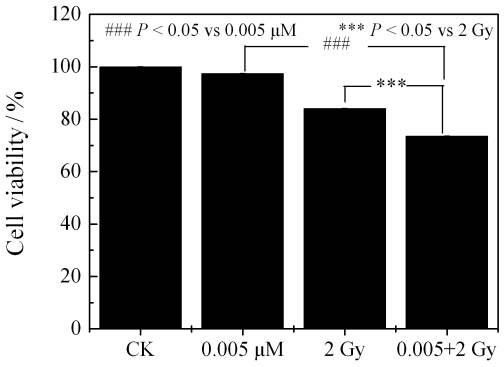

Fig. 1 CPZ significantly inhibited the proliferation of HepG2 cells exposed to carbon ion irradiation.

To investigate the effects of CPZ on cell proliferation, human hepatocellular carcinoma HepG2 cells were pretreated with 0.005, 0.01, 1, 25, 100 μmol/L CPZ for 24 h. The result suggested that CPZ could inhibit the proliferation of HepG2 cells in a dose dependent manner. Additionally, HepG2 cells were pretreated with 0.005 μmol/L CPZ for 6 h and irradiated with 2 Gy $^{12}C^{6+}$ ion beam irradiation. As shown in Fig. 1, the cell viability rate of IR+CPZ group was 73.46 ± 0.004% ($P < 0.05$), while the viability rate of IR group was 84.00 ± 0.001%. The result indicated that CPZ significantly inhibit the proliferation of HepG2 cells exposed to carbon ion irradiation. Therefore, these findings provide an opportunity to consider CPZ as a potential agent of radiation sensitivity.

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3 - 71 Researches on Radiation Related MicroRNAs and Risk Assessment of Heavy Ion Irradiation

Wang Jufang

The mechanisms of radiation induced bystander effects, functions of radiation related microRNAs and radiosensitivity of cancer and normal cells have been conducted by two- and three-dimensional cultured method during the past year in Department of Space Radiobiology. An international symposium on DNA repair and space radiobiology was successfully held in Institute of Modern Physics. There were more than 20 scientists from all over the world have taken part in the symposium. Moreover, Gansu Key Laboratory of Space Radiobiology has been in the cultivated period since July, 2014. Some of the achievements can be summarized as followings:

1) We demonstrated that miR-21 is involved in the radiation induced bystander effects (RIBE). It was found that exposure of normal human lung fibroblast MRC-5 cells to 150 MeV/u helium, 135 MeV/u carbon and 500 MeV/u iron ions could induce bystander effects through medium mediated way. Compared with the bystander cells treated with conditioned medium from non-irradiated cells, the bystander cells treated with conditioned medium from irradiated cells showed apparent increase in the frequency of micronuclei and 53BP1 foci, and dramatic decrease in survival fraction, suggesting that the RIBE could be induced by different types of charged particles. Significant upregulation of miR-21 in both directly irradiated cells and bystander cells were found by the expression levels of miR-21 precursor and its target genes. Transfection of miR-21 mimics into nonirradiated MRC-5 cells caused bystander-like effects. Elucidation of such a miRNA-mediated bystander effect is of utmost importance in understanding the biological processes related to ionizing radiation and cell-to-cell communication.

2) It was found that miR-454-3p modulated cellular radiosensitivity by regulating BTG1 which has long been recognized as a tumor suppressor gene. To investigate whether BTG1 responds to carbon ion exposure, we detected the mRNA levels and protein levels of BTG1 in renal carcinoma 786-O cells. The results implied that BTG1 response to 2.5 Gy of carbon beam significantly. To confirm that miR-454-3p participated in the process of DNA damage and repair through regulating BTG1, we transfected 786-O cells with miR-454-3p and treated the cells with 2.5 Gy of carbon beam. At 36 h after treatment, the genetic integrity of the cells was estimated by calculating the number of micronuclei in binucleated cells. As a result, the number of micronuclei increased markedly in upregulated miR-454-3p cells. However, miR-454-3p did not influence the genomic integrity of 786-O cells which were not exposed to carbon beam. Our results indicate that BTG1 contributes to maintain the genetic integrity and miR-454-3p regulates the cellular radiosensitivity after carbon ion irradiation by targeting BTG1. These findings may shed light on the potential application of microRNA in tumor radiotherapy.

3) Most of the cells in human body are in G0 phase and may remain in this stage for days or even years before resuming cell division and enter G1 phase in response to exogenous stimuli such as injury. We established a G0 cell model with MRC-5 cells by contact inhibition and investigated the radiosensitivity of G0 and G1 cells after heavy ion exposure. It was found that G0 cells exhibited radioresistance while G1 cells exhibited similar radiosensitivity to exponentially growing cells. The mechanisms underlying the low levels of oxidative stress and DNA damage of G0 cells could be the intracellular localization of P38MAPK together with RAC2, which led to their nuclear translocation in G0 cells and resulted in the inactivation of RAC2. This phenomenon was not observed in G1 cells. Thus, it was supposed that P38MAPK phosphorylation was increase the radioresistance of G0 cells. These findings can help us to obtain accurate and realistic risk assessment on normal human lung fibroblasts after heavy ion irradiation.

