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Ras相关区域家族7基因在食管鳞状细胞癌中的表达及其临床意义

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摘要：

目的：检测人食管鳞癌 (esophageal squamous cell carcinoma, ESCC)组织中Ras相关区域家族7（Ras-association domain family 7，RASSF7）基因的mRNA、蛋白表达情况及其甲基化状态，探究RASSF7 在ESCC发生发展中的作用。方法：组织标本取自河北医科大学第四医院2011—2012年间手术切除的69例ESCC原发灶组织及癌旁组织。分别应用RT-PCR及甲基化特异性PCR(methylation specific polymerase chain reaction，MSP)方法检测DNA甲基转移酶抑制剂5-氮杂-2’-脱氧胞苷（5-aza-2’-deoxycytidine, 5-Aza-dC）处理前后的4株食管癌细胞系（TE13、T.Tn、YES-2、Ec109）和69例病灶组织及其癌旁组织中RASSF7 mRNA表达水平及甲基化状态，应用免疫组织化学方法检测69例ESCC组织及相应癌旁组织中RASSF7的蛋白表达。结果：RASSF7基因在TE13、T.Tn、YES-2细胞系中表达阳性，在Ec109细胞系中表达缺失；经5-Aza-dC处理后，RASSF7在TE13、T.Tn、YES-2细胞中表达下调，在Ec109细胞中表达阳性。5-Aza-dC处理前后4株食管癌细胞系中均未检测到RASSF7 的甲基化。人ESCC组织中RASSF7 的mRNA相对表达量（0.63±0.08 vs 0.42±0.20，P<0.01）与蛋白表达阳性率\[81.2%（56/69） vs 53.6%（37/69），P<0.01\]均显著高于相应癌旁组织，且均与患者的淋巴结转移情况及分化程度有关（P<0.05或P<0 01），与TNM分期、年龄和性别无关（均P>0.05）。ESCC组织和相应癌旁组织中均未检测到RASSF7的甲基化。结论：4株食管癌细胞系、人ESCC组织和癌旁组织中RASSF7基因的表达差异与RASSF7 本身甲基化状态无关，ESCC组织中RASSF7 的高表达可能参与了ESCC的发生及转移。

关键词：食管鳞状细胞癌 Ras相关区域家族7基因 表达 甲基化

Expression of Ras-association domain family 7 gene in esophageal squamous cell carcinoma: Association with disease development and DNA methylation

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Abstract:

Objective: To assess the expression of Ras-association domain family 7 (RASSF7) gene in esophageal squamous cell carcinoma (ESCC) in association with the disease pathogenesis and progression and to evaluate the effect of DNA methylation on RASSF7 expression. Methods: Sixty-nine patients diagnosed with ESCC in Hebei Medical University-Affiliated Fourth Hospital between 2011 and 2012 were recruited. Carcinoma and its surrounding non-carcinoma tissue specimens were collected from 69 of these patients. Four esophageal cancer cell lines (TE13, T.Tn, YES-2, and Ec109) were treated with DNA methyltransferase inhibitor 5-aza-2’-detoxycytidine (5-Aza-dC). RASSF7 mRNA abundance in the 69 tissue specimens and 4 esophageal cancer cell lines after 5-Aza-dC treatment were determined by RT-PCR and methylation specific polymerase chain reaction (MSP). RASSF7 protein content in the tissue specimens were assessed by immunohistochemical staining. Results: RASSF7 mRNA was detected in TE13, T.TN, Yes-2 cells but not in Ec109 cells. Treatment with 5-Aza-dC induced RASSF7 mRNA but significantly decreased RASSF7 mRNA levels in TE13, T.Tn, and Yes-2 cells. No aberrant RASSF7 methylation was detected in any of the four esophageal cancer cell lines studied, regardless of 5-aza-dC treatment. Carcinoma tissue specimens had significantly higher abundance of RASSF7 mRNA (0.63±0 08 vs 0.42±0.20, P<0.01) and a significantly higher rate of positive immunohistochemical staining for RASSF7 protein 56(81.2% vs 53.6%, P<0.01) as compared with the non-carcinoma normal tissue specimens, and both RASSF7 mRNA and protein were associated with lymph node metastasis and histological grade of ESCC. Methylation was detected neither in ESCC specimens nor in the corresponding non-carcinoma tissue specimens. Conclusion: The differential expression of RASSF7 in different esophageal cancer cell lines, ESCC tumor tissue and non-carcinoma tissues is not related to methylation status of RASSF7. Increased expression of RASSF7 in the ESCC tissue suggests a role for RASSF7 in the pathogenesis and metastasis of ESCC.

Keywords:esophageal squamous cell carcinoma (ESCC) Ras-association domain family 7 gene (RASSF7) expression methylation

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