A Caucasian boy with Gilbert’s syndrome heterozygous for the (TA)₈ allele

A Caucasian boy was found to be heterozygous for the (TA)₈ allele with genotype (TA)₆/(TA)₈ after molecular analysis of the promoter region of exon 1A. Our finding of a (TA)₈ repeat, which was recently observed in a family of Italian descent, is reported for the first time as being present in the Greek population.

Sir,

Gilbert's syndrome is an inherited disorder of hepatic bilirubin metabolism occurring in the population with a frequency ranging from 2-13%. A variant A(TA)₇-TAA element in the promoter region of the gene for bilirubin UDP-glucuronosyltransferase-1 which reduces the efficiency of transcription initiation, has been associated with the syndrome. The molecular pathology of Gilbert's syndrome has been very recently reviewed by Sampietro and Iolascon, while analysis of the A(TA)₇-TAA motif was reported in homozygous β-thalassemia patients, as well as in glucose-6-phosphate dehydrogenase deficient neonates, providing a better understanding of the genetics of these conditions. The presence of seven TA repeats ([TA]₇) in white populations has been correlated with increased serum total bilirubin levels in Gilbert’s syndrome patients as well as in normal subjects. However, Bancroft et al. observed that people of African ancestry, in addition to 6 and 7 (TA) repeats, also had 5 and 8 repeats. The investigators suggested that the unstable UGT1A1 polymorphism may serve to fine tune the plasma bilirubin level within population groups, maintaining it at a high enough level to provide protection against oxidative damage but not so high as to cause kernicterus in infants. A recent article by Iolascon et al. was published in this journal reporting the first Caucasian case with Gilbert’s syndrome heterozygous for the (TA)₈ allele.

We report on a 3-year old Caucasian boy admitted to our Department with febrile seizures. His total serum bilirubin concentration was 2.5 mg/dL. Genotypic analysis of the promoter region of exon 1A was performed by polymerase chain reaction; amplified products were separated on 6% denaturing polyacrylamide gel and the size was determined by Apple Macintosh computer software (VISTRA 725 version 2.0 and fragmentor analysis software) (100 bp A(TA)₇-TAA allele). Our patient was found to be heterozygous for the (TA)₈ allele with genotype (TA)₆/(TA)₈ (Figure 1). We have previously analyzed the promoter region of UGT1A1 gene in 117 children and observed no other cases with the (TA)₈ repeat. This is the second case of a Caucasian patient with Gilbert’s syndrome with the rare (TA)₈ repeat following the first report from Iolascon et al. Our finding confirms the observation by Iolascon et al. that this extremely rare mutation is a recent spontaneous mutation and is the first case of a patient of Greek origin with Gilbert’s syndrome with the (TA)₈ repeat.

Aspasia Tsezou,* Maria Tziatis,° Sofia Kitsiou,* Emmanuel Kazavarakis,* Angeliki Gallia,* Emmanuel Kanavakis*
*Second Department of Pediatrics, University of Athens, P.&A.Kyriakou Children’s Hospital, Athens; °First Department of Pediatrics, University of Athens, Agia Sofia Children’s Hospital, Dept. of Molecular Medicine, Athens, Greece

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Correspondence
Aspasia Tsezou, PhD, 2nd Dept. of pediatrics, University of Athens, P. & A. Kyriakou Children’s Hospital, 115 27 Athens, Greece. Fax: international +30-1-7774383.

References