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General Summary

Our major research projects in the 2008 academic year focused on: 1) the genotoxic effects of indium chloride on micronucleus induction; 2) the comet assay for detection of DNA damage; 3) DNA damage by exposure to electromagnetic fields; 4) the effects of zinc deficiency on the induction of chromosome aberrations; 5) oxygen-induced oxidative stress; 6) methods of medical informatics education and evidence-based medicine (EBM); and 7) the risk of decompression sickness.

Research Activities

Experimental medicine

1. Influence on the antitumor effect of a static magnetic field

We have reported that co-exposure to a static magnetic field (SMF) increases the frequency of chromosome aberration induced by some chemicals (including antitumor agents). In this study, we investigated the antitumor effect of co-exposure to SMFs and bleomycin in L1210 leukemia-bearing mice. The increases in lifespan were 16.5% and 12.3% by exposure to a SMF (5T) and to bleomycin (5 mg/kg), respectively. The increase in lifespan increased to 34.6% by co-exposure to gradient SMF and bleomycin. Similarly, the increase in lifespan increased to 27.9% by co-exposure to a 5-T SMF and bleomycin.

2. Effect of SMFs on the induction of micronuclei and the production of 8-hydroxy-deoxyguanosine in mice bone marrow cells

We investigated the effects of an antioxidant chemical (ascorbic acid) on the co-mutagenic effects of a 5-T SMF and X-rays by means of the *in vivo* mouse bone marrow micronucleus test. Moreover, concentrations of 8-hydroxy-deoxyguanosine (8-OHdG) in bone marrow cells were determined to examine the level of oxidative stress. Increases in both the micronucleus frequency and the 8-OHdG concentration induced by co-exposure to X-rays and SMFs were observed, but these increases were inhibited by pretreatment with ascorbic acid. These results suggest that SMF exposure enhances micronuclei in mouse bone marrow cells by affecting the behavior of free radical species produced within cells.

3. Zinc deficiency and oxidative stress

We studied the effect of oxidative stress in esophageal lesions in zinc-deficient rats. Parakeratosis in the esophagus was partially suppressed by tempol, a free-radical scavenger. This result suggests that oxidative stress is partially related to parakeratosis in the esophagus of zinc-deficient rats.

4. A work of the method for analysis of 8-OHdG by gas chromatography/mass

spectrometry

8-OHdG is considered to be the best variable for assessing the oxidation damage of DNA. Measurement of 8-OHdG using gas chromatography/mass spectrometry was considered.

Epidemiology, EBM, investigation, and medical informatics

1. EBM

A systematized body of epidemiologic principles with which studies can be designed and judged has been established only in the last 2 decades. These principles have evolved in tandem with an explosion of epidemiologic activity covering a wide range of health problems. Our greatest concern is to clarify risk factors for adult disease and intractable diseases. We also studied the methodology of medical informatics education and EBM.

2. Oxidative stress by breathing oxygen in neonates

To clarify the carcinogenicity of target organs by oxygen exposure during the neonatal period, we studied oxidative DNA damage according to 8-OHdG in newborn rats. The oxidative DNA damage was observed to increase temporarily during oxygen exposure.

3. Outpatients with diabetes were followed up for 30 years or more. The effects of age and variability of fasting plasma glucose (FPG) levels on the onset of simple diabetic retinopathy (SDR) were analyzed. Mean levels of hemoglobin A1C and FPG were independent risk factors for the onset of simple diabetic retinopathy. The risk decreased in subjects older than 42 years, perhaps because of less variability in FPG levels.

Publications

Suzuki Y, Takagi R, Kawasaki I, Matsudaira T, Matsudaira H, Shimizu H. The micronucleus test and erythropoiesis: effects of cyclic adenosine monophosphate (cAMP) on micronucleus formation. *Mutat Res* 2008; **665**: 45-51.

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Ichiki A, Miyazaki T, Nodera M, Suzuki H, Yanagisawa H. Ascorbate inhibits apoptosis of Kupffer cells during warm ischemia/reperfusion injury. *Hepato-Gastroenterol* 2008; **55**: 338-44.