

mBAND analysis of late chromosome aberrations in human lymphocytes induced by gamma rays and Fe ions

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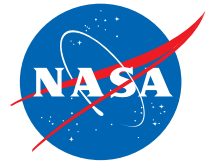
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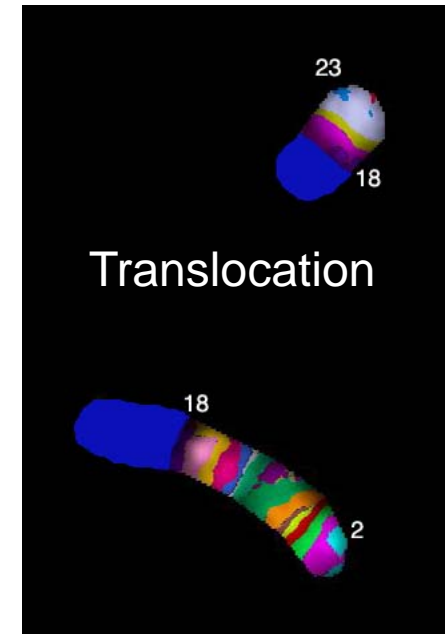
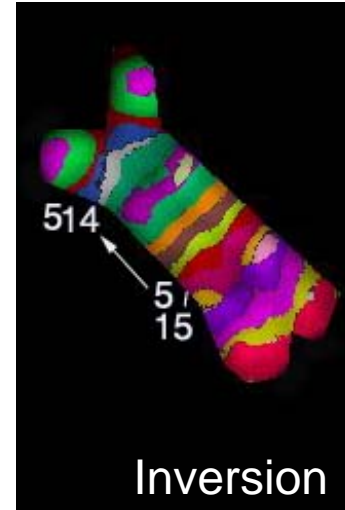
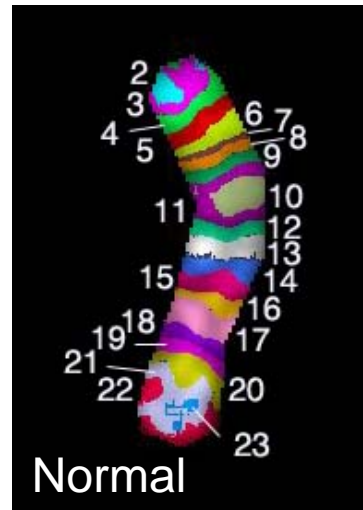
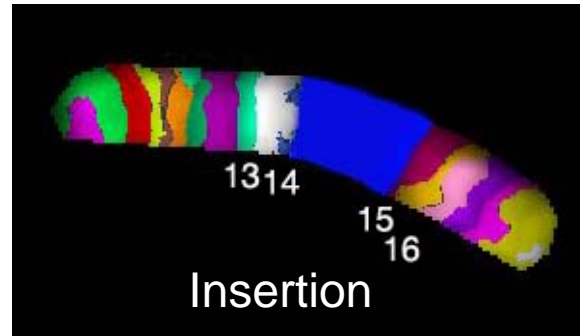
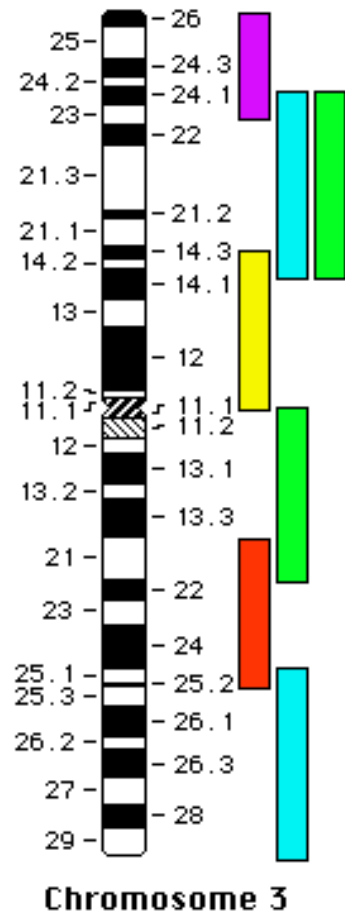
Chromosomal translocations and inversions are considered stable, and cells containing these types of chromosome aberrations can survive multiple cell divisions. An efficient method to detect an inversion is multi-color banding fluorescent *in situ* hybridization (mBAND) which allows identification of both inter- and intrachromosome aberrations simultaneously. Post irradiation, chromosome aberrations may also arise after multiple cell divisions as a result of genomic instability. To investigate the stable or late-arising chromosome aberrations induced after radiation exposure, we exposed human lymphocytes to gamma rays and Fe ions *ex vivo*, and cultured the cells for multiple generations. Chromosome aberrations were analyzed in cells collected at first mitosis and at several time intervals during the culture period post irradiation. With gamma irradiation, about half of the damages observed at first mitosis remained after 7 day- and 14 day- culture, suggesting the transmissibility of damages to the surviving progeny. Detailed analysis of chromosome break ends participating in exchanges revealed a greater fraction of break ends involved in intrachromosome aberrations in the 7- and 14-day samples in comparison to the fraction at first mitosis. In particular, simple inversions were found at 7 and 14 days, but not at the first mitosis, suggesting that some of the aberrations might be formed days post irradiation. In contrast, at the doses that produced similar frequencies of gamma-induced chromosome aberrations as observed at first mitosis, a significantly lower yield of aberrations remained at the same population doublings after Fe ion exposure. At these equitoxic doses, more complex type aberrations were observed for Fe ions, indicating that Fe ion-induced initial chromosome damages are more severe and may lead to cell death. Comparison between low and high doses of Fe ion irradiation in the induction of late damages will also be discussed.



