LETTERS TO THE EDITOR

Comments on “Cellular Therapies for Treatment of Radiation Injury after a Mass Casualty Incident” (Radiat Res 2017; 188:242-45)

Michel Drouet, Diane Riccobono and Sabine François
French Armed Forces Biomedical Research Institute, Brétigny-sur-Orge, France

It was with a great interest that we have read the articles “Cellular Therapies for Treatment of Radiation Injuries after a Mass Casualty Incident”¹ by C. Rios, J. R. Jourdain and A. L. DiCarlo and Workshop Report “Cellular Therapies for Treatment of Radiation Injury: Report from a NIH/NIAID and IRSN Workshop”² by DiCarlo et al. Indeed, there is, from our point of view too, a great need in animal model development to overcome the current limits in the use of mesenchymal stromal/stem cells (MSCs) to mitigate radiation damages at the level of numerous tissues, especially cutaneous and muscular. One of them is the low efficacy, if any, depending on the targeted tissue, of unmatched MSCs from banking that could be the first line of defense in a (military) mass casualty scenario (Percy military hospital and Centre de Transfusion sanguine des Armées). As an example, our group was unable to observe any efficacy after iterative injections of allogeneic adipocyte derived stem cells in a minipig model, which strongly contrasted with the efficacy of autologous cells (I). In this model, iterative injections of autologous cells were required to enhance cutaneous-muscular wound healing with the limitation that no early injection schedule was tested. Studies are currently being performed to explore derived strategies such as culture cell media use and micro vesicles injection but it is yet unclear whether these approaches would present any therapeutic efficacy in vivo in the context of radiation-induced injuries. In addition, it is likely that preferentially localized treatments could be achieved in this way. Albeit expensive such strategies need to be tested in large animal models such as minipig. Regarding the specific use of MSCs to cope with irradiated/war casualties the point of feasibility (or not) of allogeneic cell use, with matching constraint or after manipulation, remains the crucial one before embarking in any large approach. Finally, we would like to indicate the need to clarify the confusing point in the paper indicating that the minipig studies cited have been conducted in the “French Armed Forces Biomedical Research Institute” facility by a military team thanks to a grant from the Délegation Générale de l’Armement—all colleagues who are not from the prestigious IRSN.

REFERENCE


Editor’s note. DiCarlo et al. wish to thank the authors for pointing out an error in the original publication, as well as apologize for the inaccuracy and appreciate the clarification.

The LSS Cohort of Atomic Bomb Survivors and LNT.


Jeffry A. Siegel,* Bill Sacks† and Yehoshua Socol

² Nuclear Physics Enterprises, Marlton, New Jersey 08053 & U.S. Food and Drug Administration (Retired), Green Valley, Arizona; and ³ Department of Electrical and Electronics Engineering, Jerusalem College of Technology, Jerusalem 91160, Israel

We read with interest the articles by Grant et al. (1) and critique by Mortazavi and Doss (2) with reply by the original authors (3). In their original article, on p. 523, under the subheading “Examination of Threshold,” Grant et al. assert (emphasis added):

“The evidence of a threshold dose below which there was no dose response was examined using linear-quadratic threshold models for males and linear threshold models for females. There was no evidence of a threshold for females (estimated threshold dose of 0.08 Gy). This was not significantly different from 0 (P = 0.18) and the upper 95% confidence bound was 0.2 Gy. For males, the best estimate for a threshold dose was 0.75 Gy. Similarly, this was not significantly different from 0 (P = 0.49).”

Further, near the end of the “Summary and Discussion” section (I), the authors say (emphasis added):

“These uncertainties taken together with inconsistencies with prior LSS analyses and the findings from other studies precludes [sic] definitive conclusions that might confidently guide the development of modified radiation protection policies at this time.”

Grant et al. arbitrarily and implicitly enlist the absence of a nonzero threshold (or equivalently a threshold of zero dose) as their effective null hypothesis, which they find the data do not permit them to “reject”, i.e., their estimates for thresholds derived from the LSS data cannot be distinguished statistically from zero. Then they go on to commit a common logical fallacy. They, in effect, “accept” this null, absence of a (nonzero) threshold, as the valid scientific model.

However, failure to reject a null is not the same as confirming it to be valid, since failure to reject may only result from “insufficient data” rather than from the null’s validity. In the case of LSS, the data are indeed insufficient due to large uncertainties, as exhibited, first, from the fact that the best-estimate dose threshold, 0.75 Gy, as cited above for males, is not statistically–significantly different from zero. Second, a Monte Carlo simulation by Socol and Dobrzyński (4) confirms that the statistical power of the LSS cohort is insufficient to discriminate between the linear no-threshold (LNT) model and a threshold hypothesis. LNT is the most commonly accepted non-threshold model.

REFERENCE
