Zellweger Spectrum Disorder (PEX1-Related)

ZSD is a group of rare genetic disorders. The form of ZSD covered by this report is characterized by impaired hearing, vision, and organ function, as well as developmental disability and early death. A person must have two variants in the PEX1 gene in order to have this form of ZSD.

Overview Scientific Details

Jamie, you **have the variant** we tested.

You could pass this variant on to your children.

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

- To test for the G843D variant in the PEX1 gene.
- To identify carrier status for ZSD.

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** ZSD caused by variants in other PEX genes.

Important Ethnicities

- This test does **not** include the majority of PEX1 variants that cause ZSD in any ethnicity.

You are a carrier.

You could pass this variant on to your children.

We detected one variant for ZSD.

People with only one variant are not expected to have ZSD.

Your results may be relevant for you if you're thinking about starting a family.

If you and your partner are both carriers, each child may have a **25% chance** of having this condition. Your relatives may also wish to consider testing if they plan to have children.

About Zellweger Spectrum Disorder (PEX1-Related)

ZSD is a continuum of rare genetic disorders that can present as severe, intermediate, or mild. It is a type of peroxisome biogenesis disorder.

When symptoms develop

Symptoms are typically present at birth or develop during infancy.

Typical signs and symptoms

- Decreased muscle tone
- Seizures
- Failure to gain weight
- Impaired vision and hearing
- Developmental disability
- Early death (severe form)

Ethnicities most affected

This condition affects people of all ethnicities.

How it's treated

There is currently no known cure. Treatment focuses on managing symptoms and preventing complications.

Read more at: MedlinePlus GeneReviews National Organization for Rare Disorders

Consider talking to a healthcare professional if you are thinking about having children.

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 your family.

Share your report

If you have other concerns about your results, consult with a healthcare professional.

Print report

Learn more about this condition and connect with support groups.

Learn more

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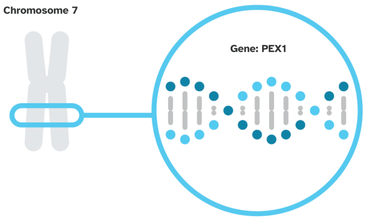
Overview Scientific Details

ZSD is caused by variants in the PEX1 gene.

PEX1

The PEX1 gene contains instructions for making a protein called peroxisome biogenesis factor 1, also known as PEX1. This protein helps peroxisomes (compartments within cells that make and break down fats and other substances) work properly. Certain variants in PEX1 disrupt peroxisome function and lead to a harmful buildup of certain substances inside of cells.

Read more at MedlinePlus



You have one variant detected by this test.

Variants Detected | View All Tested Markers

Marker Tested	Genotype*			Additional Information
G843D **Gene:** PEX1 **Marker:** i5012688	**C** Typical copy from one of your parents		**T** Variant copy from your other parent	**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** **References [1, 2, 3, 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 Details

Indications for Use

The 23andMe PGS Carrier Status Test for Zellweger Spectrum Disorder (PEX1-Related) is indicated for the detection of the G843D variant in the PEX1 gene. This test is intended to be used to determine carrier status for ZSD in adults, but cannot determine if a person has two copies of a tested variant.

Special Considerations

- This test does not include the majority of PEX1 variants that cause ZSD in any ethnicity.
- 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.

European	41%	[4, 5]

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. Ebberink MS et al. (2011). "Genetic classification and mutational spectrum of more than 600 patients with a Zellweger syndrome spectrum disorder." Hum Mutat. 32(1):59-69.
2. Hiebler S et al. (2014). "The Pex1-G844D mouse: a model for mild human Zellweger spectrum disorder." Mol Genet Metab. 111(4):522-32.
3. Maxwell MA et al. (1999). "A common PEX1 frameshift mutation in patients with disorders of peroxisome biogenesis correlates with the severe Zellweger syndrome phenotype." Hum Genet. 105(1-2):38-44.
4. Steinberg S et al. (2004). "The PEX Gene Screen: molecular diagnosis of peroxisome biogenesis disorders in the Zellweger syndrome spectrum." Mol Genet Metab. 83(3):252-63.
5. Steinberg SJ et al. (2003). "Zellweger Spectrum Disorder." [Accessed Oct 5, 2021].
6. Walter C et al. (2001). "Disorders of peroxisome biogenesis due to mutations in PEX1: phenotypes and PEX1 protein levels." Am J Hum Genet. 69(1):35-48.

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. 7, 2022	The report name and condition name in the report were updated from "Zellweger Syndrome Spectrum" ("ZSS") to "Zellweger Spectrum Disorder" ("ZSD") to reflect the current preferred terminology for this condition.
Feb. 18, 2016	Due to improvements in data analysis, some customers who previously received a "Not Determined" result for this report may see an updated result.
Oct. 21, 2015	Zellweger Syndrome Spectrum (PEX1-Related) report created.