GS01-6 siRNA delivery system using functional peptide, CH2R4H2C

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The siRNA has been expected to apply for several diseases such as cancer since siRNA specifically silences the disease-associated genes. However, effective gene carriers should be developed to overcome the low siRNA stability *in vivo*, form stable complexes and facilitate intracellular uptake of siRNA. We have synthesized the functional peptide "$CH_2R_4H_2C$" as a gene carrier. The $CH_2R_4H_2C$ condenses nucleic acid due to the positive charge and disulfide cross linkage in extracellular environment and release nucleic acid in intracellular reduction environment. In this study, several types of $CH_2R_4H_2C$ modified carriers were synthesized and the cellular uptake ability and *in vitro* silencing effect were evaluated using flow cytometry and ELISA. As a result, the $CH_2R_4H_2C$ modified stearic acid (STR-$CH_2R_4H_2C$) facilitated the cellular uptake rather than $CH_2R_4H_2C$ and showed significant silencing effect. On the other hand, by replacing the residue in both ends of $CH_2R_4H_2C$ from cysteine to glycine not to form disulfide cross linkage, the cellular uptake ability and silencing effect decreased. Furthermore the STR-$CH_2R_4H_2C$/siRNA complexes showed significant suppression of the tumor growth by injection into the tumor tissue bearing mice compared with the naked siRNA. These results indicate that our $CH_2R_4H_2C$ based carriers which has hydrophobic modification and disulfide cross linkage with cysteine were very effective and available for siRNA delivery *in vivo*. We are currently investigating the functional modification to our carriers for systemic administration.