Mutation Analysis of 12 Gaucher Disease Patients: Identification of Rare and Novel Mutations

Siebert, M.[1,2,3], Bock, H.[1,2], Michelin, K.[2], Pires, R.F.[2], Giugliani, R.[1,2,4], Coelho, J.C.[2,3], Saraiva-Pereira, M.L.[1,2,3].

[1]Laboratório de Identificação Genética, Centro de Pesquisas e [2]Serviço de Genética Médica, HCPA; [3]Depto. de Bioquímica e [4]Depto. de Genética, UFRGS, Porto Alegre, Brazil.

Gaucher disease (GD), an autosomal recessive disorder, is caused by deficiency of glucocerebrosidase (GBA) due to mutations in the gene coding for this enzyme. The GBA gene is located on chromosome 1q21 and comprises 11 exons. A highly homologous pseudogene is located 16 kb downstream from functional gene. To date, more than 250 mutations in GBA gene have been described. The aim of this study was identify the molecular profile of 12 unrelated GD patients that were previously searched for 4 common mutations (N370S, L444P, 84GG and IVS2+1) as well as del55pb and do not carry any of these mutations. DNA samples were extracted from peripheral blood. Functional gene was amplified by long-range PCR, followed by nested PCR and direct sequencing; in all methods, primers were specifically designed. Results obtained demonstrated 4 homozygous individuals for G377S mutation, 3 homozygous individuals for V398I mutation, 1 homozygous individual for N396T mutation and 1 homozygous individual for I489T. Three compound heterozygotes were also found with the following genotypes M123T/E349K, G377S/W378C, and N396T/I489T. The W378C mutation is due to a novel base change found in this study and we are currently searching samples from normal individuals for this alteration. Mutation analysis in the entire GBA gene is essential for the establishment of genotype/phenotype correlations. Association of molecular with phenotypic data is relevant for genetic counseling and orientation regarding clinical outcome as well as treatment in some cases.

Key words: Gaucher disease, GBA gene, Mutation analysis
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