Effect of Size and Pegylation of Liposomes and Peptide-Based Synthetic Lipoproteins on Tumor Targeting

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Purpose
The goal of this study is to investigate the tumor targeting potential of peptide-based synthetic lipoproteins (sHDL) by its intrinsic properties, and the effect of size and pegylation of sHDL on tumor targeting.

Methods
Two common tumor drug delivery carriers-liposomes (LIP) and pegylated liposomes (PEG-LIP), as well as pegylated sHDL (PEG-sHDL) were used as control. We examined the tumor cell specificity and cellular uptake efficiency of sHDL in scavenger receptor B-I (SR-BI) transfected and mock-treated baby hamster kidney cells (BHK-SR-BI cells and BHK-mock cells), as well as in SR-BI positive colorectal carcinoma (HCT 116) cells. We also evaluated tumor tissue penetration ability and tumor accumulation efficiency of sHDL in HCT 116 3D tumor spheroids and tumor bearing nude mice.

Results
The cellular uptake efficiency of sHDL was 3.6 times higher in BHK-SR-BI cells relative to BHK-mock cells, and the cellular uptake of sHDL in HCT 116 cell was inhibited by 32% by an anti-SR-BI antibody, indicating sHDL could be efficiently and specifically recognized and uptaken by tumor cells mediated by SR-BI receptor (Figure 1). sHDL with super-small sizes (9.6 ± 0.2 nm) exhibited much stronger penetration ability into the tumor spheroids compared with LIP (130.7 ± 0.8 nm) and (PEG-LIP, 101 ± 2 nm) (Figure 2). Modifying PEG on sHDL affected the binding of nanoparticles with SR-BI, therefore both cellular uptake efficiency and penetration ability of PEG-sHDL (12.1 ± 0.1 nm) were significantly decreased compared with sHDL. Furthermore, in the tumor bearing nude mice, sHDL showed 12- and 3- fold higher in vivo solid tumor accumulation as compared with LIP and PEG-LIP.

Conclusion
sHDL showed high tumor targeting efficiency on cellular, tissue-organ, and whole-body levels. These results suggest the biomimetic sHDL nanoparticles possess promising intrinsic tumor-targeted properties with established human safety to facilitate clinical translation.