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## “Metabolic profile as a potential modifier of long-term radiation effects on peripheral lymphocyte subsets in atomicbomb survivors”

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### Study Findings

This study revealed that the percentage of naïve CD4 T cells (a subset of CD4 T cells that has not yet encountered antigens and is known to decrease with age) among peripheral lymphocytes was inversely associated with radiation dose; and that naïve CD4 T-cell percentages were also inversely associated with obesity-related indicators such as body mass index (BMI). Furthermore, analyses that adjusted for high-density lipoprotein (HDL) cholesterol levels found a positive association between radiation dose and NK-cell percentages.

### Explanation

This study examined the association between the percentage of peripheral lymphocyte subsets (T cells, B cells, NK cells, etc.) and radiation dose as well as obesity-related indicators, among the participants of the Adult Health Study (AHS) conducted by the Radiation Effects Research Foundation.

### 1. Study Purpose

Radiation dose-related changes in the composition and function of peripheral lymphocytes are still today observed in atomic bomb survivors, and changes in metabolic profiles,\* including cholesterol levels, are also suggested. With the understanding in recent years of a strong association between obesity and the composition and function of peripheral lymphocytes, this study tested the hypothesis that the long-term effects of radiation on lymphocyte subsets may be modified by obesity-related metabolic profiles.

\*Metabolic profile: In this study, an aggregation of various biomarkers related to obesity and metabolic diseases.

### 2. Study Methods

Counts of peripheral lymphocyte subsets among 3,113 atomic bomb survivors who participated in AHS health examinations in Hiroshima and Nagasaki during the period from 2000 through 2002 were measured using flow cytometry; linear regression analysis was then conducted to determine statistical associations of subset percentages in the entire lymphocyte population with radiation dose, as well as with metabolic profile indicators (BMI, serum total cholesterol, HDL cholesterol, CRP,\* HbA1c levels, and prevalence of diabetes mellitus and fatty liver).

\*CRP: C-reactive protein, which is induced by inflammation and detected even in mild inflammatory responses related to obesity.

### 3. Study Results

#### (1) Association between metabolic profile indicators and lymphocyte subsets

Indicators related to obesity and related diseases, including high BMI and low HDL cholesterol levels, were positively associated with T<sub>H</sub>1- and B-cell percentages, and inversely associated with naïve CD4 T-cell and NK-cell percentages. T<sub>H</sub>1 is a helper T-cell subset involved in inflammatory response.

#### (2) Association between radiation exposure and lymphocyte subsets

As in previous studies, a negative association between radiation dose and naïve CD4 T-cell

percentages was observed. Furthermore, regression analysis with adjustment for such metabolic profile indicators as HDL cholesterol levels showed that NK-cell percentages increased with an increase of radiation dose. A positive association between NK-cell percentages and aging was also detected. In AHS participants exposed to relatively lower doses, e.g., less than 0.5 Gy, however, we did not observe a statistically significant association between radiation exposure and these lymphocyte subsets.

(3) Interaction between radiation exposure and metabolic profiles

Interaction between radiation dose and CRP levels had negative effects on B-cell percentages, suggesting that a combination of exposure to higher radiation doses and enhanced inflammation may lead to a decrease in B-cell percentages.

### Study Significance

The study results suggest that radiation exposure and obesity may both exacerbate one of the characteristics of the immunosenescence of T-cells: decrease in naïve CD4 T-cell percentages and increase in T<sub>H</sub>1-cell percentages. Furthermore, radiation exposure and subsequent changes in metabolic profiles, a portion of which might be affected by radiation exposure, may bring about long-term changes in the composition of lymphocyte subsets. However, it is necessary to verify the associations observed among radiation exposure, lymphocyte subsets, and metabolic profiles, as well as the relationships between observed changes and disease development, by conducting future studies, including longitudinal studies based on observations and measurements carried out at multiple points in time.

**The Radiation Effects Research Foundation** has studied A-bomb survivors and their offspring in Hiroshima and Nagasaki for around 70 years. RERF's research achievements are considered the principal scientific basis for radiation risk assessment by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) and for recommendations regarding radiation protection standards by the International Commission on Radiological Protection (ICRP). RERF expresses its profound gratitude to the A-bomb survivors and survivors' offspring for their cooperation in our studies.

*§Radiation Research*, which is an official monthly journal of the Radiation Research Society, publishes original peer-reviewed papers and review articles on radiation effects and related issues in the fields of physics, chemistry, biology, and medicine. (Impact factor in 2015: 2.67)