

简报

小剂量辐射对肿瘤细胞 K₅₆₂ 及肿瘤病人天然杀伤细胞(NK)活性的影响

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摘要 已知小剂量辐射可增强机体免疫功能。从对高本底地区的调查发现,该地区居民肿瘤死亡率及某些肿瘤发病率有所降低⁽¹⁾。NK 细胞能直接杀伤肿瘤细胞,在肿瘤免疫中起着重要的作用。本文观察小剂量辐射对肿瘤病人和正常人外周血淋巴细胞 NK 活性的相对效应以及对人红白血病细胞 (K₅₆₂ 细胞)的影响,以期从体外实验来探索较小剂量辐射对肿瘤治疗的影响。

关键词 小剂量辐射, 肿瘤细胞, Nk 活性, 刺激效应

采用 ³H-TdR 释放法测定人外周血 NK 活性^[2],共检测 21 例肿瘤病人,其中肺癌 6 例,胃癌 8 例,食道癌和恶性淋巴瘤各 3 例,鼻咽癌 1 例。所有病人采血前均未接受过治疗,同时以 10 名正常人作对照。²²⁶Ra γ 源为照射源,对人外周血进行离体照射,剂量分组如下: 0 cGy、5 cGy、10 cGy、30 cGy、50 cGy、80 cGy 和 120 cGy。Beckman 液闪仪测定 K₅₆₂ 细胞中 ³H-TdR 的每分钟放射性计数(cpm),按下式计算 NK 活性:

$$\text{NK 活性} = \frac{\text{靶细胞组 cpm} - \text{受照组残留靶细胞 cpm}}{\text{靶细胞组 cpm} - \text{对照组残留靶细胞 cpm}} \times 100\%$$

式中靶细胞组 cpm 指 K₅₆₂ 细胞组的 cpm 值,而对照组残留靶细胞 cpm 值指(未经照射的)人血分离的淋巴细胞和靶细胞混合培养一定时间后所得残留靶细胞的 cpm 值,两者相减即为被杀死的靶细胞所释放的 cpm 值,受照组残留靶细胞 cpm 指经照射的人血分离的淋巴细胞和靶细胞混合培养后残留靶细胞的 cpm 值。

肿瘤病人外周血经 50 cGy γ 射线照射后,可观察到 NK 活性显著增强,为对照组的 120.5%,其余各剂量组其 NK 活性无显著性改变。正常人外周血经 10 cGy~50 cGy 照射后,其 NK 活性均显著升高,以 50 cGy 照射组增幅较大,在各剂量组均可观察到经小剂量辐射后,正常人外周血 NK 活性升高程度有大于肿瘤病人的趋势。经检验,在 50 cGy 组两组人员外周血 NK 活性的改变有显著性差异(见表 1)。

Tab 1. Effects of low dose irradiation on blood NK activity of normal individuals and patients with cancer in vitro ($\bar{x} \pm s$)

Group	n	Dose/cGy				
		0	10	30	50	80
Control	10	100	120.8±21.0 ⁽¹⁾	107.6±19.4	140.0±21.4 ⁽²⁾	108.4±17.5
Cancer patients	21	100	109.4±22.8	102.8±13.8	120.5±19.8 ⁽²⁾⁽³⁾	98.5±10.6

⁽¹⁾p<0.05 ⁽²⁾p<0.01 (Compared to 0cGy group) ⁽³⁾p<0.05 (Compared to control)

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又以 $^3\text{H-TdR}$ 参入法观察经小剂量辐射后人肿瘤细胞 K₅₆₂ 增殖功能的改变。取对数生长期的 K₅₆₂ 细胞, 1×10^4 个/瓶, 经照射后加入 $^3\text{H-TdR}$, $3.7 \times 10^4 \text{Bq/瓶}$, 培养 6 h 后测定每分钟放射性计数。结果发现在 10 cGy 剂量组 $^3\text{H-TdR}$ 参入明显增加, 表明该剂量对 K₅₆₂ 细胞具有刺激作用。30 cGy 及 50 cGy 照射不引起 $^3\text{H-TdR}$ 参入的明显变化。当照射剂量为 80 cGy 和 120 cGy 时, K₅₆₂ 细胞的 $^3\text{H-TdR}$ 参入即明显减少, 说明该剂量下细胞功能已受到抑制(见表 2)。

Tab 2. Effects of low dose irradiation on proliferation function of K₅₆₂ cells ($\bar{x} \pm s$)

Dose/cGy	cpm/ 10^4 cells	Percentage of control/%
0	5715 $\pm$ 334	100 $\pm$ 0
5	5961 $\pm$ 338	104.4 $\pm$ 4.3
10	6552 $\pm$ 598 ⁽¹⁾	115.3 $\pm$ 14.0
30	5935 $\pm$ 516	103.8 $\pm$ 5.6
50	5221 $\pm$ 618	91.7 $\pm$ 12.4
80	4393 $\pm$ 308 ⁽²⁾	77.1 $\pm$ 6.7
120	3561 $\pm$ 290 ⁽²⁾	62.4 $\pm$ 4.6

