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## Tumor related genes (172-176)

172 Illegitimate Recombination Leading to Genetic Instability in p53-mutant Human Lymphoblastoid cells

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Allele loss and translocation are critical mutational events in human tumorigenesis. Allele loss, which is usually observed as loss of heterozygosity (LOH) by RFLP analysis in various kinds of human tumors, is generally resulted from deletion or mitotic recombination between homologous chromosomes. It is demonstrated, here, by cytogenetic analyses of LOH mutations in heterozygous thymidine kinase (tk) locus that illegitimate recombination is a major mechanism for allele loss in p53-mutant human lymphoblastoid cells. The illegitimate recombination occurred between none-homologous chlomatids after DNA replication leading to unbalanced translocations. This observation implicates p53 in the regulation of homologous recombination, and suggests a possible mechanism by which the loss of p53 function may cause genetic instability.

How will a mutation of p53 affect the sensitivity of the cell to ionizing radiation.

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Mutations of p53 gene are the most common genetic alteration observed in human cancers. Many papers reported that cells lacking normal p53 function are more resistant to ionizing radiation. We want to know which mutations of p53 affect the sensitivity to ionizing radiation. We made mutant p53 cDNAs by in vitro mutagenesis and introduced to human osteosarcoma cells, Saos-2, which are devoid of endogenous p53 gene. We got some clones of mutant p53 and examined the sensitivity of the clones to ionizing radiation.