

What is mucopolipidosis type II and III, *GNPTAB*-related?

Mucopolipidosis is a disease with variable severity and age of onset. Individuals with mucopolipidosis types II and III have defects in the GlcNAc-1-phosphotransferase enzyme, which leads to a decrease in the number of digestive enzymes in lysosomes and the accumulation of carbohydrates and fats in tissues.^{1,2,3,4} Signs and symptoms of the more severe form of the disease, type II, are due to the absence of enzyme activity, and signs and symptoms of the milder form of the disease, type III, are due to residual enzyme activity. Signs and symptoms include slow growth, heart valve abnormalities, recurrent respiratory and ear infections, skeletal abnormalities, and distinctive facial features.^{3,4} Mucopolipidosis types II and III belong to a group of diseases called lysosomal storage disorders.^{1,2}

What are the symptoms of mucopolipidosis types II and III, *GNPTAB*-related, and what treatment is available?

Individuals with type II show signs and symptoms at birth and usually do not survive past early childhood. Symptoms may include:^{1,3}

- Slow growth and hypotonia (poor muscle tone)
- Weak cry
- Developmental delay
- Bone abnormalities
- Joint problems
- Umbilical or inguinal hernia
- Heart valve abnormalities
- Distinctive facial features
- Frequent ear and respiratory infections
- Intellectual disability
- Hepatomegaly (enlarged liver)

Individuals with type III show signs and symptoms at about three years of age and usually survive into adulthood. Symptoms may include:^{2,4}

- Slow growth and short stature
- Stiff joints
- Skeletal abnormalities
- Osteoporosis (fragile bones)
- Heart valve abnormalities
- Mild corneal clouding
- Distinctive facial features
- Frequent ear and respiratory infections
- Mild intellectual disability

Treatment is supportive and focuses on prevention of complications and management of symptoms.^{1,2}

How are mucopolipidosis types II and III, *GNPTAB*-related, inherited?

Mucopolipidosis types II and III are autosomal recessive diseases caused by mutations in the *GNPTAB* gene.^{3,4} An individual who inherits one copy of a *GNPTAB* gene mutation is a carrier. Carriers are not affected with mucopolipidosis type II or III. An individual who inherits two *GNPTAB* mutations, one from each parent, is expected to be affected with mucopolipidosis type II or III.

If both members of a couple are carriers of mutations in the same gene, the risk for an affected child is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing.

Who is at risk for mucopolipidosis types II and III, *GNPTAB*-related?

Mucopolipidosis types II and III can occur in individuals of all races and ethnicities, with an estimated carrier frequency of 1 in 152.^{5,6} The conditions are common in individuals of French Canadian ancestry, specifically those from the Saguenay-Lac-Saint-Jean region of Quebec, where the carrier frequency is 1 in 39.⁷

Having a relative who is a carrier or who is affected can increase an individual's risk to be a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

What does a negative test result mean?

A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

Where can I get more information?

Genetics Home Reference: <http://ghr.nlm.nih.gov/condition/mucopolipidosis-ii-alpha-beta>

Genetics Home Reference: <http://ghr.nlm.nih.gov/condition/mucopolipidosis-iii-alpha-beta>

The International Advocate for Glycoprotein Storage Diseases (ISMARD):
http://www.ismrd.org/glycoprotein_diseases/mucopolipidosis_ii

References

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