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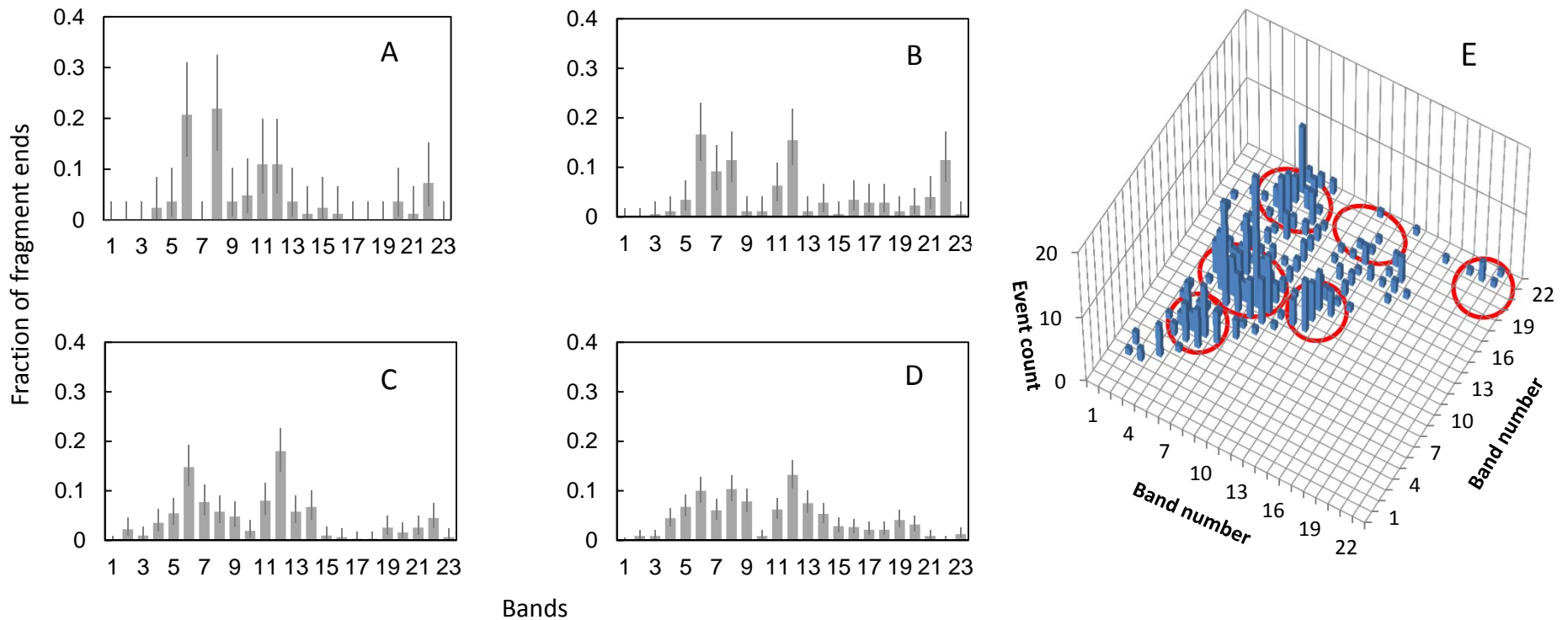
Multicolor *in situ* hybridization (mBAND)



mBAND allows identification of inter- and intrachromosome aberrations, as well as the location of the breaks in the damaged chromosome.

