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论著

结晶型硫化镍及反式-BPDE恶性转化16HBE细胞hMSH2基因甲基化的研究

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摘要 背景与目的： 对结晶型硫化镍(Nickel sulfide,NiS)及反式二氢二醇环氧苯并芘(anti-7,8,-dihydrodiol-9,10-epoxide benzo[a] pyrene,BPDE)恶性转化及成瘤的人支气管上皮细胞(Human bronchial epithelial,16HBE)hMSH2基因启动子甲基化状况及其mRNA表达进行研究，探讨镍及反式-BPDE的表遗传致癌机制。材料与方法： 采用甲基化特异性PCR(Methylation-specific PCR,MSP)法和RT-PCR法检测结晶型NiS及反式-BPDE恶性转化及成瘤的16HBE细胞hMSH2基因启动子甲基化状况及其mRNA表达，与非转化的16HBE细胞进行比较；并用去甲基化因子5-Azac(5-Aza-2′-deoxycytidine)处理有异常甲基化的细胞。 结果： 发现结晶型NiS及反式-BPDE恶性转化及成瘤的16HBE细胞hMSH2基因启动子区存在CpG岛的高甲基化；与非转化16HBE细胞比较，转化及成瘤的16HBE细胞hMSH2基因mRNA表达下降；有异常甲基化的细胞经去甲基化处理后甲基化消失。结论： 结晶型NiS及反式-BPDE恶性转化及成瘤的16HBE细胞hMSH2基因启动子区CpG岛的高甲基化使其mRNA表达下降，并可能导致hMSH2基因表达抑制，这可能是结晶型NiS及反式-BPDE诱导16HBE细胞转化和成瘤的一种表遗传致癌机制。甲基化的可逆性对今后研究其表型逆转以及药物治疗提供了重要依据。

关键词 hMSH2；基因甲基化； 硫化镍； 反式-二氢二醇环氧苯并芘

Aberrant Methylation of the hMSH2 Gene in the Nickel Sulfide and Anti-BPDE Transformed 16HBE Cells

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Abstract BACKGROUND&AIM： To study the aberrant methylation of the hMSH2 gene promoter and its mRNA expression in the nickel sulfide (NiS) and anti-7,8,-dihydrodiol-9,10-epoxide benzo[a] pyrene(anti-BPDE) transformed 16HBE cells and to explore the possible epigenetic mechanism for NiS and anti-BPDE carcinogenesis. MATERIAL AND METHODS： DNA methylation patterns in the hMSH2 gene promoter were determined by methylation-specific PCR(MSP) assay and mRNA expression was analysed by RT-PCR assay. The results were compared with the non-transformed 16HBE cells which and the aberrant methylation cells were treated with demethylating agent 5-Aza-2′-deoxycytidine. RESULTS： The hypermethylation in CpG island of the hMSH2 gene promoter was indentified in the NiS and anti-BPDE transformed 16HBE cells; comparing with non-transformed cells, hMSH2 gene mRNA expression levels of the NiS and anti-BPDE transformed 16HBE cells were reduced; treatment of the hMSH2 with 5-Azac decreased the methylation. CONCLUSION： Hypermethylation in CpG island of the hMSH2 gene promoter is known to result in mRNA expression reducing and gene silencing probably, it may represent a possible epigenetic mechanism for NiS and anti-BPDE induced cells transformation and carcinogenesis. Reversible methylation offered an important evidence for phenotype inversion and drug treatment.

Keywords hMSH2 gene methylation nickel sulfide anti-7,8,-dihydrodiol-9,10-epoxide benzo[a] pyrene

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