Electronic Supplementary Material (ESI) for Materials Advances.

Amphiphilic RGD and GHK peptides synergistically enhance liposomal delivery into cancer and endothelial cells

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Table S1. Dynamic light scattering characteristics of plain liposomes and liposomal formulations in milliQ water: hydrodynamic diameter (D_H, nm), polydispersity index (PdI) and zeta potential (ZP, mV), encapsulation efficiency (EE), loading capacity (LC), 25°C.

Composition	D_H, nm	ZP, mV	PdI	EE, %	LC, %
Unloaded					
Ctrl (Plain)	117 ± 2	55 ± 2	0.190 ± 0.002	n/a	n/a
RGD	114 ± 2	43 ± 2	0.079 ± 0.026	n/a	n/a
GHK	117 ± 1	54 ± 2	0.052 ± 0.005	n/a	n/a
RGD/GHK	112 ± 2	49 ± 1	0.061 ± 0.003	n/a	n/a
Rhodamine B (0.5 mg/mL)					
Ctrl	120 ± 10	58 ± 3	0.128 ± 0.100	53 ± 1	3.8 ± 0.1
RGD	109 ± 1	43 ± 3	0.088 ± 0.015	54 ± 2	3.9 ± 0.1
GHK	111 ± 3	52 ± 4	0.124 ± 0.017	57 ± 4	4.3 ± 0.3
RGD/GHK	109 ± 1	44 ± 2	0.147 ± 0.003	53 ± 2	3.8 ± 0.1
Doxorubicin (0.5 mg/mL)					
Ctrl	122 ± 1	52 ± 1	0.082 ± 0.022	45 ± 1	3.2 ± 0.1
RGD	114 ± 1	49 ± 4	0.087 ± 0.017	49 ± 3	3.5 ± 0.2
GHK	131 ± 1	50 ± 4	0.094 ± 0.026	53 ± 4	3.8 ± 0.3
RGD/GHK	127 ± 1	55 ± 6	0.087 ± 0.017	55 ± 3	4.0 ± 0.2
Paclitaxel (0.34 mg/mL)					
Ctrl	121 ± 4	39 ± 3	0.175 ± 0.057	74 ± 3	2.8 ± 0.1
RGD	125 ± 3	38 ± 2	0.094 ± 0.067	67 ±1	2.6 ± 0.1
GHK	138 ± 2	56 ± 3	0.124 ± 0.019	76 ± 4	2.9 ± 0.2
RGD/GHK	123 ± 4	38 ± 1	0.102 ± 0.081	72 ± 2	2.7 ± 0.1

