Targeted Hybrid Lipid-Polymer Nanoparticles for Glioblastoma Multiforme Treatment

Antonella Rocchi

University of L'Aquila, L'Aquila, Italy

Glioblastoma multiforme (GBM) is the most aggressive and common primary brain tumor in adults with rapid growth and highly infiltration. The incidence of GBM is 3-5 per 100,000 patients per year in the United States, with an average survival time of 14 months and a 5-year survival rate of below 5%.

The current standard treatment for GBM includes surgical resection followed by radiation therapy and concurrent and adjuvant chemotherapy with Temozolomide (TMZ). However, the tumor's heterogeneity and its relative resistance significantly decrease the overall survival of patients. Nanoparticles loading TMZ and selective targeting with GBM homing peptides may represent a promising strategy to menage GBM and improve the overall survival of patients. Hybrid Lipid-Polymer Nanoparticles (HLPNs) have been developed as a robust drug delivery platform with high encapsulation yield, tunable and sustained drug release, excellent serum stability, and many potentialities for selective drug delivery and targeting of specific cells and/or tissues.

LinTT1, a GBM homing peptide that uses a multistep mechanism for tumor homing and penetration, was used as targeting peptide conjugated with nanoparticles. HLPNs-LinTT1 were physicochemical characterized for average sizes, polydispersity index (PDI), and surface properties. The ability of targeting properties of HLPNs-LinTT1 with the p32 receptor, overexpressed in GBM cells, was studied by cell-free binding experiments, confocal microscopy, and FACS-based binding/internalization studies. The *in vitro* efficacy studies, the cytotoxic effect of LinTT1 and control TMZ-HLPNs was tested on cultured GBM cells by using the MTT assay.

For *in vivo* binding studies, LinTT1-TMZ-HLPNs were injected intravenously injected and systemic distribution and accumulation in the body tissues were monitored by using intravital and confocal microscopic imaging, as well as histological analysis.

Results demonstrated that LinTT1-TMZ-HLPNs represent a suitable nanocarriers for GBM therapy.