RESEARCH RESULT — Your doctor will need to confirm this result with a clinical test before using it in your care.

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Hereditary Disease Risk results

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YOUR RESULT:

We did not find anything significant for your health in the genes we looked at.

What does this mean?

Some people have changes in their genes that increase their risk of developing certain diseases.

We did not find any of these kinds of changes in your genes.

IMPORTANT!

- This report comes from a research program, so **it is a research result**. Your doctor will need to confirm these results with a clinical DNA test before using them in your care.
- **Do not change your medical care** based on this result.
- **Results provided are from an investigational device**. An “investigational device” is a device that is the subject of a clinical study.

That's good, right?

That's generally good news. But we can't say too much more. Here's why:

A lot of genes can impact your health or cause disease, and we did not look at all of them.

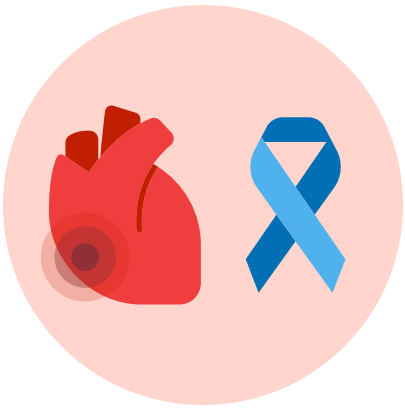
All of Us is a research program. The way we check DNA might not be the same as a doctor-ordered test. There could even be something we couldn't see or can't understand in the genes that we did look at.

What does this mean for my health and what should I do next?

This information should not change anything about how you think about your health.

- ✓ Keep taking care of yourself.
- ✓ Eat well.
- ✓ Get enough sleep.
- ✓ Exercise when you can.
- ✓ If you use tobacco, think about quitting.
- ✓ See a doctor regularly.
- ✓ Tell your doctor about your family history.

We know that these things work to help keep people healthy.



Understanding this report

This test looked at 59 genes in your DNA that can be related to serious diseases, like cancer and heart disease.

All of Us RESEARCH PROGRAM

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How did *All of Us* look at my DNA?

You gave a **blood or saliva** sample to the *All of Us* Research Program. We processed that sample to get some of your **DNA**. An *All of Us* genetics lab gave a readout of that DNA.

Because you said "Yes" to getting health-related DNA results, a specially trained scientist looked closely at some of the genes in your DNA. We wrote this report for you, based on what they found.

What if I have more questions?

You can talk to an *All of Us* genetic counselor by calling (844) 962-2385. They can answer questions about your result or help you find a local genetic counselor to talk to.

Common questions

What was done to get this result?

Actually, quite a lot! DNA is in your blood and other samples. You gave a sample to *All of Us*. We processed your sample to extract the DNA. We sent some of your DNA to a special lab. The lab gave a readout of your DNA. A specially

trained scientist checked some of the genes in your DNA for disease-causing changes. We wrote this report based on what they found.

What does this mean for my family?

Your DNA is a lot like your family member's DNA, but everyone is different. This result does not say anything about their health or their own DNA.

What was the point of looking at my DNA?

Everyone has the same set of genes, but different people can have slightly different *versions* of those genes.

Some people have a version of a gene that increases their chance of developing a serious disease. In some cases, knowing that can be life-saving. Because the information can be so important, it's worth looking at a lot of people's DNA to find these rare people.

We couldn't know what your result would be before checking your DNA.

Could my result change?

Yes. *All of Us* could look at more genes or look again at these genes as science improves. Check your *All of Us* account to make sure this is the most up-to-date version of this report.

We looked at these genes

This is the list of genes we looked at, and some of the diseases they can be related to.

There are limitations to the analysis we did. There are a lot of genes that can cause disease, and we didn't look at all of them. There could even be something we couldn't see or can't understand in the genes that we did look at.

All of Us might look at other genes in the future, or look again at these genes as science advances.

ACTA2	familial thoracic aortic aneurysm and aortic dissection
ACTC1	hypertrophic cardiomyopathy
APC	familial adenomatous polyposis
APOB	familial hypercholesterolemia
ATP7B	Wilson disease
BMPR1A	juvenile polyposis syndrome
BRCA1	hereditary breast and ovarian cancer syndrome
BRCA2	hereditary breast and ovarian cancer syndrome
CACNA1S	malignant hyperthermia susceptibility

COL3A1	vascular Ehlers-Danlos syndrome (EDS)
DSC2	arrhythmogenic cardiomyopathy
DSG2	arrhythmogenic cardiomyopathy
DSP	arrhythmogenic cardiomyopathy and dilated cardiomyopathy
FBN1	Marfan syndrome
GLA	Fabry disease
KCNH2	long QT syndrome
KCNQ1	long QT syndrome
LDLR	familial hypercholesterolemia
LMNA	dilated cardiomyopathy
MEN1	multiple endocrine neoplasia type 1 (MEN1)
MLH1	Lynch syndrome
MSH2	Lynch syndrome

MSH6	Lynch syndrome
MUTYH	*MUTYH*-associated polyposis
MYBPC3	hypertrophic cardiomyopathy
MYH11	familial thoracic aortic aneurysm and aortic dissection
MYH7	dilated cardiomyopathy and hypertrophic cardiomyopathy
MYL2	hypertrophic cardiomyopathy
MYL3	hypertrophic cardiomyopathy
NF2	neurofibromatosis type 2
OTC	ornithine carbamoyltransferase (OTC) deficiency
PCSK9	familial hypercholesterolemia
PKP2	arrhythmogenic cardiomyopathy
PMS2	Lynch syndrome
PRKAG2	hypertrophic cardiomyopathy

