3 - 74 Supression of SET8 Enhance the Radiosensitivity of A549 Cells

Pan Dong, Du Yarong, Ren Zhenxin and Hu Burong

SET8 (SET (lysine methyltransferase) domain containing 8) is a member of the SET domain-containing methyltransferase family that specifically targets H4K20 for monomethylation. It has been implicated in a diverse array of biological processes, including controlling gene transcription[1,2], maintaining genome integrity[3,4], regulating cell cycle progression[5,6], and mediating DNA damage and repair[7,8]. In addition to targeting H4K20, SET8 is also reported in methylating the tumor suppressor p53 at lysine residue 382 (p53K382me1) and repressing p53-mediated transcriptional activation of target genes. In response to ionizing radiation, p53 regulates the transcription of genes in a diverse set of pathways including DNA repair, cell cycle arrest, and apoptosis[9]. Thus, we hypothesis that SET8 may affect the cellular response to ionizing radiation by interacting with p53.

Our preliminary experimental results showed that the SET8 expression in human lung adenoeaminoma cells (A549) by western blot analysis down-regulated firstly and then upregulated after both carbon-beam and X-rays irradiation(Fig. 1). To investigate the effects of SET8 on the radiosensitivity in A549 cells, we constructed recombinant lentivirus vector containing gene fusion with small interfering RNA (siRNA) targeting SET8 and enhanced green fluorescent protein (EGFP). The A549 cells were infected by the lentivirus vector (Fig. 2(a)) and the SET8 expression was continuously suppressed (Fig. 2(b)). The clonogenic survival assay showed that the A549 cells were more radiosensitive to ionizing radiation after SET8 was suppressed (Fig. 3).

Our preliminary results suggest that SET8 play roles in the induction of radiosensitivity in cells through regulating the potential target genes. Our future work will focus on the identification of the downstream genes regulated by SET8 through gene microarray analysis and exploring more effective strategy for tumor radiotherapy.

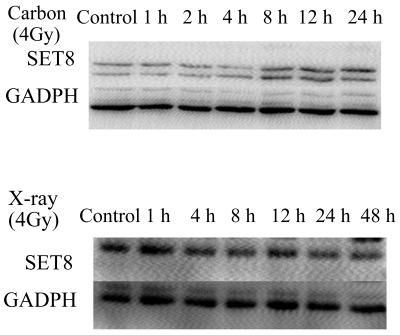

Fig. 1 The SET8 expression in A549 cells after C-beam (4 Gy) and X-ray (4 Gy) irradiation by western blot analysis.

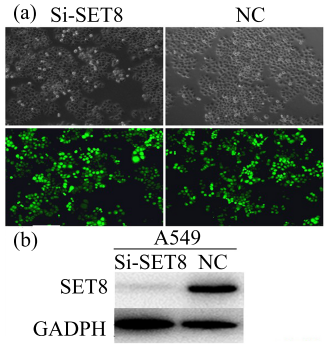

Fig. 2 (color online) The A549 cells are infected by lentivirus vector containing gene fusion with SiSET8-EGFP (a) and the SET8 expression is detected by western blot analysis (b).

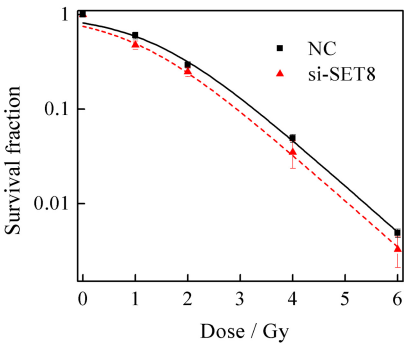

Fig. 3 (color online) The clonogenic survival of lentivirus vector infected A549 cells irradiated by X-rays. The experiment was repeated three times. The survival curve was established by Origin 8.

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