3 - 61 Mitochondrial Vicious Cycle Induced by Carbon Ions Supports the Long-lasting ROS Formation*

Wang Zhenhua, Sun Chao and Zhang Hong

As we all know ionizing radiation can promote the ROS formation in cells by water radiolysis instantly, which exerts apoptosis in the tumors. Thus, increased production of ROS is one crucial mechanism for radiotherapy[1]. However, the source of long-lasting ROS formation after radiation exposure is still not very clear.

As the powerhouse of eukaryocyte, mitochondria is also a killer organelle equipped with death effectors in controlling apoptosis, such as cyt-c and ROS, which are released when mitochondrial dysfunction[2,3]. The oxidative stress resulted from ROS generation and increase can injury mtDNA. The damages can elevate risks of mtDNA mutations, aggravate the mitochondrial dysfunction, and lead to more ROS production. Increased ROS results in further increases in oxidative stress and increased rate of mtDNA damage, thus causing a mitochondrial vicious cycle, which ultimately culminates in cell death. During starting the vicious circle, mtDNA damage and ROS generation are two main factors.

In our work, $^{12}C^{6+}$ ion beam radiation could damage mtDNA significantly, enhance the level of ROS and induce HepG2 cell death. On further research, it was found that after $^{12}C^{6+}$ion radiation the major sources of ROS and the major position of serious DNA oxidative damage were both mitochondria. These results indicated that mitochondria is one of the major sources of ROS in cells but also is the major target of cellular ROS. Finally, a feed-forward vicious cycle between mitochondrial and ROS is created to induce the long-lasting ROS formation.

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3 - 62 Impact of Carbon Ion Irradiation on Spermatogenic Cells Apoptosis in Pubertal Mice**

Li Hongyan, Zhang Hong, Xie Yi and Di Cuixia

There has been a considerable improvement in men of child-bearing age undergoing radiotherapy which often concerned about the possibility of future children[1]. In this investigation, we used TUNEL assay to analyze spermatogenic cells apoptosis in pubertal mice testes after carbon ion irradiation (CIR) that evaluate the impact of CIR on spermatogenesis in pubertal mice.

The 4 weeks of Swiss-Webster mice were whole-body irradiated with 0, 1 and 4 Gy, respectively. Testes were collected 14 d after irradiation. The histological changes in testicular tissue were observed and the apoptotic testicular cells were examined. The Johnsen score reflected the quantitative assessment of seminiferous tubules (Fig. 1(d)). Significant damage to the seminiferous tubule was observed in the irradiated groups ($P < 0.001$). Quantitative analysis of spermatogenic cells apoptosis is shown in Fig. 1(h). A significant increase in TUNEL-positive cells was found in the seminiferous tubule in the irradiated groups ($P < 0.001$). Our results showed TUNEL-positive spermatogenic cells were mainly spermatogonia, spermatocytes, early spermatids and late spermatids, and these cells seemed to be initially more susceptible to CIR toxicity.

* Foundation item: Key Program of National Natural Science Foundation of China (U1432248), Western Talent Program of Chinese Academy of Sciences (Y460040XB0), National Natural Science Foundation of China (11175222). ** Foundation item: Key Program of National Natural Science Foundation of China (U1432248), National Natural Science Foundation of China (11175222, 11205219)