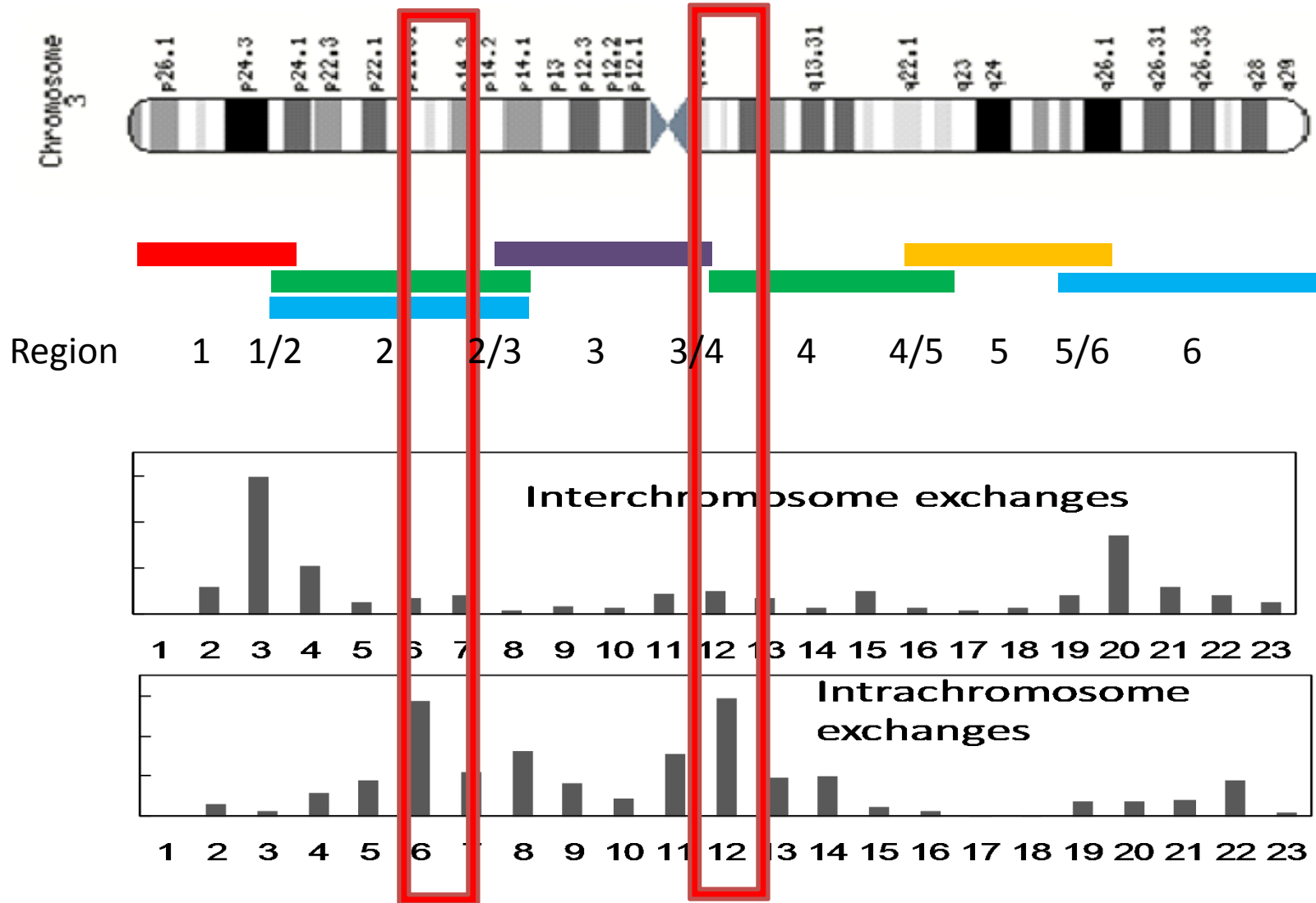
Distribution of breaks participated in intrachromosome exchanges

Human fibroblast cells (AG1522) exposed to low- and high-LET radiation

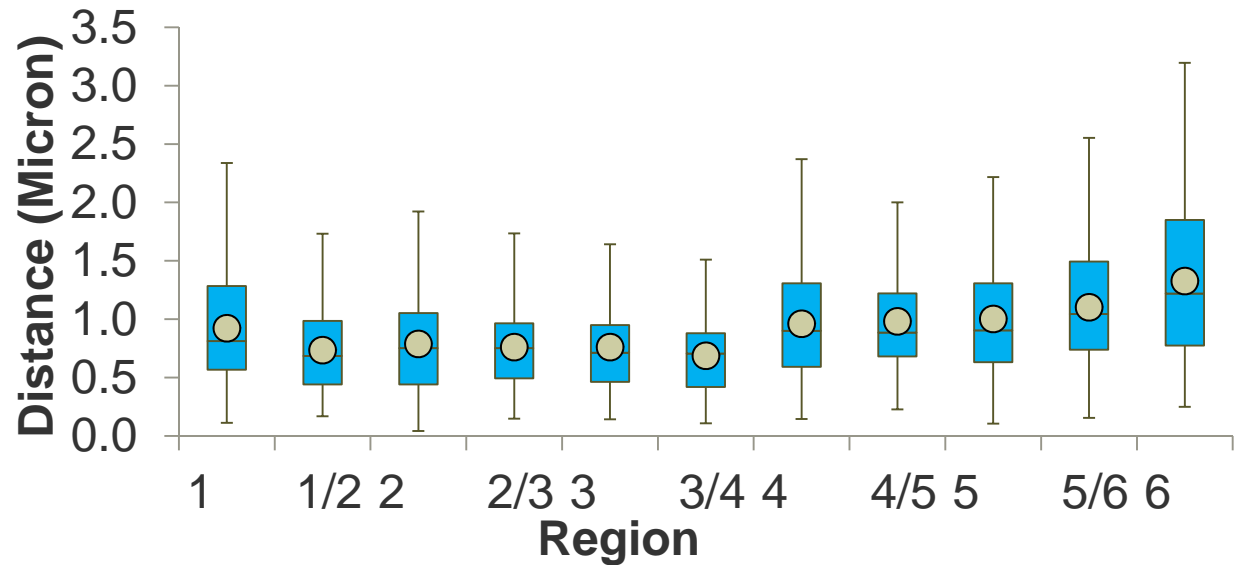
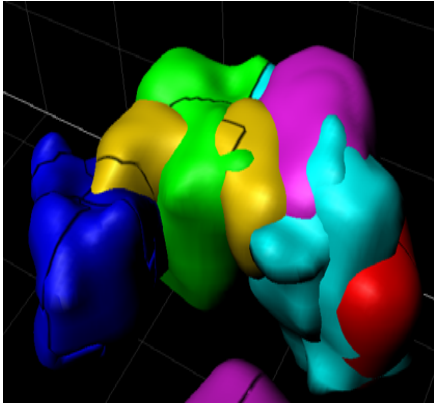


