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论著

新型分子探针近红外荧光标记Zn-DPA 监测肿瘤疗效的研究

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摘要:

目的:探讨新型分子探针近红外荧光标记Zn-DPA(Zn-DPA-PSS794)通过光学成像监测阿霉素治疗卵巢癌疗效的可行性,并与Cy5.5-annexin V光学成像效果进行比较。方法:MTT和流式细胞术分析阿霉素对卵巢癌细胞株OVCAR-8的杀伤作用。将OVCAR-8种植到裸鼠皮下,成瘤后分为对照组和治疗组,每组再分2个亚组,即DPA组和annexin V组。治疗组静脉注射阿霉素,2次后各组裸鼠分别进行Zn-DPA-PSS794光学显像和Cy5.5-annexin V光学显像,并进行定量分析。处死裸鼠,分离肿瘤,切片后进行HE染色,Western印迹检测肿瘤组织中caspase-3蛋白表达水平。结果:阿霉素对OVCAR-8的IC50为6 μmol/L,阿霉素能体外诱导OVCAR-8凋亡、坏死,总效率达35%。阿霉素治疗裸鼠移植瘤48 h后,Zn-DPA-PSS794光学成像和Cy5.5-annexin V光学成像均为阳性,而对照组2种光学成像结果均为阴性,对照组和治疗组肿瘤部位的荧光强度差异有统计学意义(P<0.001)。肿瘤组织HE染色示肿瘤细胞核大,深染。治疗组中caspase-3蛋白高表达,而对照组低表达。结论:Zn-DPA-PSS794光学成像能有效监测阿霉素治疗OVCAR-8荷瘤裸鼠的疗效,与Cy5.5-annexin V显像效果类似。

关键词: Zn-DPA annexin V 光学成像 卵巢癌 阿霉素 疗效监测

Near-infrared fluorescent zinc-dipicolylamine: a new molecular imaging probe to monitor the efficiency of chemotherapy

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Abstract:

Objective To investigate the feasibility of a novel molecular probe of Zn-DPA-PSS794 to monitor the efficiency of doxorubicin to ovarian cancer and compare with Cy5.5-annexin V. Methods Efficiency of doxorubicin to OVCAR-8 cells in vitro was measured by MTT assay and flow cytometry. The in vivo studies were performed on an OVCAR-8 xenograft tumor model. Mice were divided into a control group and a treatment group. Each group was divided into 2 subgroups, DPA and annexin V. In the treatment group, the mice were treated with doxorubicin for 2 doses. All mice were performed optical imaging by Zn-DPA-PSS794 or Cy5.5-annexin V, respectively and then sacrificed. The tumor was separated and stained by HE. The expression of caspase-3 protein was measured by Western blot. Results The IC50 of doxorubicin to OVCAR-8 was 6 μmol/L. The percentage of apoptosis and dead cells was 35% after doxorubicin treatment. In the optical image, photons accumulated in the tumor either by Zn-DPA-PSS794 or Cy 5.5-annexin V in the treatment group. That was negative in the control group. The fluorescence intensity had significant difference between the 2 groups(P<0.001). The nuclei were big and stained with deep color after the cells were stained with HE. The caspase-3 expression was high in the treatment group, while it was low in the control group. Conclusion Zn-DPA-PSS794 as a probe used by optical imaging can monitor the efficiency of doxorubicin to OVCAR-8 xenograft tumor, which is similar to Cy5.5-annexin V.

Keywords: Zn-DPA annexin V optical imaging ovarian cancer doxorubicin monitoring efficiency

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参考文献:

[1] Haberkorn U, Markert A, Mier W, et al. Molecular imaging of tumor metabolism and apoptosis [J]. Oncogene, 2011,16.

[2] Vangestel C, Peeters M, Mees G, et al. In vivo imaging of apoptosis in oncology: an update [J]. Mol Imaging, 2011,26.

[3] Smith B A, Xiao S, Wolter W, et al. In vivo targeting of cell death using a synthetic fluorescent molecular probe
[J]. Apoptosis, 2011,16(7):722-731.

[4] Edgington L E, Berger A B, Blum G, et al. Noninvasive optical imaging of apoptosis by caspase-targeted activity-based probes
[J]. Nat Med, 2009, 15(8):967-973.

[5] Sun D, Yang K, Zheng G, et al. Study on effect of peptide-conjugated near-infrared fluorescent quantum dots on the clone formation, proliferation, apoptosis, and tumorigenicity ability of human buccal squamous cell carcinoma cell line BcaCD885
[J]. Int J Nanomedicine, 2010, 5:401-405.

[6] Petrovsky A, Schellenberger E, Josephson L, et al. Near-infrared fluorescent imaging of tumor apoptosis
[J]. Cancer Res,2003, 63(8):1936-1942.

[7] Smith B A, Akers W J, Leevy W M, et al. Optical imaging of mammary and prostate tumors in living animals using a synthetic near infrared zinc(II)-dipicolylamine probe for anionic cell surfaces
[J]. J Am Chem Soc, 2010,132(1):67-69.

[8] Niu G, Chen X. Apoptosis imaging: beyond annexin V
[J]. J Nucl Med, 2010, 51(11):1659-1662.

[9] Collingridge D R, Glaser M, Osman S, et al. In vitro selectivity, in vivo biodistribution and tumour uptake of annexin V radiolabelled with a positron emitting radioisotope
[J]. Br J Cancer, 2003, 89(7):1327-1333.

[10] Li X, Link J M, Stekhova S, et al. Site-specific labeling of annexin V with F-18 for apoptosis imaging
[J]. Bioconjugate Chem, 2008, 19(8), 1684-1688.

[11] 田蓉,孙红芳,匡安仁,等.细胞凋亡近红外线荧光显像在评价肿瘤放疗早期疗效中的作用
[J].中国临床医学影像杂志,2008,19(12):846-849,871. TIAN Rong, SUN Hongfang, KUANG Anren, et al. Evaluation of early efficacy of tumor radiation therapy using NIRF imaging
[J].Journal of China Clinic Medical Imaging,2008, 19(2): 846-459, 871.

[12] Zhang R, Lu W, Wen X, et al. Annexin A5-Conjugated Polymeric Micelles for Dual SPECT and Optical Detection of Apoptosis
[J]. J Nucl Med, 2011, 52(6):958-964.

[13] Frey B, Schildkopf P, R del F, et al. AnnexinA5 renders dead tumor cells immunogenic-implications for multimodal cancer therapies
[J]. J Immunotoxicol, 2009, 6(4): 209-216.

[14] Vanderheyden J L, Liu G Z, He J, et al. Evaluation of Tc-99m-MAG(3)-annexin V: influence of the chelate on in vitro and in vivo properties in mice
[J]. Nucl Med Biol, 2006, 33(1), 135-144.

[15] DiVittorio K M, Leevy W M, O’ Neil E J, et al. Zinc(II) coordination complexes as membrane-active fluorescent probes and antibiotics
[J]. Chembiochem, 2008, 9(2): 286-293.

[16] Adams K E,Ke S,Kwon S,et al. Comparison of visible and near-infrared wavelength-excitable fluorescent dyes for molecular imaging of cancer
[J]. J Biomed Opt, 2007, 12(2): 024017.

[17] Smith B A, Gammon S T, Xiao S. In vivo optical imaging of acute cell death using a near-infrared fluorescent zinc-ipicolylamine probe
[J]. Mol Pharm, 2011, 8(2): 583-590.

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[J]．中南大学学报(医学版)，2006,31(01)：45-56

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