and Space Radiobiology had been held in Institute of Modern Physics. More than 20 scientists from Institute of Modern Physics, Chinese Academy of Sciences, from Institute of Applied Physics, National Academy of Sciences of Ukraine, and from Institute of Orthopedics, Lanzhou Command of CPLA took part in the symposium. Moreover, the anunal meeting of the Gansu Key laboratory of Space Radiobiology has also been successfully held on 4^{th} of November.

4 - 66 Carbon-Ion Irradiation is More Efficient to Eliminate Glioma Stem Cells

Ding Nan, Sun Fang, Zhang Xurui, Hua Junrui and Wang Jufang

Cancer stem cells (CSCs) maintain tumor growth by keeping the balance between self-renewal, proliferation and differentiation. Though CSCs occupy a tiny minority, they are the fundamental reason for the formation and recurrence of tumors. CSCs hypothesis suggests that CSCs populate an original tumor, which is resistant to treatments, and repopulate the recurrent tumor after most of the tumor has been removed. CSCs research is one of the most thriving and competitive areas in oncology research because it has the potential to become a predictive factor in radiotherapy.

Currently, carbon-ion radiotherapy has been approved for treatment of specific types of cancers including melanoma, chordoma and glioma. According to results of heavy-ion irradiation therapies from LBL, NIRS, GSI and IMP, this kind of therapy does indeed appear to have clinical advantages over other modalities such as photon irradiation. It was reported that the high linear energy transfer (LET) of carbon ion radiation has shown a higher relative biological effectiveness (RBE) compared to conventional low-LET photon radiation. Therefore, the efficiency of carbon ions inducing DNA damage, cell cycle arrest and cell death in tumor cells is higher than X-rays. Even on radio-resistant (with respect to X-rays) tumors, carbon ions still have high lethality.

We speculate that there's a relationship between heavy-ion irradiation therapy's excellent therapeutic effects and its prominent lethality to CSCs. However, relevant studies have not been reported.

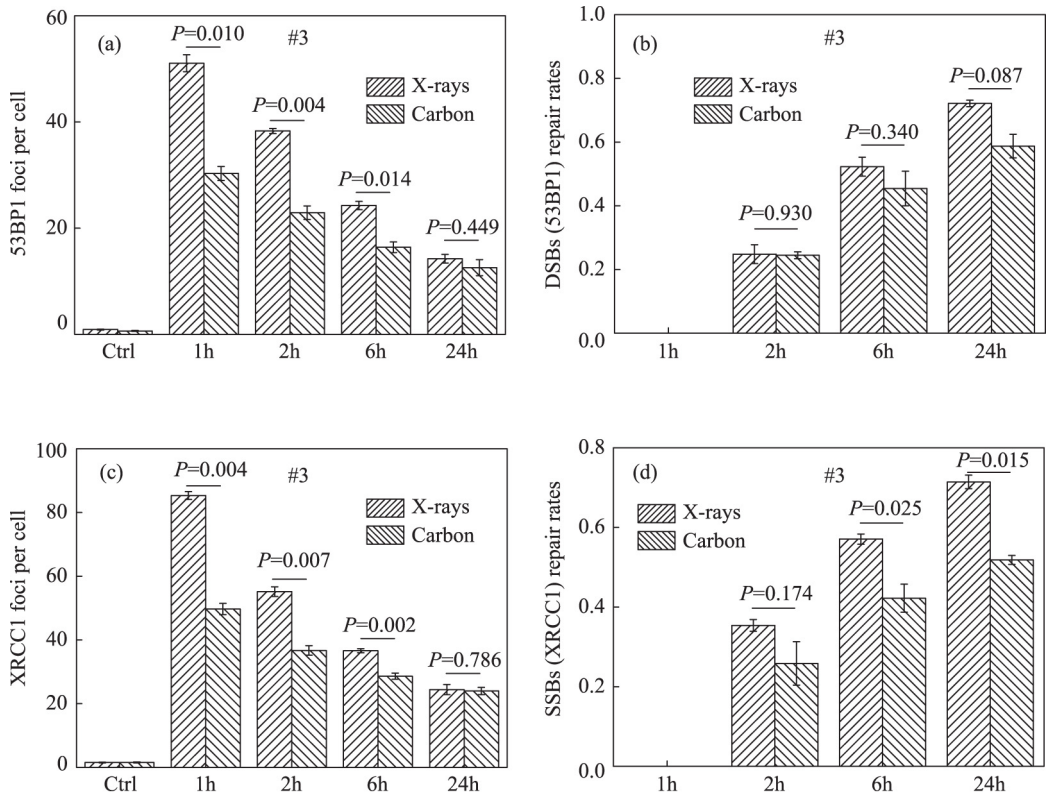

Fig. 1 Repair rate of DNA damage generated by carbon-ion was lower than that generated by X-rays in CSC.