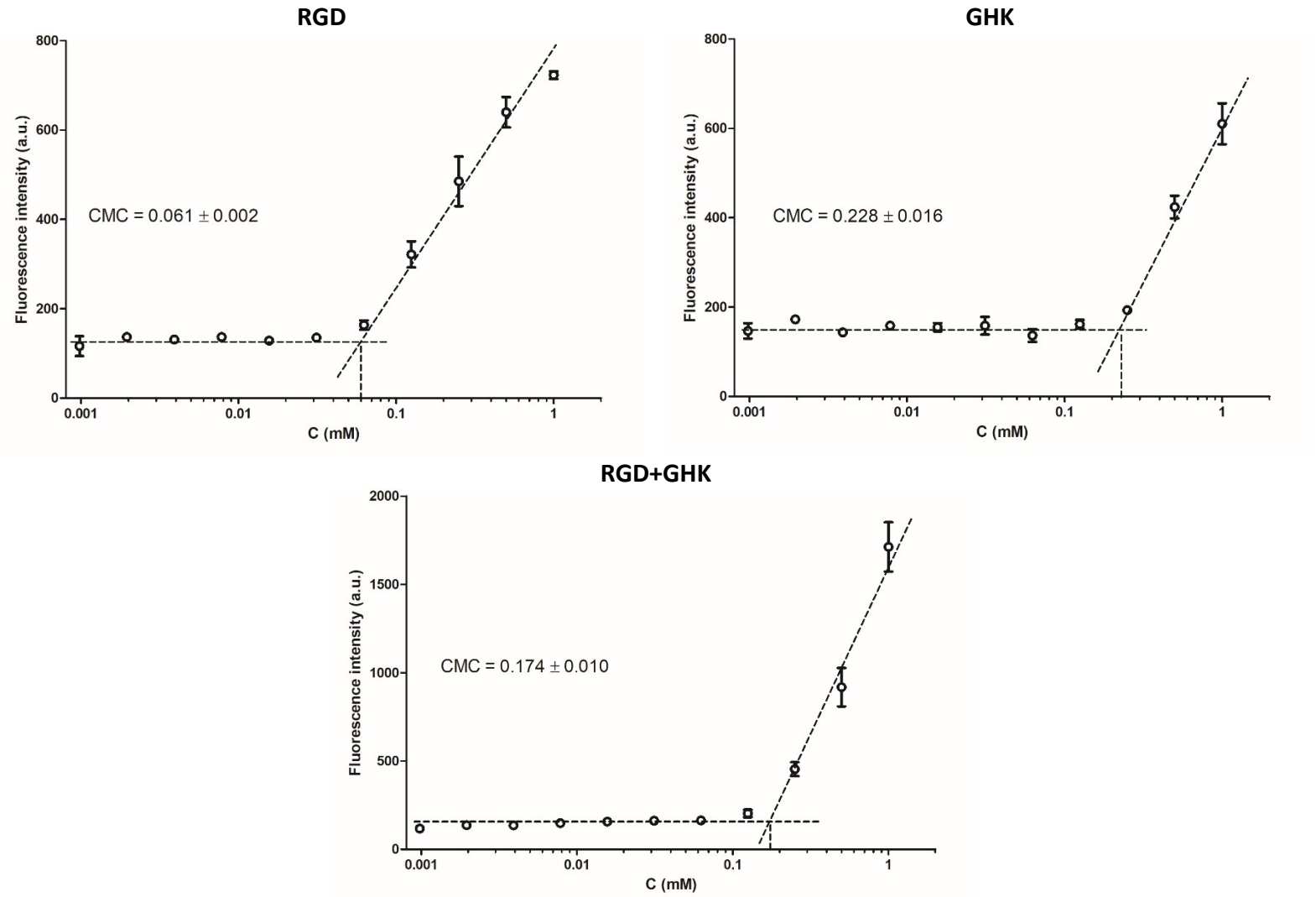

Fig. S1. Fluorescence intensity of curcumin in the presence of amphiphilic peptides at different concentrations. Critical micelle concentrations (CMC) are presented as mean (n = 3) ± SD.

