ABSTRACTS

161 Mutation-points of p53 affect the sensitivity of the cell to anticancer drugs.

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Mutations of p53 gene are the most common genetic alteration observed in human cancers. Many papers reported that cells mutated at p53 gene became resistant to anticancer drugs but some papers reported the contrary of the sensitivity to anticancer drugs. We want to know which mutations of p53 affect the sensitivity to anticancer drugs. We introduced four p53 mutants (123A, 143A, 175H, and 273H) or wild type p53 to human osteosarcoma cells, Saos-2, which are devoid of endogenous p53 gene. We examined the sensitivity of the clones to four anticancer drugs (CDDP, ACNU, ADR and BLM) and found that the sensitivity to anticancer drugs varied with the mutation-points of p53.

162 Expression of np95 Nuclear Protein during Radiation-induced Thymic Lymphomagenesis and its Distribution in Nuclei.
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We previously established a monoclonal antibody Th-10a that recognizes the 95 kDa mouse nuclear protein (np95). The nuclear protein was expressed specifically in S-phase of normal thymocytes. In contrast, unregulated expression of the nuclear protein was observed throughout the cell cycle of mouse thymic lymphoma cells. We cloned the cDNA encoding np95 by immunoscreening a λgt-11 cDNA expression library with Th-10a. Sequencing the whole 3.5 kb cDNA revealed that the np95 was a novel nuclear protein with an open reading frame (ORF) consisting of 782 amino acids. In this study, we investigated the expression of np95 nuclear protein during radiation-induced thymic lymphomagenesis and its distribution in nuclei. The results supported the possibility that aberrant expression of np95 is involved in cancer progression. The biological role of np95 during S phase is under investigation.

163 Diverse Spectrum of ras Mutations in Radiation-Induced Thymic Lymphomas.
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In order to identify the radiation signature in tumors, we have examined spontaneous,
ethylntrosourea (ENU)- or X-ray-induced thymic lymphomas (TL) isolated from the B6C3F1 female
mice for the mutations of K- and N-ras. Twenty five percent of ethylntrosourea (ENU)-induced TL
had K-ras mutation which is restricted in exon 1. In contrast, 20% of X-ray-induced TL had K-ras
mutations which were located in both exons 1 and 2. The diverse spectrum of point mutations was
found in X-ray-induced TL in codons 18 (GCT→GAC), 61 (CAA→CAC) and 63 (GAG→AAG).
These mutations were not detected in ENU-induced TL. N-ras was activated less frequently (5%)
regardless of the carcinogens. Since no mutation of either K- or N-ras was detected in spontaneous TL,
these mutations were considered to be induced by the carcinogens via direct or indirect mechanism.