Mesenchymal stromal cells (MSCs) are radio-resistant bone marrow progenitors that support hematopoiesis and its reconstitution following total body irradiation. MSCs reside in hypoxic niches within the bone marrow and tumor microenvironments. The DNA Damage Response (DDR) represents a network of signaling pathways that enable cells to activate biological responses to DNA damaging agents. Hypoxia-mediated alterations in the DDR contribute to the increased radio-resistance of hypoxic cancer cells, limiting therapeutic efficacy. The DDR is important in mediating mouse MSC radio-resistance. However, the effects of hypoxia on MSC radio-resistance are currently unknown.

In this study, we show how hypoxia increases long-term survival post irradiation and improves MSC recovery from IR-induced cell cycle arrest by the up-regulation of the DNA DSB repair machinery.

These findings have important implications for our understanding of MSC functions in supporting allogeneic bone marrow transplantation and in tumorigenesis. We are currently using these techniques to decipher the DDR of cortical and medullary thymic stromal cell lines.

**Conclusions**

1. Hypoxia increases MSC long-term survival post irradiation and improves MSC recovery from IR-induced cell cycle arrest and accelerates the resolution of highly genetic IR-induced DNA double-strand breaks.
2. HIF-1α contributes to the resolution of DSBs, probably by up-regulating different proteins involved in DSB repair by NHEJ.
3. MtECs and IT cells are highly radio-resistant and activate different checkpoint responses to genetic irradiation.

**References**


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