

小分子HIF-1 α 干扰RNA逆转鼻咽癌细胞耐药的实验

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Experimental on Drug-resistant Effect on Nasopharyngeal Cancer Cells with siRNA-HIF-1 α Silencing

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摘要

目的

探讨小分子HIF-1 α 干扰RNA对人鼻咽癌耐药细胞株CNE2/DDP耐药性的影响。方法采用药物大剂量冲击和逐渐增加剂量相结合的方法建立人鼻咽癌顺铂耐药细胞株CNE2/DDP, 瞬时转染法将HIF-1 α 小片段RNA导入CNE2/DDP细胞沉默HIF-1 α 基因, MTS法及流式细胞仪分别检测顺铂对CNE2/DDP细胞增殖、凋亡的影响, Western blot法分析细胞HIF-1 α 及MDR1表达水平。结果成功建立了人鼻咽癌顺铂耐药细胞株CNE2/DDP, 耐药系数达16。当顺铂 $\geq 1.0 \mu\text{g/ml}$ 时, CNE2组与siHIF-1 α siRNA组细胞抑制率均明显高于CNE2/DDP组与siCtrl-siRNA组 ($P < 0.05$); 同样, CNE2组与siHIF-1 α siRNA组细胞凋亡率也明显高于CNE2/DDP组与siCtrl-siRNA组 ($P < 0.05$); Western blot显示siHIF-1 α siRNA组HIF-1 α 及MDR1蛋白的表达低于CNE2/DDP组。结论小分子HIF-1 α 干扰RNA沉默HIF-1 α 提高了人鼻咽癌顺铂耐药细胞CNE2/DDP对顺铂的敏感度, 逆转了CNE2/DDP对顺铂的耐药性。

关键词: 鼻咽癌; 乏氧诱导因子-1 α ; 多药耐药

Abstract:

Objective

To investigate drug-resistant effect in a cisplatin-resistant human nasopharyngeal carcinoma (NPC) cell line CNE2/DDP with HIF-1 α silencing. Methods The drug-resistant cell line CNE2/DDP was established by a procedure of the human NPC cell line CNE2 exposed to the medium with repeated sharp high and then low but gradually increasing concentration of cisplatin. Small fragments of HIF-1 α RNA were transfected into the cell line CNE2/DDP to silence HIF-1 α by transient transfection method. Cell proliferation and apoptosis of cell line CNE2/DDP with HIF-1 α silencing were measured by MTS assay and flow cytometry analysis, respectively. Western blot were applied to detect the expression of HIF-1 α and MDR1 in cell line CNE2/DDP. Results The cisplatin-resistant human NPC cell line CNE2/DDP was established successfully and the resistance index was 16. When the concentration of cisplatin was higher than or equal to $1.0 \mu\text{g/ml}$, the inhibition rates of cisplatin on CNE2 group and siHIF-1 α siRNA group were significantly higher than that on CNE2/DDP group and siCtrl-siRNA group ($P < 0.05$). Similarly, flow cytometry analysis showed that apoptosis in CNE2 group and siHIF-1 α siRNA group were significantly higher than that in CNE2/DDP group and siCtrl-siRNA group ($P < 0.05$). Furthermore, Western blot showed that HIF-1 α and MDR1 proteins in siHIF-1 α siRNA group were significantly lower than those in CNE2/DDP group. Conclusion HIF-1 α silenced by siRNA improved the sensitivity of the cisplatin-resistant human NPC cell line CNE2/DDP to cisplatin, and reversed the

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resistance of CNE2/DDP to cisplatin.

Key words: Nasopharyngeal carcinoma Hypoxia-inducible factor 1 α Multidrug resistance

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[1]

[1] XXiao WW, Huang SM, Han F, et al. Local control, survival, and late toxicities of locally advanced

[2]

nasopharyngeal carcinoma treated by simultaneous modulated accelerated radiotherapy combined with

[3]

cisplatin concurrent chemotherapy: long-term results of a phase 2 study [J]. Cancer, 2011, 117(9): 1874-

[4] 83.

