5 - 52 Effect of Quiescence on Apoptosis Induced by Carbon Ions Radiation of Human HeLa Cells

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The radioresistance of cancer cells is a major factor leading to radiotherapy failure and poor prognosis in patients. Quiescent cells are considered a major reason for cancer radioresistance due to their larger hypoxic fraction and stronger repair ability[1]. Compared with proliferating cancer cells, quiescent cancer cells have lower sensitivity to radiotherapy and chemotherapy, and stronger repair ability[2,3]. For proliferating cells, there are certain differences in the radiosensitivity of cells in different cell cycles: M phase is the most sensitive, S phase is the most resistant, and prolonging G1 phase will increase the radioresistance of cells. For low LET γ Or X-ray irradiation, the sensitivity of proliferating cancer cells is usually significantly higher than that of quiescent cancer cells. Therefore, after radiotherapy, a considerable amount of quiescent cancer cells will still survive, and their proliferation activity will be triggered, leading to cancer recurrence. As a prospective technology in radiotherapy methods, carbon ions irradiation has shown strong cancer cell killing ability, approximately $2 \sim 3$ times that of X-ray irradiation[4]. However, the molecular mechanisms of heavy ions overcoming the radioresistance of quiescent cancer cells is not completely understood.

As shown in Fig. 1, application with carbon ions led to the apoptosis of proliferating and quiescent HeLa cells, with the proliferating cells being markedly more effective. The results revealed that carbon ions radiation induced a significant increase in cell apoptotic of quiescent HeLa cells at 12 and 24 h after radiation (from 5.14 to 8.16 and 13.75%, respectively), when compared with the controls. However, carbon ions potently induced the apoptosis of proliferating HeLa cells; The proportion of apoptotic cells was 13.74 and 17.04%, respectively. The results suggested that quiescence effectively inhibits irradiation-induced apoptosis in HeLa cells, and quiescent cancer cells have more radioresistance.

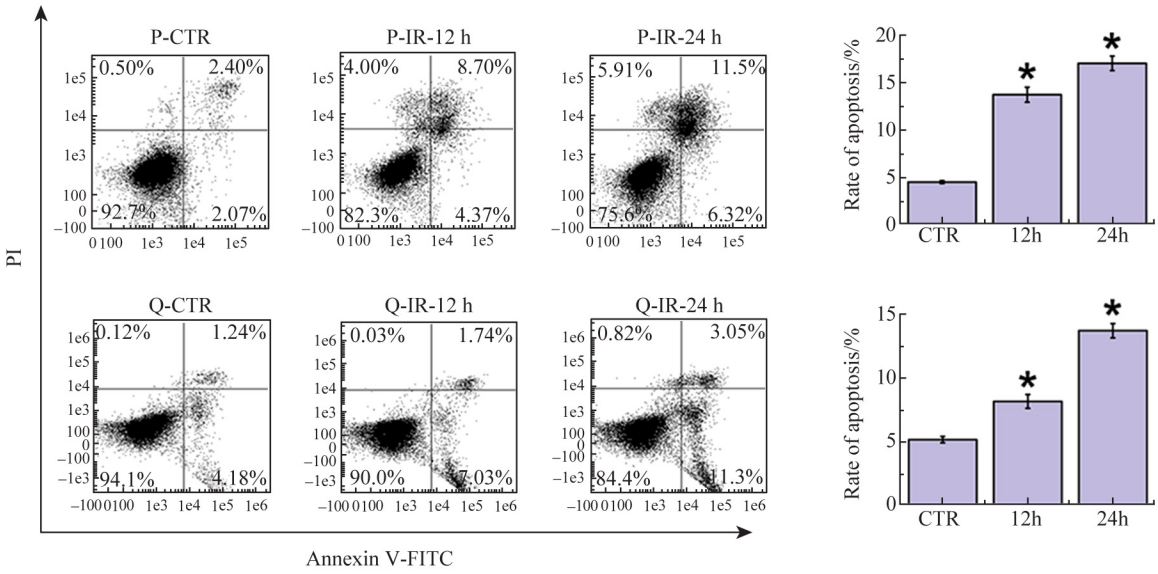

Fig. 1 (color online) Carbon ions induce the apoptosis of proliferating and quiescent HeLa cells. Cell apoptosis at 12 and 24 h after carbon-ion radiation was assessed using Annexin VFITC and PI doublestaining flow cytometry. $*P$ ¡ 0.05 compared to untreated control. P, proliferate cancer cells; Q, quiescent cancer cells.

