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研究报告

PON基因簇序列变异筛查研究

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摘要 摘要：系统筛查PON1、PON2及PON3基因编码、剪接及侧翼序列，以期发现所有潜在功能多态基因座，为进一步探讨PON基因家族与心血管疾病的关系做准备。随机选择48例冠心病患者作为筛查对象，以PCR产物直接测序检测DNA序列变异。扩增片断涵盖整个外显子，其两侧部分内含子区域及5’和3’侧翼序列。（1）13.9kb测序范围内共发现31个多态性基因座，均为单核苷酸多态（SNP），其中17个SNP为首次报道。（2）国人中SNP构成和等位基因频率与高加索人群存在显著差异。（3）一个基因内部两个或多个多态性基因座间存在完全或近乎完全连锁不平衡相当常见。中国汉族人群中PON基因簇多个潜在功能多态基因座的识别及这些基因座间的强连锁不平衡状态，为在国人中探讨PON基因簇与心血管疾病关系提供了重要的基础数据。

关键词 单核苷酸多态；遗传；PON基因簇

分类号 Q987

Polymorphisms Screening of PON Gene Cluster

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Abstract

To identify all putative functional polymorphisms of PON gene cluster in Chinese Han population. Common polymorphisms of PON1, PON2 and PON3 gene were identified by directly sequencing of genomic DNAs derived from 48 randomly selected patients with coronary heart disease. We designed PCR arrays to amplify regions up to about 1kb upstream from transcription-initiation sites, i.e., putative promoter regions, all exons and adjacent non-coding regions. In a total length of 13.9 kb explored, we identified thirty-one SNPs, of which, 17 were first reported. A new coding polymorphism was detected in PON1 gene, which gives rise to amino acid substitutions of arginine (R) for glycine (G) at codon 160, whereas L54M polymorphism, which is common in white population, was not detected in our Han population. Among the five polymorphisms identified in PON3 gene, one in the promoter regions at position –133 (C/A) was located in a potential binding site for transcription factor LF-A1. Allele frequencies of some polymorphisms are significantly different from those reported in Caucasian populations. Complete or nearly complete association between polymorphisms was frequently observed. The identified multiple putative functional polymorphisms in PON gene cluster and their linkage disequilibrium patterns in combination with the population specific frequencies are of values for futher association studies of PON gene cluster with cardiovascular disease.

Key words single nucleotide polymorphism genetics paraoxonase gene cluster

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