Letter to the Editor

Serum amyloid A1 as a biomarker for radiation dose estimation and lethality prediction in irradiated mouse-reply

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Thank you for the constructive Editorial Commentary on our recently published article "*Serum amyloid A1 as a biomarker for radiation dose estimation and lethality prediction in irradiated mouse*" (1).

We agree with the editorial author's opinion on the triage of people exposed to radiation in a large-scale event such as nuclear power plant accident, nuclear terrorist attack, or other accidents. The damage degree of person exposed to radiation is closely related to the dose. Exposure below 1 Gy, it usually does not cause obvious symptoms; 1–2 Gy total body irradiation can lead to blood cell decline, fatigue and other symptoms, but it can usually self-heal; 2–6 Gy total body irradiation can cause obvious clinical symptoms such as blood cell decline and vomiting, it can be effectively treated by anti-infection, cytokine application and bone marrow transplantation. However, there are no effective medical methods, by which patient exposed to radiation above 6 Gy could be rescued (2). Therefore, effective initial triage is essential, so limited resources can be focused on those who are need to treatment for acute radiation syndrome (ARS), by distinguishing them from those who would not. An important basis for the initial triage is the dose received by each individual. In general, the survival rate of treatment can be improved by medical treatment for the persons exposed to more than 2 Gy. Therefore, 2 Gy is usually used as a threshold for initial triage (3). At the same time, half of the lethal dose is 4 Gy, which is to say, 50% of individuals exposed to 4 Gy will die without medical treatment (4). Therefore, in the process of medical emergency for a large number of nuclear radiations wounded, in addition to screening out the wounded with a dose of more than 2 Gy, we believe that it is more important to quickly screen out the patients with lethal radiation.

Radiation biodosimetry is the main method of initial triage of radiation wounded. Dicentric chromosome assay (DCA) is a golden standard technique for biodosimetry, which is usually suitable for biological dose estimation in the range of 0.5–5 Gy (or 6 Gy). If analysis of a lower dose of radiation (for example, 0.2 Gy) is needed, thousands of cells should be accounted. The results of DCA can be obtained 2–3 days after obtaining blood samples and the sample throughput is low. DCA has high accuracy and specificity which can be used as the final dose determination technology (5). The research on the substitution technology of DCA has been ongoing. Several studies of γ-H2AX foci in lymphocytes exposed to radiation as biodosimetry are reported (6-8). However, as a marker of DNA double strand breaks (DSBs) induced by ionizing radiation, the number of γ-H2AX foci shows a significant time dynamic change with the time dynamic change of DSBs repair. The number of γ-H2AX foci increased in a few minutes after irradiation, reached its peak at 1 or 2 hours, and returns to the normal level at 24 hours after radiation (6). Fast time dynamic change limits the practical application of γ-H2AX foci. However, the γ-H2AX foci has high sensitivity and specificity, and it also could be analyzed by the automatic high-throughput method (9). It is a useful screening technology for a large number of nuclear radiations

wounded.

There are few studies on biomarkers of lethal nuclear radiation injury. Acharya *et al.* found that miRNA-30a-3p, miRNA-187-3p, miRNA-27a-3p in serum 24 hours after irradiation could predict potentially lethal radiation damage (10). Our study analyzed the feasibility of serum SAA1 protein as a protein marker for lethal radiation and got an encouraging finding.

We agree with several suggestions of editorial author. Firstly, the authors suggest more samples from patients performed radiation therapy should be used in future study. The patients of tumor radiotherapy are mostly local irradiation. In our study, we found that both local irradiation of mice and local irradiation of tumor patients can increase the level of SAA1 in serum, which suggested that the research findings of total-body irradiation mouse model maybe applicable to the accident patients of total-body irradiation. But for ethical reasons, it is difficult to verify the change of SAA1 of person exposed to radiation. Even if the patients were treated with total-body irradiation before bone marrow transplantation, it is impossible to analyze the data of several days after irradiation without bone marrow transplantation and other treatment. However, we agreed with the author's suggestion to expand the number of study population with local irradiation of tumor patients. Secondly, the editorial author raises the question of mechanism of SAA1 increase. DNA damage and stress reaction will occur within minutes to hours after irradiation, and NF-kB pathway activated may be the reason for the increase of SAA1 within 6–24 hours. Within a few days after irradiation, a large number of cell apoptosis appeared in peripheral blood lymphocytes, thymus, spleen, intestine and other radiation sensitive tissues. The toxic substances released by apoptotic cells will cause damage to the body again, which may be the reason for the increase of serum SAA1 level 5–7 days after high dose irradiation, but it needs further study.

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Footnote

Conflicts of Interest: The author has completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/atm.2020.03.215). The author has no conflicts of interest to declare.

Ethical Statement: The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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