miR-130a对胰腺癌细胞系PANC-1细胞增殖和凋亡的调控作用及其 机制探讨

《现代肿瘤医学》[ISSN:1672-4992/CN:61-1415/R] 期数: 2019年11期 页码: 1866-1871 栏目: 论著（基础研究） 出版日期: 2019-04-30

Title: **Regulation and mechanism of miR-130a on proliferation and apoptosis of pancreatic cancer cell line PANC-1**

作者: 胡 川; 段俊伟; 杨 帆; 余昌文; 戴丹菁
汉川市人民医院肿瘤科，湖北 汉川 431600

Author(s): Hu Chuan; Duan Junwei; Yang Fan; Yu Changwen; Dai Danjing
Department of Oncology，Hanchuan People's Hospital，Hubei Hanchuan 431600，China.

关键词: miR-130a; FOS样抗原1; 胰腺癌细胞; 细胞增殖; 细胞凋亡

Keywords: miR-130a; FOS like antigen 1; pancreatic cancer cells; cell proliferation; cell apoptosis

分类号: R735.9

DOI: 10.3969/j.issn.1672-4992.2019.11.005

文献标识码: A

摘要: 目的：研究miR-130a对胰腺癌细胞系PANC-1细胞增殖和凋亡的影响，并探讨其机制。方法：体外培养胰腺癌细胞PANC-1、SW 1990、MIA PaCa-2和正常胰腺上皮细胞HPDE6-C7，检测各细胞中miR-130a表达水平。将PANC-1细胞分为miR-130a低表达组（miR-130a-inhibitor组）、阴性对照组（miR-130a-NC组）和空白对照组（miR-130a-BC组）。转染48 h后，CCK-8试验检测细胞增殖情况；裸鼠皮下成瘤实验检测miR-130a对肿瘤体内生长的影响；流式细胞术检测细胞凋亡情况；TargetScan数据库预测miR-130a的靶基因，并采用蛋白免疫印迹（WB）和荧光素酶报告实验进行验证。结果：PANC-1、SW 1990、MIA PaCa-2人胰腺癌细胞中miR-130a表达水平均显著高于正常胰腺上皮细胞，差异有统计学意义（P<0.05）。转染miR-130a-inhibitor后，PANC-1细胞miR-130a相对表达量显著下调（P<0.05）；与miR-130a-NC和miR-130a-BC组比较，miR-130a-inhibitor组PANC-1细胞增殖能力显著下降（P<0.05）、裸鼠皮下肿瘤体积明显减小（P<0.05）、细胞凋亡率显著升高（P<0.05）。TargetScan数据库显示FOS样抗原1（FOSL1）是miR-130a潜在靶基因，WB和双荧光素酶报告实验证实FOSL1是miR-130a的作用靶点。结论：下调miR-130a表达通过作用于FOSL1基因抑制PANC-1细胞增殖，促进其凋亡，可能为胰腺癌的临床治疗提供新思路。

Abstract: Objective：To study the influences of miR-130a on the proliferation and apoptosis of pancreatic cancer cell line PANC-1 cell and to explore its mechanisms.Methods：Pancreatic cancer cells PANC-1，SW 1990，MIA PaCa-2 and normal pancreatic epithelial cell HPDE6-C7 were cultured in vitro.The expression of miR-130a in each cell was detected.PANC-1 cells were divided into miR-130a low expression group（miR-130a-inhibitor group），negative control group（miR-130a-NC group) and blank control group（miR-130a-BC group).After transfection for 48 h，CCK-8 assay was used to detect cell proliferation.The effect of miR-130a on the growth of tumor in vivo was detected by subcutaneous tumor formation experiment in nude mice.Cell apoptosis was detected by flow cytometry.The target genes of miR-130a were predicted by TargetScan database and verified by Western blot（WB) and luciferase assay.Results：The expression level of miR-130a in pancreatic cancer cells of PANC-1，SW 1990 and MIA PaCa-2 was significantly higher than that in normal pancreatic epithelial cells，and the difference was statistically significant（P<0.05).After transfection of miR-130a-inhibitor，the relative expression of miR-130a in PANC-1 cells was significantly reduced（P<0.05).Compared with miR-130a-NC group and miR-130a-BC group，the proliferation ability of PANC-1 cells in group miR-130a-inhibitor decreased significantly（P<0.05)，the volume of subcutaneous tumor in nude mice decreased significantly（P<0.05)，and the rate of apoptosis significantly increased（P<0.05).The TargetScan database showed that FOS like antigen 1（FOSL1) was a potential target gene for miR-130a，WB and double luciferase reporter experiments confirmed that FOSL1 was the action target of miR-130a.Conclusion：Down-regulating the expression of miR-

130a can inhibit the proliferation and promote the apoptosis of PANC-1 cells by acting FOSL1 gene，may provide new ideas for the clinical treatment of pancreatic cancer.

