# 4 - 49 Inhibiting Mitochondrial Fission Changed the Mitochondrial Responses in MDA-MB-231 Cells after Carbon Ion Irradiation

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In previous study, we found that the low-dose carbon ions induced a mid-fragmentation in mitochondria, leading to mitophagy. However, serious mitochondrial fragmentation was related to the release of cytochrome c after irradiation at the high dose. Here, we further investigated whether the mitochondrial network abnormalities were attributed to the different mitochondrial responses in MDA-MB-231 cells by down-regulating *Drp*1, since this gene has a high expression in breast cancer cells and is essential for mitochondrial fission. FIS1 functions as a receptor for *Drp*1 and regulates mitochondrial fission, our hypothesis could be further confirmed if its expression was also attenuated *Drp*1 and *FIS*1 down-regulation in MDA-MB-231 cells with siRNAs were verified at mRNA and protein levels (Fig. 1). Compared to cells treated with radiation alone and irrelevant scrambled siRNA, cells treated with siRNAs exhibited a tubular mitochondrial network significantly, indicating that mitochondrial fission was impaired in the cells after irradiation at 0.5 Gy. Moreover, the treatment with siRNAs also inhibited the high-dose radiation-induced mitochondrial punctation remarkably (Fig. 2). Fig. 3 shows that mitophagy was obviously suppressed in cells co-treated with 0.5 Gy radiation and siRNAs compared to those treated with radiation alone and scrambled siRNA. However, the increase level of mitophagy was observed after 3 Gy irradiation in the co-treatment groups. Opposite results were obtained when we analyzed the release of cytochrome c from mitochondria (Fig. 4). Collectively, our results further showed that the mitochondrial fission played a crucial role in regulating mitochondrial damage response after irradiation with carbon ions.

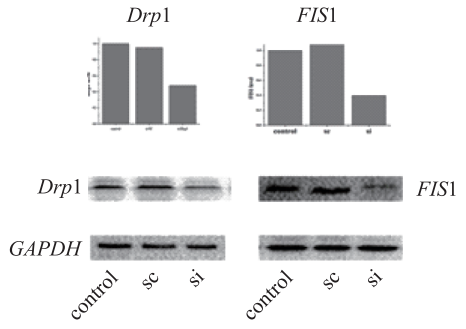



Fig. 1 Down-regulation of Drp1 (left) or FIS1 (right) in following transfection with specific siRNAs, sc: scrambled control siRNA, si-1: Drp1-siRNA, si-2: FIS1-siRNA.

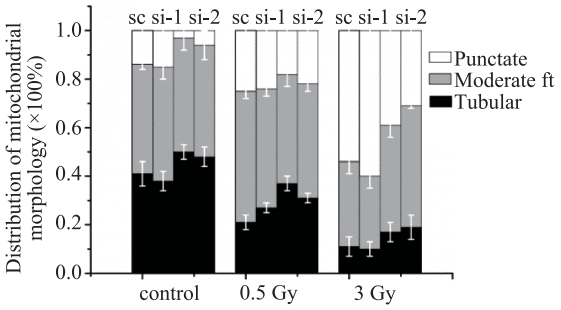



Fig. 2 Inhibition of *Dpr*1 or *FIS*1 suppressed mitochondrial fission after carbon ion irradiation.

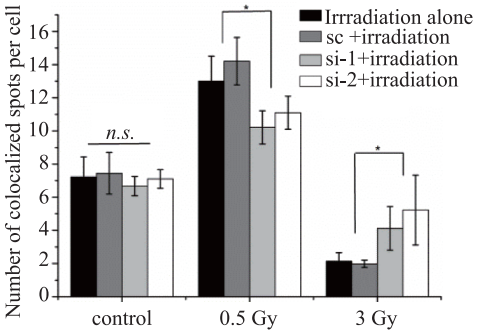
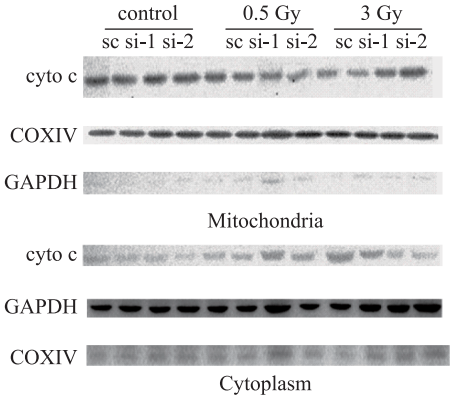



Fig. 3 Changes of mitophagy in cells co-treated with siRNAs and radiation, n.s.: no significance.



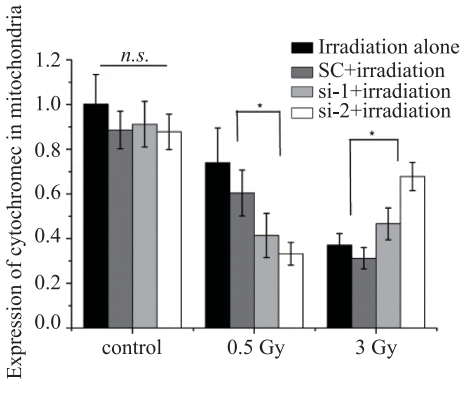




Fig. 4 Western blot analysis of cytochrome c release after co-treatment, cyto c: cytochrome c. *: $P < 0.05$, the siRNA groups versus the radiation alone and sc groups.