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“Radiation-dose response of *glycophorin A* somatic mutation in erythrocytes associated with gene polymorphisms of *p53 binding protein 1*”
Yoshida K, Kusunoki Y, Cologne JB, Kyoizumi S, Maki M, Nakachi K, Hayashi T
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**Study Findings**

Previous studies revealed that the fraction of erythrocytes with somatic mutations at the *glycophorin A* (*GPA*) gene locus increased with radiation dose in atomic-bomb survivors. It was found in the present study that the manner in which GPA mutations increased following radiation exposure (radiation-dose effects) differed by individual differences in genetic background, i.e., DNA sequences (gene polymorphisms). It also was suggested that p53 binding protein 1 (*53BP1*) plays a significant role in DNA double-strand break repair in hematopoietic stem cells following radiation exposure.

(Note) Use of letters in italics, such as in *GPA* and *53BP1*, indicates genes, whereas ordinary typeface, such as GPA and 53BP1, is used to designate proteins generated by those genes. *GPA* gene mutations are usually confirmed by the observation of protein alterations.

**Explanation**

The fraction of erythrocytes with mutations at the *GPA* gene locus is considered to be one of the indices of somatic mutations induced by ionizing radiation for estimating the degree of related genome damage and cancer risk. Previous studies of A-bomb survivors revealed that erythrocyte GPA mutations increased with radiation dose, but it also has been reported that there was significant individual difference in GPA mutation rates even after exposure to around the same radiation dose. The reason for such individual difference in GPA mutation rates was unclear, and the differences could not be explained by differences in age at exposure, sex, city, or frequency of smoking.

In the present study, we examined whether individual differences in DNA sequences (gene polymorphisms) contributed to individual differences in GPA mutation rates related to radiation exposure. In particular, because it was suspected that the difference in ability to repair DNA double-strand breaks that are caused by radiation exposure may be related to individual differences in GPA mutation rates, we focused on gene polymorphisms of the *53BP1* gene, which is related to DNA double-strand break repair. As a result, radiation-dose effects on GPA mutation rates were found to vary slightly by *53BP1* gene polymorphism (Figure).

Although erythrocytes have a short life span of around 120 days, an increase in the number of erythrocyte GPA mutations with radiation dose is still observed even now, more than 60 years after A-bomb radiation exposure. It can therefore be considered that mutations have been recorded in the *GPA* genes of longer-lived hematopoietic stem cells, which can differentiate into erythrocytes. In other words, it is assumed that many of the erythrocyte GPA mutations observed in A-bomb survivors reflect GPA mutations in hematopoietic stem cells. For this reason, and because of the relationship between erythrocyte GPA mutations and *53BP1* gene polymorphisms observed in the present study, it is suggested that a group of
proteins, including 53BP1, plays an important role in DNA double-strand break repair in hematopoietic stem cells and somatic mutations following radiation exposure.

![Figure](image-url)

Figure. Relationship among GPA mutations, radiation dose, and 53BP1 gene polymorphisms. Increase in GPA mutations varies by individual differences in DNA sequence of the 53BP1 gene. (Individuals with TCA homozygotes, TCA/GGC heterozygotes, and GGC homozygotes are shown in blue, green, and red, respectively.)

The Radiation Effects Research Foundation has studied A-bomb survivors in Hiroshima and Nagasaki for more than 60 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).

§*Mutation Research-Genetic Toxicology and Environmental Mutagenesis* is a section of *Mutation Research* (peer-reviewed journal that publishes research papers in the area of mutation research with a focus on fundamental mechanisms underlying the phenotypic and genotypic expression of genetic damage). This section publishes papers in the field of genetic toxicology, focusing on genotoxicity testing of specific agents, *in vitro* or *in vivo*, and assessment of health effects resulting from genotoxic exposures in human populations. (Impact factor in 2012: 2.220)