Genetic instability (11-16)

11 Radiation-Induced Delayed Chromosome Instability Studied by a Microcell-Mediated Chromosome Transfer

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Radiation induces genetic instability in surviving cells that are exposed to radiation. We hypothesize that radiation-induced genetic instability is initiated with some DNA lesions produced by incomplete repair of DNA strand breaks. In the present study, we examined this hypothesis using a chromosome transfer method. Mouse A9 cells containing a human chromosome 11 were used as chromosome donor cells. The A9 cells were irradiated with 15 Gy of X-rays, and then, a human chromosome 11 was introduced into unirradiated mouse m5S cells using a microcell-mediated chromosome transfer. After isolation of microcell hybrids containing an intact human chromosome 11, the rearrangement of human chromosome 11 in the microcell hybrids over 20 population doublings after irradiation was detected by FISH technique. Our preliminary result of chromosome analysis indicated that there is no difference in structural rearrangements and copy numbers between the unirradiated chromosome 11 and the 15 Gy-irradiated chromosome 11, implying that irradiated chromosomes might not be unstable in unirradiated recipient cells.

12 Radiation-Induced Genetic Instability in *Scid* Mouse Cells

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Ionizing radiation induces genetic instability in the progeny of irradiated cells. To know the relationship between double-strand breaks (DSBs) repair and the genetic instability, we studied X-ray-induced delayed chromosome aberrations in *scid* mouse cells which defect in non-homologous end joining repair of DSBs. The chromosome analysis revealed that the yield of delayed-type dicentrics in *scid* cells is higher by 2.6-fold than that in wild-type cells when they are exposed to an equivalent survival dose of X-rays. The yield of spontaneous dicentrics in *scid* cells is also higher by 1.9-fold than that in wild-type cells. These results suggest that DNA dependent protein kinase suppresses both spontaneous and radiation-induced delayed chromosome aberrations. We suggest that *scid* cells might be more susceptible to initiation and/or expression of instability than wild-type cells when they receive the equivalent survival dose.