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

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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.

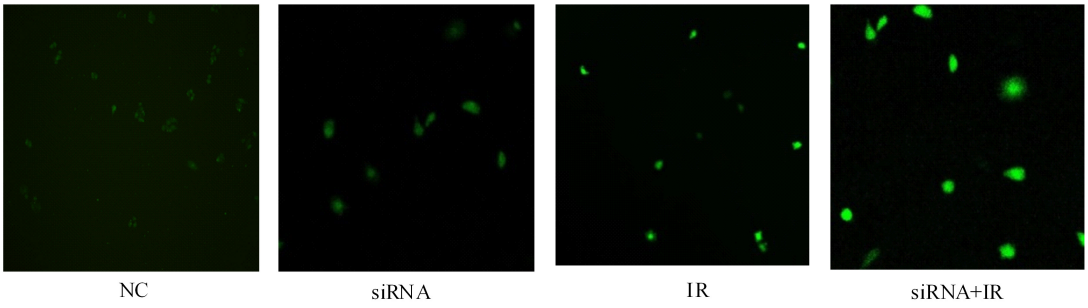

Fig. 1 (color online) Nrf2 siRNA promotes ROS accumulation in A549 cells. A549 cells were incubated with 10 μM H_2DCFH-DA for 30 min before IR. ROS was measured by fluorescence microscopy.

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