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Identification of Genes and Molecular Pathways Regulated by Synchrotron Microbeam Radiotherapy

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Synchrotron-generated microbeams radiotherapy (MRT) is a novel preclinical radiotherapy,in which synchrotron-generated X-rays are segmented by a collimator, producing intense microbeams. MRT has been shown to be extremely well tolerated by normal tissues including the central nervous system in animal models when compared to conventional radiotherapy (CRT). The aim of this study was to identify genes and molecular pathways differentially regulated by MRT versus CRT in vitro using cultured EMT6.5 cells. We hypothesized that gene expression and molecular pathway changes after MRT are different from those seen after CRT. We found that at 24 hr post-irradiation, MRT exerts a broader regulatory effect on multiple pathways than CRT. MRT regulated those pathways involved in gene transcription, translation initiation, macromolecule metabolism, oxidoreductase activity and signalling transduction in a different manner compared to CRT. We also found that MRT/CRT alone, or when combined with IFN-ɣ or LPS, up-regulated expression of Ccl2, Ccl5 or Csf2, which are involved in immune cell recruitment. Our findings demonstrated differences in the molecular pathway for MRT versus CRT in the cultured tumour cells. Our findings are consistent with the notion that radiation plays a role in recruiting tumour-associated immune cells to the tumour. Our results also suggest that a combination of MRT/CRT with a treatment targeting CCL2 or CSF2 could repress the tumour-associated immune cell recruitment, delay tumour growth and/or metastasis, and yield better tumour control than radiation alone.

Keywords or phrases (comma separated)

Pathway analysis, in vitro, tumour-associated macrophages, CCl2, CSF2

Summary

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