Summary: Low-dose Irradiation Promotes Tissue Revascularization

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Low-dose irradiation promotes tissue revascularization through VEGF release from mast cells and MMP-9-mediated progenitor cell mobilization

Beate Heissig et al. *Journal of Experimental Medicine.* 2005 Sep 19;202(6):739-50.

Definitions

Angiogenesis- Angiogenesis is the growth of new blood vessels. In order for tumors to grow and spread a cancer cell must somehow stimulate growth of new blood vessels.

Ischemic- A low oxygen state usually due to obstruction of the arterial blood supply or inadequate blood flow in the tissue.

Mast cells- Resident cell of connective tissue that contains many granules rich in histamine and heparan sulphate which results in vascular changes in response to mild injury.

Vasculature- An associated network of blood vessels in an organ.

Background

Ionizing radiation has been shown to have angiogenic potential in both malignant and nonmalignant disease, however the molecular basis of IR-induced angiogenesis is poorly understood. Angiogenesis appropriately ensues during wound healing and neovascularization when new blood supplies are required for repair or maintenance. In breast cancer, however, angiogenesis acts inappropriately to aid tumor transition from a dormant state to a malignant state. This paper finally presents an updated outline for the mechanistic induction of IR-induced angiogenesis.

Method

Gene expression and cellular mobilization was measured from irradiated and non-irradiated mice. Additionally, the revascularization capacity following low dose IR in an ischemic limb was studied in order to draw conclusions about therapeutic IR potential. Tissue necrosis was monitored in irradiated and non-irradiated mice in an effort to observe whether or not mast cells act as a vehicle for positive IR effects.

Results

Staining techniques reveal an increased population of mast cells in irradiated tissue, and it is surmised that mast cells are responsible for promoting vascular endothelial growth. Administration of molecules designed to limit mast cell capabilities effectively limit IR-induced angiogenesis, further supporting this conclusion.

Discussion

This data suggests a new mechanism by which IR alters the cellular and chemical composition of the ischemic microenvironment. Tumor growth is controlled by angiogenesis, and these new insights into IR-mediated angiogenesis offer previously uninvestigated treatment options. The team proposes that local low-dose IR may be a more effective treatment in clinical applications than those currently in use. Being aware of the particular mechanism by which IR-mediated angiogenesis is accomplished will offer clues about related epithelial-stromal crosstalk communication.

Implications for Future Research

Further studies are needed to confirm the speculation that IR-induced angiogenesis also involves the nitric oxide pathway. The team believes that growth factor-independent IR is able to modulate the tone of the vasculature to induce angiogenesis, but more experiments need to be completed in order to verify this hypothesis.