Department of Public Health and Environmental Medicine

Hiroyuki Yanagisawa, *Professor*
Shingo Yogosawa, *Assistant Professor*
Machi Suka, *Associate Professor*

General Summary

Our major research projects in the 2014 academic year focused on: (1) effects of Zn-deficient and Zn-excess ingestion on gene expression of inflammatory cytokines and chemokines in spleen macrophages in Spague Dawley rats; (2) potential mechanisms responsible for tubulointerstitial nephropathy induced by fluoride in Spague Dawley rats with unilateral ureteral obstruction; (3) transgenerational effects of maternal arsenic exposure; (4) molecular approaches toward cancer chemoprevention with food factors; (5) the decompression stress in the hyperbaric work; (6) effects of electric and magnetic fields; (7) relationships among health literacy, health information access, health behavior, and health status; (8) determination of reading comprehension of health checkup reports; (9) 8-week open-label trial of polaprezinc, a zinc complex, on treatment of pressure ulcer healing; (10) time-to-effect relationships between systolic blood pressure and the risks of nephropathy and retinopathy in patients with type 2 diabetes; and (11) association between glycosylated hemoglobin (HbA1c) variability and mortality in patients with type 2 diabetes.

Research Activities

Experimental Medicine

1. Gene expression of inflammatory cytokines and chemokines in spleen macrophages derived from rats fed Zn-deficient or Zn-excess diets

A deficiency of Zn causes growth retardation and dysfunction of the immune and reproductive systems. The present study was designed to examine the expression of inflammatory cytokines and chemokines in spleen macrophages from rats fed a Zn-deficient diet, a standard diet, or a Zn-excess diet for 6 weeks. Gene expression of *Il1b, Tnf, Ccl2* and *Ccl3b* was significantly higher in rats fed a Zn-deficient diet than in rats fed a standard diet or a Zn-excess diet.

2. Potential mechanisms responsible for tubulointerstitial nephropathy induced by fluoride in rats with unilateral ureteral obstruction

Fluoride, an environmental pollutant, is excreted from the kidney. The toxic effects of fluoride may deteriorate in animals with impaired renal function. In our previous animal experiments, ICR-derived glomerulonephritis mice, which have impaired renal function, were more seriously affected by fluoride. In this study, we used the tubulointerstitial fibrosis model (unilateral ureteral obstruction). We examined whether fluoride deteriorates the tubulointerstitial nephropathy seen in rats with unilateral ureteral obstruction.

3. Effects of maternal arsenic exposure on later generations of C3H mice

Our recent study showed that maternal arsenic exposure of C3H mice increases hepatic

tumors in male offspring and grandchildren at 74 weeks of age. In this study, we focused on other target organs. Gene expression analysis of the lungs and kidneys with real-time reverse transcriptase-polymerase chain reaction method showed differences between control and arsenic groups in male offspring and grandchildren.

4. Molecular approaches toward cancer chemoprevention with food factors

Carcinogenesis is closely related to lifestyle, including eating habits. We have attempted to establish an evidence-based cancer prevention method using food factors, including phytochemicals and trace elements. We found that equol, an isoflavandiol metabolized from daidzein, a type of isoflavone, from bacterial flora in the intestines, enhanced the inhibitory effect of brassinin, a phytoalexin from *Brassica* vegetables, on the growth of cancer cells via cell-cycle arrest and apoptosis.

5. A study of decompression stress in hyperbaric work

The decompression stress from hyperbaric work has been evaluated with the Doppler bubble detection technique. We evaluated the decompression stress by means of the Doppler technique and human herpes virus 6 (HHV-6) in saliva. The number of HHV-6 DNA in saliva was well correlated with the results of the Doppler bubble detection. We believe HHV-6 in saliva can be used as a marker to evaluate decompression stress.

6. Biological effect of electric and magnetic fields

To evaluate the biological effects of electric and magnetic fields, various mutagenicity assays were employed with various exposure conditions. As a result, no mutagenic effect was observed except after long-term exposure to a strong static magnetic field greater than 2 T. At 20 kHz, we found no effect on differentiation of mouse embryonic stem cells to myocardial cells.

Epidemiology, evidence-based medicine, investigation, and medical informatics

1. Relationship between health literacy, health information access, health behavior, and health status

A questionnaire survey was performed among health examinees at 6 healthcare facilities. We examined the relationship between health literacy, health information access, health behavior, and health status.

2. Reading comprehension of health checkup reports

A Web-based survey was performed among a sample drawn from a research panel. We determine the reading comprehension of health checkup reports in the context of health literacy.

3. Oral treatment of pressure ulcers with polaprezinc (zinc L-carnosine complex): 8-week open-label trial

We performed an open-label trial of polaprezinc with maximum 8-week treatment for chronic pressure ulcers. The results suggested that polaprezinc is effective and well tolerated and could be a candidate for the oral treatment of pressure ulcers.

4. Time-to-effect relationships between systolic blood pressure and the risks of nephropathy and retinopathy in patients with type 2 diabetes

The time-to-effect relationship with systolic blood pressure (SBP) differed for the development of nephropathy and retinopathy. The long-term effect was clear for nephropathy and was borderline for retinopathy, whereas the short-term effect was stronger and evi-

dent for both. Continuous lowering of SBP is necessary to prevent nephropathy, whereas control of SBP during the preceding 5 years seems to be important to prevent retinopathy.

5. Association between HbA1c variability and mortality in patients with type 2 diabetes

We investigated the association between the variability of HbA1c and mortality due to all causes — cancer and noncancer, including cardiovascular disease — in patients with type 2 diabetes. The variability of HbA1c is a predictor of all-cause mortality, especially non-cancer mortality including cardiovascular disease independent of the mean HbA1c level. In contrast, mean HbA1c, but not HbA1c variability, might predict cancer mortality.

Publications

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