
Delayed Growth Suppression and Radioresistance Induced by Long-Term Continuous Gamma Irradiation.
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Abstract
Biological response to ionizing radiation depends not only on the type of radiation and dose, but also on the duration and dose rate of treatment. For a given radiation dose, the biological response may differ based on duration and dose rate. We studied the properties of two human cell lines, M059K glioma and U2OS osteosarcoma, continuously exposed to γ rays for long time periods of more than five months. Growth inhibition in both cell lines was dependent on total dose when exposed to acute radiation over several minutes, whereas prolonged growth inhibition was dependent on dose rate after continuous irradiation over several months. The minimum dose rate for growth inhibition was 53.6 mGy/h. Cell cycle analysis showed G1 phase accumulation in cell populations continuously exposed to γ rays, and G2 phase accumulation in cells acutely exposed to high-dose-rate γ rays. Cells continuously exposed to γ rays continued to exhibit delayed growth suppression even after one month in an environment of background radiation, and maintained a high-level expression of c-Jun and its phosphorylation forms, as well as resistance to apoptosis induced by staurosporine and chemotherapeutic agents. These delayed effects were not observed in cells acutely exposed to 5 Gy of radiation. These results suggest that optimization of the irradiation schedule is crucial for risk estimation, protection and therapeutic utilization of ionizing radiation.

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