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论著

miR-126靶向调控IRS1,SLC7A5及TOM1基因抑制结肠癌的增殖及侵袭转移

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摘要： 目的: 通过研究miR-126在人结肠癌细胞中的表达及其对结肠癌细胞生物学行为的影响,了解miR-126在结肠癌发生发展中的作用。方法: 利用原位杂交在高密度人结肠癌组织芯片中研究miR-126的表达,通过慢病毒转染构建miR-126稳定过表达细胞系,并进一步通过体外实验研究miR-126对结肠癌细胞生物学行为的影响。结果: miR-126在人结肠癌组织中表达下调,在存在侵袭转移患者的结肠癌组织中下调尤为明显。miR-126的表达与患者是否发生转移及结肠癌临床分期、Duke's分期相关(P<0.05),且miR-126下调越明显,患者预后越差(P=0.025)。利用慢病毒转染构建的miR-126过表达SW480细胞系进行体外实验显示结肠癌细胞中恢复miR-126的表达可抑制结肠癌细胞增殖,使其出现G1期阻滞并促进结肠癌细胞凋亡、抑制结肠癌细胞迁移和侵袭能力。同时miR-126可明显增强结肠癌细胞对化疗药物奥沙利铂的敏感性。进一步生物信息学分析及qRT-PCR结合蛋白免疫印迹法验证IRS1,SLC7A5及TOM1可能为miR-126在结肠癌中的靶基因。结论: miR-126可明显抑制结肠癌的发生发展,且与结肠癌患者预后密切相关,其可能调控的靶基因为IRS1,SLC7A5及TOM1,miR-126有望成为结肠癌临床诊断及治疗的新靶点。

关键词： miR-126 结肠癌 慢病毒转染 靶基因 侵袭转移

miR-126 inhibits colon cancer proliferation and invasion through targeting IRS1, SLC7A5 and TOM1 gene

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Abstract: Objective: To explore the expression pattern and function of miR-126 in human colon cancer and the underlying mechanisms. Methods: The expression pattern of miR-126 in high-density human colon cancer tissue microarray was analyzed by in situ hybridization. Further more, the biological function of miR-126 in colon cancer in vitro was investigated by establishing a stable miR-126 over-expression cell lines. Result: The expression of miR-126 was lower in the tumor tissue, especially in metastasis tissue. The down-regulation of miR-126 was more obvious in the patients who displayed bad prognosis (P=0.025). Over-expression of miR-126 in colon cancer cell was able to inhibit cell proliferation, promote cell apoptosis and reduce the invasive ability. MiR-126 significantly enhanced the sensitivity of the colon cancer cell to chemotherapeutic drug. It has been shown that IRS1, SLC75A and TOM1 were the potential target genes of miR-126 in colon cancer. Conclusion: MiR-126 was able to inhibit the development of colon cancer and its level was closely related with the prognosis of patients with colon cancer. The potential target genes for miR-126 might include IRS1, SLC7A5 and TOM1. Therefore, miR-126 might be a therapeutic target for colon cancer diagnosis and treatment.

Keywords: miR-126 colon cancer lentivirus transfection target gene metastasis

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