illegitimate structure is frequently observed in radiation-induced acute myeloid leukemia (AML) cells in C3H/He mice. Since production of the IAP RNA is the first step of retrotransposition mechanisms and is regulated by the 5′-LTR, we compared transcriptional activity of the LTRs of type-A, D and H by the reporter assay. Transcriptions driven by D-type LTR and H-type LTR were enhanced in Balb/c-based and C3H/He-based hematopoietic cell lines, respectively. Nucleotide sequences essential for mouse strain and tissue specific regulation site in U3-region of LTR were determined.

38 Genetic Control of Spontaneous and Xray-induced Intestinal Tumorigenesis in Min Mice

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Min(multiple intestinal neoplasia) mice carry a mutant allele of the murine *Apc* locus and are predisposed to adenoma formation in the intestinal tract. Tumorigenesis in Min mice is affected by various factors including genetic background and ionizing radiation. In this report, we addressed a possibility of genetic relevance between spontaneous and X-ray induced tumorigenesis in Min mice. MSM strain is highly resistant to intestinal tumorgenesis by Min mutation. QTL analysis indicated that a newly identified modifier locus *Mom3* is a major determinant of the resistance, together with a resistant allele of *Mom1* locus. A congenic strain of *Mom 3* and a consomic strain of the chromosome in the B6-Min background resulted in more than five-fold decrease in tumor multiplicities in the intestine of Min mice. X-irradiation of the consomic mice increased their tumor incidence, almost reaching to a level in irradiated B6-Min mice. These data suggest a possibility of the crosstalk between induction by X-irradiation and suppression by *Mom3* allele in the tumorigenesis in Min mice.

39 Frequencies of Leukemia-Related Chromosome Aberrations in Hematopoietic Stem Cells of Irradiated Mice

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C3H/He mice develop acute myeloid leukemia (AML) after whole-body irradiation, and typical chromosome 2 deletions are found in the leukemic cells. We have examined the frequencies of the AML-type deletions in primitive hematopoietic cells that could be the targets of the leukemogenesis. Ten-week male C3H/He mice were exposed to 3 Gy x-rays and sacrificed after certain periods of time. Bone marrow cells were collected from femora and a single-cell suspension from each animal was divided into two parts. One part was processed with MACS to obtain Lin^+ and Lin^-Sca1^+ cells. Those cells were analyzed with FISH for the AML-type deletions. The other part of the cell suspension was cultured in methyl cellulose media, and metaphase spreads were prepared from each growing colony. Results obtained so far for 1 day post irradiation show that approximately 3% of the cells carried the AML-type deletions in both Lin^+ and Lin^-Sca1^+ subpopulations while metaphases in GM colonies were mostly of normal karyotypes except for a small number of non-clonal aberrations.

40 Cyclin D1 Overexpression in Thyroid Tumors from the Radio-contaminated Area, and its Correlation with Pin1 and Aberrant beta-Catenin Expressions

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A high prevalence of aberrant beta-catenin has been reported in radiation-associated thyroid tumors (RATT). CyclinD1 is a target activated by Wnt/beta-catenin. While, Pin1 promotes cyclinD1 expression and p53 phosphorylation induced by irradiation. This study aimed to elucidate whether Pin1 was involved in cyclinD1 and beta-catenin expression in RATT. We examined follicular adenomas (FA) and papillary carcinomas (PC). All PC displayed cyclinD1 overexpression and a cytoplasmic beta-catenin. Overexpression of cyclinD1 mRNA was observed in 45.5% of FA and 54.5% of PC. Correlation was revealed between cyclinD1 and Pin1/cytoplasmic/membrane beta-catenin expressions, and between Pin1 and cytoplasmic/membrane beta-catenin expressions in RATT. Any mutations of beta-catenin gene could not be detected. Western blot analysis demonstrated a high level of cyclinD1 and beta-catenin as well as Pin1 expressions in a PC cell line. This study supported a significance of cyclinD1 overexpression and aberrant beta-catenin in RATT. Pin1 may be an important factor to regulate cyclinD1 and beta-catenin in RATT.

41 Experimental scheme of combined effect of radiation and chemical carcinogens: dose response relationship and molecular mechanism

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We are living in the environment with numerous natural and man-made chemicals that are cancer-initiating and promoting potentials. Thus exposure to radiation could be a result of interaction with these agents. However, the quantitative assessment and mechanistic understanding of combined effects of radiation and chemical carcinogens are still insufficient. Mechanism-based cancer model is expected to greatly improve the risk assessment. We have set up an experiment for the combined effect of radiation and chemicals in order to determine the dose-response relationship including low doses. The animal models used in the