

lncRNA PVT1调控肝癌细胞放射敏感性的分子机制

《现代肿瘤医学》[ISSN:1672-4992/CN:61-1415/R] 期数: 2019年19期 页码: 3387-3390 栏目: 论著 (基础研究) 出版日期: 2019-08-29

Title: Molecular mechanism of lncRNA PVT1 regulating radiosensitivity of hepatoma cells

作者: 杨松柏¹; 龚玉竹²; 张建华³

1.陆军军医大学第一附属医院（重庆西南医院）核医学科；2.肿瘤科，重庆 400038;3.奉节县人民医院（重庆医科大学附属第二医院奉节分院）放射科，重庆 404600

Author(s): Yang Songbai¹; Gong Yuzhu²; Zhang Jianhua³

1.Nuclear Medicine Department; 2.Oncology Department, the First Hospital Affiliated to Amu (Southwest Hospital), Chongqing 400038, China; 3.Radiology Department, the Second Affiliated Hospital of Chongqing Medical University at Fengjie, Chongqing 404600, China.

关键词: PVT1; 放射敏感性; 凋亡; 增殖; 肝癌

Keywords: PVT1; radiosensitivity; apoptosis; proliferation; hepatoma

分类号: R735.7

DOI: 10.3969/j.issn.1672-4992.2019.19.008

文献标识码: A

摘要: 目的: 探讨lncRNA PVT1调控肝癌细胞对放射照射增殖、凋亡的敏感性及机制。方法: 运用qRT-PCR检测人肝癌细胞HepG2、人正常肝细胞L02中PVT1的表达。si-NC组(转染si-NC)、si-PVT1组(转染si-PVT1)、IR+si-NC组(转染si-NC后放射照射)、IR+si-PVT1组(转染si-PVT1后放射照射)均用脂质体法转染至HepG2细胞。MTT法检测各组细胞增殖; 流式细胞术检测各组细胞凋亡; Western blot检测各组细胞中p-ATM、p-p53、p-Chk2、Bcl-2、Bax的蛋白表达。结果: 与人正常肝细胞L02相比, 人肝癌细胞HepG2中PVT1的表达显著升高($P<0.05$) ; 敲减PVT1联合放射照射可明显抑制HepG2细胞增殖, 促进凋亡且可下调p-ATM、p-p53、p-Chk2、Bcl-2蛋白表达, 上调Bax蛋白表达。结论: 敲减lncRNA PVT1可通过抑制HepG2细胞增殖, 促进凋亡, 增强其对放射照射的敏感性, 为提高肝癌的治疗效率提供新靶点。

Abstract: Objective: To investigate the mechanism of lncRNA PVT1 sensitivity to proliferation and apoptosis of hepatocellular carcinoma cells irradiated by radiation. Methods: qRT-PCR was used to detect the expression of PVT1 in human hepatoma cells HepG2 and human normal liver cells L02. si-NC group (transfected si-NC), si-PVT1 group (transfected si-PVT1), IR+si-NC group (transfected si-NC and treated with radiation), IR+si-PVT1 group (transfected si-PVT1 and treated with radiation) were transfected into HepG2 cells by liposome method. The proliferation of each group was detected by MTT assay. The apoptosis of each group was detected by flow cytometry. The protein expressions of p-ATM, p-p53, p-Chk2, Bcl-2 and Bax were detected by Western blot. Results: Compared with human normal liver cell line L02, the expression of PVT1 in human hepatoma cell line HepG2 was significantly increased ($P<0.05$). PVT1 combined with radiotherapy significantly inhibited HepG2 cell proliferation, promoted apoptosis and down-regulated protein expression of p-ATM, p-p53, p-Chk2 and Bcl-2, up-regulated Bax. Conclusion: Knockdown of lncRNA PVT1 can inhibit the proliferation and promote apoptosis to enhance its sensitivity to radiation exposure of HepG2 cells, which will provide a new target for improving the therapeutic efficiency of hepatoma.

参考文献/REFERENCES

- [1] Fang TT, Sun XJ, Chen J, et al. Long non-coding RNAs are differentially expressed in hepatocellular carcinoma cell lines with differing metastatic potential [J]. Asian Pac J Cancer Prev, 2015, 15(23): 10513-10524.
- [2] Tarantino G, Magistri P, Ballarin R, et al. Oncological impact of m-tor inhibitor immunosuppressive therapy after liver transplantation for hepatocellular carcinoma: Review of the literature [J]. Front Pharmacol, 2016, 7(1): 387.
- [3] Sepehri Z, Kiani Z, Kohan F, et al. Toll like receptor 4 and hepatocellular carcinoma: A systematic

