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Abscopal Bone Marrow Stroma Suppression and Acute Death in Gut-Irradiated Mice

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Gastrointestinal (GI) button is often attributed to whole body ionizing irradiation-induced acute death (i.e. within 10 days of irradiation). The mechanisms of GI death, however, are not clear, as the two elements that seem to mediate this acute death, crypt cell damage and GI-derived bacteraemia, have been shown in some reports to be minor players. Here we present evidence that acute GI death is correlated with suppression of un-irradiated bone marrow stroma. **Methods**: Ten-week-old male C57BL/6 mice were randomized into three groups, 8–12 mice per group. Mice were positioned on their left side and x-ray irradiation at 0, 15 and 20 Gy was given to the abdominal area only at dose rate of 50 cGy/min. Body weight of the mice was monitored daily and survival rate determined for up to 42 days. Blood and bone marrow were collected from surviving mice at day 8 for bacterial growth and *ex vivo* stromal cell colony formation, respectively. Gut, liver, kidney and the lung were examined for histological abnormality. **Results**: Weight loss in both irradiated groups started one day after gut irradiation. The extent of weight loss in the 20-Gy group increased with time throughout the 8-day period. The first death in this group occurred at day 6, and survival rate dropped to 16% by day 8. By contrast, weight loss in the 15-Gy group peaked at day 5, followed by a recovery phase lasting into day 8. All mice in this group survived the 8-day period and the subsequent 6-week follow-up until the experiment was terminated. Gut irradiation resulted in changes in blood bacterial profile, crypt cell death and organ damage in both irradiated groups to a similar extent. *Ex vivo* proliferation capacity of stromal cells in bone marrow from the 20-Gy group was suppressed to less than 10% of the control level. By striking contrast, viability of stromal cells from the 15-Gy group was largely intact. **Conclusions**: Our data demonstrate clearly that gut irradiation induces cellular responses in distant organs. These results are consistent with the concept of “abscopal” effects of radiation. Since bone marrow stroma serves both as the source of stem cells as well as the support for these cells to replenish the radiation-damaged cells in the body, we hypothesize that acute GI death following irradiation is mediated by marked suppression of bone marrow stroma.