

## **Experimental studies on the protective effects of the over-expression of lentivirus-mediated SIRT6 on radiation-induced lung injury.**

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### **Abstract**

**Objective:** To investigate the protective effects of the over-expression of SIRT6 on radiation-induced lung injury in rats.

**Methods:** 72 male Wistar rats (150-120 g) were randomly divided into 3 groups (n=24). Models were made through radiating both lungs with a 6 MV-X linear accelerator. Each group was injected through the tail vein with normal saline (the control group and radiation group) and lentivirus carrying over-expressed SIRT6 (Lent-SIRT6 group) on the exact day of modeling. Changes in respiratory rates, body weight and levels of TNF- $\alpha$  and IL-6 in serum were measured respectively at 1, 2, 4 and 8 weeks after radiation. Blood routine indexes (RBCs, neutrophils and lymphocytes) were recorded, rats were sacrificed with their lung tissues taken, pathological changes of lungs were evaluated by HE staining and TNF- $\alpha$ , IL-6 and IL-1 $\beta$  were detected with ELISA at 8 weeks after radiotherapy.

**Results:** The lung structure including alveolar walls and interstitium in control group were normal, but alveolar walls in radiation group were obviously thickened and a large amount of hyperplastic fibrous tissues were found in alveolar interstitium, while the thickness and interstitial fibrosis of alveolar walls were more alleviated in Lent-SIRT6 group than in radiation group. Compared with those in control group, the respiratory rates, levels of TNF- $\alpha$  and IL-6 in serum, neutrophils and levels of TNF- $\alpha$ , IL-6 and IL-1 $\beta$  in liver all were increased, while WBCs and lymphocytes were decreased in radiation group. The differences were statistically significant ( $P < 0.05$ ). The respiratory rates, levels of TNF- $\alpha$  and IL-6 in serum, neutrophils and levels of TNF- $\alpha$ , IL-6 and IL-1 $\beta$  in liver were all decreased, and WBC and lymphocytes were increased after injection with over-expressed SIRT6. The differences were statistically significant ( $P < 0.05$ ).

**Conclusion:** SIRT6 inhibits inflammation and alleviates radioactive pneumonia and lung injury. Therefore, SIRT6 can exert certain protective effects on lung injury.

**Keywords:** SIRT6, Radioactive pneumonia, Lung injury, Inflammation.

*Accepted on October 26, 2017*

### **Introduction**

At present, lung cancer has become a malignant disease with highest incidence and mortality worldwide. The global annual death toll of cancers is up to 1.2 million, while radiotherapy is the main treatment for late-stage or postoperatively recurred lung cancer. Radiation-induced lung injury, a common complication of lung cancer after radiotherapy, not only affects lung functions but sharply reduce patients' quality of life, so it is of great significance to protect lungs of patients with radiotherapy from damages. Sirtuin is a NAD<sup>+</sup>-dependent histone deacetylase that can alter the activity of the target protein by lysine deacetylation [1-4]. The 7 widely expressed sirtuin subtypes (SIRT1-SIRT7) are encoded in mammalian genome play an important role in various physiological processes, such as cell growth and apoptosis [5]. It has been reported that SIRT1 exerts protective effects on lung injury of

different types [6,7], and the pathways SIRT1 participates in play a crucial role in this process [8]. Previous studies of this project found that SIRT6 can increase the radiosensitivity of non-small cell lung cancer [9], and exerts protective effects on radiation-induced lung injury. Therefore, the aim of this study is to transfect lentiviral vectors of over-expressed SIRT6 in the models of rats with radiation-induced lung injury and observe the protective effects of SIRT6 on radiation-induced lung injury. The research was sponsored by Natural Science Foundation of Shanghai (15ZR1434300).

### **Materials and Methods**

#### **Main reagents**

The over-expressed lentivirus vector construction of SIRT6 was completed by the Shanghai Genechem Co., Ltd; ELISA