- review [J] .Life Sci, 2017, 179(1): 80-87.
- [4] Buendia MA, Neuveut C.Hepatocellular carcinoma [J] .Cold Spring Harb Perspect Med, 2015, 5(2): a021444.
- [5] Vallard A, Rancoule C, Guy JB, et al.Biomarkers of radiation-induced DNA repair processes [J] .Bull Cancer, 2017, 104(11): 981-987.
- [6] Nickson CM, Moori P, Carter RJ, et al.Misregulation of DNA damage repair pathways in HPV-positive head and neck squamous cell carcinoma contributes to cellular radiosensitivity [J] .Oncotarget, 2017, 8(18): 29963-29975.
- [7] Jin XL, Lian JR, Guan YH.Overexpression of long non-coding RNA MINCR contributes to progressive clinicopathological features and poor prognosis of human hepatocellular carcinoma [J] .Eur Rev Med Pharmacol Sci, 2018, 22(23): 8197-8202.
- [8] Cui M, You L, Ren X, et al.Long non-coding RNA PVT1 and cancer [J] .Bio Biophy Res Commu, 2016, 471(1): 10-14.
- [9] Iyer MK, Niknafs YS, Malik R, et al.The landscape of long non-coding RNAs in the human transcriptome [J] .Nature Genetics, 2015, 47(3): 199-208.
- [10] Lu D, Luo P, Wang Q, et al.lncRNA PVT1 in cancer: A review and Meta analysis [J] .Clinica Chimica Acta, 2017, 474(2017): 1-7.
- [11] WANG F, YANG F, YUAN JH, et al.Epigenetic mechanism of fetal liver-specific lncRNA regulation of liver development and hepatocarcinogenesis [C] //National Conference on Medical Genetics.2014. [王芳, 杨富, 袁继航, 等.胎肝特异性lncRNA调控肝发育及肝癌发生的表观遗传学机制研究 [C] //全国医学遗传学学术会议.2014.]
- [12] ZHI XS, HUANG YY, ZI XY, et al.Progress in the role of long-chain non-coding RNA PVT1 in tumors [J] .Journal of Xinxiang Medical College, 2016, 33(03): 243-245,249. [职晓松, 黄筱奕, 訾晓渊, 等.长链非编码RNA PVT1在肿瘤中的作用研究进展 [J] .新乡医学院学报, 2016, 33(03): 243-245,249.]
- [13] DING CF, WU J, YANG Z, et al.Clinical value of long-chain non-coding RNA PVT1 in predicting tumor recurrence after liver transplantation in liver cancer [C] //China Organ Transplantation Congress.2014. [丁超峰, 吴健, 杨喆, 等.长链非编码RNA PVT1预测肝癌肝移植术后肿瘤复发的临床价值 [C] //中国器官移植大会.2014.]
- [14] Wang F, Yuan JH, Wang SB, et al.Oncofetal long non-coding RNA PVT1 promotes proliferation and stem cell-like property of hepatocellular carcinoma cells by stabilizing NOP2 [J] .Hepatology, 2014, 60(4): 1278-1290.
- [15] ZHU YX,FU HW,LIN X,et al.Expression of hsa-circ-PVT1 in human hepatocellular carcinoma and its clinical significance [J] .Medical Journal of Chinese People's Liberation, 2018, 43(3): 211-216. [朱元鑫, 付航玮, 林夏, 等.Hsa-circ-PVT1在肝细胞癌中的表达及意义 [J] .解放军医学杂志, 2018, 43(3): 211-216.]
- [16] ZHAO XX, WEN F, SUN HZ, et al.Progress in the role of radiation-sensitivity-regulated signaling pathways in cancer therapy [J] .Modern Oncology, 2018, 26(10): 1611-1614. [赵相轩, 温锋, 孙洪赞, 等.放射线敏感性调节信号通路在癌症治疗中的作用研究进展 [J] .现代肿瘤医学, 2018, 26(10): 1611-1614.]
- [17] Zhang XW, Bu P, Liu L, et al.Overexpression of long non-coding RNA PVT1 in gastric cancer cells promotes the development of multidrug resistance [J] .Biochemical & Biophysical Research Communications, 2015, 462(3): 227-232.
- [18] You L, Chang D, Du HZ, et al.Genome-wide screen identifies PVT1 as a regulator of Gemcitabine sensitivity in human pancreatic cancer cells [J] .Biochem Biophys Res Commun, 2011, 407(1): 1-6.
- [19] Fan H, Zhu JH, Yao XQ.Knockdown of long non-coding RNA PVT1 reverses multidrug resistance in colorectal cancer cells [J] .Molecular Medicine Reports, 2018, 17(6): 8309-8315.
- [20] Wu D, Li Y, Zhang H, et al.Knockdown of lncRNA PVT1 enhances radiosensitivity in non-small cell lung cancer by sponging miR-195 [J] .Cell Phys Biochem, 2017, 42(6): 2453-2466.

备注/Memo: -

更新日期/Last Update: 2019-08-29