>FP:</b> A polymorphism reported to affect the structure, function or expression of the gene (or gene product), but with no disease association reported as yet.</p> <p><b>R:</b> A variant entry retired from HGMD due to being found to have been erroneously included ab initio, or variant that has been subjected to correction in the literature resulting in the record becoming obsolete, merged or otherwise invalid.</p>



## Methods

### Versions

VCF Version: 2Ao0f9WCtoiAhyP2NixFbst1bb8w\_5GQ

Clinvar Database Version: FgUM\_0StTQ4PCkHW\_E7OkqqEOI.5KRqI

### Extraction

Before sequencing, DNA extraction and library preparation processes were carried-out by automated liquid handling robots. Sequencing was completed using the NovaSeq 6000 instrument (Illumina).

The Nextera DNA Flex (Illumina) library was used during sequencing.

### Analysis

Primary and secondary analysis was performed on the Illumina DRAGEN platform. Our secondary analysis extends the GATK "best practices" pipeline.

It is important to note that applying a filter will not remove any data from the VCF file; it will just annotate the "FILTER" column. Variants with the "PASS" annotation are considered high quality and may, therefore, be used for advanced downstream analysis.

Sequence data is primarily aligned to the GATK [GRCh37 reference genome](#) and mitochondria is aligned to the [Revised Cambridge Reference Sequence \(NC\\_012920.1\)](#). Additional references may have been requested though tertiary analysis is not conducted on variant calls using references other than GRCh37.

## Limitations

Test results are not interpretations. All variants reported in the genes included in the panel are reported.

Rare polymorphisms may lead to false-negative or false-positive results.

Due to limited read length and other contributing technical limitations, repeat expansions (e.g. in the Huntington gene, the SCA-genes, the myotonic dystrophy repeat region, and other similar regions) cannot be assessed with the applied method

This report is based on SNP VCF data.

## Disclaimer

Any preparation and processing of a sample from saliva collection kit to Dante Labs by a customer is assumed to belong to the email used by the customer at the moment of kit registration on the Dante Labs Genome Manager platform before the shipment of the specimen to the laboratory.

The analysis and reporting conducted by Dante Labs are based on information from one or more published third-party scientific and medical studies.

Because of scientific and medical information changes over time, your risk assessment for one or more of the conditions contained within this report may also change over time. For example, opinions differ on the importance and relative weights given to genetic factors. Also, epidemiological data isn't available for some conditions, and this report may not be able to provide definitive information about the severity of a particular condition. We recommend asking your healthcare provider to correctly interpret them. Therefore, this report may not be 100% accurate (e.g., new research could mean different results) and may not predict actual results or outcomes.

This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA). The US Food and Drug Administration (FDA) has determined that clearance or approval of this method is not necessary and thus neither have been obtained.

## Contact

Please contact [contact@dantelabs.com](mailto:contact@dantelabs.com) for more information on the contents of this report, our analysis methodology, and the limitations of this process.

Doctor's Signature

Signature

Date