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Peptide-based delivery of oligonucleotides studied by an in vitro model of blood-brain barrier

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Glioblastoma multiforme (GBM) is an aggressive malignant brain tumor with poor prognosis after interventions. A blood-brain barrier (BBB) is a major obstacle to limit the efficacy of chemotherapy and block the passage of all large molecular drugs to the brain tumor. In order to improve the delivery of therapeutic agents particularly in gene-based therapy, a peptide-based delivery was proposed in the study. A series of novel peptides were designed for dual purposes, to enhance the penetration across the BBB and to specifically target the brain cancer cells. In the study, the BBB model was set up using Transwell™ plate which is composed of two compartments. Both represent the blood side (upper) and the brain side (lower) and they were cultured with the brain endothelial cells (bEnd.3) and glioma cell line (U87), respectively. The nanocomplexes of peptide and luciferase expressing plasmid DNA (pGL3) were formed and tested in an *in vitro* model of BBB. The luciferase transfection efficacy was measured in both cell lines and also WST-1 cell viability assay was done to determine the toxicity of the complexes. PepFect 32 (PF32), a cell-penetrating peptide coupled to a targeting ligand angiopep-2, showed to be an efficient vector for pDNA delivery across the BBB model to target to glioma cells with no toxicity to both cell lines.

Biography

Artita Srimanee received her PhD in Pharmaceutical Chemistry and Phytochemistry from Faculty of Pharmacy, Mahidol University, Thailand in 2014. She joined the group of Professor Ülo Langel in the Department of Neurochemistry at Stockholm University, Sweden through a Student Exchange Program while doing her PhD in Thailand. Her research focuses on design, synthesis and modification of cell-penetrating peptides (CPPs) in order to deliver gene-based therapeutic agents to brain cancer cells. A setup in vitro model of the blood-brain barrier (BBB) using Transwell plate was designed and used to assess the transfection efficiency of nucleic acids such as siRNA and plasmid DNA delivered by CPPs. Moreover, she also studies transcytosis pathway of the nanoparticles across the BBB using brain endothelial cell line (bEnd.3) together with improvement the peptide-based vector using targeting modification strategy for the brain-targeted drug delivery.

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