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Irradiated Glioma Antigens-Pulsed Dendritic Cell Vaccine Prolonged Overall Survival through the Enhancement of CD4+ T cell Lineages on a Mouse Orthotopic Glioma Model

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Glioblastoma (GBM) is the most common malignant brain tumor in adults and is associated with a poor prognosis. Although there are many treatments but overall survival remains at about fifteen months after diagnosis. Therefore, it is important to identify new treatment to improve therapeutic effects. Dendritic cells (DCs) are the most potent antigen-presenting cells in the immune system and are capable of inducing tumor-specific effector T cells. Recent studies have demonstrated that the DC vaccines can prolong the survival of subjects afflicted with cancers. However, the efficacy of DC vaccines is abated by glioma-induced immunosuppression and lack of attention toward the immunogenicity of the tumor lysate/cells used for pulsing DCs. In the present study, the DC vaccine loaded with irradiated glioma cell lysates has been shown to prolonged overall survival in a mouse orthotopic glioma model. Further analysis showed that Anti-tumor activity induced by irradiated glioma cell lysates-pulsed DC vaccine was abrogated by depletion of CD4+ T cells, but not by depletion of CD8+ T cells. Depletion of CD4+ T-cells by anti-CD4 treatment at the time of tumor challenge demonstrated their essential role in irradiated glioma cell lysates-pulsed DC vaccine- mediated antitumor immunity. Flow cytometric analysis of tumor-infiltrating cells in mice treated with irradiated glioma cell lysates-pulsed DC vaccine showed increases in CD4+ Cytotoxic and regulatory T-cell molecule (CRTAM) + T cell but not in CD8+ CRTAM+ T cell. In the systemic immune response, irradiated glioma cell lysates-pulsed DC vaccine increased the CD4+ terminally differentiated effector memory cell. These findings suggest that the CD4+ T cells lineage signaling pathway plays an important role in response to antitumor active vaccination.