Oncolytic herpes simplex virus

Both the proteasome inhibitor bortezomib and an oncolytic herpes simplex virus 1 (oHSV)-expressing GM-CSF are FDA approved. Although proteasome blockade can increase oHSV replication, immunologic consequences, and consequent immunotherapy potential are unknown.

The Food and Drug Administration approval of immunogenic oncolytic virus (OV) has opened a new era in the treatment of advanced melanoma; however, approximately 50% of patients with melanoma develop brain metastasis, and currently there are no beneficial treatment options for such patients.

To model the progression of metastases seen in patients and to overcome the hurdles of systemic delivery of OV, we developed melanoma brain metastasis models in immunocompromised and immunocompetent mice, and tested the fate and efficacy of oncolytic herpes simplex virus (oHSV)-armed mesenchymal stem cells (MSCs). Using brain-seeking patient-derived melanoma cells and real-time in vivo imaging, we show a widespread distribution of micrometastases and macrometastases in the brain, recapitulating the progression of multifoci metastases seen in patients. We armed MSCs with different oHSV variants (MSC-oHSV) and found that intracarotid administration of MSC-oHSV, but not of purified oHSV alone, effectively tracks metastatic tumor lesions and significantly prolongs the survival of brain tumor-bearing mice. In a syngeneic model of melanoma brain metastasis, a combination of MSC-oHSV and PD-L1 blockade increases IFNγ-producing CD8+ tumor-infiltrating T lymphocytes and results in a profound extension of the median survival of treated animals. This study thus demonstrates the utility of MSCs as OV carriers to disseminated brain lesions, and provides a clinically applicable therapeutic platform to target melanoma brain metastasis [1)].

Oncolytic herpes simplex virus for glioblastoma

see Oncolytic herpes simplex virus for glioblastoma.

1)
Du W, Seah I, Bougazzoul O, Choi G, Meeth K, Bosenberg MW, Wakimoto H, Fisher D, Shah K. Stem cell-released oncolytic herpes simplex virus has therapeutic efficacy in brain metastatic melanomas. Proc Natl Acad Sci U S A. 2017 Jul 25;114(30):E6157-E6165. doi: 10.1073/pnas.1700363114. Epub 2017 Jul 14. PubMed PMID: 28710334; PubMed Central PMCID: PMC5544283.