

Gaucher Disease StripA^{ssay}

INTENDED USE

The *ViennaLab* Gaucher Disease StripA^{ssay} provides materials for the isolation of DNA from human whole blood, the *in vitro* amplification of glucocerebrosidase (GBA) gene sequences, and the subsequent detection of eight mutations and two recombinant alleles by reverse-hybridization.

INTRODUCTION

Gaucher disease is the most prevalent glycolipid storage disorder known. The disease is of autosomal recessive inheritance and characterized by glucocerebrosidase deficiency due to mutations in the GBA gene located on chromosome 1q. Since the GBA sequence was first published in 1985, more than 120 disease-producing alleles have been described. These include point mutations as well as complex alleles resulting from genetic rearrangements between the functional gene and the nearby pseudogene.

Enzyme deficiency results in accumulation of glucocerebroside within the reticuloendothelial system, leading to a very heterogeneous range of clinical manifestations, among them hepatosplenomegaly, anemia, thrombocytopenia, bone marrow suppression, bone lesions, and hyperpigmentation. The disease is panethnic and has been divided into three clinical phenotypes (types I-III), with the chronic non-neuronopathic type I being most common.

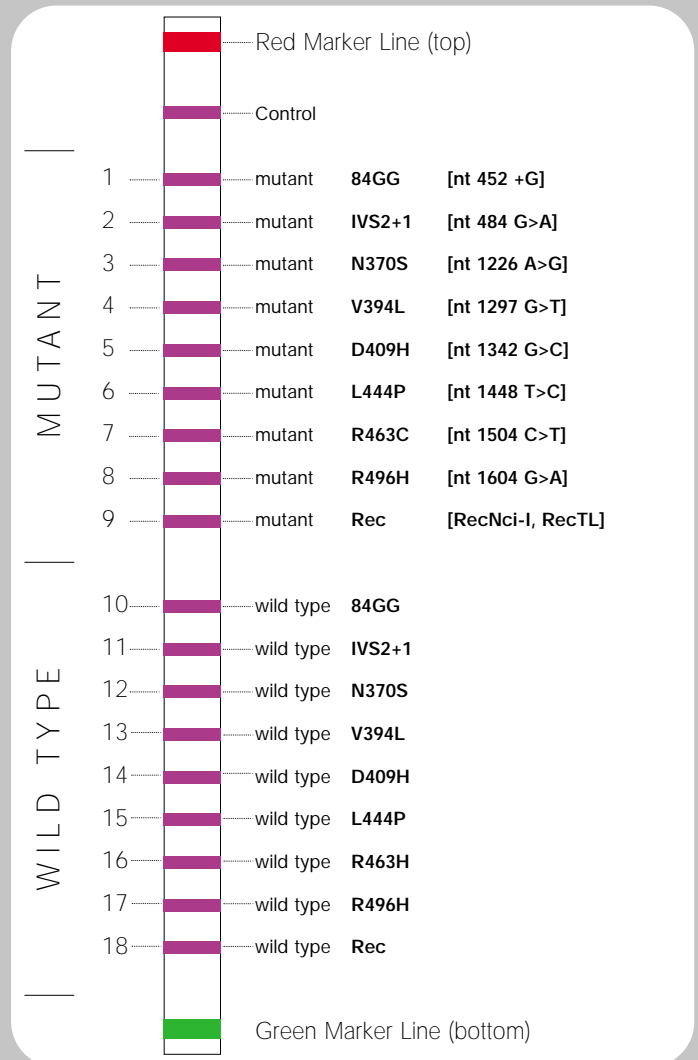
In the Ashkenazi Jewish population type I disease frequency is estimated to 1 in 500, with a carrier rate of approximately 1 in 10. Enzyme replacement therapy is available for Type I Gaucher disease, resulting in clinical improvement and increased quality of life.

PRINCIPLES OF THE ASSAY

The Gaucher Disease StripA^{ssay} is based on the reverse-hybridization principle, and includes three successive steps: DNA is isolated from anticoagulated blood by a rapid and convenient procedure. Then, GBA gene sequences are *in vitro* amplified and biotin-labelled in two multiplex amplification reactions. Finally, the amplification products are selectively hybridized to a test strip, which contains oligonucleotide probes (wild type- and mutant-specific) immobilized as parallel lines. Bound biotinylated sequences are detected using streptavidin-alkaline phosphatase and color substrates.

The assay covers eight of the most frequent GBA mutations: 84GG [452 +G], IVS2+1 [484 G>A], N370S [1226 A>G], V394L [1297 G>T], L444P [1448 T>C], R496H [1604 G>A] and two recombinant alleles [RecNci-I, RecTL].

References: Sorge J., West, C., Westwood, B., Beutler, E. (1985), Proc. Natl. Acad. Sci. USA 82, 7289-7293. Beutler, E., Gelbart, T. (1998), Blood Cells Mol. Dis. 24, 2-8.



Gaucher Disease^{StripA^{ssay}}

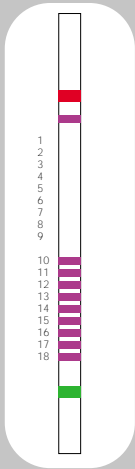
TEST RESULTS:

For each polymorphic position, one of three possible staining patterns may be obtained:

1. wild type probe only: *normal genotype*
2. wild type and mutant probe: *heterozygous genotype*
(«carrier» individual)
3. mutant probe only: *homozygous mutant genotype*
(«affected» individual)

EXAMPLES:

(A.) normal



(B.) L444P heterozygous



(C.) N370S - L444P compound heterozygous



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