Title: *GNPTAB*-Related Disorders *GeneReview* – Diagnostic testing used in the past
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Testing used in the Past to Confirm the Diagnosis of *GNPTAB*-Related Disorders

Enzyme assay. Testing of GNPTAB enzyme activity is not routinely performed as part of clinical diagnostic evaluations. In the past, demonstration of significant deficiency (1%-10% of normal) of the enzyme UDP-*N*-acetylglucosamine: lysosomal hydrolase *N*-acetylglucosamine-1-phosphotransferase (GNPTA) (EC 2.7.8.17), encoded by *GNPTAB*, confirmed the diagnosis of ML IIIαβ [Kudo et al 2005, Kudo et al 2006]. Although enzyme activity In GNPTAB-related disorders is deficient in all tissues (including leukocytes), the deficiency is pathogenic only in mesenchymal cells.

Phase-contrast or electron microscopic (EM). Demonstration of large amounts of dense cytoplasmic inclusions (I-cells) in cultured fibroblasts was previously used to help confirm the diagnosis of ML II and ML IIIαβ.

Note: On electron microscopy (EM) the mesenchymal cells in any tissue reveal large numbers of cytoplasmic vacuoles comprising swollen lysosomes bound by a unit membrane. The contents are pleomorphic, but not dense. This phenomenon observed in ML II, ML IIIαβ, and ML IIIγ, is not observed in any other lysosomal storage disorder.

The **activity of lysosomal enzymes** is severely reduced in I-cells, but significantly increased in the corresponding culture media.

References

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