[5]

[2] NNg WT, Lee MC, Hung WM, et al. Clinical outcomes and patterns of failure after intensity-modulated

[6]

radiotherapy for nasopharyngeal carcinoma [J]. Int J Radiat Oncol Biol Phys, 2011, 79(2): 420-8.

[7]

[3] ZZhu H, Chen XP, Luo SF, et al. Hypoxia-inducible factor-1 α dependent expression and

[8]

significance of the related multidrug resistance genes induced by hypoxia in human hepatocarcinoma

[9]

cell [J]. Zhonghua Wai Ke Za Zhi, 2005, 43(5): 277-81. [朱虹, 陈孝平, 罗顺峰, 等. 缺氧诱导因子1 α 依赖性缺氧

[10]

诱导人肝癌细胞多药耐药相关基因的表达及意义 [J]. 中华外科杂志, 2005, 43(5): 277-81.]

[11]

[4] SSui J, Wu J, Li X, et al. The expression and significance of hypoxia inducible factor-1 α and

[12]

microvessel density in human nasopharyngeal carcinoma [J]. Lin Chuang Er Bi Yan Hou Tou Jing Wai Ke

[13]

Za Zhi, 2008, 22(6): 269-72. [隋军, 吴金鹏, 李晓江, 等. 缺氧诱导因子-1 α 与微血管密度在人鼻咽癌中的表达及相关

[14]

性研究 [J]. 临床耳鼻咽喉头颈外科杂志, 2008, 22(6): 269-72.]

[15]

[5] CChen J, Qian GS, Huang GJ, et al. Establishment of a multidrug resistance cell line from human lung

[16]

adenocarcinoma cells and its biologic features [J]. Di San Jun Yi Da Xue Xue Bao, 2001, 23(2): 135-137.

[17]

[陈杰, 钱桂生, 黄桂君, 等. 人肺腺癌多药耐药细胞系的建立及其生物学特征 [J]. 第三军医大学学报, 2001, 23

[18]

[2] ::135-7.]

[19]

[6] WWakabayashi A,Takeda T,Tsuiji K,et al.Antiproliferative effect of adiponectin on rat uterine

[20]

leiomyoma ELT-3 cells [J] .Gynecol Endocrinol,2011,27(1): 33-8.

[21]

[7] BBaba Y,Nosho K,Shima K,et al.HIF1A overexpression is associated with poor prognosis in a cohort

[22]

of 731 colorectal cancers [J] .Am J Pathol,2010,176(5):2292-301.

[23]

[8] LLu X,Yan CH,Yuan M,et al.In vivo dynamics and distinct functions of hypoxia in primary tumor

[24]

growth and organotropic metastasis of breast cancer [J] .Cancer Res,2010,70(10): 3905-14.

[25]

[9] EEckert AW,Schutze A,Lautner MH,et al.HIF-1alpha is a prognostic marker in oral squamous cell

[26]

carcinomas [J] .Int J Biol Markers,2010,25(2):87-92.

[27]

[10] Munipalle PC,Viswanath YK,Davis PA,et al.Prognostic value of hypoxia inducible factor 1alpha in

[28]

esophageal squamous cell carcinoma [J] .Dis Esophagus,2011,24(3): 177-81.

[29]

[11] Wu XH,Qian C,Yuan K.Correlations of hypoxia-inducible factor-1alpha/ hypoxia-inducible factor-

[30] 2alpha expression with angiogenesis factors expression and prognosis in non-small cell lung cancer

[J

[31]]

.ChChin Med J (Engl),2011,124(1):11-8.

[32]

[12] Semenza GL.Intratumoral hypoxia,radiation resistance,and HIF-1 [J] .Cancer Cell,2004,5(5): 405-



[33] 6.

[34]

[13] Chen L,Feng P,Li S,et al.Effect of hypoxia-inducible factor-1alpha silencing on the sensitivity

[35]

of human brain glioma cells to doxorubicin and etoposide [J] .Neurochem Res,2009,34(5):984-90.

