GNPTAB gene

N-acetylglucosamine-1-phosphate transferase subunits alpha and beta

Normal Function

The *GNPTAB* gene provides instructions for making two different parts, the alpha and beta subunits, of an enzyme called GlcNAc-1-phosphotransferase. This enzyme is made up of two alpha (α), two beta (β), and two gamma (γ) subunits. The gamma subunit is produced from a different gene, called *GNPTG*. GlcNAc-1-phosphotransferase helps prepare certain newly made enzymes for transport to lysosomes. Lysosomes are compartments within the cell that use digestive enzymes called hydrolases to break down large molecules into smaller ones that can be reused by cells.

GlcNAc-1-phosphotransferase is involved in the first step of making a molecule called mannose-6-phosphate (M6P). M6P acts as a tag that indicates a hydrolase should be transported to the lysosome. Specifically, GlcNAc-1-phosphotransferase transfers a molecule called GlcNAc-1-phosphate to a newly produced hydrolase. In the next step, a molecule is removed to reveal an M6P attached to the hydrolase. Once a hydrolase has an M6P tag, it can be transported to a lysosome.

Health Conditions Related to Genetic Changes

Mucolipidosis II alpha/beta

Around 50 mutations in the *GNPTAB* gene have been found to cause mucolipidosis II alpha/beta. These mutations prevent the production of any functional GlcNAc-1-phosphotransferase. Without this enzyme, hydrolases cannot be tagged with M6P and transported to lysosomes. Instead, hydrolases end up outside the cell and have increased digestive activity. The lack of hydrolases within lysosomes causes large molecules to accumulate there. Conditions that cause molecules to build up inside lysosomes, including mucolipidosis II alpha/beta, are called lysosomal storage disorders. The signs and symptoms of mucolipidosis II alpha/beta are most likely caused by the lack of hydrolases within lysosomes and the effects these enzymes have outside the cell.

Mucolipidosis III alpha/beta

Mutations in the *GNPTAB* gene have also been found to cause mucolipidosis III alpha/

beta. Affected individuals have mutations that result in reduced activity of GlcNAc-1-phosphotransferase, which disrupts tagging of hydrolases with M6P. Digestive enzymes that do not receive the M6P tag end up outside the cell, where they have increased activity. The shortage of these digestive enzymes within lysosomes causes large molecules to accumulate there. Mucolipidosis III alpha/beta is also considered to be a lysosomal storage disorder. The signs and symptoms of mucolipidosis III alpha/beta are most likely due to the shortage of hydrolases inside lysosomes and the effects these enzymes have outside the cell.

Other Names for This Gene

- alpha-beta GlcNAc-1-phosphotransferase
- DKFZp762B226
- GlcNAc phosphotransferase
- GlcNAc-1-phosphotransferase
- GNPTA
- GNPTA_HUMAN
- KIAA1208
- MGC4170
- N-acetylglucosamine-1-phosphate transferase
- N-acetylglucosamine-1-phosphate transferase alpha and beta subunits
- N-acetylglucosamine-1-phosphate transferase, alpha and beta subunits
- UDP-N-acetylglucosamine-lysosomal-enzyme N-acetylglucosamine
- uridine 5'-diphosphate-N-acetylglucosamine: lysosomal hydrolase N-acetyl-1-phosphotransferase

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of GNPTAB (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=79158[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28GNPTAB%5BTIAB%5D%29+OR+%28%28GlcNAc+phosphotransferase%5BTIAB%5D%29+OR+%28GNPTA%5BTIAB%5D%29+OR+%28N-acetylglucosamine-1-phosphate+transferase%5BTIAB%5D%29+OR+%28uridine+5'-diphosphate-N-acetylglucosamine%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- N-ACETYLGLUCOSAMINE-1-PHOSPHOTRANSFERASE, ALPHA/BETA SUBUNITS; GNPTAB (https://omim.org/entry/607840)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/79158)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=GNPTAB[gene])

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Genomic Location

The *GNPTAB* gene is found on chromosome 12 (https://medlineplus.gov/genetics/chromosome/12/).

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