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

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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.

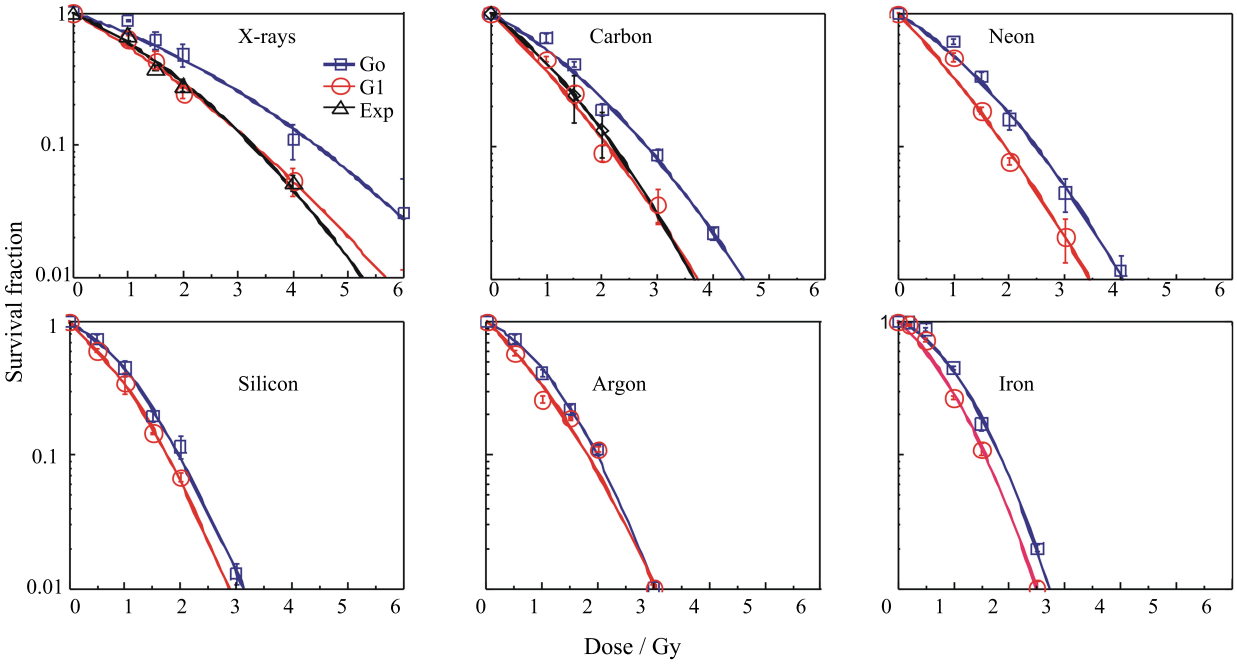

Fig. 1 (color online) Survival curves of G0 cells and G1 cells exposed to various type of radiation. Cell survival was measured with routine colony-forming assay right after exposure. Data were from three independently repeated experiments and the bars represented the standard error of the means (SEM).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

With routine colony forming assay, we obtained survival curves of cells exposed to various kinds of HZE particles with different energy and linear energy transfer (LET). The sensitivity of exponentially growing cells to both X-rays and 290 MeV/u carbon ions was very similar to G1 cells, which are more sensitive than G0 cells (Fig. 1). In order to confirm the higher radioresistance of G0 cells than G1 cells, we compared their difference in DNA damage and repair by counting 53BP1 foci induced by 0.5 Gy of radiation. As shown in Fig. 2, all particles robustly induced 53BP1 foci in both cell models in 1 h after irradiation and the foci decreased in 24 h. However, both the induction and the decrease of foci were obviously dependent on the type of radiation.

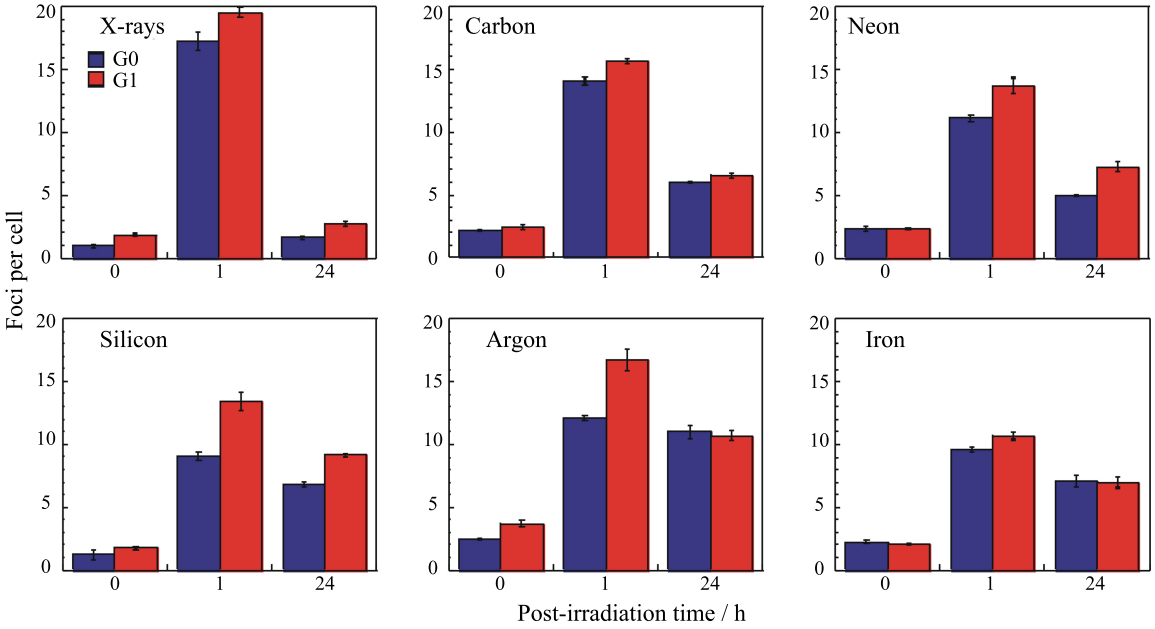

Fig. 2 (color online) Kinetics of 53BP1 foci induced by various kinds of radiation. After exposure to 0.5 Gy of X-rays or HZE particles, cells were fixed and DNA damages were visualized with anti-53BP1 antibody. Data obtained from three independent replicationswere presented as mean ± SE.

References

[1] L. T. Dauer, A. L. Brooks, Hoel, et al., Radiat. Prot. Dosim, 140(2010)103.
[2] M. Durante, A. Kronenberg. Adv Space Res, 35(2005)180.
[3] P. L. Olive, J. P. Banath, R. E. Durand, et al., Radiat. Res, 178(2012)35.
[4] N. C. Lea, S. J. Orr, K. Stoeber, et al, Mol. Cell. Biol, 23(2003)2351.
[5] C. Liu, T. Kawata, N. Shigematsu,et al., Radiat. Res, 174(2010)566.
[6] C. Catena, P. Villani, D. Conti, et al., Mutat. Res, 311(1994)231.
[7] E. Del Terra, A. Francesconi, D. Donnini, et al, Thyroid, 13(2003)747.
[8] J. M. Encinas, M. E. Vazquez, R. C. Switzer, et al., Exp. Neurol, 210(2008)274.