158 Cellular Origins of Rat Lung Tumors Induced by Inhalation Exposures to Plutonium Dioxide

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To investigate the origins of target epithelial cells for radiation-induced rat lung tumors, 135 primary tumors induced by inhalation exposures to plutonium(Pu) dioxide aerosols, as compared to 21 primary tumors induced by X-ray irradiations, were examined by immunohistochemistry for Type II cell-specific SP-A and Clara cell-specific CC-10. In Pu-induced tumors, SP-A or CC-10 was highly detected from adenomas and adenocarcinomas, whereas most of adenosquamous and squamous cell carcinomas were negative for both antigens. In X-induced tumors, about a third of adenomas and adenocarcinomas were positive for SP-A or CC-10, while both antigens were all negative in adenosquamous and squamous carcinomas. These findings indicate that radiation-induced lung adenomas and adenocarcinomas would be derived mainly from Type II and/or Clara cells as described in ICRP Pub.66(1994) and NCRP Rep.125(1997), but squamous tumors would be from different epithelial cells or otherwise might loose antigens during the carcinogenic processes.

159 Phenotypic Reversion of an X-Ray-Induced Transformant of Mouse m5S by Introduction of a Human Chromosome 11

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The purpose of this study is to establish a new model system to know how delayed chromosome instability is involved in radiation carcinogenesis. We isolated an X-ray-induced transformant, cl.6110, from mouse m5S cells. To obtain a phenotypic revertant from cl.6110 cells, we transferred a human chromosome 11 into cl.6110 cells by microcell fusion. The FISH analysis revealed that one of revertant, cl.6110R-8, retained a human chromosome 11 in 99% of the microcell hybrid. To examine the phenotype of the revertant, the cells were assay for focus-forming ability in monolayer culture. The result indicated that the focus-forming ability of cl.6110R-8 cells was completely suppressed as compared to the parental cl.6110 cells. These results indicate that a human chromosome 11 suppresses transformed phenotypes of cl.6110 cells. Thus, cl.6110R-8 cells are useful for a model system to study the relationship between radiation-induced delayed chromosome instability and re-acquisition of the transformed phenotypes.

160 Analysis of Tumor Suppressor Regions in Radiation-Induced Lymphomas of *Fas* Heterozygous Deficient Mice

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Mutations of *Fas* gene have been reported mainly in lymphoid-lineage malignancies, and the *Fas* gene has been considered to be a tumor suppressor gene (Muschen *et al*. J. Mol. Med. 78, 312, 2000). To examine an involvement of *Fas* gene as a tumor suppressor gene in radiation lymphomagenesis, we examined the loss of heterozygosity (LOH) in the lymphomas from [BALB/cHeA x MRL-MpJ/Fas^{lpr}]F_1 [(C x *lpr*)F_1], and [MSM/Ms x MRL-MpJ/Fas^{lpr}]F_1 [(M x *lpr*)F_1], hybrid mice. The F_1 mice were exposed to four doses of 1.7 Gy or 2.5 Gy of X-rays. Developed lymphomas were analyzed for the LOH by PCR and PAGE. Lymphoma development has been observed efficiently in both F_1 hybrids. LOH was frequently observed at *D12Mit279* on chromosome 12 (23/42, 54%) and rarely on chromosomes 4, 6 and 16 in (C x *lpr*)F_1 mice. LOH was also observed on chromosomes 4 (21%) and 12 (71%) in (M x *lpr*)F_1 mice. Lymphomas from both F_1 hybrids did not indicate allelic loss on chromosome 19 containing *Fas* locus. No wild-type allele of the *Fas* gene was lost in 51 lymphomas from (M x *lpr*)F_1 mice. These results do not suggest that *Fas* gene predominantly involved in the radiation lymphomagenesis.