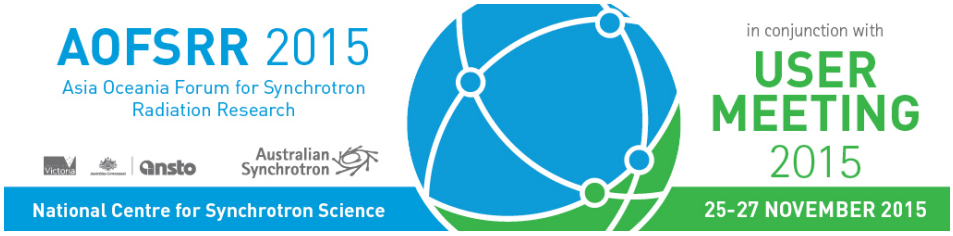

Contribution ID : **85** Type : **Oral**

The innate immune system is associated with gene expression modulation in skin distant from irradiated sites.

Thursday, 26 November 2015 11:00 (30)

Microbeam radiotherapy (MRT) utilizes high intensity synchrotron generated X-rays collimated planar microbeams (~25 μm). MRT showns promise for cancer treatment, effectively ablating tumours while causing less normal tissue damage compared to conventional broadbeam (BB) radiotherapy. Synchrotron radiation also has low scattering making it ideal to investigate non-targeted, systemic radiation effects (i.e., abscopal effects). Although abscopal effects such as non-targeted tumour shrinkage and DNA damage are observed in distant tissue, the molecular mechanism is unknown. To investigate the molecular radiation response in distant non-target tissue, hind flanks of C57BL/6J mice were irradiated with synchrotron MRT and BB and gene expression levels were measured in distant skin. DNA damage response genes, Trp53 and Mdm2, are decreased in distant skin after both BB and MRT. To determine if these effects are due to the innate immune system, immunodeficient mice were irradiated with MRT. These mice showed no decrease in the Trp53 and Mdm2 genes in distant skin. Furthermore, Trp53 increases in distant skin from macrophage depleted mice. Also, in distant skin from Ccl2 deficient mice, the levels of Mdm2 and the inflammatory genes, Tgfb1, Tnfa, and Ccl22 increases. In conclusion, the innate immune system is associated with suppression of genes in distant tissue which otherwise may induce inflammation in response to radiation-induced cytokines.

Keywords

microbeam radiotherapy, MRT, abscopal effects, innate immune system

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Session Classification : Radiotherapy and Radiobiology

Track Classification : Radiotherapy and Radiobiology