Chromatin Folding, Fragile Sites, and Chromosome Aberrations Induced by Low- and High-LET Radiation

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Abstract

We previously demonstrated non-random distributions of breaks involved in chromosome aberrations induced by low- and high-LET radiation. To investigate the factors contributing to the break point distribution in radiation-induced chromosome aberrations, human epithelial cells were fixed in G1 phase. Interphase chromosomes were hybridized with a multicolor banding in situ hybridization (mBAND) probe for chromosome 3 which distinguishes six regions of the chromosome in separate colors. After the images were captured with a laser scanning confocal microscope, the 3-dimensional structure of interphase chromosome 3 was reconstructed at multi-mega base pair scale. Specific locations of the chromosome, in interphase, were also analyzed with bacterial artificial chromosome (BAC) probes.

Both mBAND and BAC studies revealed non-random folding of chromatin in interphase, and suggested association of interphase chromatin folding to the radiation-induced chromosome aberration hotspots. We further investigated the distribution of genes, as well as the distribution of breaks found in tumor cells. Comparisons of these distributions to the radiation hotspots showed that some of the radiation hotspots coincide with the frequent breaks found in solid tumors and with the fragile sites for other environmental toxins. Our results suggest that multiple factors, including the chromatin structure and the gene distribution, can contribute to radiation-induced chromosome aberrations.

Introduction

Location of breaks participated in inter- and intrachromosome exchanges after gamma exposure

Results

The Distance between Different Regions of Chromosome 3 and the Center of the Chromosome 3D Domain

Distribution of Angles Extended to the Neighboring Regions

Conclusions

- The regions towards the telomeres are likely to occupy the peripheral area of the chromosome domain. These heterochromatin regions locating in the peripheral of the chromosome domain may provide the structural support, define the chromosome territory, and maintain the chromosome integrity.
- The present results showed that Band D-8 tends to locate near the interior of the chromosome domain, and are localized closely to Band D-13 and Band E-22. This finding is consistent with the frequency of intra-chromosome exchanges between breaks in these regions.
- The non-random breakpoint distribution in chromosome 3 after radiation exposure may be associated with the folding of chromatin in interphase.
- Other factors, including the location of the fragile sites and transcription activities, may also contribute to the distribution of radiation-induced inter- and intra- chromosome exchange hotspots.
- The distribution of breaks participated in inter- and intra-chromosome exchanges found in chromosome 3 of solid tumors is in partial agreement with radiation induced chromosome exchange hotspots.