⚠ **RESEARCH RESULT** — Do NOT use this result to make any changes to your medicines.

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Medicine and Your DNA results

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Before we get to your results, here is some helpful information about genes and medicine.

This test looked at a few of the genes in your DNA that can affect how medicines are used. The technical term for this kind of information is “pharmacogenetics.”

Our genes affect how we respond to medicine.

- They do that in many different ways. Some genes help move medicines to the right part of the body.
- Some genes help break down medicines and clear them from your body.
- Some genes even change medicines into a form that makes them work properly.

What is this kind of information used for?

Doctors and pharmacists use this kind of information when they consider why medicines work differently for different people.

But doctors and pharmacists don't make decisions based on just DNA. Some other important considerations can be age, weight, health, diet, and other medicines you are taking at the same time.

IMPORTANT!

- **If your doctor has prescribed medicine for you, keep taking it.** It can be dangerous to stop taking a medicine, or to change the dose or timing of it, without first asking your doctor.
- This report comes from a research program, so **it is a research result**. That means that neither you nor your doctor should use it to make any changes to your medicines. Your doctor would need a clinical test if they wanted to use this information.
- **Share this report with your doctor** so they can decide if they should order that clinical test for you.

- **Results provided are from an investigational device**. An “investigational device” is a device that is the subject of a clinical study.

Understanding this report

There are three parts to this report:

1. "Your genetic results" shows the genes we checked and which versions of the genes we saw in your DNA.
2. "DNA and medicine" indicates some medicines that may be impacted by your genetics. Please remember: the only way to know for sure is by talking to a doctor or pharmacist.
3. "Next steps" talks about why you might share this report with your doctor.

GENETICS AND MEDICINE

Your genetic results

How to read your results:

Each result shows three things

1. Gene

The **genes** we checked. Gene names are usually a string of letters and numbers. They are often pronounced just by spelling them out.

2. Version

The **versions** of the genes you have. Everyone has the same genes, but some people can have different versions that can work slightly differently. For genes that affect medicine, the versions of the genes are named things like *1, *2, or *3. Sometimes they're named after the place in the world where they were first observed.

3. What it means

These terms describe how quickly or slowly your versions of these genes will do their work, or "metabolize."

Your Results:

Gene

CYP2C19

The *CYP2C19* gene is a "metabolizer" gene. These genes play a role

Version

*1/*1

What it means

Normal Metabolizer

in how quickly or slowly medicines are used, or metabolized, by the body.

A normal metabolizer gene may cause the body to process medicines at an average rate. If so, some medicines may stay in the body for the usual amount of time. The medicines work the way we expect them to.

Gene

DPYD

The *DPYD* gene is a "metabolizer" gene. These genes play a role in how quickly or slowly medicines are used, or metabolized, by the body.

Version

*1/*1

What it means

Normal Metabolizer

A normal metabolizer gene may cause the body to process medicines at an average rate. If so, some medicines may stay in the body for the usual amount of time. The medicines work the way we expect them to.

Gene

G6PD

The *G6PD* gene makes a substance that protects red blood cells from damage. Red blood cells carry oxygen to all the different parts of the body. People with changes in this gene

Version

B

What it means

Normal

A "normal" version of this gene may act at an average rate. This means that some medicines are unlikely to damage a person's red blood cells.

may not make enough of this substance to protect their red blood cells. This means if they take certain medicines, their red blood cells might get damaged.

Gene

NUDT15

The *NUDT15* gene is a "metabolizer" gene. These genes play a role in how quickly or slowly medicines are used, or metabolized, by the body.

Version

*1/*1

What it means

Normal Metabolizer

A normal metabolizer gene may cause the body to process medicines at an average rate. If so, some medicines may stay in the body for the usual amount of time. The medicines work the way we expect them to.

