



High expression of HIF-2 α and its anti-radiotherapy effect in lung cancer stem cells

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ABSTRACT. Hypoxia-inducible factor-2 alpha (HIF-2 α) has been shown to regulate cell stemness, although the expression and effects of HIF-2 α in lung cancer stem cells remained unclear. This study investigated HIF-2 α expression in lung cancer stem cells, as well as the relationship between HIF-2 α expression and radioresistance in lung cancer cells. Stem-like cells (CD133⁺) in the non-small-cell lung cancer cell line A549 were enriched by serum-free culture conditions, and CD133⁺ cells were sorted via fluorescence-activated cell sorting. A549 cells were treated with middle-infrared radiation, and the level of HIF-2 α expression was determined by a quantitative polymerase chain reaction assay and western blot analysis. The level of HIF-2 α expression in tissue sections from 50 cases of clinically confirmed non-small-cell lung cancer was determined via immunohistochemical analysis, and its correlation with prognosis after radiotherapy was analyzed. HIF-2 α levels in CD133⁺ cells were significantly higher than those in CD133⁻ cells ($P = 0.032$). However, after radiation treatment, these levels were significantly upregulated in both CD133⁺ and CD133⁻ cells ($P = 0.031$ and $P = 0.023$, respectively). After irradiation, the proportions of apoptotic, dead, and autophagic CD133⁺ A549 cells were

considerably lower than those of CD133⁺ A549 cells ($P < 0.05$). Furthermore, the recovery of carcinoembryonic antigen to pre-radiation levels was more rapid in lung cancer patients with high levels of HIF-2 α expression, and these patients had shorter survival times ($P = 0.018$). HIF-2 α is highly expressed in lung cancer stem cells, which may lead to radioresistance. In conclusion, HIF-2 α is a potential prognostic marker for lung cancer.

Key words: Lung cancer stem cell; HIF-2 α ; Anti-therapy; CD133; Radiation