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甲基化修饰对人宫颈癌细胞系中FHIT基因的调控

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Pattern of FHIT Gene 5’ CpG Island Methylation Contribute to Human Cervical Carcinoma Cell Tumorigenesis

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- 摘要
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全文: PDF (551 KB) HTML (0 KB) 输出: BibTeX | EndNote (RIS) 背景资料

摘要 目的 探讨FHIT在子宫颈癌发生中的作用及FHIT基因失活的机制。方法 培养宫颈癌细胞C-33A、HeLa、CasKi、SiHa及人脐静脉血管内皮细胞ECV-304,进行5-aza-dC干预前后FHIT基因在5株细胞中的甲基化分析,并通过逆转录聚合酶链式反应和免疫荧光化学染色方法检测5-aza-dC干预前后FHIT基因在5株细胞中的表达。结果 4种宫颈癌细胞均存在FHIT基因的甲基化,正常对照细胞ECV-304在5-aza-dC干预前后均未见明显FHIT基因扩增产物。4株宫颈癌细胞在5-aza-dC化学干预前均未见明显FHIT的荧光着色,而干预后的细胞胞浆中可见FHIT的表达强度明显增强,尤其在10^{-6} M及2×10^{-6} M干预浓度下的表达最强（P〈0.05）;干预48h、72h后FHIT的表达与干预24h的类似。ECV-304细胞在5-aza-dC化学干预前后的胞浆均可见到FHIT的阳性表达,其表达强度之间无明显差异（P〉0.05）。结论 FHIT基因的甲基化在宫颈癌中是频发事件,甲基化可能是FHIT基因沉默及宫颈癌发生的重要机制。

关键词： 脆性组氨酸三联体基因(FHIT) 人宫颈癌细胞系 5-aza-dC DNA 甲基化 免疫荧光

Abstract: Objective To determine whether hypermethylation of FHIT played an important role in cervical tumorigenesis. Methods By incubating DNA in the presence of a methylase , we investigated the methylation of FHIT in four cervical cancer cell lines and one human umbilical vein endothelial cell line treating with the DNA methyltransferase inhibitor , 5-aza-2’-deoxycytidine (5-aza-dC) . The expression of FHIT was also monitored by RT-PCR and immunofluorescence technique before and af ter 5-aza-dC treatment . Results We found that methylation of FHIT occured in the four cervical cancer cell lines instead of the ECV-304. Through RT-PCR and immunofluorescence technique , we found that the expression of FHIT , which could hardly be detected in all four cervical cancer cells , was significant different af ter 5-aza-dC treatment . However , the ECV-304 cell expressed FHIT at constant levels before and af ter 5-aza-dC t reatment . Conclusion We concluded that hypermethylation of FHIT gene occurred f requently in cervical tumorigenesis. And hypermethylation within the regulatory sequences of FHIT gene might be an important means for its inactivation in cervical cancer.

Key words: Fragile Histidine Triad Gene (FHIT) Human cervical cancer cell lines 5-aza-2’-deoxycytidine DNA methylation Immunofluorescence technique

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