Synthesis of novel non-viral vectors using cell penetrating peptides

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The development of specific and effective gene delivery system without a toxic reaction is strongly awaited for gene therapy. The cell uptake, intracellular trafficking such as escape from endosome, intranuclear trafficking and transcription of genes such as plasmid DNA are important to achieve sufficient gene expression. Cell penetrating peptides (CPP) and nuclear localization signals have been focused attention as effective carriers to deliver the gene and protein into cells. We have investigated to develop a novel non-viral vector in which Tat analog with Cys-Gly-NH_2 added to C terminus of HIV-Tat (48-57) known as CPP was chemically-conjugated with cholesterol pullulan (CP-Tat) self-assembled hydrogel nanospheres, by disulfide linkage. The pDNA would be release with Tat analogs from CP-Tat by cleavage of S-S linkage under the cytosol environment. CP-Tat having positive charge enhanced luciferase activity of pCMV-Luc in COS-7 cells and showed higher cell viability than PEI and Lipofectamine, indicating that the synthesized CP-Tat would be safe and effective vector. Moreover, modified Tat analog enhanced intracellular trafficking efficiency compared with intact Tat peptide. In this symposium, we would like to report on current results of our approaches to synthesis gene vectors linked several kinds of CPP.