In our present study, human glioma CSCs and murine models of virus induced glioma were used to investigate whether heavy ions offer a biological advantage over conventional X-rays in glioma. We found that, compared with

X-rays irradiation, Carbon-ion irradiation can induce more DNA damages in GSCs, the repair rate of DNA damage generated by carbon-ion was lower than that generated by X-rays in GSCs (Fig. 1) and compared with X-rays, heavy-ion could significantly reduce GSCs viability (Fig. 2). In the *in vivo* experiment, compared with X-rays, carbon-ion could significantly (P=0.0004) kill the glioma stem cells in the mice brains (Fig. 3).

Taken together, carbonion irradiation could induce lethality in the GSCs more efficiently than X-rays. Carbon-ion irradiation provides a significant performance over X-rays in targeting and inducing lethality in GSCs.

A. 53BP1 foci per cell of the #3 GSCs after irradiated with 2 Gy X-rays or carbon ions. B. 53BP1 foci (DSBs) repair rates of the #3 GSCs after irradiated with 2 Gy X-rays or carbon ions. C. XRCC1 foci per cell of the #3 GSCs after irradiated with 2 Gy X-rays or carbon ions. D. XRCC1 foci (SSBs) repair rates of the #3 GSCs after irradiated with 2 Gy X-rays or carbon ions.

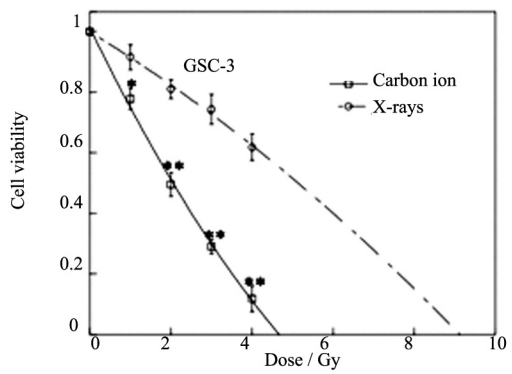

Fig. 2 Cell viability of #3 GSCs irradiated by 0 ∼ 4 Gy carbon-ion and X-rays.

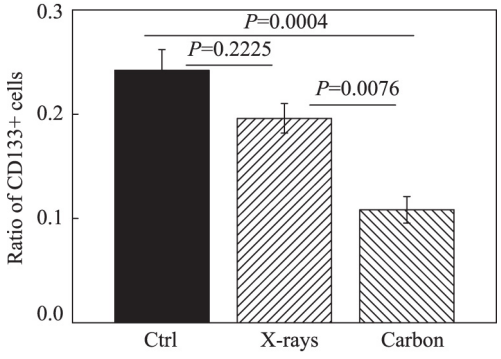

Fig. 3 Compared with X-rays, carbon-ion could significantly kill the glioma stem cells in the mice brains.

4 - 67 *miR*-300 Modulates the Cellular Radiosensitivity Through Targeting *p*53 in Human Non-small Cell Lung Cancer A549 Cells

He Jinpeng, Wei Wenjun, Feng Xiu, Hua Junrui, Lu Zhiwei, Jin Liangliang, Ding Nan, Zhang Yanan, Li He and Wang Jufang

microRNAs (miRNAs) perform crucial roles in mediation of the cellular radiosensitivity by influencing DNA damage repair, cell cycle checkpoint, apoptosis, radio-related signal transduction pathway and microenvironment[1−3]. Our previous study have suggested that $miR-300$, whose expression is correlated positively with the cellular resistance to chemotherapy drug cis-platin in human ovarian cancer cells[4], is involved in the cellular response to the DNA damages induced by ionizing radiation[5]. However, the underlying molecular mechanisms remain unclear.

In the present study, the effects of $miR-300$ on the cellular DNA damage repair, cell cycle arrest and apoptosis were investigated in human non-small cell lung cancer cell line A549 cells. The results showed that ectopic expression of $miR-300$ by transfection with pre-$miR-300$ in A549 cells not only substantially enhanced the cellular DNA damage repair ability (Fig. 1), but greatly reduced the G2 cell cycle arrest and apoptosis induced by ionizing radiation. Bioinformatics analysis indicated that $p53$ is a putative target gene of $miR-300$, and the luciferase reporter assay demonstrated that miR-300 directly bind to the 3'-UTR of p53 mRNA (Fig. 2). Furthermore, overexpression of $miR-300$ significantly suppressed the p53 protein expression levels in A549 cells, indicating $p53$ is a direct target gene of $miR-300$. Of note, $miR-300$ could enhance the cellular radioresistance by inhibition of p53-related apoptosis and senescence signal pathways.

In summary, these data suggest that *miR*-300 functions as an important regulator for ionizing radiation induced DNA damage responses by targeting p53 and may lead to new potential strategies for enhancement of tumor radiosensitivity.