$n=6$ ⁽¹⁾ $p<0.05$ ⁽²⁾ $p<0.01$

小剂量辐射对 NK 细胞刺激作用的发生机制尚不明确, 据报道, 经 10 cGy 左右的小剂量辐射后, 淋巴细胞受到激活^[3]。NK 细胞为辐射抗性细胞^[4]。一般认为, 辐射刺激作用的剂量和所观察参数的放射敏感性是相关的, 即放射敏感性越高, 发生辐射刺激作用的剂量就越低^[5]。在本实验中, 观察到正常人外周血经 10 cGy 和 50 cGy 照射后, NK 活性增强, 而 30 cGy 照射后却无显著性差异, 推测经 10 cGy 照射后 NK 活性的升高, 可能由于受激活的淋巴细胞释放出某些淋巴因子(干扰素、白细胞介素 2 等), 作用于 NK 细胞, 使其活性增强^[6], 而 50 cGy 照射后 NK 活性的增强, 可能由于 γ 射线对 NK 细胞直接刺激作用所致。一般认为, NK 细胞杀伤机理是通过释放一种 NK 细胞毒因子而起到杀伤作用^[7]。肿瘤病人可能由于其 NK 细胞功能已受损^[8], 分泌该种因子的量有所下降, 从而使 NK 活性升高幅度低于正常人。

小剂量辐射对肿瘤细胞有无刺激作用, 也是值得注意的问题。K₅₆₂ 细胞经 10 cGy 辐照后, $^3\text{H-TdR}$ 参入明显增加, 当剂量达 50 cGy 以上时, $^3\text{H-TdR}$ 参入下降, 说明小剂量辐射对肿瘤细胞也具有刺激作用, 在应用较小剂量辐射治疗肿瘤时, 虽可提高 NK 细胞活性但需防止刺激肿瘤细胞的增生, 故应选择合适的辐照剂量, 使其既能刺激 NK 细胞的功能, 又对肿瘤细胞具有抑制作用。

本文采用的是体外实验的方法, 与在体照射相比可能存在某些差异, 尚须进一步研究。

参 考 文 献

- 1 Nambi K S. Health Phys., 1987, 52: 653
- 2 苏燎原等. 癌症, 1990, 9(5): 378
- 3 杜泽吉等. 辐射研究与辐射工艺学报, 1994, 12(1): 59
- 4 王宜强等. 军事医学科学院院刊, 1993, 17(2): 104
- 5 鞠桂芝等. 中华放射医学与防护杂志, 1989, 9(1): 8
- 6 吴易元等. 中国免疫学杂志, 1985, 1(2): 55
- 7 林飞卿等主编: 医学基础免疫学, 上海医科大学出版社, 上海, 1990: 72~79
- 8 苏燎原等. 癌症, 1985, 4(1): 15

EFFECTS OF LOW DOSE IRRADIATION ON TUMOR CELLS AND TUMOR PATIENT'S BLOOD NK ACTIVITY IN VITRO

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ABSTRACT In this paper, relative effects of LDI on NK activity of blood lymphocytes in normal subjects and cancer patients in vitro and effects of LDI on K_{562} cells were studied. NK activity was determined by ^3H -TdR release assay. 21 patients and 10 normal individuals blood were analysed. All samples were irradiated by ^{226}Ra γ -rays with doses 0, 5, 10, 30, 50, 80, 120 cGy separately. The results indicated that the NK activity of lymphocytes in cancer patient's blood increased significantly in 50 cGy irradiation group (120.5% of control). No significant changes were found in other dose groups. While in normal subjects, NK activity increased at both dose groups, 10 and 50 cGy. The peak value of NK activity appeared at dose of 50 cGy. The tendency of the increase of NK activity in normal subjects after LDI was higher than that in patients. There was significant difference of NK activity changes between two groups of persons after 50 cGy irradiation. ^3H -TdR incorporation was used to study the effects of LDI on K_{562} cells. The result showed that ^3H -TdR incorporation in K_{562} cells increased significantly after 10 cGy irradiation. It indicated stimulating effect. As the dose is above 80 cGy, ^3H -TdR incorporation decreased significantly, which indicated that the stimulating effect disappeared.

KEYWORDS Low dose irradiation, Tumor cell, NK activity, Stimulating effect

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EFFECTS OF LOW DOSE IRRADIATION ON THE SPLENIC MACROPHAGES FUNCTION IN MICE

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ABSTRACT It is known that low dose ionizing radiation stimulated the immune functions in human subjects and mice. In order to examine the situation of macrophages a series of changes in the immune system in Kunming mice following low dose whole body irradiation were observed based on the study of macrophages from spleen. The present study was designed by whole body X-rays with the doses of 50, 75, 100 and 250 mGy, respectively. The dose rate was 12.5 mGy/min. All the results showed that low dose irradiation may enhance the function of macrophages on the reaction of lymphocytes to ConA, and increase content of IL-1 from macrophages.

KEYWORDS Low dose irradiation, Splenic macrophages, IL-1, Splenic lymphocytes