The genetics of Pompe disease

Pompe disease is a rare genetic disorder affecting approximately 1 in 40,000 men and women across all ethnic groups. The disease results from the deficiency of an enzyme called acid alpha glucosidase (GAA), which breaks down the complex sugar glycogen. Accumulation of glycogen becomes toxic and damages cells and tissues, particularly muscles.

Symptoms can develop either early in childhood (infantile-onset) or later in life (late-onset). These classifications are based on the age of symptom onset, how much the cell and tissue damage affects the person's organs, and rate of progression. People with absent or minimal GAA activity generally have severe, early-onset disease, while people with more GAA activity generally have a later-onset condition—although exceptions have been reported.

Since Pompe disease is a genetic condition, it's inherited from a person's parents. Everyone has two copies of the *GAA* gene. If someone has one faulty copy of the gene, they do not show any symptoms and are called a "carrier." If both parents are carriers, they have a 25% chance of having a child with two faulty copies (and, as a result, developing Pompe disease).

Treatment for both infantile and late-onset forms of Pompe disease is enzyme replacement therapy.

How can genetic testing for Pompe disease help?

Genetic testing can:

confirm or clarify a clinical diagnosis, helping you and your healthcare provider make informed medical decisions, including treatment, surveillance, and preventive options.

identify other at-risk relatives for whom genetic testing is recommended.

inform reproductive options. A genetic diagnosis is required to access reproductive preventive techniques such as pre-implantation genetic testing through IVF.

Who should consider genetic testing?

This test is intended for any individual, child or adult, who has a suspected clinical diagnosis of Pompe; progressive limb-girdle muscular weakness; or an abnormal newborn screen result for Pompe. Further, any individual with prior low acid alpha-glucosidase (GAA) enzyme activity should consider genetic testing for Pompe disease.

Family members of pople diagnosed with Pompe disease should also consider testing. Invitae offers a family variant testing program.

For those who have a family history of Pompe disease and are planning a family themselves, Invitae offers comprehensive carrier screening. Invitae's comprehensive carrier panel costs $250 USD and can be ordered through your healthcare provider or through a family planning clinic.

Why should I choose Invitae for genetic testing?

Invitae is a CLIA-certified and CAP-accredited genetic testing company whose mission is to bring comprehensive genetic information into mainstream medicine to improve healthcare for billions of people. We strive to make high-quality genetic testing affordable and accessible.

The Invitae Pompe Disease Test analyzes the *GAA* gene, which is the only gene known to cause Pompe disease (also called glycogen storage disease, type II [GSD II]). Testing for Pompe disease is also available as part of our broader Invitae Comprehensive Lysosomal Storage Disorders Panel.
To assist healthcare providers in distinguishing Pompe disease (including the later onset form) from other diseases that can have similar symptoms, we also offer the *GAA* gene as part of the Invitae Limb-Girdle Muscular Dystrophy Panel and the Invitae Comprehensive Muscular Dystrophy Panel.

Simple billing, no surprises

When genetic testing is not covered through your healthcare system, you have the option to pay $250 USD for your diagnostic genetic testing. This option requires upfront payment before test results are released. In addition, your healthcare provider must place the order online and provide your e-mail address so that we can send you a link to pay online using a credit card.

How to order a test

- Speak to your healthcare provider to discuss testing options. To help guide your discussion, we have a letter outlining the specifications of the test that you can share with your doctor.

- Invitae will work with your healthcare provider to answer any questions about the testing, ordering, or billing process. The self-pay cost is $250 USD.

- A saliva, cheek swab or blood sample is required and collection kits can be sent directly to your home to assist with remote consultations.

- Invitae's turnaround time is 10–21 days from when your sample arrives at our San Francisco lab.

- The results are sent to your ordering clinician via Invitae's secure online portal.

For more information

Contact your local representative for Australia and New Zealand at apac@invitae.com.

Reference: Kishnani, PS, *et al.* Pompe disease diagnosis and management guideline. *Genet. Med.* 2006; 8(5):267-88.

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