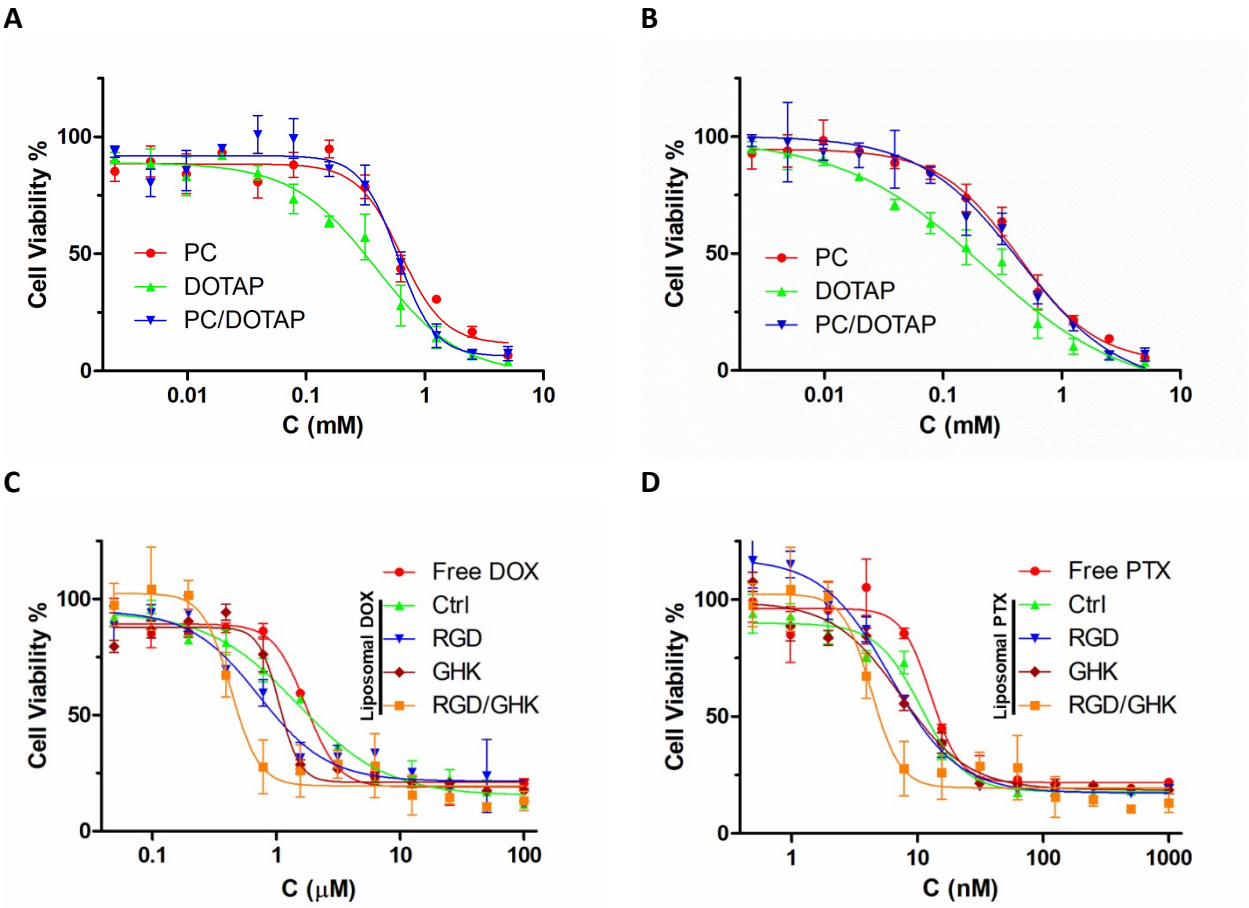

Fig. S2. Relative cell viability curves for serially diluted liposomal formulations (MTT assay). Effect of plain liposomes on PC-3 cells (A) and HSF (B) (72 h, PC+DOTAP concentration is shown). Effect of free and encapsulated drugs on PC-3 cells (C) and HUVECs (D) (24 h, drug concentration is shown). Data are presented as mean (n = 3) ± SD.

