

- 148 The Roles of DNA Polymerase I in Chromosome Instability in *Escherichia coli*  
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We investigated spontaneous mutagenesis in the endogenous tonB gene of *E. coli* strains deficient in Pol I activities. In DpolA strain, deficient in both klenow and 5->3 exonuclease domains, the most frequent mutation event was deletion, followed by -frameshift, +frameshift, and duplication. In polA107 strain, deficient in 5->3 exonuclease domain, the most frequent mutation events were +frameshift and duplication. Previous study revealed that in polA 1 strain, which is deficient in klenow domain, the most frequent mutation events were deletion and -frameshift (AGEMIZU et al. 1999). These results indicate that 5->3 exonuclease domain of Pol I processes duplication and +frameshift events, and klenow domain processes deletion and -frameshift events. In many cases of mutant sequences, GC rich repeated sequences were detected near the mutated regions, suggesting GC repeated sequences are unstable in *E. coli*. In eukaryotes, such repeated sequences are called as microsatellite. Pol I seems to have an ability to stabilize microsatellite. It is known that mammalian FEN1 and yeast RAD27 are homologues of 5->3 exonuclease of *E. coli* Pol I. Thus we argue that FEN1 and RAD27 may also play a role in stabilization of their own genome.

- 149 The Effect of DNA Repair Defects on the Induction of Delayed Chromosome Aberrations by Radiation  
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Ionizing radiation induces chromosomal instability in the progeny of irradiated cells. To know the effect of DNA repair defects on the induction of delayed chromosome aberrations, we used *scid* mouse cells defected in non-homologous end-joining and Rad54 knockout (-/-) DT40 cells defected in homologous recombination. The Rad54 (-/-) DT40 cells were transferred with a human chromosome 2 by microcell fusion to monitor chromosomal instability. The cells were irradiated with X-rays and delayed chromosome aberrations were investigated over 20 cell divisions postirradiation. The chromosome analysis revealed that radiation increases the frequency of delayed dicentrics of which telomere sequences are retained at a fused site, suggesting that telonomic instability might be involved in the formation of delayed chromosome aberrations. Furthermore, we demonstrated that the *scid* cells are more susceptible to telonomic instability, suggesting that DNA-PKcs might be involved in the maintenance of telomere function.

- 150 Radiation induction of genomic instability as assayed by the somatic reversion of a pink-eyed allele.  
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The biological effect of irradiation has been attributed to DNA damage. However, the relationship between DNA damage and repair does not account for delayed mutation and bystander effect. We have investigated whether or not radiation has ability to induce genomic instability. In this study delayed and in direct somatic mutation at the pink-eyed dilution locus was investigated. F1 mice were born between irradiated male C3H p-j mice and female B6 p-un mice. Pigmentation of retinal pigment epithelium was examined for the frequency of a maternal p-un gene reversion. 6Gy-irradiation to sperm increased the reversion frequency to two times. Analysis of the distribution of pigmented cells indicated that the frequency of reversion was elevated in the irradiated group throughout the development of pigment epithelium cells. Additionally, this increase of the mutation frequency was observed only for irradiation to the spermatozoa stage, but not of the spermatogonia stage. Furthermore P53 knockout mouse is examined to understand the mechanism of this phenomenon.