Table S1. Peptides with CD4 recognition sequences for targeting of lipid nanoparticles.

CD4-BP	A.A.	Peptide Sequence	Description
2	16	CKGIRIGPGRAVYAAE	Consensus sequence gp120 $V3_1$
4	28	CARRPKFYRAPYVKNHPNVWGPWVAYGP	ST40 CD4 Antibody Mimetic$_2$

CD4-BP: CD4 Binding Peptide, A.A.: Amino Acids, 1:[21], 2: [22]

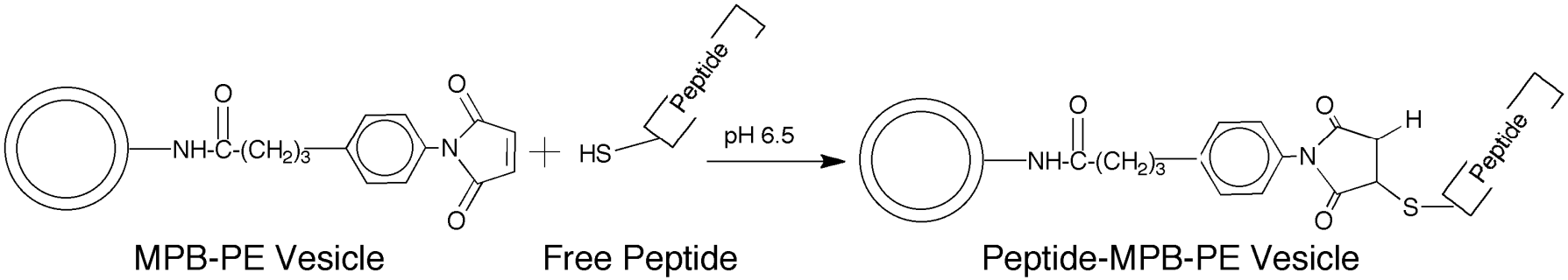

Figure S1. Covalent coupling of peptides to MPB-PE containing liposomes.
Schematic representation of peptides containing a terminal cysteine with –SH group coupling to nanoparticles containing a proportion of lipid with a maleimide linker. Lipid nanoparticles are prepared with 1.1-2.4 mole percent of MPB-PE. Peptides are coupled to nanoparticles at pH 6.5 through covalent binding of the cysteine SH to the maleimide on the lipid, forming a stable thioether linkage. Not drawn to scale.

Table S2. Comparison of anti-HIV efficacy of Indinavir loaded in CD4-targeted and control lipid nanoparticles
a: Samples analyzed based on the half-maximum inhibitory concentration EC_{50} (μM) values. Additional controls of targeted LNP without Indinavir (empty LNPs) were also evaluated. The effects of total drug exposure time are also presented. b: Lipid Nanoparticles.

Total Exposure Time(min)	**Anti-HIV Efficacy of Indinavir (EC_{50}, μM)**					
	Soluble	**CD4-BP2 LNP[b]**	**CD4-BP4 LNP**	**Control LNP**	**Empty CD4-BP2 LNP**	**Empty CD4-BP4 LNP**
15	>25	>25	7.52± 0.76	>25	>25	>25
30	>25	>25	6.47±0.21	>25	>25	>25
60	0.49± 0.09	0.13± 0.03	0.12± 0.04	>25	>25	>25