Increase of radiosensitivity in human tumor cells

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Ionizing radiation is a technique that is commonly used to shrink tumors although there still is high risk of relapse depending on the tumor. New strategies to increase the efficiency of this technique have been highlighted in recent scientific studies related to cancer therapy.

DNA double-strand break (DSB) is a typical damage induced by ionizing radiation and therefore mechanisms related to DNA repair can be considered as promising targets for combination with radiotherapy. Mis-repaired or unrepaired breaks can destroy mechanisms that are vital for proper cellular function. In mammalian cells, the DNA DSBs induced by irradiation are most often repaired by a pathway, which is known as nonhomologous end joining (NHEJ). The DNA-dependent protein kinase catalytic subunit (DNA-PKcs) is the key protein in this pathway, which can re-ligate the DNA broken ends without need to template. Considering the important role of DNA-PKcs in DSB repair, any agent that can inhibit this protein or knock-down its related gene can be used to enhance the sensitivity of tumor cells to radiation.

To study the radiosensitivity of DNA-PKcs depleted or deficient cells, epidermoid carcinoma and colorectal carcinoma cells were treated by either small interfering RNA which down-regulates the DNA-PKcs gene, or by either of two potent inhibitors of DNA-PKcs. After both treatments, depleted cells showed reduced ability to repair DSB. The reduction became even more significant when both treatments were combined. Using these treatments, we showed that cells with depletion or deficiency of DNA-PKcs are more sensitive to ionizing radiation.

Degree project in biology, Master of science (2 years), 2 0 13
Examensarbete i biologi 45 hp till masterexamen, 2 0 13
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