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Form 6

Grant No.

20—G48

Research Report

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Organization (at the start of the grant period): Hirosaki University

Title of Research:

Exploring a Healthy Neighborhood Living Environment to Combat Age-related Diseases: Telomere Length as a Biomarker of Aging

Purpose of Research: (200 words)

Neighborhood environment (NE) factors play a pivotal role in a healthy aging of a community. Understanding the NE factors that influence the risk of age-related diseases would help to prevent the age-related diseases. On the other hand, telomere length (TL) is considered as a robust biomarker of biological aging. TL are oligomer sequences located in the end of chromosomal DNA. TL shortening is associated with many age-related diseases such as hypertension, diabetes, and cancer. Previous studies only provided fragmented information with suggestive measurement of NE. Although the link between environmental arsenic (As) and cadmium (Cd) exposure and blood pressure has been revealed, there is no study that explains the mechanistic pathway involving arsenic/cadmium-induced TL shortening and increased blood pressure. This study hypothesized that the individuals with higher exposure to environmental toxic trace elements such as As and Cd would have shorter TL which in turn may increase blood pressures and risks of hypertension. Thus, the objectives of this study aimed at determining whether biological aging, TL, differs by the different environmental trace elements exposure, and at identifying the effects of environmental toxic trace elements on the associations of TL and cardiometabolic risks

Content/Methodology of Research: (400 words)

This study was a community-based cross-sectional study which utilized the data of approximately 1067 participants of age more than 19 years of 2019 Iwaki Health Promotion Project. The project is large scale annual comprehensive health up survey among the residents in Iwate area of Aomori prefecture. Aomori Prefecture is reported as the prefecture with shortest life expectancy in Japan. It could be resulted from the higher mortality and prevalence of age-related diseases. Thus, it is important to understand the factors influencing the disease risks, that have significantly triggered the increased mortality rate.

The participants first underwent a questionnaire survey which covers the general characteristics (age, sex, occupation, educational background etc.), medical and drug history, lifestyle (smoking, drinking, exercise, food-related behaviors etc.). To identify the age-related diseases, risk profiles such as blood sugar level, blood pressure, and blood cholesterol level were also assessed by the trained research team. Spot urine sample was collected by the research team and trace elements concentrations in the urine was measured using octuplet collision/reaction cell inductively coupled-plasma mass spectrometer (ICP-MS). The current study included the following data of the Iwaki health promotion project.

(i) *Neighborhood Environmental Exposure/Factors:* In this study, environmental trace elements exposure was

considered as neighborhood environment (NE) factors. The environmental exposure was objectively evaluated by ICP-MS to reflect the trace elements concentrations in the urine.

(ii) *Outcomes*: In this study, primary outcome is leucocyte telomere length (TL). TL was assessed by G tail telomere hybridization protection assay. The secondary outcomes are the age-related disease of increased blood pressure or hypertension.

(iii) *Covariates*: Socioeconomic status, and personal history (smoking, alcohol drinking, etc.) was included as covariates.

Regarding the statistical analysis, first, descriptive analysis was done using means, frequency, and percentage. Later, regression analysis was performed to evaluate the associations between environmental trace elements concentration, TL and blood pressure/hypertension in relevance. All data analysis was performed using Stata Software (StataCorp, Texas, USA).

Conclusion/Observation (200 words)

This study is the first study to report the effect of NE on biological aging which in turn may correlate with the risks of age-related diseases. The study identified that systolic blood pressure (SBP), diastolic blood pressure (DBP) and pulse pressure (PBP) were significantly higher in the high Cd concentration group while TL was significantly shorter. In case of As exposure, SBP and pulse pressures were significantly higher in the high concentration group. Meanwhile, the current study determined a negative association between TL and blood pressures. These findings suggested that environmental Cd and/or As exposure may play a role in the associations of TL and increased blood pressures. The data analysis is ongoing and the results of stratified analysis will support the evidence of how the associations of TL and blood pressures could be differed by the environmental trace elements. The findings gave a beneficial baseline information of estimating the effect of NE factors on age-related diseases.