Reference

[1] K. Kyrylkova, S. Kyryachenko, M. Leid, et. al., Meth. Mol. Bio., 887(2012)41.

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4 - 63 Suppression of Radiation-induced Migration of Non-small Cell Lung Cancer through Inhibition of Nrf2-Notch Axis

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Nuclear factor E2 related factor 2 (Nrf2) is a transcription factor that is associated with tumor growth and resistance to radiation. The canonical Notch signaling pathway is also crucial for maintaining non-small cell lung cancer (NSCLC). Aberrant Nrf2 and Notch signaling has repeatedly been showed to facilitate metastasis of NSCLC. Here, we show that radiation induce Nrf2 and Notch1 expression in NSCLC. Knockdown of Nrf2 enhanced radiosensitivity of NSCLC and reduced epithelial-to-mesenchymal transition. Importantly, we found that knockdown of Nrf2 dramatically decreased radiation-induced NSCLC invasion(Fig. 1) and significantly increased E-cadherin, but reduced N-cadherin and matrix metalloproteinase (MMP)-2/9 expression. We found that Notch1 knockdown also upregulated E-cadherin and suppressed N-cadherin expression. Nrf2 contributes to NSCLC cell metastatic properties and this inhibition correlated with reduced Notch1 expression. These results establish that Nrf2 and Notch1 downregulation synergistically inhibit radiation-induced migratory and invasive properties of NSCLC cells.

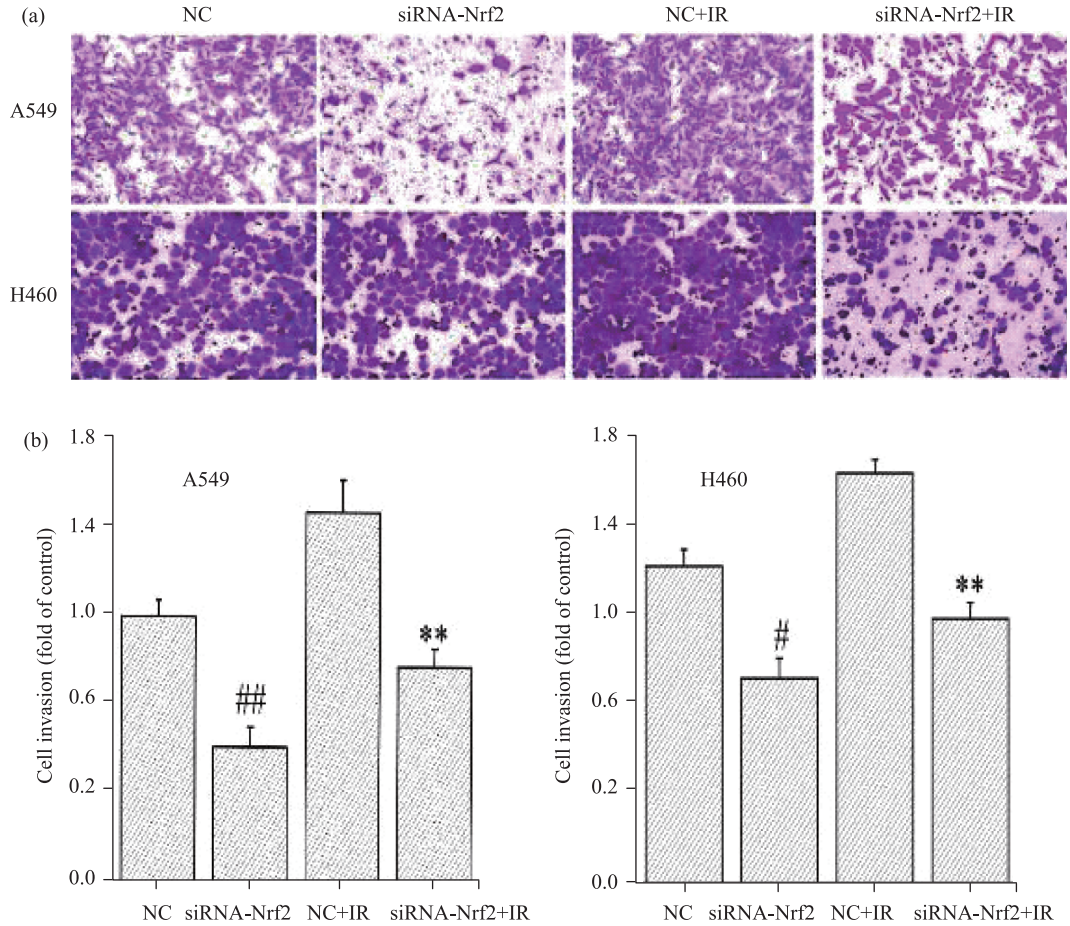

Fig. 1 (color online) Suppression of Nrf2 attenuated EMT in NSCLC cells. (a) and (b) Transwell invasion assay in A549 and H460 cells. The cells were then treated with or without the siNRA-Nrf2, or irradiation. The images (original magnification, ×200) were taken at 0 h and 24 h. The data are from triplicate experiments. $^{\#}P < 0.05$ and $^{\#\#}P < 0.01$ versus NC group. $^{*}P < 0.05$ and $^{**}P < 0.01$ versus irradiation-treated groups.