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Dendritic cell vaccines for cancer stem cells.

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Accumulating evidence suggests that only a fraction of neoplastic cells, defined as cancer stem cells (CSC), are responsible for tumor perpetuation. Recent data suggest that neurospheres (NS) from glioblastoma multiforme (GBM) are enriched in CSC. The characterization of this subpopulation of brain tumor cells with a potent tumorigenic activity supports the cancer stem cell hypothesis in solid tumors and may imply that cancer cells are differentially targeted by treatments, including dendritic cell (DC) immunotherapy. To test therapeutic strategies, a good model mimicking the characteristics of GBM-NS and GBM-AC (Adherent Cells) was necessary. One of the most frequently used murine brain tumor models is the GL261 glioma cell line. To see whether GL261 cells could mimic the growth of human GBM-CSC we let them grow in EGF/bFGF without serum. After 5 days neurospheres were visible in the culture medium and were proliferating continuously. The characterization in vivo and in vitro demonstrates that GL261-NS satisfy criteria used to identify CSC and are more immunogenic than AC. DC loaded with GL261-NS lysates protect mice against tumors from both GL261-NS and GL261-AC. Our results suggest that only DC vaccination against neurospheres can restrain the growth of a highly infiltrating and aggressive model of glioma and may have implications for the design of novel, more effective immunotherapy trials for malignant glioma and possibly other malignancies.

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