Low-dose irradiated mesenchymal stromal cells break tumor defensive properties in vivo.

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Abstract

Solid tumors, including gliomas, still represent a challenge to clinicians and first line treatments often fail, calling for new paradigms in cancer therapy. Novel strategies to overcome tumor resistance are mainly represented by multi-targeted approaches, and cell vector-based therapy is one of the most promising treatment modalities under development. Here, we show that mouse bone marrow-derived mesenchymal stromal cells (MSCs), when primed with low-dose irradiation (irMSCs), undergo changes in their immunogenic and angiogenic capacity and acquire anti-tumoral properties in a mouse model of glioblastoma (GBM). Following grafting in GL261 glioblastoma, irMSCs migrate extensively and selectively within the tumor and infiltrate predominantly the perivascular niche, leading to rejection of established tumors and cure in 29\% of animals. The therapeutic radiation dose window is narrow, with effects seen between 2 and 15 Gy, peaking at 5 Gy. A single low-dose radiation decreases MSCs inherent immune suppressive properties in vitro as well as shapes their immune regulatory ability in vivo. Intra-tumorally grafted irMSCs stimulate the immune system and decrease immune suppression. Additionally, irMSCs enhance peri-tumoral reactive astrocytosis and display anti-angiogenic properties. Hence, the present study provides strong evidence for a therapeutic potential of low-dose irMSCs in cancer as well as giving new insight into MSC biology and applications. This article is protected by copyright. All rights reserved.