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基础研究

食管鳞癌中p16基因启动子区甲基化及其表达

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p16 Gene Methylation and Expression in Esophageal Squamous Cell Carcinoma

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摘要 目的探讨食管鳞癌（ESCC）p16基因甲基化的状况及其表达与食管鳞癌临床病理特征之间的关系。方法采用甲基化特异性PCR方法（MSP）分别检测75例食管癌组织、癌旁组织和切缘组织p16基因启动子区域CpG岛甲基化状态。采用Envision免疫组化法检测食管癌组织及癌旁组织的p16蛋白的表达。结果75例标本中，食管癌组织、癌旁组织和切缘细织p16基因甲基化率分别为41．3%（31／75）、13．3%（10／75）和6．67%（5／75）。癌组织和癌旁组织P16蛋白的阳性表达率分别为29．3%（22／75）和56．7%0（17／30）。31例癌组织p16基因甲基化阳性标本中有2例（6．4%）检测到P16蛋白的表达，而44例癌组织p16基因甲基化阴性标本中有20例（45．5%）检测到P16蛋白的表达。食管癌组织p16基因甲基化率显著高于癌旁组织和切缘组织（P〈0.01），P16蛋白表达与p16基因甲基化呈负相关。p16基因启动子区甲基化与食管癌的组织学分级、肿瘤部位无明显相关，与临床分期、淋巴转移密切相关。结论p16基因甲基化在食管癌发生发展中起着重要作用，食管鳞癌的分期和淋巴结转移与p16基因甲基化之间有密切关系。

关键词： 食管鳞癌 p16基因 DNA甲基化 甲基化特异性PCR

Abstract： Objective To detect the hypermethylation status of the 5’Cp G island locating in the promoter region of p16/ IN K4 gene and it s expression in esophageal squamous cell carcinoma (ESCC) , and to ana2lyze the relationship between the aberrant methylaion of p16/ IN K4 gene and clinical manifestation. Meth2ods The hypermethylation of the p16/ IN K4 promoter region was detected by methylation specific poly2merase chain reaction (MSP) in all esophageal cancer tissues ,adjacent tissues and each corresponding edge of dissection. With Envision immunohistochemist ry , both esophageal carcinoma tissue and their adjacent mucosa tissue were stained by using the multiclonal antibody against the human P16 protein respectively. Results In 75 cases of ESCC , hypermethylation of the p16/ IN K4 promoter region was detected in 5 ca2ses of dissected edge tissues 6. 67 %(5/ 75) ,10 cases of adjacent normal esophageal mucosa 13. 3 %(10/ 75) ,31 cases of ESCC tissue 41. 3 %(31/ 75) , respectively. The positive rate of p16 gene expression was 29. 3 %(22/ 75) in ESCC tissues ,56. 7 %(17/ 30) in adjacent mucosa tissues. p16 gene expression was de2tected in 5 of 31 cases of (16. 1 %) p16 methylation positive ESCC and 17 of 44 cases of (38. 6 %) p16 methylation negative ESCC. There is a notable difference of hypermethylated rate between lat ter cancer2ous lesion group and both former normal group s (P < 0. 01) . There are obvious negative correlation be2tween p16 gene methylation and p16 gene expression (P < 0. 01) . No correlation was found between exist2ence of 5’Cp Gisland of p16 gene hypermethylation in ESCC tissues and histological grade , the position of tumor ,but correlated closely with clinical stages and lymphoid metastasis. Conclusion The result sup2port s that the p16/ IN K4 gene promoter hypermethylation might be involved in the pathogenesis of squa2mous cell carcinoma of the esophagus ,and which is closely correlated with the TNM stage and lymphnode metastasis in ESCC.

Key words： Esophageal squamous cell carcinoma p16 gene DNA methylation Methylation specific PCR

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