Gene

SLCO1B1

The *SLCO1B1* gene helps move some medicines out of the body when they are done working. People with changes in this

Version

*1/*15

What it means

Decreased Function

A “decreased function” version of this gene may act at a rate that is much slower than average. This means

gene may have a harder time removing these medicines from their body. This means those medicines may build up in the body and cause muscle pain.

some medicines may increase your risk of developing muscle pain.

Gene

TPMT

The *TPMT* gene is a "metabolizer" gene. These genes play a role in how quickly or slowly medicines are used, or metabolized, by the body.

Version

*1/*1

What it means

Normal Metabolizer

A normal metabolizer gene may cause the body to process medicines at an average rate. If so, some medicines may stay in the body for the usual amount of time. The medicines work the way we expect them to.

Gene

UGT1A1

The *UGT1A1* gene is a "metabolizer" gene. These genes play a role in how quickly or slowly medicines are used, or

Version

*1/*1

What it means

Normal Metabolizer

A normal metabolizer gene may cause the body to process medicines at an average rate. If so, some

metabolized, by the body.

medicines may stay in the body for the usual amount of time. The medicines work the way we expect them to.

GENETICS AND MEDICINE

DNA and medicine

This table points out some medicines that may be affected by your genetic results.

If you are taking one of these medicines, talk with your doctor or pharmacist about whether ordering a clinical pharmacogenetic test is right for you.

These medicines MAY BE impacted

In some cases, pharmacogenetic information may help doctors and pharmacists choose medicines and doses.

Gene
SLCO1B1

- simvastatin (Zocor®)

Just because a medicine is listed here doesn't mean that you should or should not be taking it. Some people with these genetic results still process these medicines normally.

Important! Genetic information is really just one piece of the puzzle.

- It won’t tell us if a medicine will definitely work.
- It won’t tell us if a medicine will definitely cause side effects or won’t work at all.
- It won’t tell us exactly how much medicine someone should take.
- It only applies to medicines that you eat, drink, or inject. It doesn't apply to medicines that are rubbed on your skin or used in your eyes or ears.

If your doctor has prescribed medicine for you, keep taking it. It can be dangerous to stop taking a medicine, or to change the dose or timing of it, without first asking your doctor.

Next steps

What’s next?

- **Share this report with your doctor** so they can determine if they should order a clinical pharmacogenetic test.
- Ordering a clinical pharmacogenetic test could be helpful if you see a medicine you're currently taking on the table titled "These medicines MAY BE impacted by your genetics."
- Do **not** use this report to make changes to any medicine you take. If your doctor has prescribed medicine for you, keep taking it. It can be dangerous to stop taking a medicine, or to change the dose or timing of it, without first asking your doctor.

What if I have questions?

Ask your doctor or pharmacist.

Because *All of Us* is a research program, we cannot give advice about your medicines specifically.

? Common questions

How do I know if this matters for me?

Ask your doctor or pharmacist. Because *All of Us* is a research program, we cannot give advice about your medicines specifically.

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 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 and 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 doesn’t say anything about their health or their own 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.

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 & Alleles

This analysis aims to detect the presence or absence of any of the following alleles, or genotypes at the specified positions: *CYP2C19*: *2, *3, *4, *6, *8, *9, *10, *16, *17, *22, *24, *35; *DPYD*: c.1905+1G>A (*2), c.1129-5923C>G, c.1679T>G (*13), c.2846A>T; *G6PD*:A-202A_376G; A-968C_376G; Asahi; Aures; Canton, Taiwan-Hakka, Gifu-like, Agrigento-like; Chinese-5; Ilesha; Kaiping, Anant, Dhon, Sapporo-like, Wosera; Kambos; Kalyan-Kerala, Jamnaga, Rohini; Mediterranean, Dallas, Panama, Sassari, Cagliari, Birmingham; Quing Yuan, Chinese-4; Seattle, Lodi, Modena, Ferrara II, Athens-like; Sibari; Ube Konan; Union, Maewo, Chinese-2, Kalo;

