Phenylketonuria and Related Disorders

PKU is part of a spectrum of related genetic disorders. These disorders are characterized by intellectual disability, seizures, and skin problems. A person must have two variants in the PAH gene in order to have one of these disorders.

Overview | Scientific Details

Jamie, you **do not have the variants** we tested.

You could still have a variant not covered by this test.

0 variants detected

in the PAH gene

How To Use This Test

This test does not diagnose any health conditions.

Please talk to a healthcare professional if this condition runs in your family, you think you might have this condition, or you have any concerns about your results.

Review the Carrier Status tutorial

See Scientific Details

Intended Uses

- Tests for **multiple variants** in the PAH gene.
- To identify carrier status for PKU and related disorders.

Limitations

- Does **not test** for all possible variants for the condition.
- Does **not report** if someone has two copies of a tested variant.

Important Ethnicities

- This test is most relevant for people of **Northern European** descent, particularly those of **Irish** ancestry.
- This test does **not** include a large fraction of PAH variants that cause PKU and related disorders in people of other ethnicities.

You are likely not a carrier.

This result is relevant for you because you have **Irish** ancestry.

We ruled out the most common variants for PKU and related disorders in people of Irish descent.

You still have a chance of being a carrier for PKU or a related disorder.

You may still have up to a **1 in 179 chance** of carrying a variant not covered by this test.

See Scientific Details

About Phenylketonuria and Related Disorders

Also known as: Phenylalanine Hydroxylase Deficiency, Hyperphenylalaninemia

When symptoms develop

Symptoms typically develop soon after birth.

Typical signs and symptoms

- Intellectual disability
- Seizures
- Behavioral problems
- Eczema

Ethnicities most affected

These conditions occur worldwide, but are more common in people of Irish, European, Turkish, and East Asian descent.

How it's treated

There is currently no known cure. Diet management throughout life may help reduce common PKU symptoms. For some people, use of medication can prevent phenylalanine levels from becoming too high.

Read more at: Genetics Home Reference GeneReviews Mayo Clinic

Consider talking to a healthcare professional if you are concerned about your results.

If you're starting a family, a genetic counselor can help you and your partner understand if additional testing might be appropriate.

Connect with a GC

Share your results with a healthcare professional.

Print report

Learn more about this condition and connect with support groups.

Learn more

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PKU is part of a spectrum of related genetic disorders. These disorders are characterized by intellectual disability, seizures, and skin problems. A person must have two variants in the PAH gene in order to have one of these disorders.

Overview | Scientific Details

PKU and related disorders are caused by variants in the PAH gene.

PAH

Chromosome 12

The PAH gene contains instructions for making an enzyme called phenylalanine hydroxylase. This enzyme helps break down an amino acid called phenylalanine, which is found in some foods. Certain variants in PAH disrupt its function, resulting in a harmful buildup of phenylalanine.

Read more at GeneEx's Home Reference

You have no variants detected by this test.

