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论著

DNA修复酶基因MGMT启动子区异常甲基化与食管癌的关系

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摘要 背景与目的： 分析食管癌组织中MGMT启动子区CpG岛甲基化状态和食管癌发病风险的关系，探讨MGMT基因启动子的异常甲基化在食管癌筛查及早期诊断中的意义。 材料与方法： 对江苏淮安的91例新发食管癌病例的癌组织、癌旁组织及外周血血浆样本提取DNA，应用甲基化特异性PCR(MSP)分析MGMT启动子区CpG岛的甲基化状态；对食管癌组织和癌旁组织提取总RNA，采用SYBR GREEN I 实时荧光定量逆转录-聚合酶链反应(RT-PCR)测定MGMT的mRNA水平。 结果： MGMT启动子区CpG岛异常甲基化与食管癌发病风险增高有关联 (OR=7.750, 95%CI=2.736～21.955)；MGMT启动子区CpG岛甲基化状态与MGMT mRNA水平无显著相关；血浆循环DNA中MGMT启动子区CpG岛甲基化与癌组织中MGMT启动子区CpG岛甲基化相关(P<0.01)，血浆循环DNA中MGMT启动子区CpG岛甲基化检出率与癌组织中MGMT启动子区CpG岛甲基化检出率中度相关(Kappa=0.603, P<0.01)。 结论： MGMT基因的启动子区CpG岛的异常甲基化与食管癌发病风险增加有关；检测血浆循环DNA中MGMT基因启动子的异常甲基化，可为食管癌的筛查、早期诊断提供有价值的信息。

关键词 食管癌； MGMT； 甲基化； 循环DNA

Correlation of Promoter Hyper-methylation of O6-methylguanine-DNA Methyltransferase Gene and the Risk for Esophageal Cancer

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Abstract BACKGROUND AND AIM:To analyze whether promoter methylation of O6-methylguanine-DNA methyltransferase (MGMT) gene is associated with the risk for esophageal squamous cell carcinoma(ESCC), and to evaluate the clinical significance in the screening and early diagnosis of ESCC. MATERIALS AND METHODS: 91 patients with newly diagnosed, untreated esophageal cancer were recruited in the present study. Esophageal cancer tissues, tissues adjacent to the tumors and peripheral blood were collected to determine CpG island hypermethylation of the promoter. Methylation specific PCR(MSP) was used to examine the methylation status of MGMT gene, total mRNA was extracted from esophageal cancer tissues and tissues adjacent to the tumors, expression levels of MGMT gene were measured by quantitative real-time reverse transcription-PCR. RESULTS:The risk for ESCC showed significant correlation to promoter hypermethylation of MGMT gene (OR=7.750, 95%CI=2.736～21.955). There was no significant correlation between methylation status and mRNA level. Hypermethylation of MGMT gene in plasma from ESCC patients was significantly correlated to that in tumor tissue(P<0.01). The detection rate of CpG island hypermethylation of MGMT promoter in plasma was moderately correlated with that in tumor tissue(Kappa=0.603, P<0.01). CONCLUSION: This study suggested that CpG island hyper- methylation of MGMT gene was associated with an enhanced risk for ESCC. Detection of the aberrant methylation in the promoter of MGMT gene from ESCC patient plasma might provide valuable information for the screening and early diagnosis of ESCC.

Keywords esophageal cancer O6-methylguanine-DNA methyltransferase methylation circulating DNA

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