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碱基切除修复通路基因XRCC1、hOGG1多态性与吸烟对肺癌患者生存的影响

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Effects of Base Excision Repair Pathway Gene XRCC1 hOGG1 Polymorphisms and Smoking on the Survival of Lung Cancer Patients

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全文: PDF (724 KB) HTML (1 KB) 输出: BibTeX | EndNote (RIS) 背景资料

摘要 DNA损伤修复作为维持体内基因稳定性和修复DNA损伤的重要机制，在肿瘤的发生、发展、转归及预后中发挥重要作用，DNA损伤修复基因多态性通过影响DNA损伤修复能力进而影响肿瘤患者生存。本研究旨在探讨DNA损伤修复基因XRCC1、hOGG1多态性对肺癌患者生存的影响。方法：收集420例原发性非小细胞肺癌病例，采用TaqMan SNP技术检测肺癌患者外周血DNA XRCC1（rs25487）和hOGG1（rs1052133）多态性。采用Kaplan-Meier 法分析生存情况，Log-rank 法进行单因素检验，Cox 回归用来计算调整混杂因素的风险比（Hazard Ratio， HR）。结果：患者临床特征和预后风险的分析显示，年龄≥60岁和病理分期晚期（Ⅲ/Ⅳ期）是影响肺癌预后的独立危险因素，P值分别为1.000E-4和3.828E-11。DNA修复基因XRCC1和hOGG1多态性与肺癌患者生存情况的分析未见不同基因型的生存曲线的分布具有统计学差异。按照吸烟情况分层后，在轻度吸烟者（吸烟量<40包/年）中，携带hOGG1突变型G等位基因较携带野生型C基因型生存率低（P=0.021 3），经Cox回归分析显示携带G等位基因的患者死亡风险为野生型的8.24倍。而在非吸烟者和重度吸烟者中未见多态性对患者生存的影响。结论：本研究首次发现碱基切除修复通路基因hOGG1 rs1052133多态性对肺癌患者生存存在一定影响，尤其是在轻度吸烟者中，携带突变型等位基因增大肺癌患者死亡风险，相关机制有待进一步大规模样本验证。

关键词： 非小细胞肺癌 XRCC1 hOGG1 多态性 吸烟 预后

Abstract: Single nucleotide polymorphisms (SNPs) in DNA repair genes are believed to be associated with the survival of lung cancer patients because of their effects on the DNA repair capacity. This work aimed to define the role of DNA repair gene SNPs in non-small cell lung cancer (NSCLC) patients, and investigate the association of lung cancer survival with SNPs of x-ray repair cross-complementing group1 (XRCC1) and human 8-oxoguanine glycosylase1 (hOGG1). Methods: The Taqman SNP method was used to detect SNPs in XRCC1 (rs 25487) and hOGG1 (rs 1052133) genes, and evaluate their association with the overall survival of 420 Chinese patients with lung cancer. The association of lung cancer survival with genetic polymorphisms were evaluated by the Kaplan-Meier method and log-rank test. The Cox regression model was used to calculate the adjusted hazard ratio. Results: Advanced cancer stage and advanced age were independently associated with the overall survival of lung cancer patients (P = 1.000E-4 and P = 3.828E-11), respectively. XRCC1 and hOGG1 polymorphisms were not statistically associated with lung cancer survival in the total population studied. After stratification by smoking status and smoking amount, individuals with the hOGG1 mutant G genotype had a higher hazard ratio of death than those with the hOGG1 wild CC genotype in light smokers (log-rank P = 0.021 3, HR = 8.24). However, no association was found in nonsmokers and heavy smokers. Conclusion: To our knowledge, this is the first study to reveal the prognostic roles of the hOGG1 G genotype in the survival of Chinese NSCLC patients and patients with different smoking statuses. The data indicated that the hOGG1 G genotype was associated with lung cancer survival in light smokers. Large and well-designed studies with diverse populations and functional evaluations are warranted to confirm these findings.

Key words: NSCLC(Non-small cell lung cancer) XRCC1 (X-ray repair cross-complementing group1) hOGG1 (Human 8-oxoguanine glycosylase1) Polymorphism Smoking Prognosis

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