Breakpoint distribution for chromosome fragment ends participating in intra-chromosomal exchanges induced by γ -rays of low dose rate (Panel A), neutrons (Panel B), γ -rays of high dose rate (Panel C) or Fe ions (Panel D). Most of the intrachromosome exchanges occurred between a break in band 5-9 and one in band 11-13 (Panel E). (From Hada et al. 2011).

mBAND painting of human chromosome 3

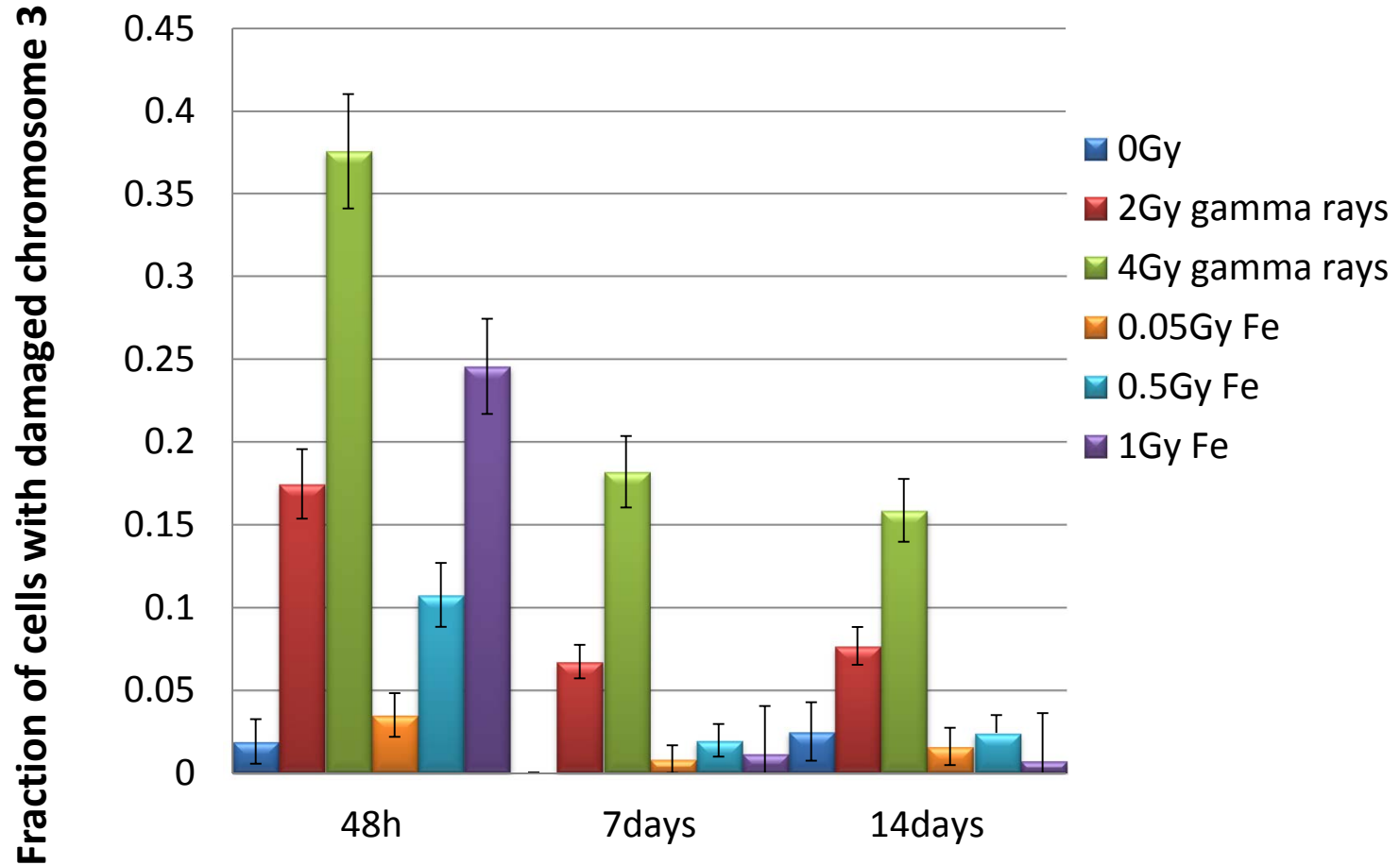


Distance between the center of each region and the center of the chromosome domain

