Paper published in *Radiation Research*[§]

"Radiation and Age-associated Changes in Peripheral Blood Dendritic Cell Populations among Aging Atomic Bomb Survivors in Japan"

Junko Kajimura, Heather E. Lynch, Susan Geyer, Benjamin French, Mika Yamaoka, Ivo D. Shterev, Gregory D. Sempowski, Seishi Kyoizumi, Kengo Yoshida, Munechika Misumi, Waka Ohishi, Tomonori Hayashi, Kei Nakachi, Yoichiro Kusunoki

Radiat Res; 189(1):84-94, 2018/1
(doi: 10.1667/RR14854.1)

Study Findings

We have examined the relationship of A-bomb radiation exposure with counts and functional profiles of circulating dendritic cells (DCs), which play an important role in immunological activation. The results of our study do not indicate any radiation-related change in the number and function of DCs in the blood of those exposed to radiation from the atomic bombings more than 60 years ago.

Explanation

1. Study Purpose

Previous immunological studies of A-bomb survivors have suggested that radiation exposure accelerates aging of the immune system. However, effects of A-bomb radiation exposure on DCs, key coordinators for activation and functional differentiation of the immune system, specifically T-cell immunity, had not yet been examined. This study measured counts and functional profiles of circulating conventional DCs (cDCs)* and plasmacytoid DCs (pDCs)** in the peripheral blood of Adult Health Study (AHS) A-bomb survivor participants to elucidate the relationship of such numerical and functional changes with radiation dose, sex, and age.

*Conventional dendritic cell (cDC): One of the DC subgroups, cDCs recognize foreign substances that invade the body, including pathogens. They present information involving such foreign substances to other immune cells, including T cells, and thus play a command role in the eradication of such pathogens.

**Plasmacytoid dendritic cell (pDC): One of the DC subgroups, pDCs are not adept at presenting information about foreign substances as cDCs; however, pDCs produce large amounts of virus-suppressing Type I interferon in response to viral infection.

2. Study Methods

We collected peripheral blood from 229 A-bomb survivors in Hiroshima who participated in the AHS during the period from 2011 through 2013 (ages 66–91) and measured and separated cDCs and pDCs using a cell sorter. To examine the function of these separated DCs in vitro, we assessed gene expression levels and cytokine/chemokine* production following Toll-like receptor (TLR)** stimulation.

*Cytokine/chemokine: Cytokines are a broad category of proteins released from cells that play an important role in biological defense, including immunity and inflammation. Chemokines are a family of cytokines, and they assist the migration of immune cells to the site of inflammation.

**Toll-like receptor (TLR): TLRs are sentinel receptors expressing in immune cells such as DCs and macrophages. TLRs recognize structurally conserved molecules derived from invading pathogens and promptly activates the innate immune system. (Innate immunity is a non-specific, inborn immune system that eliminates pathogens regardless of type.)

3. Study Results

(1) Changes in cell counts

- Relationship with radiation dose

  The absolute number (count per unit volume of blood) of pDCs significantly decreased with increasing radiation dose only in women (r = -0.17, p = 0.035). There was no significant association between the absolute number of cDCs and radiation dose in either gender.

- Relationship with age

  The absolute numbers of cDCs (r = -0.17, p = 0.033) and pDCs (r = -0.26、p = 0.004) significantly decreased with age. This decreasing trend was particularly marked in women.

(2) Functional changes

- Relationship with radiation dose

  No significant effect of radiation dose was observed in gene expression levels following TLR stimulation, but inflammatory cytokine/chemokine production levels had a tendency to increase with radiation dose.

- Relationship with age

  Gene expression levels following TLR stimulation significantly decreased with age in cDCs (p = 0.048), but no significant effect was observed in pDCs. Furthermore, cytokine/chemokine production levels following TLR stimulation in cDCs decreased with age.

Study significance

The present study among AHS participants revealed that human DC counts and functional profiles continued to decrease even after age 70. It is known that cDCs play a stronger role in the activation of T-cell-mediated immunity than pDCs, but age-related functional decline was observed in cDCs. The possibility exists that the aging-related decline in T-cell function may be caused by deterioration in cDC-mediated activation. Furthermore, changes in pDC counts in relation to radiation dose and age were observed in women, but not men suggesting sex differences in the effects of radiation dose and age. Taken together, the counts and functional profiles of DCs circulating in the blood of those who survived for an extended period after A-bomb radiation exposure generally recovered to normal levels, i.e., levels typical for the unexposed group of the same generation.

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 2016/2017: 2.539)