Nanoparticle drug delivery systems

- ROS-Responsive Cinnamaldehyde Polymer Nanoparticles Loaded with Puerarin for the Treatment of Atherosclerosis
- A Polysaccharide-Based Fluorescent Polymer Carrier for Natural Product Delivery and Gastric Cancer Inhibition
- Assessment and evaluation of melatonin loaded PLGA injectable nanosuspension for the treatment of subarachnoid hemorrhage: Preclinical study
- Theranostic Role of Advanced Nanotechnological Tools in Early Brain Metastases in Lung Cancer: An Updated Review
- Gambogic acid-iron nanozymes as effective carriers for enhanced chemotherapy by inducing excessive autophagy and oxidative stress
- Carbon Dot-Based Nanoparticles: A Promising Therapeutic Approach for Glioblastoma
- Ginsenoside F2-modified liposomes delivering FTY720 enhance glioblastoma targeting and antitumor activity via ferroptosis
- Recent Advances in the Delivery of Bone Morphogenetic Proteins for Targeting Glioma: An Updated Review

Nanoparticle drug delivery systems are engineered technologies that use nanoparticles for the targeted delivery and controlled release of therapeutic agents. The modern form of a drug delivery system should minimize side-effects and reduce both dosage and dosage frequency.

Poly(lactic-co-glycolic acid) (PLGA) NPs are coated with various poloxamers, including F68, F98, or F127, via physical adsorption to render particle surfaces non-adhesive, thereby resisting interactions with brain extracellular matrix. F127-coated PLGA (F127/PLGA) NPs provide markedly greater distribution in healthy rat brains compared to uncoated NPs and widespread coverage in orthotopically-established brain tumors. Distribution analysis of variously-sized F127/PLGA NPS determines the average rat brain tissue porosity to be between 135 and 170 nm while revealing unprecedented brain coverage of larger F127/PLGA NPs with an aid of hydraulic pressure provided by CED. Importantly, F127/PLGA NPs can be lyophilized for long-term storage without compromising their ability to penetrate the brain tissue. Further, 65- and 200-nm F127/PLGA NPs lyophilized-reconstituted and administered in a moderately hyperosmolar infusate solution show further enhance particle dissemination in the brain via osmotically-driven enlargement of the brain tissue porosity. The combination of F127/PLGA NPs and osmotic tissue modulation provides a means with a clear regulatory path to maximize the brain distribution of large NPs that enable greater drug loading and prolong drug release [1)].

Hyaluronan (HA)-grafted lipid-based nanoparticles (LNPs). These LNPs having an ionized lipid were previously shown to be highly effective in delivering small interfering RNAs (siRNAs) into various cell types. LNP's surface was functionalized with hyaluronan (HA), a naturally occurring glycosaminoglycan that specifically binds the CD44 receptor expressed on GBM cells.

Cohen et al. found that HA-LNPs can successfully bind to glioblastoma GBM cell lines and primary neurospheres of GBM patients. HA-LNPs loaded with Polo-Like Kinase 1 (PLK1) siRNAs (siPLK1) dramatically reduced the expression of PLK1 mRNA and cumulated in cell death even under shear flow that simulate the flow of the cerebrospinal fluid compared with control groups. Next, a human

GBM U87MG orthotopic xenograft model was established by intracranial injection of U87MG cells into nude mice. Convection of Cy3-siRNA entrapped in HA-LNPs was performed, and specific Cy3 uptake was observed in U87MG cells. Moreover, convection of siPLK1 entrapped in HA-LNPs reduced mRNA levels by more than 80% and significantly prolonged survival of treated mice in the orthotopic model. Taken together, this results suggest that RNAi therapeutics could effectively be delivered in a localized manner with HA-coated LNPs and ultimately may become a therapeutic modality for GBM [2].

Solid lipid nanoparticles (SLNs) conjugated with tamoxifen (TX) and lactoferrin (Lf) were applied to carry anticancer carmustine (BCNU) across the blood-brain barrier (BBB) for enhanced antiproliferation against glioblastoma multiforme (GBM). BCNU-loaded SLNs with modified TX and Lf (TX-Lf-BCNU-SLNs) were used to penetrate a monolayer of human brain-microvascular endothelial cells (HBMECs) and human astrocytes and to target malignant U87MG cells. The surface TX and Lf on TX-Lf-BCNU-SLNs improved the characteristics of sustained release for BCNU. When compared with BCNU-loaded SLNs, TX-Lf-BCNU-SLNs increased the BBB permeability coefficient for BCNU about ten times. In addition, TX-BCNU-SLNs considerably promoted the fluorescent intensity of intracellular acetomethoxy derivative of calcein (calcein-AM) in HBMECs via endocytosis. However, the conjugated Lf could only slightly increase the fluorescence of calcein-AM. Moreover, the order of formulation in the inhibition to U87MG cells was TX-Lf-BCNU-SLNs>TX-BCNU-SLNs>Lf-BCNU-SLNs>BCNU-SLNs. TX-Lf-BCNU-SLNs can be effective in infiltrating the BBB and delivering BCNU to GBM for future chemotherapy application [3]

1)
Negron K, Kwak G, Wang H, Li H, Huang YT, Chen SW, Tyler B, Eberhart CG, Hanes J, Suk JS. A Highly Translatable Dual-arm Local Delivery Strategy To Achieve Widespread Therapeutic Coverage in Healthy and Tumor-bearing Brain Tissues. Small. 2023 Jan 17:e2207278. doi: 10.1002/smll.202207278. Epub ahead of print. PMID: 36651002.
2)
Cohen ZR, Ramishetti S, Peshes-Yaloz N, Goldsmith M, Wohl A, Zibly Z, Peer D. Localized RNAi Therapeutics of Chemoresistant Grade IV Glioma Using Hyaluronan-Grafted Lipid-Based Nanoparticles. ACS Nano. 2015 Jan 8. [Epub ahead of print] PubMed PMID: 25558928.
3)
Kuo YC, Cheng SJ. Brain targeted delivery of carmustine using solid lipid nanoparticles modified with tamoxifen and lactoferrin for antitumor proliferation. Int J Pharm. 2016 Feb 29;499(1-2):10-9. doi: 10.1016/j.ijpharm.2015.12.054. Epub 2015 Dec 22. PubMed PMID: 26721730.