S10-6 Development of systemic siRNA delivery system for cancer RNAi therapy

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RNA interference (RNAi) therapy with small interfering RNA (siRNA) is expected as a potent treatment strategy for intractable diseases such as cancer. Whereas local injection of siRNA drugs has entered clinical trials one after another, systemic injection of them is quite limited because of a problem of DDS technology. In the present study, a novel polycation liposome (PCL) was developed to achieve systemic delivery of synthetic siRNA for cancer treatment. We newly synthesized dicetylphosphate-tetraethylenepentaamine (DCP-TEPA) for siRNA delivery and found potent transfection activity of PCL containing DCP-TEPA (TEPA-PCL). In addition, we examined lipid composition of PCL and nitrogen/phosphorus ratio of PCL/siRNA, and obtained the most potent transfection activity. Next, pharmacokinetics of Alexa750-labeled siRNA in tumor-bearing mice was examined using *in vivo* imaging system to design TEPA-PCL for systemic injection. For this purpose, TEPA-PCL was modified with polyethyleneglycol (PEG) and Ala-Pro-Arg-Pro-Gly, a peptide for targeting angiogenic endothelium. Alexa750-labeled siRNA in TEPA-PCL for systemic injection retained in the bloodstream for a long time and accumulated in the tumor. Systemic delivery of siRNA with TEPA-PCL might be useful for cancer RNAi therapy.