Study on the radiosensitivity of carbon ion($^{12}\text{C}^{6+}$) beam to different lung adenocarcinoma cell lines

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Objective To investigate the radiosensitivity differences of different doses of carbon ion radiation different types of lung adenocarcinoma cell lines.

Method 4 lung adenocarcinoma cell lines, A549, H1299, H460, and H1975, were cultured in RPMI-1640 complete nutrient solution containing FBS to 70%. Respectively using 0, 1, 2, and 4 Gy $^{12}\text{C}^{6+}$ heavy ion beam to irradiate 4 cell lines, which was delivered by Wuwei carbon ion therapy system developed by institute of modern physics, Chinese academy of sciences. Continue cultured to 24h and 48h, using cell clone forming test to detect cell clone rate, cell count assay (CCK 8) to detect cell inhibition rate and flow cytometry analysis to test cell cycle and apoptosis respectively. RT-PCR and immunofluorescence confocal assay were used to measure expression of STAT3, TGF- β 1, e-cadherin and mmp-2 related molecules.

Results The results of cloning formation test showed that with the increase of irradiation dose, the cell cloning formation rate was inhibited, and the inhibition effect was successively H1975, H460, A549, and H1299. Compared with the 0Gy group, the inhibition effect of 4Gy group was the most significant. Cell count test results show that after different doses of carbon ion beam irradiation, the 4 cell lines showed different inhibition effect, the inhibition rate was successively H460, A549, H1299 and H1975, inhibition effect was significantly increased with the increase of irradiation dose ($p < 0.05$) at 24h, 48h and 72h. Flow cytometry analysis results showed that the cell cycle was significantly blocked in the G2/M phase after carbon ion beam irradiation, and this blocking effect was most significant at 24h ($p < 0.05$), and the blocking effect was successively H1975, H460, H1299, and A549. With the increase of radiation dose, apoptosis rate

increased obviously. RT-PCR (real time PCR) and immunofluorescence confocal assay showed that with the increase of irradiation dose, the expression levels of STAT3, e-cadherin and mmp-2 decreased accordingly, but TGF- β 1 decreased in the transcription level and did not change in protein level ($p > 0.05$).

Conclusion Carbon ion beam can inhibit the proliferation of lung adenocarcinoma cells by changing the extracellular and intracellular signal molecules, and induce cells to G2/M phase arrest, so as to induce apoptosis and inhibit the proliferation and metastasis of lung adenocarcinoma cells.

Fig. 1 Clonal survival curve

Fig. 2 The proliferation curve at 24H after irradiation with different doses

Chart. 1 cell cycle arrest

Chart. 2 cell The apoptosis rate of different dose irradiation

Chart. 3 Expression of related molecules by different dose irradiation

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