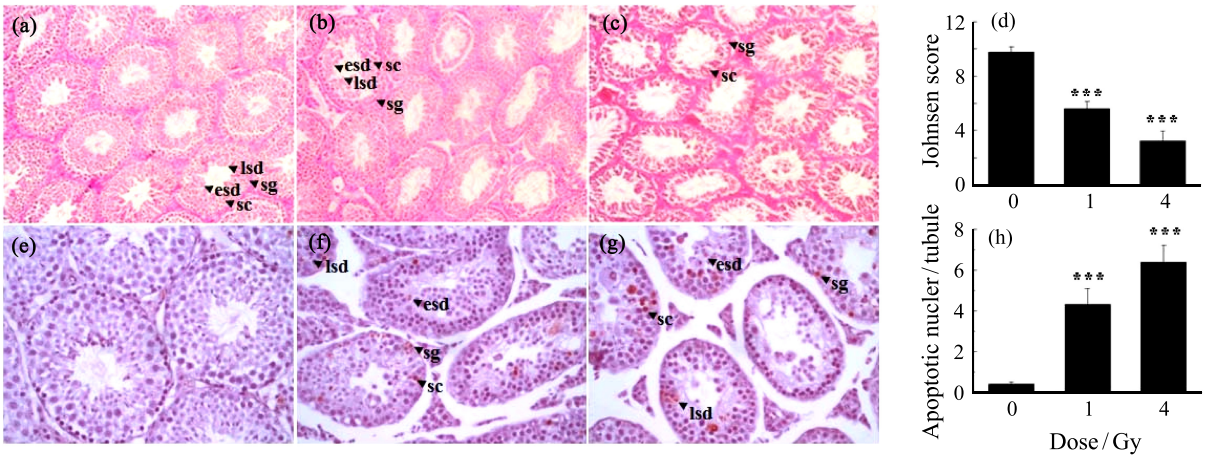

Fig. 1 (color online) 0 Gy (a), 1 Gy (b), 4 Gy (c). Photomicrographs of sections stained with H&E (magnification 200 ×): sg, spermatogonia; sc, spermatocytes; esd, early spermatids; lsd, late spermatids; lc, Leydig cell. Severe degeneration of spermatogenic cells in the seminiferous tubule (*), arrows indicate Sertoli cells in the seminiferous tubule (c). Representative photomicrographs of TUNEL staining: 0 Gy (e), 1 Gy (f), 4 Gy (g). Arrows indicate TUNEL-positive cells in the seminiferous tubule (magnification 400 ×): sg, spermatogonia; sc, spermatocytes; esd, early spermatids; lsd, late spermatids. Testicular damage as evaluated by the Johnsen score (d). Histogram of apoptotic-positive spermatogenic cells from mouse testis (h). Values represent the average ± S.E.M. Asterisks indicate a statistically significant difference from control: $***P < 0.001$ on one-way ANOVA with Duncan's post hoc analysis.

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3 - 63 Toxicity of Mitochondrial Singlet Oxygen Inducer on Zebrafish Embryo*

Zhou Xin, Wang Yupei and Zhang Hong

Mitochondrial singlet oxygen is a potential signal molecule to regulate mitochondrial biogenesis[1]. However, it is hard to distinguish mitochondrial ROS from cytoplasmic ROS in vitro. To overcome this issue, we recently developed a specific mitochondrial singlet oxygen inducer-Mitochondros. The toxicity of Mitochondros has been verified in vitro. However, the in vivo toxicity of mitochondros has not been investigated. Here we employed the zebrafish embryo to study the toxicity of mitochondros in vivo.

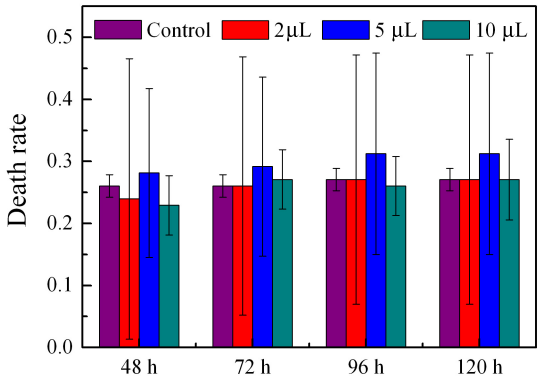

Fig. 1 (color online) The death rate of zebrafish embryo within 120 hours after exposure to various concentration of Mitochondros.

Zebrafish embryos were kept in E3 medium with the addition of various concentration of mitochondros ranging from 2∼10 μl/mL. The embryo death, as indicated by cardiac arrest and/or Egg condensation was scored at 48, 72, 96 and 120 hpf. The embryo death rate was calculated by dead embryo versus the total number of embryo scored. As shown in Fig. 1, no significant embryo death was observed at this concentration range of mitochondros within 120 h after egg fertilization.

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* Foundation item: Key Program of National Natural Science Foundation of China (U1432248), National Natural Science Foundation of China (11175222, 11205219), Western Talent Program of Chinese Academy of Sciences (Y460040XB0, Y160180XB0)