参考文献/REFERENCES

[1]Bailey P，Chang DK，Nones K，et al.Genomic analyses identify molecular subtypes of pancreatic cancer［J］.Nature，2016，531(7592)：47-52.
[2]Llop E，E Guerrero P，Duran A，et al.Glycoprotein biomarkers for the detection of pancreatic ductal adenocarcinoma［J］.World J Gastroenterol，2018，24(4)：2537-2554.
[3]Swl DG，Eskander MF，Kasumova GG，et al.Stereotactic body radiotherapy for unresected pancreatic cancer：A nationwide review［J］.Cancer，2017，123(21)：4158-4167.
[4]Hong CA，Nam YS.Functional nanostructures for effective delivery of small interfering RNA therapeutics［J］.Theranostics，2014，4(12)：1211-1232.
[5]González-Quintana V，Palma-Berré L，Campos-Parra AD，et al.MicroRNAs are involved in cervical cancer development，progression，clinical outcome and improvement treatment response（Review）［J］.Oncol Rep，2016，35(1)：3-12.
[6]Shen S，Guo X，Yan H，et al.A miR-130a-YAP positive feedback loop promotes organ size and tumorigenesis［J］.Cell Research，2015，25(9)：997-1012.
[7]Wu LM，Wu SG，Chen WW，et al.Construction of nude mouse models bearing subcutaneous tumors：Human osteosarcoma cell lines MG63，U2OS and 143B［J］.Journal of Clinical Rehabilitative Tissue Engineering Research，2015，81(27)：4277-4281.［吴丽美，伍绍国，陈卫文，等.构建裸鼠皮下荷瘤模型：人骨肉瘤细胞株MG63、U2OS和143B［J］.中国组织工程研究，2015，81(27)：4277-4281.］
[8]Kang YA，Li NF，Hu YR，et al.Study on detection of expression of GIRK4 gene in renal tissue of SD rats by Western-blotting［J］.Journal of Clinical and Experimental Medicine，2013，12(4)：241-242.［康永安，李南方，胡燕荣，等.蛋白质印迹法检测GIRK4在SD大鼠肾脏组织的表达［J］.临床和实验医学杂志，2013，12(4)：241-242.］
[9]Nair VB，Manasa VG，Sinto MS，et al.Differential expression of microRNAs in uterine cervical cancer and its implications in carcinogenesis:An integrative approach［J］.Int J Gynecol Cancer，2018，28(3)：553-562.
[10]Lin S，Gregory RI.MicroRNA biogenesis pathways in cancer［J］.Nature Reviews Cancer，2015，15(6)：321-333.
[11]Mody H，Hung SW，Pathak R，et al.miR-202 diminishes TGFbeta receptors and attenuates TGFbeta1-induced EMT in pancreatic cancer［J］.Mol Cancer Res，2017，15(8)：1029-1039.
[12]Zhu Y，Gu J，Li Y，et al.MiR-17-5p enhances pancreatic cancer proliferation by altering cell cycle profiles via disruption of RBL2/E2F4-repressing complexes［J］.Cancer Lett，2018，412(3)：59-68.
[13]Jiang H，Yu WW，Wang LL，et al.miR-130a acts as a potential diagnostic biomarker and promotes gastric cancer migration，invasion and proliferation by targeting RUNX3［J］.Oncol Rep，2015，34(3)：1153-1161.
[14]Cappellesso R，Galasso M，Nicolè L，et al.miR-130A as a diagnostic marker to differentiate malignant mesothelioma from lung adenocarcinoma in pleural effusion cytology［J］.Cancer Cytopathol，2017，125(8)：635-643.
[15]Pan Y，Wang R，Zhang F，et al.MicroRNA-130a inhibits cell proliferation，invasion and migration in human breast cancer by targeting the RAB5A［J］.Int J Clin Exp Pathol，2015，8(1)：384-393.
[16]Hu Y，Li J，Li SY，et al.Expression level of FOSL2 protein in Uygur patients with type 2 diabetes mellitus in Xinjiang［J］.China Journal of Modern Medicine，2016，26(5)：26-30.［胡颖，李军，李思源，等.FOS样抗原2蛋白表达在新疆维吾尔族2型糖尿病中的应用［J］.中国现代医学杂志，2016，26(5)：26-30.］
[17]Chen X，Zhao M，Huang J，et al.MicroRNA-130a suppresses breast cancer cell migration and invasion by targeting FOSL1 and upregulating ZO-1［J］.J Cell Biochem，2018，119(6)：4945-4956.
[18]Vallejo A，Valencia K，Vicent S.All for one and FOSL1 for all：FOSL1 at the crossroads of lung and pancreatic cancer driven by mutant KRAS［J］.Mol Cell Oncol，2017，4(3)：e1314239.
[19]Vallejo A，Perurena N，Guruceaga E，et al.An integrative approach unveils FOSL1 as an oncogene vulnerability in KRAS-driven lung and pancreatic cancer［J］.Nat Commun，2017，8(1)：14294-14305.
[20]Elangovan IM，Vaz M，Tamatam CR，et al.FOSL1 promotes KRAS-induced lung cancer through amphiregulin and cell survival gene regulation［J］.Am J Respir Cell Mol Biol，2017，58(5)：625-635.

备注/Memo: -

更新日期/Last Update: 2019-04-30