

Summary

Primary glioblastoma multiforme (GBM) is an aggressive brain tumor that has no cure. Despite valiant efforts, prognosis for patients remains dismal. A promising new therapy involves the use of oncolytic viruses (OVs) that can specifically replicate and lyse in cancers, without spreading in normal tissues. Results from recent clinical trials with OV have revealed the safety of this approach, although evidence for efficacy remains elusive. We have observed that host immune responses elicited upon OV treatment are limiting for OV replication and propagation. Efforts to increase viral replication in tumors should enhance OV mediated tumor oncolysis. We hypothesize that reduction in tumor blood vessels prior to OV therapy will reduce host inflammatory cell infiltration of brain tumor tissue. This will result in improved OV replication and spread, enhancing efficacy of OV therapy. We will evaluate the effect of pretreatment with anti-angiogenic therapy on therapeutic efficacy of OV treatment in immune competent rodent models of glioma. We will elucidate the mechanism of enhancement of OV mediated tumor oncolysis by anti-angiogenic pretreatment. The significance of this translational grant is that it will lead to development of a rational treatment strategy that can move rapidly from bench to bedside of patients battling brain tumors.