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**Assessment of therapeutic efficacy and fate of engineered human mesenchymal stem cells for cancer therapy.**

[Sasportas LS](#), [Kasmieh R](#), [Wakimoto H](#), [Hingtgen S](#), [van de Water JA](#), [Mohapatra G](#), [Figueiredo JL](#), [Martuza RL](#), [Weissleder R](#), [Shah K](#).

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The poor prognosis of patients with aggressive and invasive cancers combined with toxic effects and short half-life of currently available treatments necessitate development of more effective tumor selective therapies. Mesenchymal stem cells (MSCs) are emerging as novel cell-based delivery agents; however, a thorough investigation addressing their therapeutic potential and fate in different cancer models is lacking. In this study, we explored the engineering potential, fate, and therapeutic efficacy of human MSCs in a highly malignant and invasive model of glioblastoma. We show that engineered MSC retain their "stem-like" properties, survive longer in mice with gliomas than in the normal brain, and migrate extensively toward gliomas. We also show that MSCs are resistant to the cytokine tumor necrosis factor apoptosis ligand (TRAIL) and, when engineered to express secreted recombinant TRAIL, induce caspase-mediated apoptosis in established glioma cell lines as well as CD133-positive primary glioma cells in vitro. Using highly malignant and invasive human glioma models and employing real-time imaging with correlative neuropathology, we demonstrate that MSC-delivered recombinant TRAIL has profound anti-tumor effects in vivo. This study demonstrates the efficacy of diagnostic and therapeutic MSC in preclinical glioma models and forms the basis for developing stem cell-based therapies for different cancers.

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