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Hepatocyte micronucleus assay in young rats: comparison of 2 strains

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【Purpose】We are investigating the utility of the young rat liver micronucleus assay as a genotoxicity assay. Because Sprague Dawley rats are commonly used in toxicity studies, we compared the responses of SD rats and Fischer F344 rats in the assay.

【Chemicals】para-Dimethylaminoazobenzene (DAB), 2-acetylaminofluorene (2-AAF), diethylnitrosamine (DEN), dimethylntrosamine (DMN), 2,4-diaminotoluene (2,4-DAT) and quinoline.

【Methods】Using 4-week-old male rats of both strains, we tested 6 chemicals at doses that evoked positive responses in the F344 rat. After 3, 4, or 5 days of dosing, we prepared hepatocytes specimens by perfusion with collagenase and stained them by the AO (acridine orange) / DAPI (4′,6-diamidino-2-phenylindole dihydrochloride) double fluorescent staining method. We examined 2000 cells from each animal and recorded the number of micronucleated hepatocytes (MNHEP) and the number of mitotic cells.

【Results】The frequency of MNHEP was similar for the two strains for DMN and DEN though we found some differences among the times of specimen preparation, but not for 2,4-DAT and 2-AAF. We will report strain differences in the frequency of MNHEP and the results of the remaining 2 chemicals.

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Nature of micronuclei induced in reticulocytes of p53-null mice after radiation, a preliminary report

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Null(-/-) mice for atm and those for p53 are hypersensitive to X-ray induced micronucleus (MN) formation in peripheral blood reticulocytes to similar extent (Kagawa et al., 2004, JEMS). This finding and other data support the hypothesis that ATM-P53 pathway is playing an important role in defense of somatic cells from chromosome damage induced by radiation. Since ATM is activated by double strand breaks in DNA (DSBs), this hypothesis implies that excess number of MNs induced in p53(-/-) status after radiation mostly represent acentric fragments due to DSBs. The present study was designed to determine where MNs increased in p53(-/-) mice over the wild-type level after radiation are free from centromere. For this purpose, we adopted the FISH technique reported by Hande et al. (1996) with a little modification. The centromere probe we used is STARFISH. A spindle poison colchicin (CH) was used at an i.p. dose of 1 mg/kg as positive control. It was noticed in a preliminary experiment that a large fraction of MNs detected in p53(-/-) mice 24h after CH treatment were positive for the centromere signal. Results obtained for MNs detected 48h after X-irradiation at a dose of 1 Gy are to be presented and discussed.

p53遺伝子欠損マウスの末梢赤血球で放射線によって誘発された核の本性（予報）

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