Variants Detected | View All Tested Markers

Marker Tested	Your Genotype*			Additional Information
F39L Gene: PAH Marker: **i4000470**	G Typical copy from one of your parents	G Typical copy from your other parent		**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** References [3, 6, & 28, 36, 38] | ClinVar
L48S Gene: PAH Marker: **rs5030841**	A Typical copy from one of your parents	A Typical copy from your other parent		**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** References [2, 11, 14-26, 28, 29, 30, 32, 36] | ClinVar
I65T Gene: PAH Marker: **i4000472**	A Typical copy from one of your parents	A Typical copy from your other parent		**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** References [5, 9, 28-22, 25, 26, 29, 36] | ClinVar
R111X Gene: PAH Marker: **i4000473**	G Typical copy from one of your parents	G Typical copy from your other parent		**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** References [3, 11, 13, 13, 24, 28, 31, 36] | ClinVar
R158Q Gene: PAH Marker: **i3003397**	C Typical copy from one of your parents	C Typical copy from your other parent		**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** References [3, 11, 14, 19, 28, 25, 29, 36] | ClinVar
R243Q Gene: PAH Marker: **i4000481**	C Typical copy from one of your parents	C Typical copy from your other parent		**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** References [1, 12, 13, 28, 24, 36] | ClinVar
R243X Gene: PAH Marker: **i3003398**	G Typical copy from one of your parents	G Typical copy from your other parent		**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** References [3, 11, 22, 25, 32, 36] | ClinVar
R252W Gene: PAH Marker: **i3003399**	G Typical copy from one of your parents	G Typical copy from your other parent		**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** References [3, 28, 22, 23, 26, 29, 32, 36] | ClinVar
R261Q Gene: PAH Marker: **rs5030849**	C Typical copy from one of your parents	C Typical copy from your other parent		**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** References [3, 11, 13, 14, 22, 31, 32, 36] | ClinVar
Q272X Gene: PAH Marker: **i4000487**	C Typical copy from one of your parents	C Typical copy from your other parent		**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** References [3, 25, 26, 27, 29, 36] | ClinVar
E280K Gene: PAH Marker: **i4000476**	C Typical copy from one of your parents	C Typical copy from your other parent		**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** References [3, 28, 22, 25, 32, 36] | ClinVar
P281L Gene: PAH Marker: **i3003401**	G Typical copy from one of your parents	G Typical copy from your other parent		**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** References [3, 10, 11, 12, 22, 32, 36] | ClinVar
A309S Gene: PAH Marker: **rs5030853**	C Typical copy from one of your parents	C Typical copy from your other parent		**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** References [3, 9, 22, 25, 32, 33, 36] | ClinVar
L349V Gene: PAH Marker: **i4000476**	G Typical copy from one of your parents	G Typical copy from your other parent		**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** References [2, 3, 5, 10, 22, 36] | ClinVar
E390G Gene: PAH Marker: **i3003403**	T Typical copy from one of your parents	T Typical copy from your other parent		**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** References [3, 6, 18, 11, 36] | ClinVar
A403V Gene: PAH Marker: **rs5030857**	G Typical copy from one of your parents	G Typical copy from your other parent		**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** References [1, 3, 4, 33, 36] | ClinVar
R408W Gene: PAH Marker: **rs5030858**	G Typical copy from one of your parents	G Typical copy from your other parent		**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** References [3, 11, 14, 28, 25, 29, 36] | ClinVar
R408Q Gene: PAH Marker: **i3003404**	C Typical copy from one of your parents	C Typical copy from your other parent		**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** References [1, 5, 14, 28, 32, 36] | ClinVar
R413P Gene: PAH Marker: **rs2934899**	C Typical copy from one of your parents	C Typical copy from your other parent		**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** References [3, 12, 13, 16, 24, 36] | ClinVar
Y414C Gene: PAH Marker: **i3003405**	T Typical copy from one of your parents	T Typical copy from your other parent		**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** References [3, 5, 14, 28, 22, 26, 29, 36] | ClinVar
IVS10-11G>A Gene: PAH Marker: **rs5030655**	C Typical copy from one of your parents	C Typical copy from your other parent		**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** References [1, 5, 14, 28, 23, 26, 29, 32] | ClinVar
IVS12+1G>A Gene: PAH Marker: **rs5030661**	C Typical copy from one of your parents	C Typical copy from your other parent		**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** References [1, 3, 4, 14, 16, 26, 29] | ClinVar

*This test cannot distinguish which copy you received from which parent. This test also cannot determine whether multiple variants, if detected, were inherited from only one parent or from both parents. This may impact how these variants are passed down.

23andMe always reports genotypes based on the 'positive' strand of the human genome reference sequence (build 37). Other sources sometimes report genotypes using the opposite strand.

Test Interpretation

This report provides an estimate of the chances of still being a carrier for people who do not have the carrier(s) tested. This is known as the **post-test carrier risk**.

Post-test carrier risk is based on the average chance of being a carrier for a given ethnicity and the carrier detection rate of the test for a given ethnicity.

View technical article on estimating post-test carrier risk.

Post-Test Carrier Risk

This report provides an estimate of the post-test carrier risk for people of Irish, Northern European, Turkish, Chinese, Korean, and Japanese descent only.

- For people with partial ethnicity from one or more groups mentioned above, post-test carrier risk depends on the exact mixture in the person's background.
- Post-test risk for other ethnicities cannot be provided because sufficient data is not available.

