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MicroRNA-203在人食管鳞癌组织和细胞中的表达及其基因的甲基化状态

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摘要：

目的：检测人食管鳞状细胞癌（esophageal squamous cell carcinoma, ESCC）组织及细胞中MicroRNA-203(miR-203)的表达及其基因的甲基化状态，探讨miR-203在ESCC发生及发展中的作用。方法：选取河北医科大学第四医院2008—2011年间手术切除的83例ESCC原发灶组织及癌旁组织标本，实时定量PCR与甲基化特异性PCR（methylation specific PCR，MSP）分别检测其miR-203的表达及其编码基因的甲基化状态。用DNA甲基化转移酶抑制剂5-氮杂-2’-脱氧胞苷（5-aza-2’-deoxycitydine, 5-Aza-dC）处理食管癌细胞系（TE1、TE13、YES-2、EC109、T.TN），实时定量PCR与MSP分别检测5-Aza-dC处理对食管癌细胞中miR-203的表达及其基因甲基化状态的影响。结果：五种食管癌细胞中miR-203的表达均相对较低，且呈高甲基化状态。5-Aza-dC处理后，miR-203的表达均显著升高（ P <0.05或 P <0.01）；YES-2细胞中miR-203编码基因的甲基化程度显著降低，其余4种细胞均转变为非甲基化状态。miR-203在ESCC组织中的表达显著低于癌旁组织（0.54±0.11 vs 1.00±0 01， P <0.01），启动子区甲基化率显著高于癌旁组织\[62.65%（52/83) vs 7.23% (6/83)， P <0.01\]，并且两者均与TNM分期和组织分化程度有关（ P<0.05）。发生miR-203编码基因甲基化的ESCC组织中miR-203的表达显著低于未发生甲基化的ESCC组织（ P <0 0 5）。结论： miR-203在ESCC组织与细胞中呈低表达，与食管鳞癌的发生、发展有关，且其启动子区甲基化可能是导致其表达沉默的机制之一。

关键词：食管鳞癌 微小RNA-203 DNA甲基化 表达

Expression and methylation status of microRNA-203 gene in tissues and cells of esophageal squamous cell carcinoma

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Abstract:

Objective: To investigate the expression, methylation status and functional role of miR-203 in pathogenesis of ESCC. ethods: Eighty-three patients diagnosed with ESCC in Hebei Medical University-Affiliated Fourth Hospital between 2008 and 2011 were recruited. Biopsy specimens were collected from primary tumors and the corresponding adjacent tissues. Quantitative real-time RT-PCR (qRT-PCP) and methylation specific PCR (MSP) were used to respectively detect the mRNA abundance and methylation status of miR-203 gene in the collected specimens. Five esophageal cancer cell lines (TE1, TE13, T.TN, Yes-2, and EC109) were treated with DNA methyltransferase inhibitor 5-Aza-2’-detoxycytidine (5-Aza-dC) Levels of CpG methylation of the miR-203 gene and miR-203 were assessed by qRT-PCR and MSP, respectively, 72 h after 5-Aza-dC treatment. Results： Relatively low levels of miR-203 mRNA and hypermethylation were detected in all the five untreated esophageal cancer cell lines. After 5-Aza-dC treatment, miR-203 mRNA was increased in all five cell lines studied and the methylation level of miR-203 was decreased in YES-2 cells and complete miR-203 unmethylation occurred in TE1, TE13, T.TN, and EC109 cells. The abundance of miR-203 mRNA was significantly lower (0.54±0.11 vs 1.00±0.01, P<0.05) and the methylation frequency of miR-203 promoter was significantly higher (62.65%vs 7.23%,P<0.05) in ESCC tissues than in corresponding tissues. Both miR-203 mRNA abundance and methylation frequency were all correlated with TNM stage and pathological differentiation (P<0.05). The expression of miR-203 in ESCC with miR-203 methylation was significantly lower than that in ESCC without miR-203 methylation (P<0.05). Conclusion： Aberrantly low expression of miR-203 is closely related to the development and progression of ESCC and promoter DNA methylation is one of the possible mechanisms underlying miR-203 inactivationin ESCC.

Keywords:esophageal squamous cell carcinoma (ESCC) microRNA-203 DNA methylation expression

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