The Japan Radiation Research Society

129

Transient DNA inhibition produces proliferative tetraploid V79 cells which have both increased drug resistance and genomic instability with a propensity for gene amplification

[1]Toshio MORI, [1,2]Mitsumasa W. HASHIMOTO, [2]Osamu NIKAIDO, [3]Keizo TANO, [4]Keiji SUZUKI and [4]Masami WATANABE.; [1]Nara Medical Univ., [2]Kanazawa Univ., [3]Kyoto Univ., and [4]Nagasaki Univ.

To investigate a relationship between cell cycle arrest and genomic instability, V79 cells were treated with various concentrations of aphidicolin, an inhibitor of DNA synthesis, for 54 hours, then the emergence of tetraploid cells and of methotrexate-resistant (MTX^r, 150 nM) colonies were measured. Indeed, aphidicolin produced tetraploid cells and induced MTX^r cells in a concentration-dependent manner. Although almost no tetraploid cells were observed in spontaneously-occurring MTX^r cells, aphidicolin-induced MTX^r cells contained more tetraploid cells with increasing aphidicolin concentrations. Diploid and tetraploid MTX^r clones were isolated and were cultured with stepwise increased MTX selection for 3 months. Although the former obtained only 5,000 nM MTX resistance, the latter obtained more than 40,000 nM MTX resistance. In the latter clones, the increased resistance of MTX was associated with the increased gene copy numbers of *dhfr*, dihydrofolate reductase. In contrast, the former did not show any *dhfr* gene amplification even at the stage of 5,000 nM MTX resistance. These results indicate that transient DNA inhibition produces tetraploid cells which have both increased MTX resistance and genomic instability with a propensity for gene amplification during stepwise MTX selection.

130

The induction and the fate of chromosome aberrations by ionizing radiation in human fibroblast cells

Mieko MIYAKE , Seiji KODAMA , Keiji SUZUKI , Masami WATANABE
Div-Radiat.Biol.,Nagasaki Univ.

Dicentrics and rings have been used for a biological marker to estimate genetic damage because of their clear recognition by eyes. However, cells with dicentrics or rings would be dead since cell division was greatly prevented by those aberrations. So if we want to know the role of chromosome aberrations in the process of carcinogenesis, it is better to detect stable type of aberrations (translocations) than unstable type of aberrations (dicentrics and rings).Therefore, in this study we examined the induction and the fate of translocations by ionizing radiation in human fibroblast cells using fluorescence in situ hybridization (FISH) to compare those of dicentrics. We found that stable translocations would be remained in the population and be passed on during cell division.

131

Distribution of Chromosomal Breakpoints in Bone Marrow Cells of C3H/He Mice Exposed to γ-ray in vivo

Nobuhiko BAN, Tomoko KUSAMA and Yoshiro AOKI
Department of Radiological Health, Faculty of Medicine, University of Tokyo; Tokyo 113.

Bone marrow cells of whole-body irradiated mice were cytogenetically analyzed to detect radiation-sensitive chromosomal sites that may play important role in leukemogenesis. Eight-week male C3H/He mice were exposed to ^{137}Cs γ-ray at the dose of 3 Gy, and sacrificed for metaphase preparation 24 hours after irradiation. Chromosome banding was achieved by double staining with DAPI (4',6-diamidino-2-phenylindol) and actinomycin D. In 150 metaphases analyzed so far, a total of 158 breakpoints was observed. The breakpoints distribute throughout the genome, and no hot spot is likely. It is inferred, if breakage of specific chromosome is an initiating event of radiation-induced acute myeloid leukemia, probability of the event is not so high.

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