

论文

原发性肝细胞癌与 *IL-2*、*IFN-γ* 基因多态性关系

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摘要:

目的 探讨细胞因子 *IL-2* 基因-330T/G(rs2069762)位点和 *IFN-γ* 基因-1615C/T(rs2069705)、+5171A/G(rs2069727)位点单核苷酸多态性与原发性肝细胞癌(HCC)发生的关系。**方法** 采用医院为基础的病例对照研究方法于2007年6月—2010年7月在广西医科大学第一附属医院和广西肿瘤医院收集784例HCC患者和同期在广西医科大学第一附属医院及广西区医院体检中心1 017名健康对照人群进行环境暴露调查;采用Taq-Man荧光定量PCR技术对上述位点进行分型,应用logistic回归模型分析组间基因-环境和基因-基因的交互作用。**结果** *IFN-γ*的-1615C/T和+5171A/G位点存在连锁不平衡($D' = 0.976, r^2 = 0.549, P = 2.22 \times 10^{-16}$),单倍型CG在人群中发生频率 < 0.03 ,其他3种单倍型CA、TA、TG频率在病例组和对照组间分布差异均无统计学意义($P > 0.05$);*IL-2*-330T/G和*IFN-γ*-1615C/T、+5171A/G3个位点的基因型在HCC患者和健康对照人群中分布差异均无统计学意义($P > 0.05$);吸烟、饮酒和携带HBV等环境暴露因素与-330T/G位点的突变基因G对HCC的发生有协同作用,交互作用指数S分别为1.38、1.50、1.03;吸烟、饮酒、有肝癌相关家族史和携带HBV等环境暴露因素与-1615C/T、+5171A/G位点的基因多态性在HCC患病风险中存在负交互作用;logistic回归分析结果表明,携带*IL-2*的-330T/G位点突变基因G并且同时携带*IFN-γ*的-1615C/T、+5171A/G位点的突变纯合子TT/GG能增加HCC患病风险($OR = 1.84, 95\% CI = 1.08 \sim 3.83$)。结论 *IL-2*基因-330T/G和*IFN-γ*基因-1615C/T、+5171A/G位点多态性与环境暴露因素存在交互作用,基因-环境、基因-基因交互作用可能增加HCC发生风险。

关键词: 原发性肝细胞癌(HCC) 病例对照研究 *IL-2* *IFN-γ* 单核苷酸多态性(SNP)

Gene polymorphism of *IL-2*, *IFN-gamma* and primary hepatocellular carcinoma

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Abstract:

Objective To explore the association of interleukin-2(*IL-2*)-330T/G(rs2069762),interferon gamma (*IFN-γ*)-1615C/T(rs2069705) and +5171A/G(rs2069727) single nucleotide polymorphisms(SNPs) with the incidence of primary hepatocellular carcinoma(HCC),and to provide the reference for HCC risk assessment.Methods A hospital-based case-control study was carried out.Totally 784 HCC patients from First Affiliated Hospital of Guangxi Medical University and Guangxi Cancer Hospital and 1 017 controls from Physical Examination Center of First Affiliated Hospital of Guangxi Medical University and Guangxi People's Hospital were investigated with a environmental exposure questionnaire during June 2007-July 2010.TaqMan fluorescence quantitative PCR technology was adopted to detect the SNPs of the genes.The interactions of gene-environment and gene-gene were analyzed with logistic regression model.Results -1615C/T and +5171A/G of *IFN-γ* had linkage disequilibrium ($D' = 0.976, r^2 = 0.549, P = 2.22 \times 10^{-16}$).The frequency of haplotype CG was less than 0.03 in the study population.CA,TA and TG had no statistically significant difference among the three groups($P > 0.05$).There were no statistically significant differences in the polymorphisms of *IL-2* -330T/G,*IFN-γ*-1615C/T and +5171A/G between HCC patients and controls ($P > 0.05$).The interactions of *IL-2*-330T/G mutant allele G with smoking,alcohol drinking and carrying HBV were positive with the synergy indexes(S) of 1.38,1.50,and 1.03,respectively.The individuals carrying *IL-2*-330T/G mutant gene G and both *IFN-gamma*-1615C/T and +5171A/G mutant homozygote (TT and GG) had increased risk of HCC(odds ratio=1.84,95% confidence interval:1.08-3.83).Conclusion There are interactions among polymorphisms of *IL-2*-330T/G and *IFN-γ*-1615C/T,+5171A/G and the environmental exposure.The gene-environment and gene-gene interaction may increase the risk of HCC.

Keywords: primary hepatocellular carcinoma case-control study interleukin 2 gene interferon gamma gene single nucleotide polymorphism

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