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5 - 53 Research Progress and Clinical Application of Boron Carrier in BNCT Therapy

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Boron neutron capture therapy (BNCT) is a form of radiotherapy in which the patient is firstly injected with a boron-containing drug. Because of its strong affinity for cancer cells, drug quickly collects in the tumor cells and rarely in normal tissue[1]. Next, the patient's tumor site needs to be irradiated with thermal neutrons. When the thermal neutron is captured by ^{10}B in the tumor cell, an^{11}B is formed and fissions to produce a more destructive α particle and a ^{7}Li recoil nucleus, which can then precisely kill the tumor cell (Fig. 1). The produced low-energy α particles and ^{7}Li recoil nuclei have high linear energy transfer and high cell biological effects. Their range in the tissue is equivalent to the diameter of one cell, most of the energy of particles is deposited in the nucleus, which is a sensitive site for radiation damage in cells. Therefore, alpha particles and ^{7}Li nuclei can kill tumor cells precisely and have little damage to the surrounding tissue[2,3].

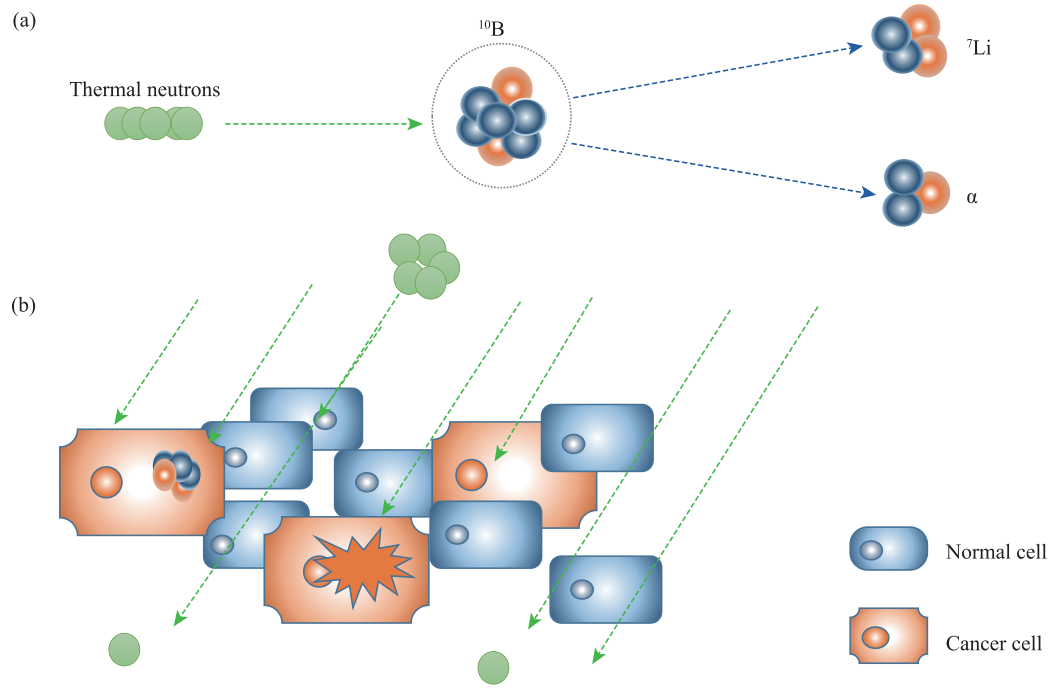

Fig. 1 (color online) Schematic diagram of BNCT principle. (a) after neutron irradiation, boron-containing cells undergo nuclear fission to produce α particles and ^{7}Li recoil nuclei, (b) BNCT treatment kills tumor cells without damaging normal cells.

The development of novel ^{10}B delivery agents with high tumor selectivity is undoubtedly one of the most important needs for the success of BNCT. Currently, the development of third generation boron carriers based on the second-generation boron carriers ^{10}B-BSH and $L-^{10}$B-BPA is expected to increase the boron concentration ratio of tumor cells to normal tissue as well as to blood, resulting in more efficient boron-containing drugs[4]. Mainly amino acids, antibodies, nucleosides, porphyrins, peptides, nanomaterials, *etc.* can improve the specificity of boron carriers for tumor cells[5] (Fig. 2).

In clinical treatment, second-generation boron agents are widely used and have achieved remarkable results in tumors such as glioblastoma multiforme, head and neck tumors and melanoma. Third-generation boron carriers are in a development boom as well as in preliminary clinical trials, and more clinical trials are needed to validate their anti-tumor effects. At present, the development of BNCT still faces a number of problems, the first of which is the insufficient intra-tumoral ^{10}B content and the gap between its T/N and T/B values and the actual