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Synchrotron MRT radiation induces DNA damage and inflammatory response in normal mouse tissues distant from the irradiated volume

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Discovery of the radiation-induced bystander effect (RIBE) demonstrates that cell death and genomic instability are not restricted to cells that are directly exposed to ionising radiation. The RIBE refers to a situation where cells that have not been directly exposed to IR behave as though they have been exposed. This phenomenon presents real clinical consequences such as increased risk of secondary malignancies and inflammatory diseases after localised radiotherapy. Past reports indicate pronounced increase of DNA damage in bystander cells, especially in those of highly proliferative tissues. The fluctuations of the host's immunological response elicited by localised radiation exposure are a proposed mechanism of the bystander effect. Our aim was to establish the contributions of DNA damage response and the immunological components in the propagation of the RIBE, by using synchrotron-generated irradiation of immune-compromised mice. The Imaging and Medical Beamline (IMBL) at the Australian Synchrotron made it possible to investigate a new pre-clinical modality, microbeam radiation therapy (MRT), which yields superior therapeutic benefit while also preserving neighbouring healthy tissues in animal models, contrary to the broad beam modality currently used in hospitals. The MRT beam is generated when a single X-ray beam is split by a collimator, producing a lattice of planar microbeams. Wild-type C56BL/6 and Balb/c mice and immune-compromised mice (macrophage-depleted, CCL2 K/O and NSG) were irradiated with 10 Gy peak dose of MRT in an 8x8 mm^2 area on the right hind leg, with a dose rate of 49 Gy/sec. At 3 and 6 days post-irradiation, irradiated skin and unirradiated tissue samples were collected and probed for DNA damage using the ɣ-H2AX assay, apoptotic cell death and local immune response. Pronounced and robust DNA damage, apoptotic cells and immunological response were discovered in intestinal crypt cells of wild-type mice; these events were compromised in immune-deficient mice. The role of immune system components in propagation and persistence of systemic genome destabilisation after localised irradiation will be discussed.

Keywords or phrases (comma separated)

Radiation-induced bystander effect, MRT, DNA damage, immune response

Are you a student?

Yes

Do you wish to take part in</br>the Student Poster Slam?

Yes

Are you an ECR? (<5 yrs</br>since PhD/Masters)

No

What is your gender?

Female

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