



## CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:  
RP100861

Project Title:  
A new pharmacoviral approach to treat Malignant Gliomas

Award Mechanism:  
Individual Investigator

Principal Investigator:  
Costa-Mattioli, Mauro

Entity:  
Baylor College of Medicine

### Lay Summary:

Malignant gliomas (MGs) are the most lethal form of human cancer. Patients with MGs respond poorly to most available therapeutic modalities. Thus, more effective therapies are desperately needed. Oncolytic viruses constitute a promising therapy against MGs. However, the antiviral response greatly counteracts its clinical application. The mTOR signaling pathway has been implicated in i) the induction of the antiviral response and ii) glioma tumorigenicity. Accordingly, we have developed a new "pharmacoviral" approach in which the highly specific inhibitor of mTORC1, rapamycin, in combination with VSVd51M, the prototype for VSV-based oncolytic therapies, dramatically prolongs the survival of immunocompetent rats afflicted with MGs. More importantly, VSVd51M selectively killed tumor, but not normal cells in MG-rats treated with rapamycin. Thus, reducing the antiviral response through inhibition of mTOR is an effective strategy to augment the therapeutic activity of VSVd51M. The main goal of this grant is discover cures for MG through a better understanding of i) the molecular mechanism underlying host-pathogen interaction and ii) the biology of MGs. We will characterize our pharmacoviral approach in clinically relevant MG-animal models. We will try to further improve our pharmacoviral approach. Finally, we will study the effects of a much more powerful mTOR inhibitor, either alone or in combination with VSVd51M. The outcome from these translational studies will have a major impact in both cancer therapy and human health.