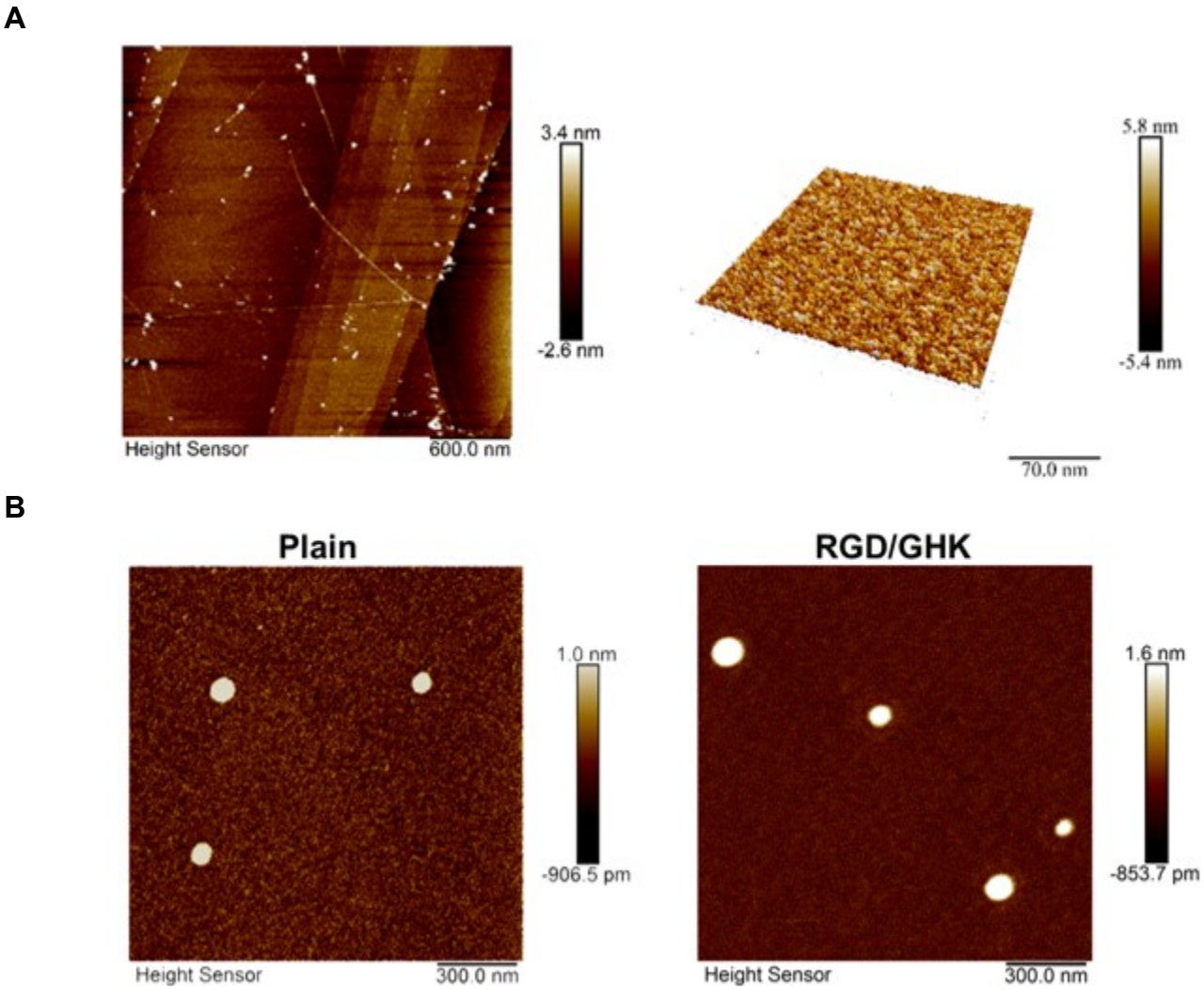

Fig. S3. AFM images of PC/DOTAP liposomes on HOPG (A) and mica (B) surfaces. Liposomes were added to the substrate surface at a concentration of ca. 1 mM lipids and dried before detection.

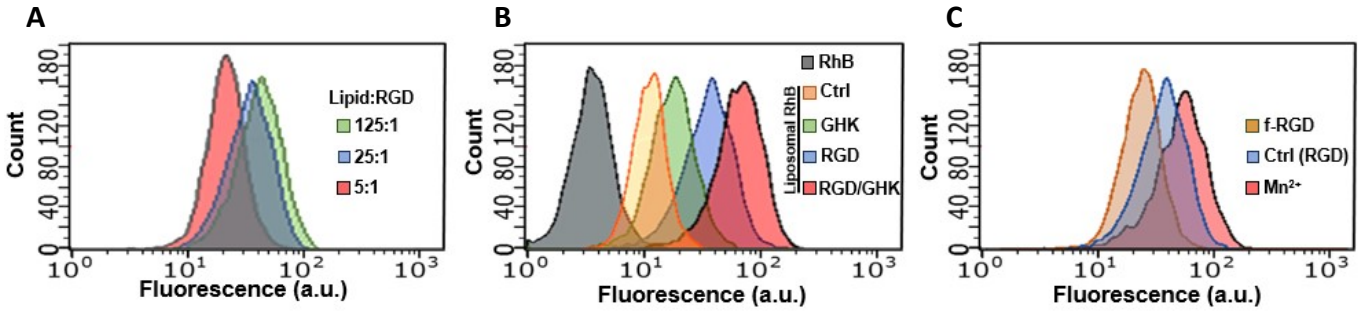

Fig. S4. Representative flow cytometry charts of RhB fluorescence in PC-3 cells treated with peptide-modified PC/DOTAP liposomal formulations: A. Effect of lipid:peptide (RGD) ratio. B. Effect of RGD, GHK, RGD/GHK peptides (lipid:peptide ratio 25:1). C. Effect of manganese chloride and free peptides (f-RGD).

