遗传 2007 29 (1): 37—40 ISSN: 0379-4172 CN: 11-5450/R

研究报告

粘多糖贮积症Ⅱ型患者*IDS*基因的2个新突变

窦薇[1]，彭超[1]，郑俊克[1]，顾学范[2]

1. 上海交通大学医学院附属新华医院, 上海 200092;
2. 上海市儿科医学研究所, 上海 200092

收稿日期 2006-3-5 修回日期 2006-5-9 网络版发布日期 2006-12-4 接受日期

摘要

为了研究粘多糖贮积症II型(MPS Ⅱ)患者发病的分子遗传学机制，采用PCR扩增艾杜糖-2-硫酸酯酶(*IDS*)基因突变热点区(外显子2、3、5、7、8和9)、DNA测序分析和限制性内切酶图谱分析的方法，对2个粘多糖贮积症Ⅱ型家系进行了遗传突变分析。结果表明，2个家系患者的*IDS* 基因分别出现IVS 6-1g→a和c.1587~1588 ins T 2个新突变。前者属于单碱基替换，位于内含子6的3′端剪接位点，导致跨外显子剪接；后者属于插入突变，插入点位于外显子9的cDNA 1,587和1,588碱基之间，是迄今为止报道的人类*IDS*基因插入突变中最接近肽链末端的突变，导致移码突变和转录提前终止。经限制性酶切分析，证实2个家系中的患者母亲是突变基因的携带者，符合该病X染色体隐性遗传的规律。另外,在对随机抽取的50名正常人及另外6名不相关的粘多糖病人的测序分析中，未检测到这2个突变，说明不是多态性。对于筛查所得的2个新突变是否是患者的致病原因，尚需进一步证实。

关键词 粘多糖贮积症Ⅱ型 MPSⅡ 艾杜糖-2-硫酸酯酶 IDS 家系 突变

分类号

Detection of two novel mutations of iduronate-2-sulfatase gene in pa-tients with mucopolysaccharidosis type Ⅱ

DOU Wei[1], PENG Chao[1], ZHENG Jun-Ke [1], GU Xue-Fan [2]

1. *Xinhua Hospital, Shanghai Jiao Tong University, School of Medicine, Shanghai* 200092, *China;* 2. *Shanghai Institute for Pediatric Research, Shanghai* 200092, *China*

Abstract

<P>In the present study, through PCR amplification and direct sequencing of mutation “hotspots”, we were able to identify two novel mutations in the human iduronate-2-sulfatase (<EM>IDS</EM>) gene in two patients from unrelated families with mucopolysaccharidosis type Ⅱ (MPS Ⅱ). The novel mutation IVS 6 -1g→a affected the 3′ splice acceptor site of intron 6, and was predicted to result in exon skipping. The novel mutation c.1587-1588 ins T involved a single base insertion be-tween nucleotides 1,587 and 1,588 in exon 9, and was predicted to result in frame shift and premature termination. The two novel mutations did not occur in 6 other unrelated MPS patients or in 100 alleles from normal individuals, indicating that they were not polymorphisms. The PCR-restriction enzyme digestion showed that the two newly identified mutations were of maternal origin, which was consistent with the X-linked recessive disorder. These findings suggest that the <EM>IDS</EM> gene mutations could be detected by amplifying mutation “hotspots”, direct sequencing and restriction digestion analysis, and the newly identified mutations may be disease-causing.</P>

Key words mucopolysaccharidosis type Ⅱ MPS Ⅱ iduronate-2-sulfatase IDS family mutation

DOI: 10.1360/yc-007-0037

通讯作者 顾学范 guxuefan@online.sh.cn