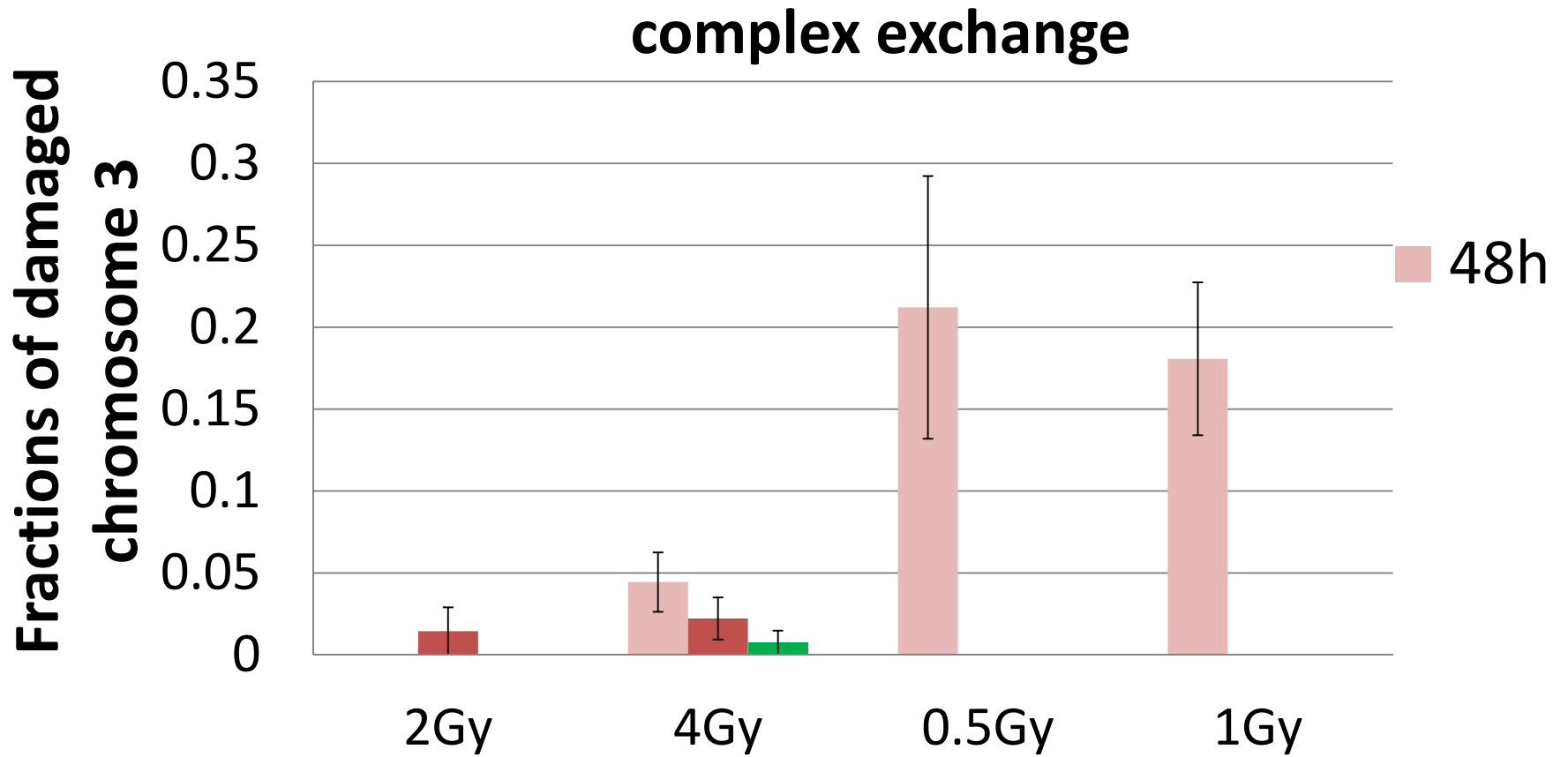


Chromatin in the p-arm tended to locate towards the interior of the chromosome domain, whereas chromatin in the q-arm tended to locate towards the exterior of the chromosome domain.

