miRNA-98-5p靶向HMGA2调控结直肠癌细胞增殖、侵袭和上皮间质转化

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Title: miRNA-98-5p inhibits proliferation，invasion and EMT of colorectal cancer cells by targeting HMGA2

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摘要: 目的：研究miRNA-98-5p在结直肠癌细胞中的表达水平及对癌细胞增殖和侵袭的影响，探讨miRNA-98-5p在结直肠癌中的临床意义及可能的分子机制。方法：收集2016年8月至2018年2月手术切除的结直肠癌组织标本60份,实时荧光定量PCR法检测结直肠癌组织和癌旁组织中miRNA-98-5p的表达水平,免疫组化检测分析HMGA2的表达强度。分析miRNA-98-5p与结直肠癌肿瘤生物学特征和HMGA2表达的相关性。实时荧光定量聚合酶链反应（qRT-PCR）检测miRNA-98-5p在结直肠癌细胞中的表达情况；应用miRNA-98-5p模拟物转染人结直肠癌HCT116细胞，CCK-8法检测细胞增殖情况，Transwell小室法检测细胞侵袭情况，Western blot检测HMGA2、E-cadherin和Vimentin蛋白表达。采用双荧光素酶活性实验验证miRNA-98-5p对HMGA2的靶向作用。构建裸鼠皮下移植瘤模型，观察肿瘤生长状况。结果：结直肠癌组织miRNA-98-5p的表达水平低于癌旁组织，结直肠癌组织HMGA2的表达水平高于癌旁组织(P < 0.05)。相关性分析显示，HMGA2表达强度与miRNA-98-5p表达水平呈负相关(r=-0.536,P < 0.001)。miRNA-98-5p在结直肠癌细胞中表达水平低于对应结直肠黏膜正常细胞（P < 0.05）；与转染阴性对照细胞比较，转染miRNA-98-5p模拟物的HCT116细胞增殖水平和侵袭能力均受到抑制（P < 0.05），HMGA2、Vimentin蛋白表达水平降低，E-cadherin表达增高。双荧光素酶报告基因结果提示HMGA2是miRNA-98-5p的靶基因。裸鼠皮下成瘤实验结果显示与Blank组和NC组相比，实验组肿瘤生长缓慢，重量明显降低。结论：miRNA-98-5p在结直肠癌细胞中表达下调，且miRNA-98-5p通过调节HMGA2的表达从而影响结直肠癌细胞增殖、侵袭和上皮间质转化状态。

Abstract: Objective:To investigate the role of miRNA-98-5p on the proliferation and invasion of colorectal cancer cells and the possible regulatory mechanisms between miRNA-98-5p and HMGA2.Methods:From August 2016 to February 2018,60 surgical specimens were collected.There expression of miRNA-98-5p and HMGA2 at mRNA level in colorectal cancer tissues and paracancerous tissues were quantified by quantitative real-time PCR.The correlation between miRNA-98-5p and the biological features of colorectal cancer as well as HMGA2 expression was analyzed.The expression of miRNA-98-5p in colorectal cancer was detected by real-time PCR.The miRNA-98-5p was overexpressed by Lipofectamine 3000 transfection with miRNA-98-5p mimics.The effects of miRNA-98-5p on cell proliferation and invasion abilities were detected by CCK-8 assay and Transwell assay.The protein expression of high mobility group A2 (HMGA2),E-cadherin and Vimentin was determined by Western blot.The regulatory mechanism between HMGA2 and miRNA-98-5p in HCT116 cells was detected by dual-luciferase reporter assay.Subcutaneous tumor formation model in nude mice was used to evaluate the effects of miRNA-98-5p on tumor growthin vivo.Results:The expression of miRNA-98-5p was significantly decreased compared with adjacent tissues (P < 0.05).The protein expression of HMGA2 was significantly increased compared with adjacent tissues.The HMGA2 and miRNA-98-5p expression were negatively correlated(r=-0.536,P < 0.001).The

results of CCK-8 assay and Transwell assay showed that overexpression of miRNA-98-5p significantly reduced the proliferation and invasion abilities of colorectal cancer cells ($P < 0.05$).Overexpression of miRNA-98-5p decreased the protein level of HMGA2.Also,it upregulated the expression of E-cadherin and downregulated the expression of Vimentin.The result of dual-luciferase-3' UTR reporter assay confirmed that miRNA-98-5p bound to the 3' UTR of HMGA2.In vivo subcutaneous tumor formation experiment revealed that miRNA-98-5p mimics inhibited the growth and volume of injected tumor.Conclusion:miRNA-98-5p may suppress the colorectal cancer cell proliferation,invasion and epithelial-mesenchymal transition (EMT) by down-regulation of HMGA2.

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备注/Memo: -

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