This study could provide scientific basis for safety of CORM-3 applied to the clinic.

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3 - 67 *MiR*-449a Overexpression Enhances the Radiosensitivity in Prostate Cancer Cells*

Mao Aihong, Liu Yang and Zhang Hong

Multiple links between *miRNA* activity and cancer have been established. Several *miRNAs* have been described as oncogenes while others act as tumour suppressors[1]. *MiR*-449a is a member of *miR*-34 family which locates on human chromosome 5q11.2, a region identified as a susceptibility locus in a variety of malignancies, including prostate cancer[2]. In line with the tumor-suppressive role of *miR*-34, *miR*-449a was shown to be significantly down-regulated in prostate cancer cell lines and tissue relative to normal tissues and plays a critical role in growth of prostate cancer cells [3,4].

In the present study, the pre-*miR*-449a and its flanking 200 bp sequence was cloned to the multi-clone site (MCS) of H1-MCS-CMV-GFP-SV40-Hygrcmycin, and the plasmid was transfected in the human prostate cancer cell (LNCaP), the expression of *miR*-449a was detected by Real-Time PCR. The biologic activity of mature *miR*-449a was determined by fluorescence quench method. The results showed that the expression of LNCaP was much higher than control group. H1-MCS-CMV-GFP-SV40-Hygrcmycin could efficiently express mature *miR*-449a with biologic activity. In the further study, we also found that overexpression of *miR*-449a in LNCaP cells inhibited proliferation and enhanced apoptosis induced by X-rays(as shown in Figs. 1 and 2).

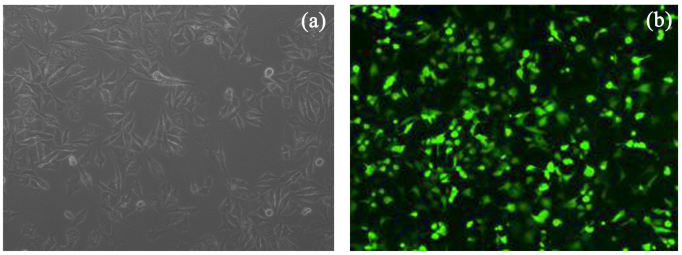

Fig. 1 (color online) LNCaP cells transfected with *miR*-449a overexpression vector. (a) Normal LNCaP cells before transfected. (b) LNCaP cells transfected with 5 μg *miR*-449a overe-xpression vector plasmid DNA or miRcon31control plasmid DNA (H1-MCS-CMV-GFP-SV40-Hygrcmycin) for 48 h.

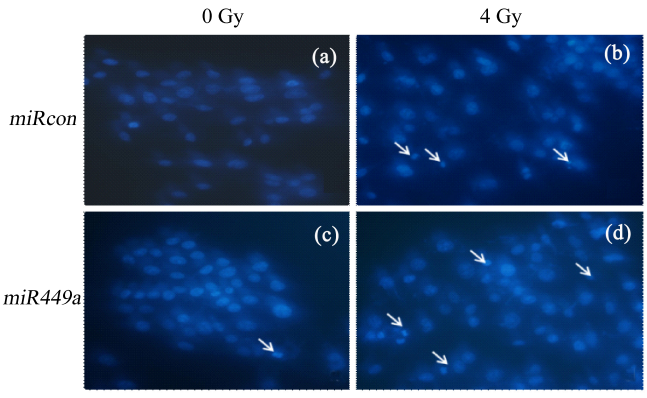

Fig. 2 (color online) *miR*-449a overexpression enhances apoptosis induced by X-rays in prostate cancer LNCaP cells. LNCaP cells were stained by Hoechest 333258 post-irradiation 4 Gy X-rays at 48 h. LNCaP were transfected with *micron* (a), (b) and *miR*-449a(c), (d).

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3 - 68 Loss of Nrf2 Enhances the Radiosensitivity in Human Lung Cancer Cells *

Zhao Qiuyue and Zhang Hong

Nuclear factor erythroid 2-related factor 2 (Nrf2) is a crucial transcription factor regulating the expression of antioxidant genes. Under oxidative stress conditions or other stimulus, Nrf2 translocating from the cytoplasm into the nucleus, binds to antioxidant response elements, and increases the expression of antioxidant enzymes[1,2]. Constitutive Nrf2 activation in many tumors enhances cell survival and resistance. For instance, high level of Nrf2 is observed in non-small cell lung cancer A549 cells[3,4]. The gain of Nrf2 function has been implicated in the resistance of cancer cells to radiation therapy.

Under ionizing radiation, it has been confirmed that ROS plays main role in the cytotoxic action. In this work, cells were irradiated with X-rays at a dose of 4 Gy and 4 groups were studied: Negative control group (NC), the cells transfected 48 h with Nrf2 siRNA group (siRNA), irradiated group (IR), and irradiated cells after transfection group (siRNA+IR). Our results showed the cells transfected with Nrf2 siRNA increased the level of ROS without the radiation exposure compared with negative group. Knocking down Nrf2 can increased ROS accumulation in irradiated cells compared with cells exposed to radiation alone (Fig. 1). Increasing the level of ROS may change redox state of the cell, and then affect cell survival and increase radiosensitivity.

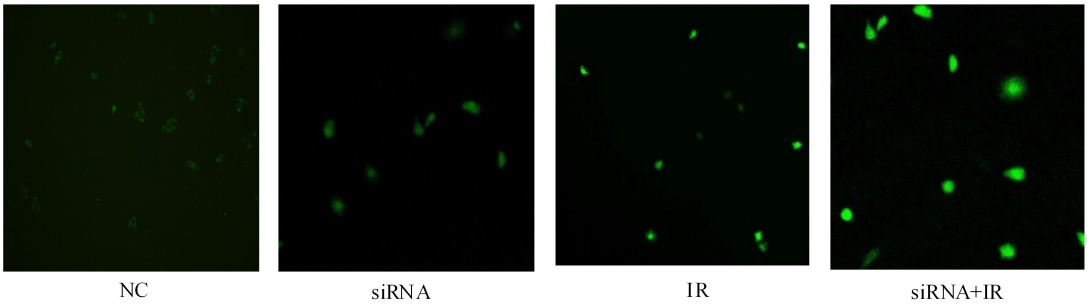

Fig. 1 (color online) Nrf2 siRNA promotes ROS accumulation in A549 cells. A549 cells were incubated with 10 μM H_2DCFH-DA for 30 min before IR. ROS was measured by fluorescence microscopy.

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