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General Summary

Our major research projects in the 2011 academic year focused on: 1) analysis of oxidative DNA damage, 2) evaluation of mutagenic potential related to diabetes mellitus (DM), 3) a method for analyzing 8-hydroxy-deoxyguanosine (8-OHdG) with matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI/TOF MS), 4) evaluation of fatigue following the compressed air work using human herpesvirus (HHV) 6 in saliva, 5) evidence-based medicine (EBM), 6) a questionnaire survey on drug information, 7) prevalence of menopausal symptoms, 8) associations between body weight and cardiovascular risk factors, 9) ecological studies of suicide, 10) annual changes in the suicide mortality rate in Japan, 11) effects of L-carnosine and its zinc complex polaprezinc on pressure-ulcer healing, 12) long-term follow-up study of type 2 DM, and 13) mental health in the workplace.

Research Activities

Experimental Medicine

1. Analysis of oxidative DNA damage

Analysis of 8-OHdG, an indicator of oxidative DNA damage, and deoxyguanosine (dG) was performed with a high-performance liquid chromatography-electrochemical detector/ultraviolet detector. The ratio of 8-OHdG/dG in zinc-excess rats was increased, compared with that in the control group. The ratio of 8-OHdG/dG in indium oxide (In_2O_3) or indium hydroxide ($\text{In}(\text{OH})_3$) was not increased.

2. Evaluation of mutagenic potential related to DM

The effects of streptozotocin-induced DM in rats were studied with flow cytometry to measure micronuclei in both the reticulocyte and normochromatic erythrocyte populations in peripheral blood. The micronucleus frequency in DM rats tended to be higher even 4 weeks after treatment with streptozotocin. This result suggests that high blood glucose levels are associated with increased micronucleus frequency. In the future, more detailed studies will be required to confirm this finding, including its reproducibility for evaluating the risk of carcinogenesis by DM.

3. A method for analyzing 8-OHdG with MALDI/TOF MS

The best indicator of the oxidation damage of DNA is 8-OHdG. Then, easurement of 8-OHdG with MALDI/TOF MS was done.

4. Evaluation with HHV-6 in saliva of fatigue following work in compressed air

Many caisson workers report severe fatigue after working in compressed air. We used HHV-6 in saliva to evaluate the fatigue of these workers. Although working hours were short, HHV-6 DNA copy numbers after hyperbaric work were significantly higher than

those after normobaric work. The fatigue of workers in compressed air caissons might be induced by exposure to hyperbaric conditions.

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 diseases and intractable diseases. We also studied the methodology of medical informatics education and EBM.

2. A questionnaire survey on drug information

A self-administered questionnaire was distributed to approximately 2,000 health examinees at a Japanese healthcare center to examine drug-information-seeking behavior of Japanese people and their attitudes toward drug information.

3. Prevalence of menopausal symptoms

Questionnaire surveys on menopausal symptoms were conducted among 50- and 60-year-old women who lived in northern Kawasaki. We determined the prevalence of menopausal symptoms among community-dwelling Japanese women and projected the number of women with menopausal symptoms in Japan from 2009 to 2055.

4. Associations between body weight and cardiovascular risk factors

Using 2008 and 2009 health examination data, we examined 1-year changes in body weight and cardiovascular risk factors among Japanese male workers. The effect of weight gain on cardiovascular risk factors was compared between younger (25-44 years) and older (45-64 years) groups.

5. Ecological studies of suicide

Using 2005 national census data, we examined the associations between age-adjusted suicide rates and socioeconomic factors in 47 prefectures and 358 medical care zones.

6. Annual changes in the suicide mortality rate in Japan

The suicide in Japan increased rapidly from 1998, and prevention of suicide is an important issue. Regional differences in suicide rates have previously been noted. The present study analyzed the relationship between 25 factors and the suicide mortality rate in each prefecture according to sex.

7. Effects of L-carnosine and its zinc complex polaprezinc on pressure-ulcer healing

We performed an interventional study examining the effects of L-carnosine and its zinc complex polaprezinc on the healing of chronic pressure ulcers. The results of this trial suggest that L-carnosine and polaprezinc are both beneficial for the treatment of pressure ulcers.

8. Long-term follow-up study of type 2 DM

We investigated the relationship between HbA1c variability and all-cause mortality in patients with type 2 DM. We recommend that attention should be paid to HbA1c variability as well as to the HbA1c level in the treatment of these patients, even if they are not elderly.

9. Mental health in the workplace

Mental health in the workplace is increasingly recognized as a serious problem. Several

questionnaires have been created to assess mental health in Japan. Concrete questions are important for managing stress in the workplace. The purpose of this study was to investigate stress in the workplace with a new questionnaire.

Publications

Ozaki S, Atsumi T, Hayashi T, Ishizu A, Kobayashi S, Kumagai S, Kurihara Y, Kurokawa MS, Makino H, Nagafuchi H, Nakabayashi K, Nishimoto N, Suka M, Tomino Y, Yamada H, Yamagata K, Yoshida M, Yumura W, Amano K, Arimura Y, Hatta K, Ito S, Kikuchi H, Muso E, Nakashima H, Ohsone Y, Suzuki Y, Hashimoto H, Koyama A, Matsuo S, Kato H. Severity-based treatment for Japanese patients with MPO-ANCA-associated vasculitis: the JMAAV study. *Mod Rheumatol.* 2012; **22**: 394-404. Epub 2011 Sep 18.

Suka M, Hayashi T, Kobayashi S, Ito S, Yumura W, Ozaki S. Improvement in health-

related quality of life in MPO-ANCA-associated vasculitis patients treated with cyclophosphamide plus prednisolone: an analysis of 18 months of follow-up data from the JMAAV study. *Mod Rheumatol.* 2012 Feb 4. Epub ahead of print.

Reviews and Books

Suka M, Taniuchi A, Igarashi S, Kudo Y, Sato S, Yanagisawa H, Ishizuka B. Menopausal symptoms among community-dwelling 60-year-old Japanese women. In: Menopause-state of the art. Roma: CIC Edizioni Internazionale; 2011. p. 475-8.