# PGM3-congenital disorder of glycosylation

## Description

*PGM3*-congenital disorder of glycosylation (*PGM3*-CDG) is an inherited condition that primarily affects the immune system but can also involve other areas of the body. The pattern and severity of this disorder's signs and symptoms typically vary.

Most people with *PGM3*-CDG have impaired immune function (immune deficiency). Many have a shortage of white blood cells (leukopenia), which normally protect the body from infection. Because affected individuals lack the necessary immune cells to fight off certain bacteria, viruses, and fungi, they are prone to repeated and persistent infections that often occur in the lungs, ears, skin, or gastrointestinal tract. In severe cases of *PGM3*-CDG, impaired bone marrow function may lead to a decrease in the production of all blood cells, resulting in a condition called bone marrow failure. Affected individuals usually also have allergies, asthma, or an inflammatory skin condition called eczema. People with *PGM3*-CDG may develop autoimmunity, which occurs when the body attacks its own tissues and organs by mistake. Persistent illness may cause affected children to grow more slowly than other individuals.

Additionally, people with *PGM3*-CDG often have abnormally high levels of immune system proteins called antibodies (also known as immunoglobulins), particularly immunoglobulin E (IgE). Antibodies help protect the body against infection by attaching to specific foreign particles and germs, marking them for destruction. The effect of abnormal levels of antibodies in *PGM3*-CDG is unclear.

People with *PGM3*-CDG often have intellectual disability, delayed development, and weak muscle tone (hypotonia). Many affected individuals have skeletal abnormalities involving the ribs or bones in the hands, feet, or spine. Some people with this condition have distinct facial features, such as a flat or sunken appearance of the middle of the face (midface hypoplasia), small chin (micrognathia), full lips, downturned corners of the mouth, and wide nostrils that open to the front rather than downward. *PGM3*-CDG can also cause problems in the lungs, gastrointestinal tract, and kidneys.

Lifespan varies widely in people with *PGM3*-CDG; some do not survive past infancy while others live into late adulthood.

## Frequency

*PGM3*-CDG is a rare disorder, although its prevalence is unknown. Approximately 40

people with the condition have been described worldwide.

## Causes

Mutations in the *PGM3* gene cause *PGM3*-CDG. This gene provides instructions for making an enzyme called phosphoglucomutase 3 (PGM3). The PGM3 enzyme is involved in a process called glycosylation, which attaches groups of sugar molecules ( oligosaccharides) to proteins. During this process, complex chains of sugar molecules ( oligosaccharides) are added to proteins and fats (lipids). Glycosylation modifies proteins and lipids so they can perform a wider variety of functions.

Mutations in the *PGM3* gene lead to the production of a PGM3 enzyme with reduced activity. Without a properly functioning enzyme, glycosylation cannot proceed normally. The wide variety of signs and symptoms in *PGM3*-CDG are likely due to impaired glycosylation of proteins and lipids that are needed for the normal function of many organs and tissues. Immune system proteins are highly dependent on glycosylation to function normally, which likely explains why people with *PGM3*-CDG have immune deficiency.

Learn more about the gene associated with PGM3-congenital disorder of glycosylation

- PGM3

## Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

## Other Names for This Condition

- AGM1 deficiency
- CID due to PGM3 deficiency
- Combined immunodeficiency due to PGM3 deficiency
- Deficiency of N-acetylglucosamine-phosphate mutase 1
- Deficiency of phosphoglucomutase 3
- Immunodeficiency 23
- Immunodeficiency with hyper IgE and cognitive impairment
- Immunodeficiency-vasculitis-myoclonus syndrome
- PGM3 deficiency
- PGM3-CDG
- PGM3-related congenital disorder of glycosylation
- Phosphoglucomutase 3 deficiency

- Phosphoglucomutase deficiency type 3

## Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Immunodeficiency 23 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C4014371/)

Genetic and Rare Diseases Information Center

- PGM3-CDG (https://rarediseases.info.nih.gov/diseases/4331/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Catalog of Genes and Diseases from OMIM

- IMMUNODEFICIENCY 23; IMD23 (https://omim.org/entry/615816)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28PGM3%5BALL%5D%29+AND+%28Congenital+Disorders+of+Glycosylation%5BALL%5D%29%29+OR+%28%28PGM3%5BALL%5D%29+AND+%28immunodeficiency%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

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