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MicroRNA-10a通过靶向作用E2F3抑制肝癌细胞的增殖

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摘要：

目的：探讨微小RNA-10a（microRNA-10a，miR-10a）对肝癌细胞增殖的影响及其作用机制。方法：收集广西医科大学附属肿瘤医院肿瘤科2001年10月至2005年7月144例肝癌患者手术切除的肝癌组织和癌旁组织（距癌灶组织边缘2~5 cm）标本，Real-time PCR法分析144例肝癌组织及癌旁组织中miR-10a的表达量。在肝癌细胞（QGY-7701、Huh7、PCL/PRF/5）中转染miR-10a 模拟物，Real-time PCR法检测转染后细胞miR-10a的表达水平；CCK-8法检测过表达miR-10a的肝癌细胞的增殖水平，流式细胞术检测过表达miR-10a的肝癌细胞的凋亡和细胞周期；生物信息学预测并以Western blotting检测过表达miR-10a的肝癌细胞中转录因子E2F3的表达量。结果：与癌旁组织相比，肝癌组织中的miR-10a显著低表达\[（-9.89±1 68） vs （-7.84±1.97）， P =0.000\]。转染miR-10a模拟物后肝癌细胞系中miR-10a的表达量是转染对照小RNA组或空白组细胞的16倍左右。过表达miR-10a可显著抑制7种肝癌细胞（QGY-7701、QGY-7703、Huh7、PCL/PRF/5、HepG2、BeL-7402、SMMC-7721）的增殖（均 P <0.05），并引起肝癌细胞细胞周期G 1/S期阻滞，但并不能诱导肝癌细胞发生凋亡。生物信息学预测显示E2F3是miR-10a可能的靶分子，Western blotting检测显示过表达miR-10a可明显抑制肝癌细胞中E2F3的表达\[（0.50±0.12) vs (0.79±0.21)， P <0.05\]。结论：人肝癌组织中低表达miR-10a，转染miR-10a模拟物后多种肝癌细胞的增殖均受到明显抑制，其机制可能与miR-10a靶向作用转录因子E2F3并阻滞肝癌细胞细胞周期于G 1/S期有关。

关键词：肝癌 微小RNA-10a 增殖 转录因子 E2F3 G 1/S期阻滞

MicroRNA-10a inhibits hepatocellular carcinoma cell proliferation through targeting E2F3

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Abstract:

Objective: To investigate the role of microRNA-10a (miR-10a) in hepatocellular carcinoma (HCC) growth. Methods: Paired HCC and adjacent non-tumor tissue specimens were surgically collected from 144 patients who were diagnosed with primary HCC in Guangxi Medical University-Affiliated Tumor Hospital between October 2001 and July 2005. HCC QGY-7701, Huh7, and PCL/PRF/5 cells were transfected with miR-10a mimics or scramble control miRNA. The abundance of miR-10a in both tissue specimens and transfected cells was quantified by real-time PCR and E2F3 protein in transfected cells was assessed by Western blotting. Proliferation of the transfectants was assessed by a colorimetric cell counting assay. Cell cycle progression and apoptosis of the transfectants were assessed by FACS. Results: The abundance of miR-10a mRNA was significantly lower in HCC tissue specimens than in normal tissue specimens (-9.89±1 68 vs -7 84±1.97, P =0.0001). HCC cells transfected with miR-10a mimics had miR-10a abundance 16 times higher than both wild-type HCC cells and HCC cells transfected with the control miRNA with scrambled sequences. Overexpression of miR-10a resulted in significant increases in suppression of HCC cell proliferation (P <0.05） and G 1 phase arrest. In contrast, overexpression of miR-10a had no influence on apoptosis of HCC cells. Bioinformatics suggested that transcription factor E2F3 might be a downstream target of miR-10a and the expression of E2F3 in HCC cells transfected with miR-10a was significantly lower than in wild-type HCC cells and HCC cells transfected with the control miRNA (0 50±0.12 vs 0.79±0.21, P <0.05). Conclusion: MiR-10a may suppress HCC cell proliferation through G 1 phase arrest in an E2F3-dependent mechanism.

Keywords:hepatocellular carcinoma microRNA-10a（miR-10a) transcription factor E2F3 proliferation G 1/S phase arrest

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