[36]

[14] Ma C,Zhou GY,Xiao Y,et al.Reversion the multidrug resistance of human breast carcinoma cells by

[37]

RNA interference targeting HIF-1 alpha gene [J] .Zhonghua Bing Li Xue Za Zhi,2006,35(6): 357-60. [马超

[38]

,周庚寅,肖颖,等.RNA干扰沉默缺氧诱导因子-1 α 逆转乳腺癌的耐药性 [J] .中华病理学杂志,2006,35(6): 357-60.

[39]]

[40]

[15] Zhu H,Chen XP,Luo SF,et al.Involvement of hypoxia-inducible factor-1-alpha in multidrug

[41]

[42]

[16] Britz-Cunningham SH, Adelstein SJ. Molecular targeting with radionuclides: state of the science [J]

[43]

. J Nucl Med, 2003, 44(12): 1945-61.

- [1] 王耕;黄韬;薛家鹏;王明华;惠震. 三羟异黄酮对人乳腺癌MCF-7/ADM细胞体外抑瘤效应、细胞周期及凋亡的影响[J]. 肿瘤防治研究, 2011, 38(8): 886-890.
- [2] 陈漫霞;姚振江;陈思东;王漫云;许雅;蔡旭玲. 原发性肝细胞癌中P-gp、Topo II α 和P53的表达及意义[J]. 肿瘤防治研究, 2011, 38(3): 278-280.
- [3] 李伟忠;王晓燕;霍秋菊. 环氧合酶-2抑制剂对人舌鳞癌Tca8113/BLM细胞MDR1/P-gp表达的影响[J]. 肿瘤防治研究, 2011, 38(1): 9-12.
- [4] 杜 芹;魏 玲;姜 超;杨锡贵. 人恶性淋巴瘤细胞Raji长春新碱耐药株Raji/VCR的建立及其生物学特性[J]. 肿瘤防治研究, 2010, 37(07): 751-753.
- [5] 梁 虹;茆俊卿;张 育;高 娜;沈维干;顾 健. 马钱子碱对白血病K562/AO2细胞多药耐药性的逆转作用[J]. 肿瘤防治研究, 2010, 37(07): 739-743.
- [6] 王天晓;雷凯健. 异汉防己碱增强多药耐药肿瘤细胞对阿霉素的敏感性及其机制[J]. 肿瘤防治研究, 2009, 36(1): 1-4.
- [7] 杨叶;侯培珍;张娟. 川芎嗪联合氟尿嘧啶对胃癌细胞SGC-7901/ADR的杀伤作用[J]. 肿瘤防治研究, 2008, 35(9): 624-626.
- [8] 蒋旭琴;包明红;梅晓冬. 鞣酸对LLC/cMOAT细胞多药耐药性的逆转机制[J]. 肿瘤防治研究, 2008, 35(9): 630-634.
- [9] 王磊;柯红;任东明;王一羽. 阿霉素纳米粒对人白血病多药耐药细胞株HL-60/ADR多药耐药性的逆转作用[J]. 肿瘤防治研究, 2008, 35(7): 527-528,.
- [10] 李洽;刘春萍;明洁;田元;黄韬. 复发性乳腺癌化疗药物敏感性的体外实验[J]. 肿瘤防治研究, 2008, 35(2): 132-133.
- [11] 梁川;吴绪峰;陈慧君. 卵巢癌中MDR1的表达及其临床意义[J]. 肿瘤防治研究, 2008, 35(10): 723-726.
- [12] 贾长河;康谊;王文玉;任颖. 胃癌耐药基因检测对临床化疗的指导意义[J]. 肿瘤防治研究, 2008, 35(10): 711-714.
- [13] 郭立杰;蔡骏. 大黄素抗肿瘤作用的研究进展[J]. 肿瘤防治研究, 2008, 35(08): 605-608.
- [14] 张梅春;赵子文;曾 军. **survivin** 反义寡核苷酸逆转顺铂诱导的人肺腺癌细胞凋亡耐受作用[J]. 肿瘤防治研究, 2007, 34(8): 560-564.
- [15] 黄程辉;曹培国. 甲基莲心碱对乳腺癌**MCF-7/Adr**细胞**MDR**逆转的研究[J]. 肿瘤防治研究, 2007, 34(5): 351-354.