Post-test carrier risk for relevant ethnicities

Irish	1 in 179	[21]
Northern European	1 in 197	[21]
Turkish	1 in 66	[21]
Chinese	1 in 39	[34]
Korean	1 in 62	[21]
Japanese	1 in 348	[21]

Test Details

Indications for Use

The 23andMe PGS Carrier Status Test for Phenylketonuria and Related Disorders is indicated for the detection of 23 variants in the PAH gene. This test is intended to be used to determine carrier status for PKU and related disorders in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Irish and Northern European descent.

Special Considerations

- PKU and related disorders can be managed with appropriate treatment.
- Symptoms of these disorders vary in severity depending on which variants are causing the condition.
- There are currently no professional guidelines in the U.S. for carrier testing for these conditions.

Test Performance Summary

Carrier Detection Rate & Relevant Ethnicities

The "carrier detection rate" is an estimate of the percentage of carriers for this condition that would be identified by this test. Carrier detection rate differs by ethnicity and is provided only where sufficient data is available.

Irish	82%	[35]
Northern European	75% (averaged across multiple countries)	[35]
Turkish	63%	[7]
Chinese	29%	[15]
Korean	28%	[12]
Japanese	42%	[12]
Eastern European	63 to 95%, depending on country of ancestry	[35]
Western European	46 to 87%, depending on country of ancestry	[35]
Southern European	32 to 85%, depending on country of ancestry	[35]

Analytical Performance

Accuracy was determined by comparing results from this test with results from sequencing. Greater than 99% of test results were correct. While unlikely, this test may provide false positive or false negative results. For more details on the analytical performance of this test, refer to the package insert.

Warnings and Limitations

- This test does not cover all variants that could cause this condition.[1]
- This test does not diagnose any health conditions.
- Positive results in individuals whose ethnicities are not commonly associated with the tested variants are less reliable. Individuals in this situation should consider genetic counseling and follow-up testing.
- Share results with your healthcare professional for any medical purposes.
- If you are concerned about your results, consult with a healthcare professional.

See the Package Insert for more details on use and performance of this test.

[1] Variants not included in this test may be rare, may not be available on our genotyping platform, or may not pass our testing standards.

References

1. **Berdiel T et al. (2002).** "Two novel genetic lesions and a common IRA-responsive mutation of the PAH gene in Italian patients with hyperphenylalaninemia." **Mol Genet Metab. 77(1):69-4.** "
2. **Blk-Mlutowski M et al. (2013).** "Molecular genetics of PKU in Poland and potential impact of mutations on BH4 responsiveness." **Acta Biochim Pol. 60(4):815-6.** "
3. **BIOPKU Database** "
4. **Correia M et al. (2011).** "Natural phenylalanine hydroxylase variants that confer a mild phenotype affect the enzyme's conformational stability and oligomerization equilibrium." **Biochim Biophys Acta. 1812(12):1635-45.** "
5. **Desviat LR et al. (2004).** "Tetrahydrobiopterin responsiveness: results of the BH4 loading test in 31 Spanish PKU patients and correlation with their genotype." **Mol Genet Metab. 83(1-2):57-62.** "
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7. **Dokouhaki SP et al. (1991).** "Molecular genetics and impact of residual in vitro phenylalanine hydroxylase activity on tetrahydrobiopterin responsiveness in Turkish PKU population." **Mol Genet Metab. 102(2):95-21.** "
8. **Perroud SM et al. (1991).** "Relation detection in phenylketonuria by using chemical cleavage of mismatch importance of using probes from both normal and patient samples." **Am J Hum Genet. 49(1):75-83.** "
9. **Gersting SW et al. (2006).** "Loss of function in phenylalanine is caused by impaired molecular motions and conformational instability." **Am J Hum Genet. 83(5):5-17.** "
10. **Gersting T et al. (2001).** "In vitro expression of 24 naturally occurring mutant variants of phenylalanine hydroxylase correlation with metabolic phenotypes and susceptibility toward protein aggregation." **Mol Genet Metab. 72(2):152-65.** "

See all references

Change Log

Your report may occasionally be updated based on new information. This Change Log describes updates and revisions to this report.

Date	Change
Dec. 9, 2011	The carrier frequency and carrier detection rate were updated for customers who self-report having Chinese ancestry. The chances of still being a carrier were also updated for customers with no variants detected who self-report having Chinese ancestry.
Aug. 18, 2010	Phenylketonuria and Related Disorders report created.

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