Comment

Definition of the correct sequence in the donor splice site of intron 2 in the human glucose 6-phosphate translocase gene

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Recently, Gerin et al. [1], using a candidate gene approach, have identified mutations of a putative human glucose 6-phosphate translocase (G6PT1), homologous to bacterial transporters of hexose 6-phosphate in two patients with glycogen storage disease type 1b (GSD1b). Annabi et al. [2], using homozygosity mapping on eight consanguineous families, have localized the gene for GSD1b to a 3.0 cM region on chromosome 11q23. In the Unigene database (National Center for Biotechnology Information, USA), the putative gene has been mapped electronically to a human transcript, number A007J44, located between D11S939 and D11S924 (117.9–120.8 cM), a region equivalent to a chromosome location of 11q23.3. The gene has subsequently been physically mapped to the same position by in situ hybridization [3].

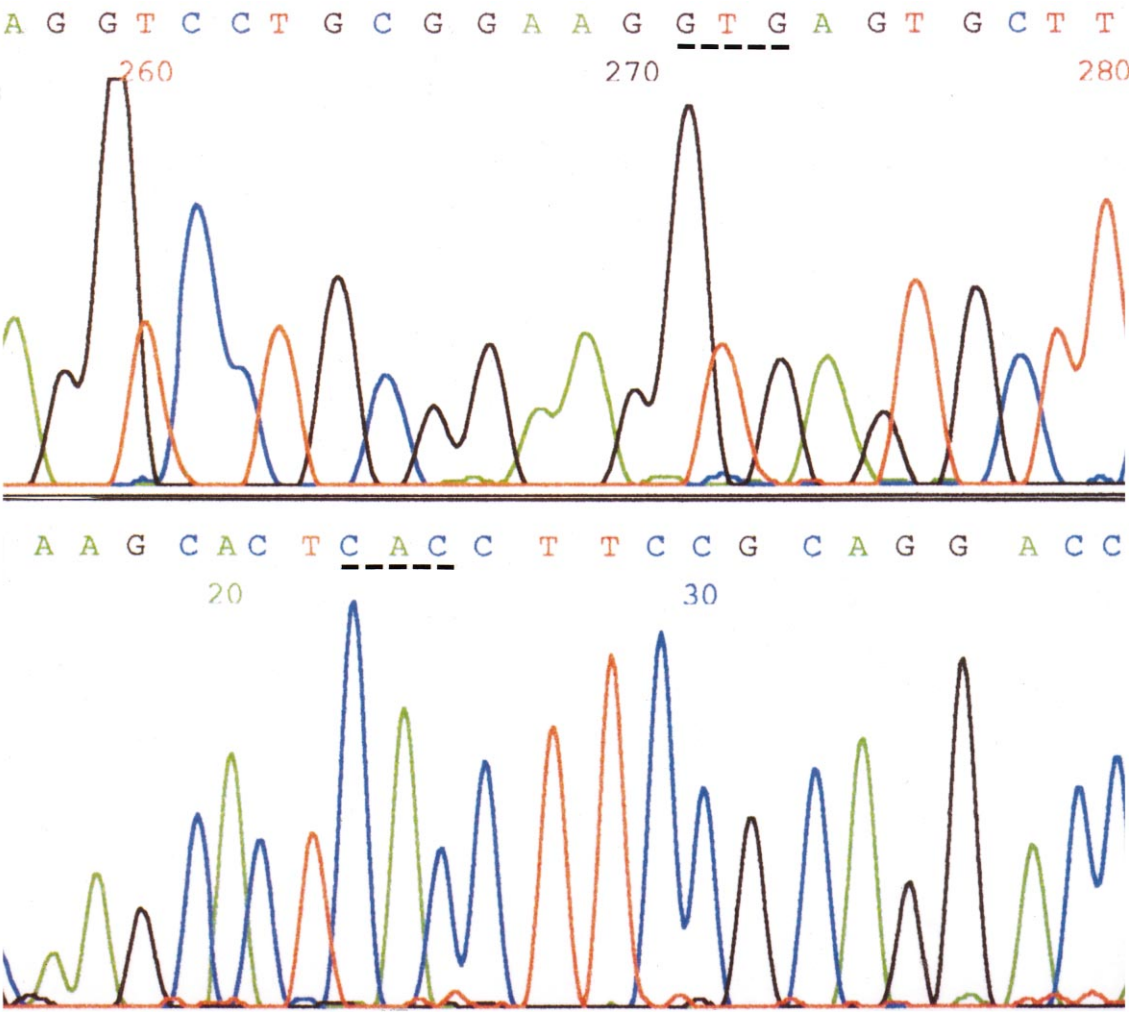

Fig. 1. DNA sequence of the human glucose 6-phosphate translocase gene at the exon 2/intron 2 boundary. Sequences of the forward strand (upper panel) and reverse strand (lower panel) are shown. The sequence variation is underlined.

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A number of mutations have been identified in G6PT1 gene [4]. A splicing mutation involving deletion of three bases at the donor splice site of intron 2, i.e. IVS2+1delGTG, has been reported by Macolongo et al. (patient number 10) [3]. The DNA sequence at the donor splice site reported by the authors was 5′-gtggtgagtg-3′, whereas the mutation deleted one gtg trinucleotide at the 5′ end, i.e. 5′-gtgagtg-3′. This mutation was detected in the mother and father of the patient. The authors suggested that this mutation is likely to determine a splicing error between exons 2 and 3, even though no direct proof was presented since mRNA from this patient was not available.

In the course of mutation analysis of the G6PT1 gene in a patient with GSD1b, we have identified the same deletion in homozygous form by direct sequencing in both directions. However, we also detected the same homozygous deletion in 30 normal Chinese individuals by DNA sequencing in both directions Fig. 1. All subjects provided informed consent. These results suggest that IVS2+1delGTG is not the cause of genetic disease. Our findings were subsequently confirmed by Marcolongo et al. [5] who, after having been made aware of the above results, have discovered the occurrence of a cloning artifact in their original clone which resulted in insertion of a GTG triplet in the donor splice site of intron 2.

References

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