Glioblastoma multiforme is the most common primary brain tumor in adults, accounting for the majority of 18,500 cases of primary brain tumors diagnosed each year in the U.S. It has a dismal prognosis with a 12-15 month median survival despite multimodality treatment. Novel therapeutic agents are urgently needed.

MV-CEA is a novel viral agent deriving from the Edmonston vaccine strain of measles virus. The virus has been engineered to produce CEA, that serves as a trackable marker of viral gene expression and can be used for monitoring of viral therapy in vivo. In preclinical work we have demonstrated significant antitumor potential of the virus, both in vitro and in vivo against glioblastoma animal models. CEA levels in the serum represented a good correlate of viral gene expression in these models. Toxicology studies of CNS administration of MV-CEA were performed in $Ifnar^{ko}$ CD46 Ge mice, which are susceptible to measles virus replication, and non-human primates (Rhesus macaques), and they support the safety of the proposed approach. Furthermore, in an ongoing clinical trial of intraperitoneal administration of MV-CEA in patients with recurrent ovarian cancer, doses up to 10^7 TCID50 have been well tolerated without dose limiting toxicity having been observed.

Our hypothesis is that MV-CEA will be a safe and effective agent for treatment of recurrent glioblastoma multiforme. We also hypothesize that the detection of CEA in patient serum can serve as an effective means of following viral gene expression, which could allow dose optimization in future applications of this agent. We propose to conduct a phase I trial of MV-CEA in patients with recurrent glioblastoma multiforme with the following objectives: a) to assess the safety of intratumoral and resection cavity administration of MV-CEA in patients with recurrent glioblastoma multiforme and to determine the maximum tolerated dose of MV-CEA in this setting; the maximum viral dose to be administered in this trial is 2×10^7 TCID50; b) to characterize the profile of viral gene expression at each dose level as manifested by serum CEA concentrations and to assess viremia, viral replication, and measles virus shedding and persistence; c) to determine humoral and cellular immune response to the injected virus and correlate it with toxicity, viremia, CEA levels, and response; and d) to assess in a preliminary fashion the antitumor activity of this approach.