Viangchan, Jammu; *NUDT15*: *2, *3; *SLCO1B1*: *5, *15, *17; *TPMT*: *2, *3A, *3B, *3C; *UGT1A1*: *6, *27, *28, *36, *37

Phenotypes

Normal Function / Normal Metabolizer / Normal	The gene may act at a rate that is considered average.
Intermediate Metabolizer / Likely Intermediate Metabolizer	The gene may act at a rate that is considered slower than average.
Variable (*G6PD*)	The gene may act at a rate that is considered slower than average, but can be different for different people.
Poor Function / Decreased Function / Poor Metabolizer / Likely Poor Metabolizer / Deficient / Deficient with CNSHA (chronic nonspherocytic hemolytic anemia)	The gene may act at a rate that is considered much slower than average.
Rapid Metabolizer	The gene may act at a rate that is considered faster than average.

Ultra-rapid Metabolizer	The gene may act at a rate that is considered much faster than average.
Indeterminate	This result could not be reported for technical reasons.

Medications

Only the following gene/drug interactions were considered: *CYP2C19* [amitriptyline (Elavil®), citalopram (Celexa®), clobazam (Onfi®), clomipramine (Anafranil®), clopidogrel (Plavix®), doxepin (Sinequan®), escitalopram (Lexapro®), imipramine (Tofranil®), sertraline (Zoloft®), trimipramine (Surmontil®), voriconazole (Vfend®), flibanserin (Addyi®), pantoprazole (Protonix®), brivaracetam (Briviact®)]; *DPYD* [capecitabine (Xeloda®), fluorouracil (Adrucil®)]; *G6PD* [chloramphenicol (note: this doesn't apply to medicines that are rubbed on your skin or used in your eyes or ears), dabrafenib (Tafinlar®), dapsone, hydroxychloroquine (Plaquenil®), local anesthetic containing drugs (e.g. articaine, chloroprocaine, lidocaine, mepivacaine, ropivacaine, tetracaine), mafenide (Sulfamylon®), methylene blue, nalidixic acid (NegGram®), nitrofurantoin (Macrobid®, Macrodantin®, Furadantin®), pegloticase (Krystexxa®), phenazopyridine, primaquine, probenecid (Col-Benemid®), rasburicase (Elitek®), sodium nitrite, sulfacetamide (note: this doesn't apply to medicines that are rubbed on your skin or used in your eyes or ears), sulfamethoxazole/trimethoprim (Bactrim®, Septra®), sulfanilamide, sulfasalazine (Azulfidine®), sulfonylurea drugs [chlorpropamide (Diabinese®), glimepiride (Amaryl®), glipizide (Glucotrol®), glyburide (Diabeta®), tolazamide (Tolinase®), tolbutamide (Orinase®)], tafenoquine (Krintafel®)]; *NUDT15* [azathioprine (Imuran®), mercaptopurine

(Purinethol®), thioguanine]; *SLCO1B1* [simvastatin (Zocor®)]; *TPMT* [azathioprine (Imuran®), mercaptopurine (Purinethol®), thioguanine]; *UGT1A1* [atazanavir (Reyataz®), belinostat (Beleodaq®), irinotecan (Camptosar®)]

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, results were incorrect < 0.12% of the time.
- This analysis does not detect all possible variants in the tested genes. When *1 (or B in the case of *G6PD*) is reported, it indicates that none of the alleles listed above were identified; it does not rule out the presence of an allele not analyzed by this test and does not rule out the possibility that a non-normal allele is present. This analysis cannot phase variants.
- The reported result may be refined as new alleles are added to the analysis.
- In some cases, observed data can be consistent with more than one possible diplotype, and in these cases the diplotype may be reported as “indeterminate”.
- This analysis cannot distinguish between the more common *1/*3A and the more rare *3B/*3C diplotypes in *TPMT*; clinical phenotypic testing can distinguish between these alleles.
- 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.

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