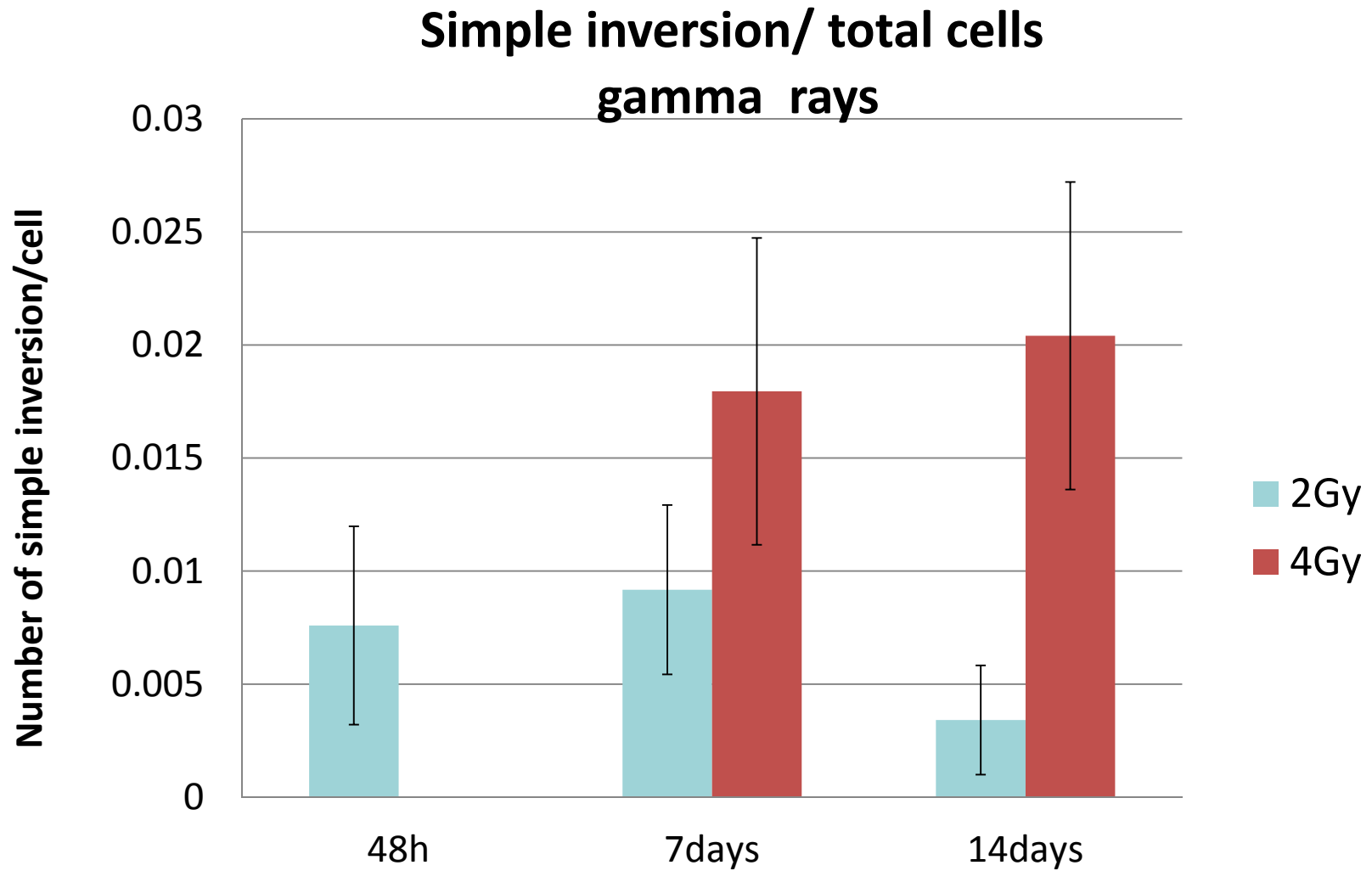
Frequency distribution of cells containing aberrant chromosome 3 of human lymphocytes



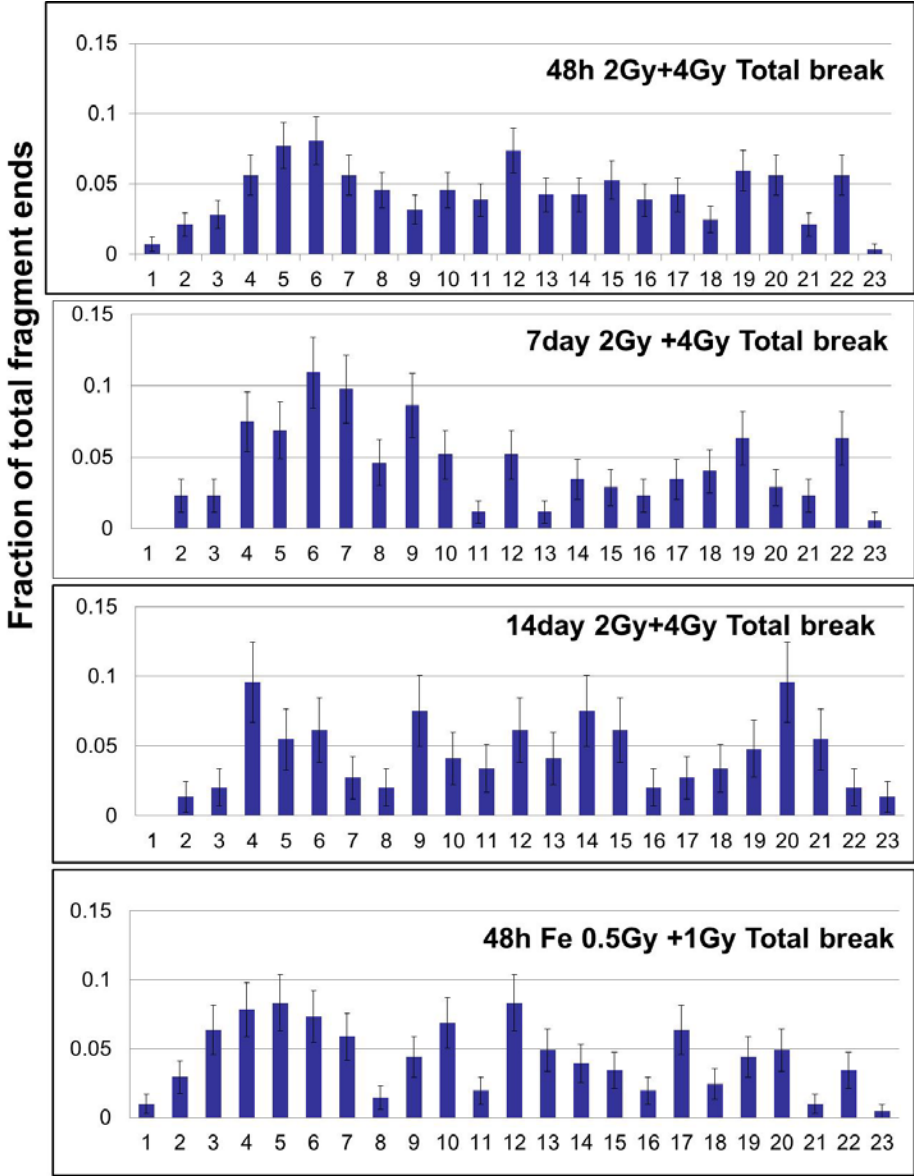
Interchromosomal exchanges in human chromosome 3 induced by gamma rays or Fe ions



