

Pep-1 peptide is a well-known cell penetrating peptide (PTD, protein transduction domain) that transports full-length proteins to the nucleus of the cell.

Tumor-targeting and **blood brain barrier** (BBB)-penetrating are highly desirable for the treatment of glioma.

In a study, Guo et al., developed Pep-1& borneol-bifunctionalized **carmustine**-loaded micelles (Pep-1/Bor/CMS-M) capable of targeting to IL-13 receptor-overexpressed glioma and penetrating the brain microvascular endothelial cells-associated physiologic barriers. Pep-1/Bor/CMS-M were nearly spherical particles with a diameter of 32.6 ± 1.1 nm and zeta potential of -21.3 ± 3.1 mV. Carmustine (CMS) released from Pep-1/Bor/CMS-M in pH 7.4 was significantly faster than in acidic environments. In human glioma **BT325** cellular studies, Pep-1/Bor/CMS-M remarkably increased the cytotoxicity, notably improved the internalization and effectively induced the cell apoptosis. Likewise, in human brain microvascular endothelial cells (HBMEC) cells, Pep-1/Bor/CMS-M obviously promoted the cellular uptake, rapidly decreased the transepithelial electrical resistance (TEER) and thereby of enhancing the ability of penetration. In orthotopic Luc-BT325 glioma tumor-bearing nude mouse models, the stronger fluorescence signal and longer retention were observed in brain tissues compared with other controls, after single administration of DiD-labelled Pep-1/Bor/M (DiD/Pep-1/Bor/M). Importantly, Pep-1/Bor/CMS-M displayed the strongest inhibition of tumor growth, the longest survival period and low systemic toxicity in treating orthotopic glioma tumor-bearing nude mice. Simultaneous functionalization of Pep-1 and borneol offers a novel strategy for designing CMS-based nanomedicine and precisely treating glioma ¹⁾.

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Guo X, Wu G, Wang H, Chen L. Pep-1&Borneol-bifunctionalized carmustin-loaded micelles enhance anti-glioma efficacy through tumor targeting and BBB penetratings. J Pharm Sci. 2018 Dec 8. pii: S0022-3549(18)30796-2. doi: 10.1016/j.xphs.2018.11.046. [Epub ahead of print] PubMed PMID: 30537472.

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