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General Summary

Our major research projects in the 2007 academic year focused on: 1) the genotoxic effects of vitamin E and its derivatives on micronucleus induction; 2) the genotoxic effects of indium chloride on micronucleus induction; 3) the comet assay for detecting DNA damage; 4) DNA damage by exposure to electromagnetic fields (EMFs); 5) effects of zinc deficiency on the induction of chromosome aberrations; 6) oxygen-induced oxidative stress; 7) the genotoxicity of methylenedioxymethamphetamine (MDMA) as an illegal drug of abuse; 8) methods of medical informatics education and evidence-based medicine (EBM); and 9) the risk of decompression sickness.

Research Activities

Experimental medicine

1. A genotoxicity study of several derivatives of vitamin E that react as antioxidants (a collaborative study with Kyoritsu Pharmaceutical University)

A genotoxicity study of several derivatives of vitamin E was performed. Chinese hamster lung (CHL/IU) cells were exposed separately to both vitamin E derivatives and vitamin E. The number of chromosomal aberrations and micronucleus frequencies was comparable in the vitamin E derivatives and vitamin E.

2. Effects of indium chloride on micronucleus induction

Recently, concerns have been raised about the possible toxic effects of indium compounds used to diagnose myelopoiesis and of ceramics used in the production of transparent conductive films for flat-panel liquid crystal and plasma displays. The frequency of micronuclei induced by indium chloride increased in *in-vivo* micronucleus tests in BALB/c mice. Indium chloride also induced micronuclei on the *in-vitro* micronucleus test, but negative results were obtained on chromosome aberration testing with CHL/IU cells.

3. A possible mechanism for the enhancement by co-exposure to static magnetic fields of micronucleus formation by mutagens

We have previously found that co-exposure to static magnetic fields (SMFs) increases the frequency of micronuclei induction by several mutagens. In the present study, it became clear that the increase in the frequency of micronuclei induction by co-exposure to SMFs and chemicals was blocked by pretreatment with the antioxidant ascorbic acid. Moreover, an increase in 8-hydroxy-deoxyguanosine in bone marrow cells was observed after exposure to SMFs. These results suggest that exposure to SMFs enhances the

reaction of mutagen-related radicals and DNA.

4. DNA damage by exposure to EMFs

We studied the effect of the co-exposure to EMFs and bleomycin on DNA damage using the comet assay. DNA damage induced by bleomycin in brain cells was increased by co-exposure to EMFs (50 Hz, 10 mT, 6 hours). Tempol, a radical scavenger, partially suppressed the DNA damage induced by bleomycin.

5. Effects of zinc deficiency on the induction of chromosome aberrations

An estimated 30% of Japanese have zinc deficiency. We studied whether zinc deficiency increases the risk of carcinogenesis. We found that the frequency of micronuclei increased 4 weeks after zinc-deficient food was first given. In addition, 8-hydroxy-deoxyguanosine was induced in bone marrow cells. These results suggest that an oxidative state is aggravated by zinc deficiency and induces micronuclei.

6. Oxidative stress by breathing oxygen in rat neonates

To clarify the carcinogenicity of target organs by oxygen exposure during the neonatal period, we studied oxidative DNA damage in animals.

7. Genotoxicity of MDMA as an illegal drug of abuse

The illegal use of MDMA has recently become a social problem. Orally ingested MDMA reacts with nitrites in the stomach and is metabolized into *N*-nitroso-MDMA. We synthesized *N*-nitroso-MDMA and studied its genotoxicity using the micronucleus and chromosomal aberration tests. The genotoxicity of *N*-nitroso-MDMA was observed with both tests.

Epidemiology, EBM, investigation, and medical informatics

1. Epidemiology, EBM, and medical informatics

A systematized body of epidemiologic principles with which studies can be designed and judged has been established only in the last two 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. A survey of risk of decompression sickness

To prevent decompression sickness in caisson workers and commercial divers, we have used the ultrasonic bubble detection technique to study the risk of decompression sickness under high-pressure mixed gas.

Publications

Yoshioka H, Shimizu H, Toyama Y, Miyakoshi Y, Suzuki Y, Takagi R. Genotoxicity study of illegal drug MDMA and its nitroso derivative N-MDMA by micronucleus and chromosomal aberration tests using chinese hamster lung fibroblast cell line. *Environ Health Prevent Med* 2007; **12**: 129-37.

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