

# Mucopolipidosis III Alpha/Beta

Subjects: Genetics

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## Definition

Mucopolipidosis III alpha/beta is a disorder that affects many parts of the body. Signs and symptoms of this condition typically appear around age 3 and worsen slowly over time.

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## 1. Introduction

Individuals with mucopolipidosis III alpha/beta grow slowly and have short stature. They also have stiff joints and dysostosis multiplex, which refers to multiple skeletal abnormalities seen on x-ray. Many affected individuals develop low bone mineral density (osteoporosis), which weakens the bones and makes them prone to fracture. Osteoporosis and progressive joint problems also cause bone pain that becomes more severe over time in people with mucopolipidosis III alpha/beta.

People with mucopolipidosis III alpha/beta often have heart valve abnormalities and mild clouding of the clear covering of the eye (cornea). Their facial features become slightly thickened or "coarse" over time. Affected individuals may also develop frequent ear and respiratory infections. About half of people with this condition have mild intellectual disability or learning problems. Individuals with mucopolipidosis III alpha/beta generally survive into adulthood, but they may have a shortened lifespan.

## 2. Frequency

Mucopolipidosis III alpha/beta is a rare disorder, although its exact prevalence is unknown. It is estimated to occur in about 1 in 100,000 to 400,000 individuals worldwide.

## 3. Causes

Mutations in the *GNPTAB* gene cause mucopolipidosis III alpha/beta. This gene provides instructions for making a part (subunit) of an enzyme called GlcNAc-1-phosphotransferase. This enzyme helps prepare certain newly made enzymes for transport to lysosomes. Lysosomes are compartments within the cell that use digestive enzymes to break down large molecules into smaller ones that can be reused by cells. GlcNAc-1-phosphotransferase is involved in the process of attaching a molecule called mannose-6-phosphate (M6P) to specific digestive enzymes. Just as luggage is tagged at the airport to direct it to the correct destination, enzymes are often "tagged" after they are made so they get to where they are needed in the cell. M6P acts as a tag that indicates a digestive enzyme should be transported to the lysosome.

Mutations in the *GNPTAB* gene that cause mucopolipidosis III alpha/beta result in reduced activity of GlcNAc-1-phosphotransferase. These mutations disrupt the tagging of digestive enzymes with M6P, which prevents many enzymes from reaching the lysosomes. Digestive enzymes that do not receive the M6P tag end up outside the cell, where they have increased activity. The shortage of digestive enzymes within lysosomes causes large molecules to accumulate there. Conditions that cause molecules to build up inside lysosomes, including mucopolipidosis III alpha/beta, are called lysosomal storage disorders. The signs and symptoms of mucopolipidosis III alpha/beta are most likely due to the shortage of digestive enzymes inside lysosomes and the effects these enzymes have outside the cell.

Mutations in the *GNPTAB* gene can also cause a similar but more severe disorder called mucopolipidosis II alpha/beta. These mutations completely eliminate the function of GlcNAc-1-phosphotransferase. Mucopolipidosis III alpha/beta and mucopolipidosis II alpha/beta represent two ends of a spectrum of disease severity.

### 3.1. The Gene Associated with Mucopolysaccharidosis III Alpha/Beta

- GNPTAB

## 4. 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.

## 5. Other Names for This Condition

- ML III
- ML IIIA
- mucopolysaccharidosis III
- mucopolysaccharidosis III, variant
- mucopolysaccharidosis IIIA
- pseudo-Hurler polydystrophy

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## Keywords

genetic conditions