The Torch
Vol. 2 (7)

Angiopeptide-2 conjugates in nanoparticle delivery across the blood-brain barrier to treat glioblastoma multiforme

Nallagatla Laxmi Koustubha

Cure for different forms of brain cancers has always been unresolved. Glioblastoma multiforme (GBM) is one of the most common types of primary brain cancer. Providing radiation therapy and chemotherapy against this potentially subside the tumour growth but affect the non-neoplastic tissues of the brain. Relapse of GBM after surgeries within a span of 9 months is a grief drawing aspect in the patients. Drug delivery for brain tumour site has been a cumbersome process owing to competitive binding of ligands/inhibitors, lysosomal degradation after receptor-mediated endocytosis, technical errors resulting in poor targeting efficiency, etc. To transfer non-neoplastic drugs to the tumour site, it is essential for a drug to overcome the blood-brain barrier (BBB). BBB is highly impermeable to molecules >400Da, a defence mechanism adopted by the brain to prevent the entry of microorganisms, toxins, drugs and other high molecular weight substances within the brain. To attain permeability, the drug has to bind to a receptor that is highly expressed on BBB in GBM patients. In different cancers, cancer cells abnormally express cell surface receptors, which are used as biomarkers for cancer detection or can aid in drug delivery through receptor-mediated transcytosis (RMT). Similarly, in GBM, LRP-1 (low-density lipoprotein receptor protein-1) is overexpressed and mediates transcytosis of multiple ligands, such as angiopep-2, lactoferrin, transferrin, melanotransferrin and other associated proteins.

Of them all, angiopep-2 effectively traverses across BBB, hence this peptide sequence is conjugated with nanoparticles containing anticancer drugs to target neoplastic cells in the brain. Angiopep-2 is a 19mer peptide derived from the human Kunitz domain. The additional advantage of these conjugates is to prevent deaths as a result of drug dosage intolerance. Anticancer drugs, such as doxorubicin, temozolomide, paclitaxel, chlorotoxin, daunorubicin, etc. are capable of causing severe side effects as they are administered in high doses to prevent metastasis. However, angiopep-2 conjugates specifically target tumour cells by preventing healthy tissue damage due to drug toxicity. Enhanced permeability retention effect (EPR) substantially increases the nanoparticle intake and provides an alternative route rather than RMT. Administering high dosage drugs induces stress on the liver and kidneys during drug metabolism. Angiopep-2 nanoparticles are proteolytically degraded, which prevents organ failures as they are administered in optimal ratios. In recent years, nanoparticle drug delivery has taken ladders to increase the quality and survival rates of cancer patients by escalating to several new combinations of conjugated drugs especially brain cancers to confer the fidelity of these conjugates in cancer treatment.

Keywords: Glioblastoma multiforme, Blood-brain barrier, Angiopeptide-2, Neoplastic cells, Receptor-mediated endocytosis

Citation:
Nallagatla Laxmi Koustubha. Angiopeptide-2 conjugates in nanoparticle delivery across the blood-brain barrier to treat glioblastoma multiforme. The Torch. 2021. 2(7). Available from: https://www.styvalley.com/pub/magazines/torch/read/angiopeptide-2-conjugates-in-nanoparticle-delivery-across-the-blood-brain-barrier-to-treat-glioblastoma-multiforme.