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研究报告

一个中国Gilbert综合征家系的遗传学分析

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摘要 对一个中国汉族Gilbert综合征遗传家系致病基因突变位点进行鉴定，以期了解该病的分子遗传学基础。首先提取先证者基因组DNA，PCR扩增尿苷二磷酸葡萄糖醛酸转移酶UGT1A1基因的5个外显子，以琼脂糖电泳鉴定PCR产物，纯化后直接测序鉴定。基因扫描显示，与血清胆红素水平密切相关的UGT1A1基因在第1和第5外显子存在纯合突变，而 UGT1A1基因启动子区域和内含子/外显子剪接边界位点序列未检测到突变。进一步对其他家系成员该基因的相应位点进行突变检测，结果显示他们在第1和第5外显子也存在杂合突变，其中还有两个成员在启动子区域检测到(TA)插入突变。对家系成员未抗凝新鲜血液进行生化检测证实了基因突变分析的结果。综合以上结果发现该家系三种突变并存，致病因素为第1和/或第5外显子突变，为显性遗传，两种突变位点纯合导致先证者出现严重胆红素代谢功能障碍。该家系因此成为Gilbert综合征突变位点及其致病机理研究的一个典型临床病例。

关键词 Gilbert综合征；基因突变；UGT1A1

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Genetic Analysis of the UGT1A1 Gene Mutation Sites in a Chinese Family Suffered from Gilbert's Syndrome

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Abstract

To learn the variation in the gene for UGT1A1 enzyme, the genetic mechanism in a Chinese Han nationality family suffered from Gilbert's syndrome was studied. At first, genomic DNA from peripheral blood of the sufferer in this family was used for amplifying all of the five exons of the UGT1A1 gene by PCR, and then direct sequencing of the PCR product was applied to analyze gene mutation. The results showed that there existed a G-->A homozygous transition at nucleotide 211 leading the substitution of arginine for glycine at position 71 of corresponding protein product (G71R) and a T-->G homozygous transition at nucleotide 1456 leading the substitution of aspartic acid for tyrosine at position 486 of corresponding protein product (Y486D). No mutation was detected in promoter region and the splicing junction sites. The relevant mutation sites of the other family members were sequenced and identified to be heterozygous in the two above-mentioned mutation sites and in the TA repeat mutation in the promoter region. Furthermore, fresh blood samples were collected from all of the members to detect the serum bilirubin levels to determine the sufferer. The result was consistent with the mutation analysis. It could thus be inferred that this family was caused by mutation in the open reading frame of the gene UGT1A1.

Key words bilirubin uridine 5'-diphosphate-glucuronosyltransferase gene mutation Gilbert's syndrome

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