Congenital Disorder of Glycosylation Type 1a (PMM2-CDG)

PMM2-CDG is a rare genetic disorder that affects the nervous system and other parts of the body. It is characterized by developmental delay, muscle weakness, and failure to gain weight. A person must have two variants in the PMM2 gene in order to have this condition.

Overview Scientific Details

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

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

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 PMM2 gene.
- To identify carrier status for PMM2-CDG.

Limitations

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

Important Ethnicities

- This test is most relevant for people of **Ashkenazi Jewish** and **Danish** descent.
- This test does **not** include a large fraction of PMM2 variants that cause PMM2-CDG in people of Dutch descent.

You are likely not a carrier.

This result may be less relevant for you because the variants that cause PMM2-CDG are rarely found in people of your ethnicity.

We ruled out the tested variants for PMM2-CDG.

These variants are most common in people of **Ashkenazi Jewish or Danish** descent.

You still have a chance of being a carrier for PMM2-CDG.

We cannot estimate your chances because this condition is rare and not well studied in your ethnicity.

About Congenital Disorder of Glycosylation Type 1a (PMM2-CDG)

Also known as: Carbohydrate-Deficient Glycoprotein Syndrome Type 1a, Jaeken Syndrome, Phosphomannomutase 2 Deficiency, CDG1a

When symptoms develop

Symptoms typically develop in infancy.

Typical signs and symptoms

- Developmental delay
- Muscle weakness
- Failure to gain weight
- Small head size and distinct facial features

Ethnicities most affected

This condition is most common in people of European descent, particularly of Danish and Dutch descent.

How it's treated

There is currently no known cure. Treatment focuses on nutritional, occupational, speech, and physical therapy.

Read more at: MedlinePlus GeneReviews National Organization for Rare Disorders

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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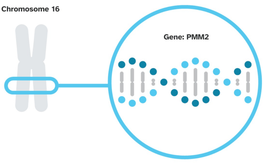
Overview Scientific Details

PMM2-CDG is caused by variants in the PMM2 gene.

PMM2

The PMM2 gene contains instructions for making an enzyme called phosphomannomutase 2 (PMM2). PMM2 plays a role in the process of attaching sugar molecules to proteins. This modification is necessary for the stability and proper function of many proteins. Certain variants in the PMM2 gene lead to lower activity of the PMM2 enzyme.

Read more at MedlinePlus



You have no variants detected by this test.

Variants Detected | View All Tested Markers

Marker Tested	Your Genotype*		Additional Information
R141H **Gene:** PMM2 **Marker:** I5912680	**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, 4, 9] | ClinVar
F119L **Gene:** PMM2 **Marker:** I5912679	**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, 2, 4, 6] | 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 variant(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 Danish and Dutch 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

Ashkenazi Jewish	1 in 699	[8]
Danish	1 in 479	[7]
Dutch	1 in 119	[7]

Test Details

Indications for Use

The 23andMe PGS Carrier Status Test for Congenital Disorder of Glycosylation Type 1a (PMM2-CDG) is indicated for the detection of two variants in the PMM2 gene. This test is intended to be used to determine carrier status for PMM2-CDG in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Ashkenazi Jewish and Danish descent.

Special Considerations

- Severity of symptoms can vary in people with this disorder, even when the same variants are involved.
- Individuals with two copies of the R141H variant have not been observed. This is likely because having two copies of this variant is not compatible with life [Shi et al., 2017]. Thus, if two individuals both carrying only the R141H variant have children, it is not expected that these children would be at risk for PMM2-CDG.
- There are currently no professional guidelines in the U.S. for carrier testing for this condition.

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.

Ashkenazi Jewish	96%	[8]
Danish	89%	[7]
Dutch	58%	[7]

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.*
- This test does not diagnose any health conditions.
- Positive results in individuals whose ethnicities are not commonly associated with this condition may be incorrect. 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.

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

References

1. **Andreotti G et al. (2013). "Biochemical phenotype of a common disease-causing mutation and a possible therapeutic approach for the phosphomannomutase 2-associated disorder of glycosylation." Mol Genet Genomic Med. 1(1):32-44.**
2. **Bjursell C et al. (2000). "PMM2 mutation spectrum, including 10 novel mutations, in a large CDG type 1A family material with a focus on Scandinavian families." Hum Mutat. 16(5):395-400.**
3. **Kjaergaard S et al. (1998). "Absence of homozygosity for predominant mutations in PMM2 in Danish patients with carbohydrate-deficient glycoprotein syndrome type 1." Eur J Hum Genet. 6(4):331-6.**
4. **Kjaergaard S et al. (2001). "Congenital disorder of glycosylation type Ia (CDG-Ia): phenotypic spectrum of the R141H/F119L genotype." Arch Dis Child. 85(3):236-9.**
5. **Lam C et al. (2005). "PMM2-CDG." [Accessed Aug 25, 2021).**
6. **Matthijs G et al. (2000). "Mutations in PMM2 that cause congenital disorders of glycosylation, type Ia (CDG-Ia)." Hum Mutat. 16(5):386-94.**
7. **Scholten E et al. (2000). "Lack of Hardy-Weinberg equilibrium for the most prevalent PMM2 mutation in CDG-Ia (congenital disorders of glycosylation type Ia)." Eur J Hum Genet. 8(5):367-71.**
8. **Shi L et al. (2017). "Comprehensive population screening in the Ashkenazi Jewish population for recurrent disease-causing variants." Clin Genet. 91(4):599-604.**
9. **Vega AI et al. (2011). "Expression analysis revealing destabilizing mutations in phosphomannomutase 2 deficiency (PMM2-CDG): expression analysis of PMM2-CDG mutations." J Inherit Metab Dis. 34(4):929-39.**

Change Log

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

Date	Change
Nov. 3, 2021	The carrier detection rate was updated for Dutch and the carrier frequency was updated for customers who self-report having Dutch or Danish ancestry. The chances of still being a carrier were also updated for customers with no variants detected who self-report having Dutch or Danish ancestry.
Dec. 9, 2019	Information specific to people of Ashkenazi Jewish descent was added. Customers who self-report having Ashkenazi Jewish ancestry may now see carrier frequency, carrier detection rate, and post-test carrier risk information specific to that ancestry.
Feb. 18, 2016	Due to improvements in data analysis, some customers who previously received a "Not Determined" result for I5912686 may see a genotype at this marker. This may also update the overall report result for these customers.
Oct. 21, 2015	Congenital Disorder of Glycosylation Type 1a (PMM2-CDG) report created.