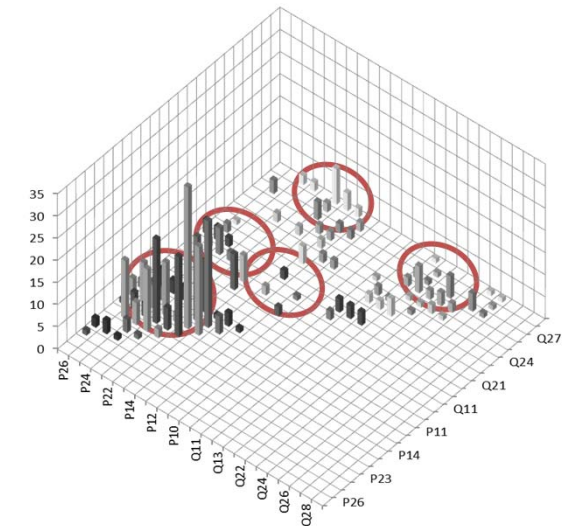
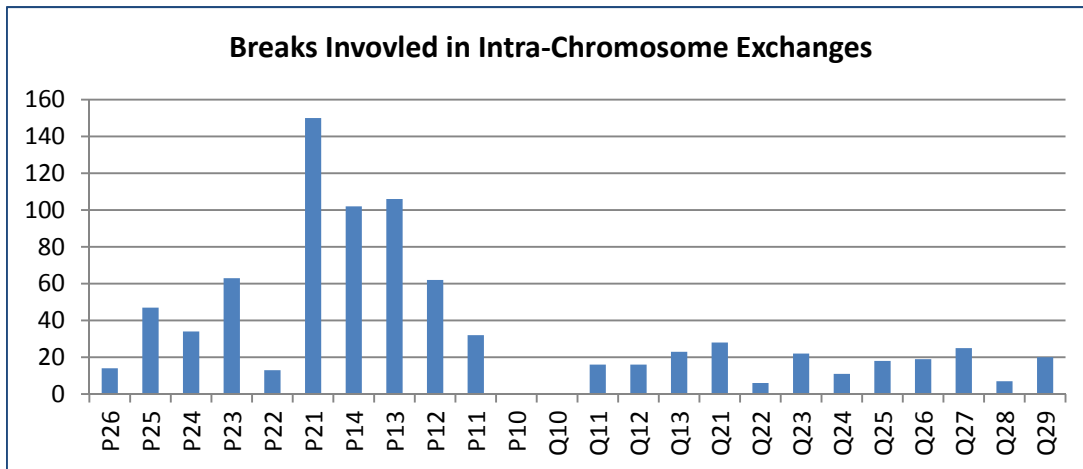
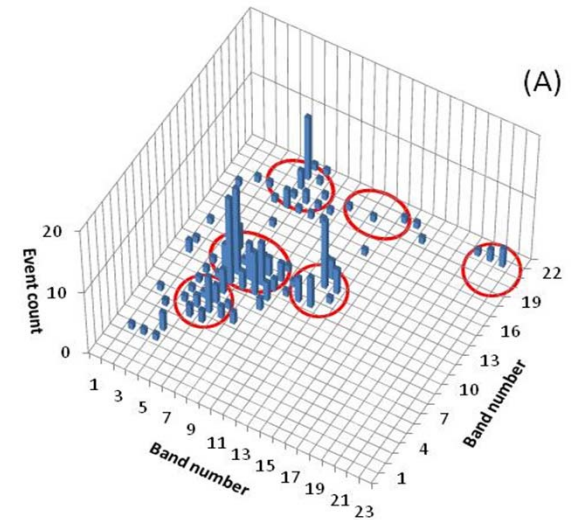
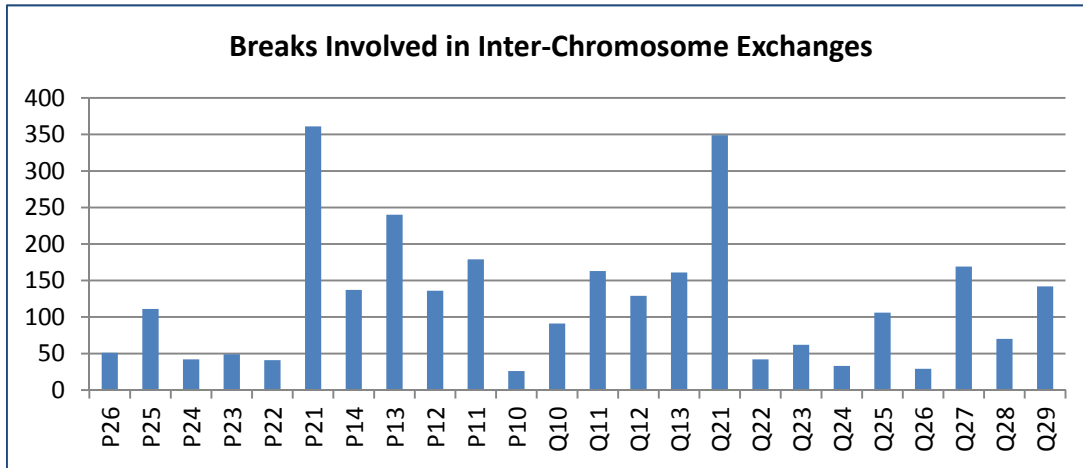
Frequency of simple inversions in chromosome 3 induced by gamma-rays