3 - 72 Biological Effects of Space Radiation on Human Quiescent Fibroblasts

Ding Nan, Pei Hailong, He Jinpeng, Li He, Hu Wentao, Wang Jufang and Zhou Guangming

Health risk associated with exposure to high-charge and -energy (HZE) particles in outer space has been discussed a lot mainly because its accurate assessment is complex and multifactorial[1−3]. Exponentially growing cells are the most widely used *in vitro* model for risk assessment. However, majority of the cells in human body stay quiescent (in G0 phase) even though some cells, such as liver cells and stem cells, can resume cell cycle and enter G1 phase in response to exogenous stimuli such as injury[4]. Therefore, it is reasonable to use G0 cells as an *in vitro* experimental model for risk assessment of space radiation.

It has been revealed that G0 cells own enhanced repair fidelity than cycling cells on chromosome repair kinetics[5]. Consistently, X-rays induce significantly fewer micronuclei in G0 human lymphocytes than G1 lymphocytes[6] and rat thyroid FRTL-5 cells in G0 phase are more resistant to UV-induced apoptosis than actively proliferating counterparts[7]. However, it is also reported that quiescent neural stem cells, rather than their rapidly dividing progeny, are very sensitive to radiation[8].

Since it is more instructive to evaluate potential cancer risk from space travel by investigating quiescent cells' response after HZE irradiation, we established G0 and G1 cell models with human normal embryonic lung fibroblast MRC-5 cells by releasing cells from contact inhibition and compared their biological effects induced by various kinds of heavy ion particles in this study.

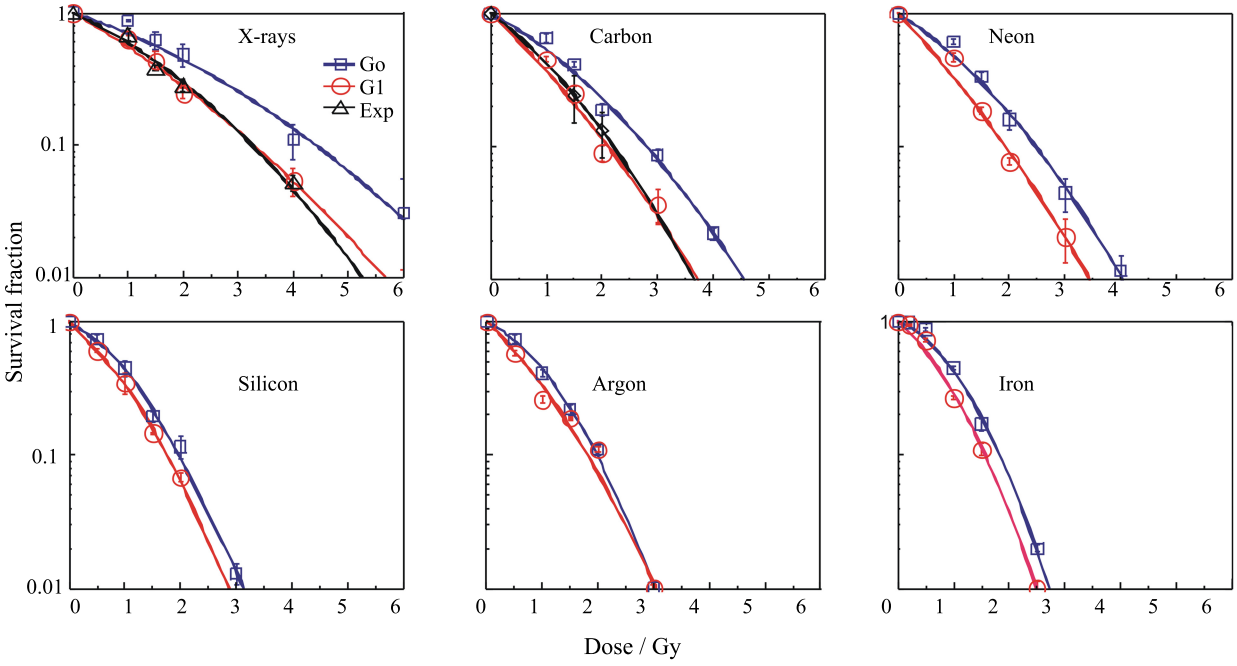

Fig. 1 (color online) Survival curves of G0 cells and G1 cells exposed to various type of radiation. Cell survival was measured with routine colony-forming assay right after exposure. Data were from three independently repeated experiments and the bars represented the standard error of the means (SEM). Exp, exponentially growing cells.