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Praveena Velpurisiva
University of Massachusetts Lowell

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POLYMERIC NANOPARTICLES FOR TARGETED COMBINATION TREATMENT OF TEMOZOLOMIDE RESISTANT GLIOBLASTOMA MULTIFORME (GBM)

Praveena Velpurisiva, MS^{1,5}, Brandon Piel, BS², Jack Lepine, MS³, Prakash Rai, PhD^{4,5}

¹Department of Biological Sciences, ²Research Associate, ³Core Research Facility, ⁴Department of Chemical Engineering, ⁵Biomedical Engineering and Biotechnology Program, University of Massachusetts, Lowell

Glioblastoma Multiforme (GBM) is an aggressive cancer that originates from astrocytes and spreads to spinal cord and other parts of the brain. Increase in replication of glial cells leads to advantageous mutations in the tumor. According to the cancer statistics from 2015 about 15,320 deaths were reported due to GBM. Five-year survival is less than 5% making GBM a dreadful form of cancer. Current treatment involves complex invasive surgery, followed by chemotherapy and radiation. The goal of this study is to develop a combination therapy to treat GBM using Poly (lactic-co-glycolic acid) (PLGA) nanoparticles encapsulated with two drugs namely gefitinib and GSK461364, each with a unique target. Gefitinib is a Tyrosine Kinase inhibitor, which competes for ATP-binding site of EGFR-TK. GSK461364 is a Polo-like Kinase (PLK-1) inhibitor that blocks the G2/M transition in tumor cell cycle. These distinct hydrophobic drugs are tested on U-87 MG (human malignant glioma) cell line. PLGA is attached to Polyethylene glycol (PEG), which is conjugated to transferrin receptor binding peptide. These transferrin peptides bind to transferrin receptors (TfR) or CD71 and enable the entry of PLGA-PEG nanoparticles across the Blood Brain Barrier (BBB). Results of characterization, TEM, SEM images, *in vitro* drug release profiles, stability, cytotoxicity assay, flow cytometry data of uptake of the nanoparticles will be presented.

Contact:

Praveena Velpurisiva
University of Massachusetts Lowell
praveena_velopuri@student.uml.edu