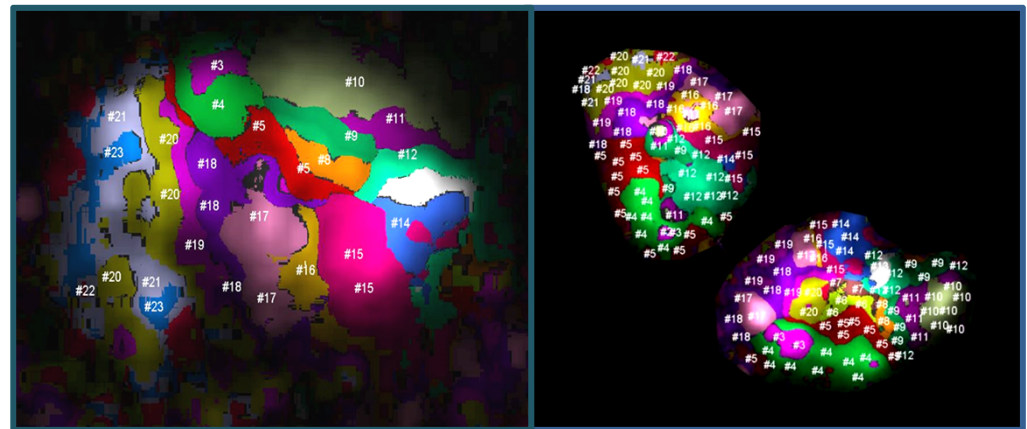
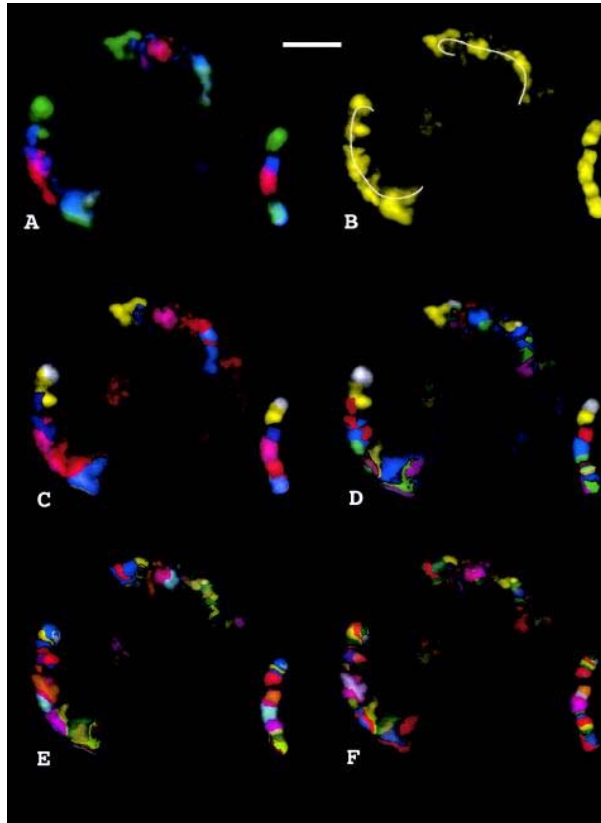
Distribution for total chromosome ends for lymphocytes



Location of breaks that participated in inter- and intra- chromosome exchanges in solid tumors



Comparison of organizations of interphase chromosome between human lymphocytes and human fibroblasts



Lemke et al. [Am J Hum Genet.](#) 2002

Conclusions

- About half of the cells initially damaged in chromosome 3 by gamma rays within the first mitosis remained for this long term culture, while about 1/5 or less of the cells damaged with Fe ions remained for this long term culture.
- Interestingly, simple inversions in chromosome 3 were found in only the 7 and 14 day samples. It is not clear whether cells containing simple inversions had already progressed through the first cell division at 48 hr, or the simple inversions were induced after the first cell division.
- The breakpoint distribution in chromosomes collected at 7 days, but not at 14 days, post irradiation appeared similar to the distribution in cells collected within the first cell cycle post irradiation. Further investigations are needed to determine whether some of the aberrations were formed after 7 days of cell culture.
- The distribution of break ends participated in interchromosome exchanges for human lymphocytes after radiation exposure was different from the previously published distribution for human mammary epithelial cells, indicating that interphase chromatin folding structures play a role in the distribution of radiation-induced breaks.

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