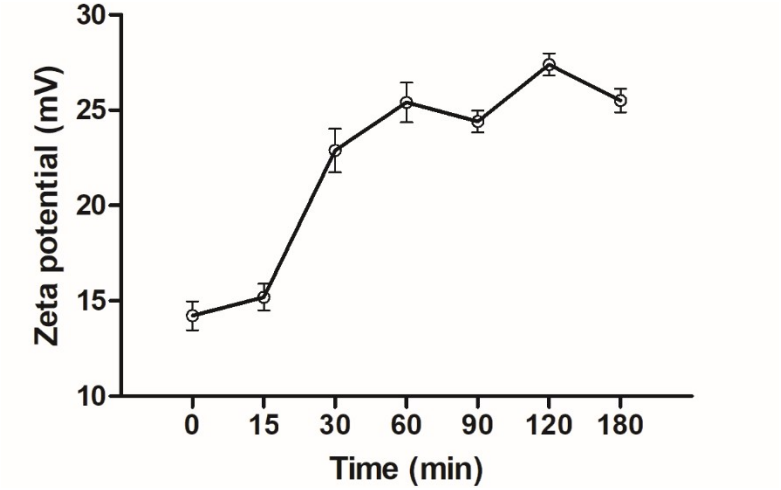

Fig. S5. Change of zeta potential of PC/DOTAP liposomes upon *in situ* co-incubation with C_{12}-GGGHK-NH_2 peptide in HEPES buffer for 2 h. Lipid:peptide ratio was 25:1. Data are presented as mean (n = 3) ± SD.

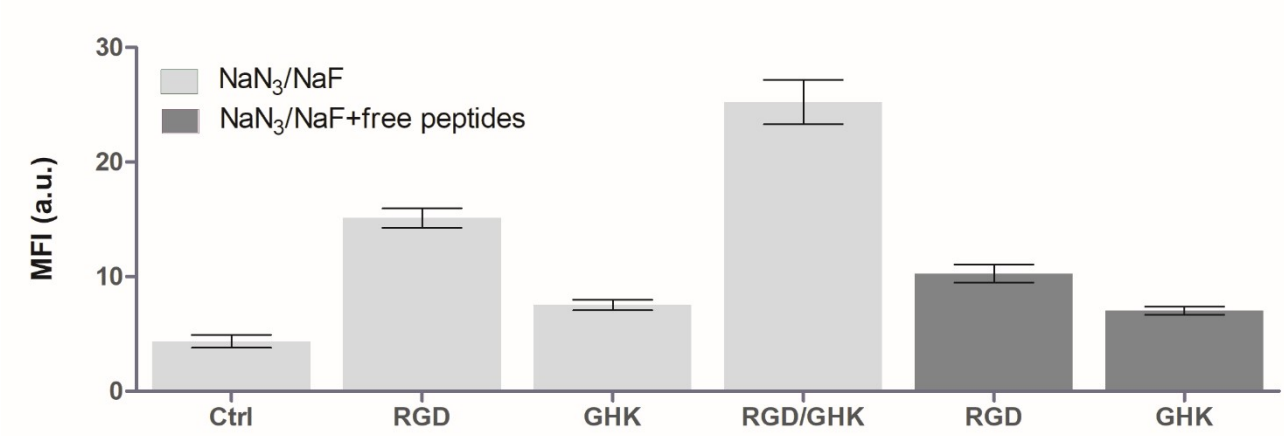

Fig. S6. Mean fluorescence intensities (MFI) of RhB in HUVECs treated with peptide-modified PC/DOTAP liposomal formulations in the presence of inhibitors (NaN_3/NaF and free RGD or GHK peptides).