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Tumor Biology 7: Stem Cells in Cancer 2 Abstract #1021

Neural stem cell can mediate immune therapy for brain tumor

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Neural stem cells are capable of tracking migratory and invasive brain tumor. In the present study we isolated neural stem-like cells from whole bone marrow of adult C57BL/6 mice. These bone marrow derived neural stem-like cells (BM-NSCs) grew as spheres morphologically indistinguishable from the neurospheres of fetal brain derived neural stem cells and expressed neural stem cell marker. Upon in vitro differentiation, the BM-NSCs were capable of producing progenies of three lineages, neurons, astrocytes, oligodendrocytes. After in vivo implantation, the cells were capable of tracking intracranial glioma cells by migrating into tumor mass, tumor "satellite" or in immediate proximity to and intermixed with invading tumor "islands". We combined this tumor tracking property of BM-NSCs with gene therapy by transducing the cells with a new discovered cytokine IL-27 that plays a role in the initiation of T help cell 1 responses. BM-NSCs transduced by an adenoviral vector carrying the single-chain IL-27 cDNA or by an empty vector as control were injected into the brain of C57BL/6 mice that were bearing intracranial GL26 gliomas. Approximately 50% mice survived intracranial gliomas after the implantation of IL-27 transduced BM-NSCs. In contrast, the implantation of empty vector transduced BM-NSCs did not rescue the intracranial glioma-bearing mice. Enhanced T cells infiltration within the tumor masses was observed in the mice treated with IL-27 expressing BM-NSCs. Cytotoxic T lymphocyte (CTL) assay of spleen cells from the survived mice shown tumor-specific CTL activities against GL26. In addition, the IL-27 expressing BM-NSCs treated mice that survived intracranial glioma were resistant to intracranial rechallenge with the same GL26 glioma cells. Consistent with this observation, increased IFN- ϵ^3 expression was detected within the brain after the rechallenge. Furthermore, depleting particular lymphocytes demonstrated that CD8+ T cells were crucial for the antitumor activity of IL-27 expressing BM-NSCs. Taken together, these data demonstrated that BM-NSCs can be used as a targeting vehicle to track migratory and invasive tumor cells within the central nervous system, and that IL-27 as a new cytokine has potent ability to induce tumor-specific antitumor activity and protective immunity. These findings suggest that IL-27 expressing BM-NSCs may have therapeutic potential for treating brain tumors.

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