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Letter to the Editor

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Dear Editor,

The comments made by Dr Chadwick [1] were critical of the balance provided in our article ‘Non-targeted effects and radiation-induced carcinogenesis: a review’ [2]. Our review examined the literature discussing the potential role of non-targeted effects (including the bystander effect) in radiation-induced cancers. Our conclusion, which we stand by, is that while the associated risks are low and do not require immediate changes to current radiation protection practices, it is still prudent to conduct studies in order to shed light on the potential mechanisms leading to non-targeted effects.

Dr Chadwick’s criticisms seem to derive from his belief that the bystander effect is either not real or insignificant in calculating risk. He notes that we did not discuss the possibility that some experiments describing bystander effects may not adequately account for factors such as background effects. Our review did not identify background effects as a gap or inconsistency in non-targeted effect studies since this ‘sole parameter’ as stated by Dr Chadwick, was clearly taken into account in several of the outstanding studies we chose to reference. For example, Wu et al [3], which is listed as reference 65 in Burtt et al [2], demonstrated a clear 2–3 fold increase in mutation frequency (with up to four particle traversals per cell) after background mutation frequencies were taken into account. They reported a preexisting level of mutation of 43 ± 15 mutants per 10^5 survivors in the A5 hybrid cell population under study. Furthermore, the experimental control A5 hybrid cells and mock irradiated cells showed a similar plating efficiency and mutant yield compared to controls. It is our opinion that simply accounting for background effects, as suggested [1] is unlikely to account for the increase in radiation-mediated mutations. The studies referenced in our review provide an overwhelming weight of evidence that supports the existence of various non-targeted effects where appropriate controls have been chosen. However, clearly accounting for background effects and plating efficiency in future work could add to the scientific rigor supporting the existence of non-targeted effects and their potential role in radiation-induced carcinogenesis.

There is a vast and continuously increasing amount of literature describing the underlying mechanisms of non-targeted effects on cell signaling and cancer risk, both in vitro and in vivo; our recommendation to incorporate these ideas into models of risk assessment seems prudent. Our opinion is that continued investigation of non-targeted effects is strongly warranted and the numerous and well controlled papers that describe these effects should be considered in models of risk assessment. To ignore these many studies and further research in this field...
would be a disservice to the pursuit of a comprehensive understanding of the mechanisms of biological effects of radiation at low and very low doses.

Kindest regards,

Julie Burtt, Patsy Thompson, and Robert Lafrenie

References