to 4 Gy ionizing radiation combined with BTB showed a marked reduction in red /green fluorescence intensity ratio at 24 h post radiation, suggesting a loss of Ψm, which is important to sensitize the cancer cells. The finding of the present study providing a novel inhibition target for enhancing radiosensitivity and BTB could be a potential radiosensitizer in radiation therapy.

Reference

[1] Fabrice Ivanes, Stefania Cocco, Jemma Gatliff, et al., British Journal of Pharmacology, 171(2014)4193.

4 - 65 Researches on Assessment, Protection and Mechanisms of Ionizing Radiation in Department of Space Radiobiology

Wang Jufang

Ionizing radiation existing in heavy ion cancer therapy, nuclear device, spaceflight or terror attack is one of the major threats to human health and public security. During the past year, the main research task of Department of Space Radiobiology focus on the assessment, protection and underlying mechanisims of ionizing radiation both in vitro and in vivo.

Noninvasive biomarkers that can rapidly assess the exposure degree in the early stage of ionizing event are urgently needed for optimal medical treatments when an unexpected accident happens. Serum microRNAs (miRNAs) are ideal biomarkers because they are stable in responding to the changes of environments, conservative in different species and easy for collection. To identify serum miRNAs for the assessment of exposure degree, 8-weeks-old Kunming mice were whole-body exposed to 0.5 and 2 Gy of X-rays, carbon ions and iron ions.

The miRNA PCR array was performed to analyze the expression profiles of the serum miRNAs at 24 h after exposure. A specific signature with 12 radio-sensitive miRNAs was identified for further validation. After 0.1∼2.0 Gy of iron ion, X-ray or carbon ion irradiation, $miR-183-5p$, $miR-9-3p$, $miR-200b-5p$, $miR-342-3p$ and $miR-574-5p$ were selected as universal radio-sensitive biomarkers because they responded to all three kinds of ionizing radiation significantly. Finally, we developed a model including those five miRNAs by multiple logistic regression analysis from all three kinds of radiation data to assess the exposure risk scores (ERS):

$$\mathrm{ERS} = 0.300 + 0.125(X_{miR-183}) + 0.112(X_{miR-9}) + 0.154(X_{miR-200b})$$

$$-0.083(X_{miR-342}) - 0.062(X_{miR-574})$$

The receiver operating characteristic (ROC) analysis showed the model could predict the exposure degree with high specificity and sensitivity. The ERS values obtained from the model had significant difference for the assessment of exposure degree (ED): 0 for dose of 0 Gy, 1 for dose around 0.1 Gy and 2 for dose between 1∼2 Gy.

The radiation protective effects of the GANRA nanoparticles against X-ray radiation in lymphoblast cells were observed. Cell cytotoxicity, proliferation and cytokinesis-block micronucleus assay were conducted to evaluate the toxicity and radio-protective effects of GANRA nanoparticles. The results indicated that GANRA-nanoparticles exhibited low toxicity, while providing high radio-protective effects for lymphoblasts against X-ray radiation. It was also found that GANRA-nanoparticles acted as free radical scavenger, suggesting that GANRA-nanoparticles had the potential to be used as a safe and efficient radio-protectant.

Nuclear Receptor-binding SET domain2 (NSD2) is a histone methyltransferase that is abnormally expressed in Wolf-Hirschhorn syndrome(WHS) and many kinds of carcinomas including melanoma. We used p53 wild-type human melanoma cell line 92-1 as a cell model to study the funtion of NSD2 in radiation respons. Firstly, 92-1 cells were exposed to four different kinds of DNA damage inducer to prove that NSD2 was downregulated at protein levels which was related to upregulation of p53 and its downstream p21 after severe DNA damage. Then, it was verified that p21 mediated the degradation of NSD2 by premature activation of the APC/Ccdh1 in G2/M arrest by the RNA interference technology after induction of DNA damage. Finally, the DNA damage responses of 92-1 cells exposed to X-rays or hydroxyurea were detected. It was found that the functions of NSD2 in DNA damage respons which was induced by X-rays or hydroxyurea were different. It was p53, rather than p21 which directly repressed the transcription of NSD2, and the repression depended on a certain post-translational modification of p53 which was obviously different between the two different treatments.

In addition, it was found that radiation altered $miR-142-3p$ and $Bod1$ expression and thus contributed to early stages of radiation-induced genomic instability in carcinoma cells. An International Symposium on Bone Science

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.

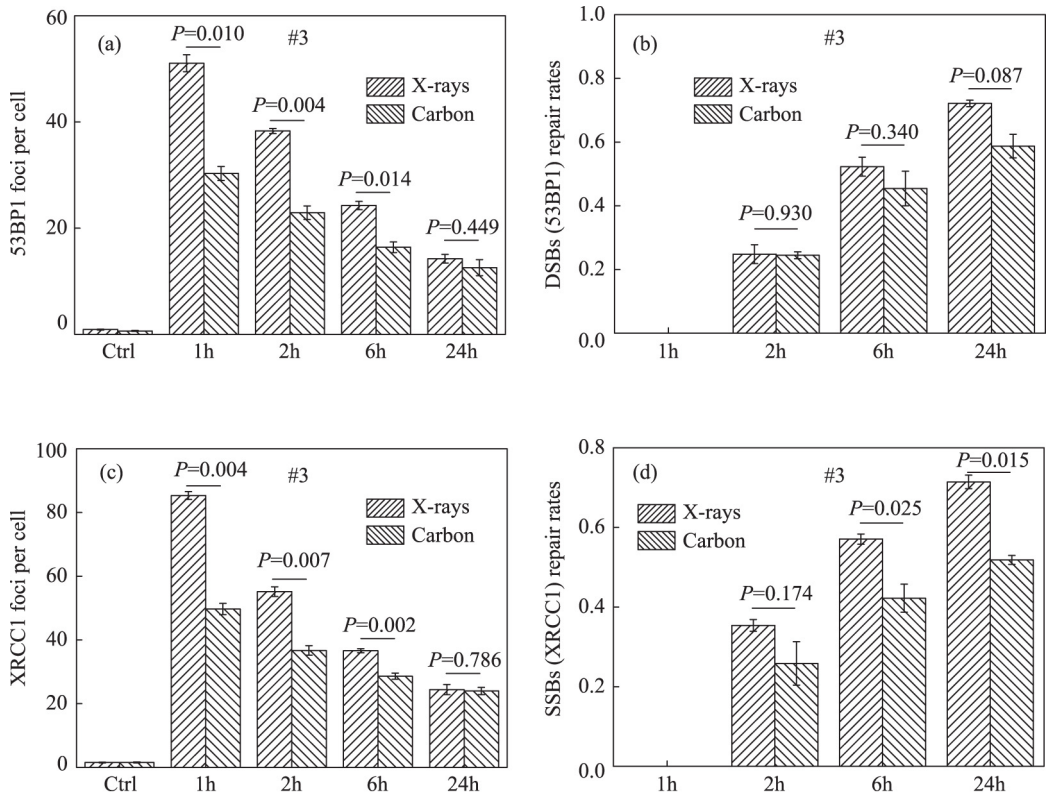

Fig. 1 Repair rate of DNA damage generated by carbon-ion was lower than that generated by X-rays in CSC.

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