PTEN	*PTEN* hamartoma tumor syndrome
RB1	retinoblastoma
RET	multiple endocrine neoplasia type 2 (MEN2)
RYR1	malignant hyperthermia susceptibility
RYR2	catecholaminergic polymorphic ventricular tachycardia
SCN5A	Brugada syndrome and long QT syndrome
SDHAF2	paragangliomas 2
SDHB	paragangliomas 4
SDHC	paragangliomas 3
SDHD	paragangliomas 1
SMAD3	Loeys-Dietz syndrome
SMAD4	juvenile polyposis syndrome
STK11	Peutz-Jeghers syndrome

TGFBR1	Loeys-Dietz syndrome
TGFBR2	Loeys-Dietz syndrome
TMEM43	arrhythmogenic cardiomyopathy
TNNI3	hypertrophic cardiomyopathy
TNNT2	dilated cardiomyopathy and hypertrophic cardiomyopathy
TP53	Li-Fraumeni syndrome
TPM1	hypertrophic cardiomyopathy
TSC1	tuberous sclerosis complex
TSC2	tuberous sclerosis complex
VHL	von Hippel-Lindau syndrome
WT1	Wilms tumor

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Methods and limitations

This section has some technical information about the test that was performed.

Methodology

This report represents the analysis of a sample submitted as a part of the *All of Us* Research Program. The sample was collected at a program partner or with an at-home collection kit. The sample was stored and the DNA was extracted at Mayo Clinic. Genetic data was generated at Broad Institute and interpreted at Color Health.

Genomic DNA was extracted from the submitted sample and sequenced using Illumina Next Generation Sequencing. Sequence data was aligned to a reference genome, and variants were identified using a suite of bioinformatic tools designed to detect single nucleotide variants and small insertions/deletions.

This test was developed and its performance characteristics determined by the *All of Us* Research Program, with clinical laboratories accredited by the College of American Pathologists (CAP) and certified under the Clinical Laboratory Improvement Amendments (CLIA) to perform high-complexity testing.

Genes & Transcripts

ACTA2 (NM_001613), *ACTC1* (NM_005159), *APC* (NM_000038), *APOB* (NM_000384), *ATP7B* (NM_000053), *BMPR1A* (NM_004329), *BRCA1* (NM_007294), *BRCA2* (NM_000059), *CACNA1S* (NM_000069), *COL3A1* (NM_000090), *DSC2* (NM_024422), *DSG2* (NM_001943), *DSP* (NM_004415), *FBN1* (NM_000138), *GLA* (NM_000169), *KCNH2* (NM_000238), *KCNQ1* (NM_000218), *LDLR* (NM_000527), *LMNA* (NM_005572; NM_170707), *MEN1* (NM_130799), *MLH1* (NM_000249), *MSH2* (NM_000251), *MSH6* (NM_000179),

MUTYH (NM_001128425), *MYBPC3* (NM_000256), *MYH11* (NM_001040113), *MYH7* (NM_000257), *MYL2* (NM_000432), *MYL3* (NM_000258), *NF2* (NM_000268), *OTC* (NM_000531), *PCSK9* (NM_174936), *PKP2* (NM_004572), *PMS2* (NM_000535), *PRKAG2* (NM_016203), *PTEN* (NM_000314), *RB1* (NM_000321), *RET* (NM_020975), *RYR1* (NM_000540), *RYR2* (NM_001035), *SCN5A* (NM_198056), *SDHAF2* (NM_017841), *SDHB* (NM_003000), *SDHC* (NM_003001), *SDHD* (NM_003002), *SMAD3* (NM_005902), *SMAD4* (NM_005359), *STK11* (NM_000455), *TGFBR1* (NM_004612), *TGFBR2* (NM_003242), *TMEM43* (NM_024334), *TNNI3* (NM_000363), *TNNT2* (NM_001001430), *TP53* (NM_000546), *TPM1* (NM_001018005), *TSC1* (NM_000368), *TSC2* (NM_000548), *VHL* (NM_000551), *WT1* (NM_024426)

Limitations

- **Results provided are from an investigational device.**
- **Because this report is based on data derived from a research study, this information cannot be used to diagnose, cure, mitigate, treat, or prevent disease.**
- **These results could be incorrect.** Based on validation data, true positives were missed < 0.25% of the time.
- This test may not detect all variants in the analyzed genes. Copy number variation, structural variants, and large chromosomal events are not analyzed or reported. The following genes have additional limitations: *PMS2*: exons 12-15 are not analyzed. *APOB*: only codon 3527 is analyzed.
- The *All of Us* Research Program only reports pathogenic and likely pathogenic variants within the genes specified above in the “Genes & Transcripts” section. Variants conferring only recessive carrier status, and variants in other genes are not reported.
- In very rare cases, such as allogeneic bone marrow transplant, or recent blood transfusion (within 7 days of providing the sample), the results of this

analysis may reflect the DNA of the donor. DNA quality may be affected if a participant has received chemotherapy within 120 days of providing the sample, or if the participant has an active hematological malignancy. In addition, certain organ transplants or diseases (liver, kidney, heart) may limit the relevance of the results.

Would you like to give us some feedback?

What do you think of your Hereditary Disease Risk results?

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