174 LOH Analysis of Mouse Hepatocellular Carcinoma Cell Lines and Its Relationship with the Biological Feature.

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We analyzed loss of heterozygosity (LOH) in cell lines from mouse hepatocellular carcinomas induced by radiation exposure to C3HxC57BL F1 (or C57BLxC3H F1) mice using microsatellite DNA polymorphic markers on chromosome 4, 7, 14, or 17. On chromosome 4, we observed LOH in 31% of the cell lines and the weak expression on one allele (PLOH) in 25% of those. In this 56% of LOH, the C57BL allele was lost, or weakened, more frequently. And we found the highest incidence of LOH at the loci around D4Mit220. We also observed LOH and / or PLOH on chromosome 7, 14, or 17 in 6%, 25%, 12% of the cell lines, respectively. Moreover, we investigated the relationship between LOH on chromosome 4 and the ability of proliferation in the soft agar as the marker of the biological features. We found that 69% of the cell lines, in which the C57BL allele was lost on chromosome 4, could grow in soft agar culture. On the other hand, only 20% of those, in which the C3H allele was lost on chromosome 4, and 27% of those without LOH on chromosome 4, could grow in the same condition.

These data indicate that there are some important genes on chromosome 4 in mouse hepatocarcinogenesis. We are now investigating some genes related to these biological features using the differential display method.

175 Molecular Analysis of p53 Gene Mutations in Skin Cancers of the A-bomb Survivors.

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Among A-bomb survivors, an increased risk of skin cancer is observed. We have analyzed changes in the p53 tumor suppressor gene in skin cancers from survivors to identify any foot-prints as a result of exposure to ultraviolet light (UV) and ionizing radiation (IR). These cancer cases included Bowen's disease, basal cell carcinoma, and squamous cell carcinoma, but not melanoma. After PCR amplification of exons 5-8 using DNA extracted from paraffin-blocks, mutations were detected by PCR-SSCP and then identified by direct sequencing. Interestingly, the mutation spectra among tumors derived from different areas of the body seemed to depend on whether they were exposed to UV and/or IR. These results will help us to elucidate the mechanisms of radiation-induced skin carcinogenesis.