Supplementary Information

Method

Zeta Potential and Dynamic Light Scattering

In zeta potential and dynamic light scattering experiments, a Malvern Zetasizer Nano-ZS ZEN 3600 (Malvern Instruments, USA) instrument was used with a detector angle of 173°. Samples were prepared to have a final AON concentration of 1 µM. Peptide concentrations were calculated accordingly to have the PA/AON ratios indicated. PA-only samples were prepared at a final concentration of 100 µM PA. PA/AON ratio of 30:1 was used in dynamic light scattering measurements. At least three measurements were done with automatic subreadings.

Cell viability assay

MCF-7 cells were seeded at a cell density of 1 x 10^4 cells per well in 96 well-plates with standard medium. After 24 h, medium was exchanged with serum free medium and PA solutions were administered at final concentrations of 200 µM, 100 µM, 50 µM, 25 µM, 12.5 µM, 6.25 µM, 3.12 µM. After 24 h of incubation, medium was discarded and Alamar Blue (Invitrogen) assay was performed. Cells were incubated with 10% Alamar Blue in serum free media for 4 h. Then, fluorescence at 560/590nm excitation/emission was measured with a microplate reader (Molecular Devices Spectramax M5). Fluorescence intensity was normalized to non-treated control and shown as percent viability.

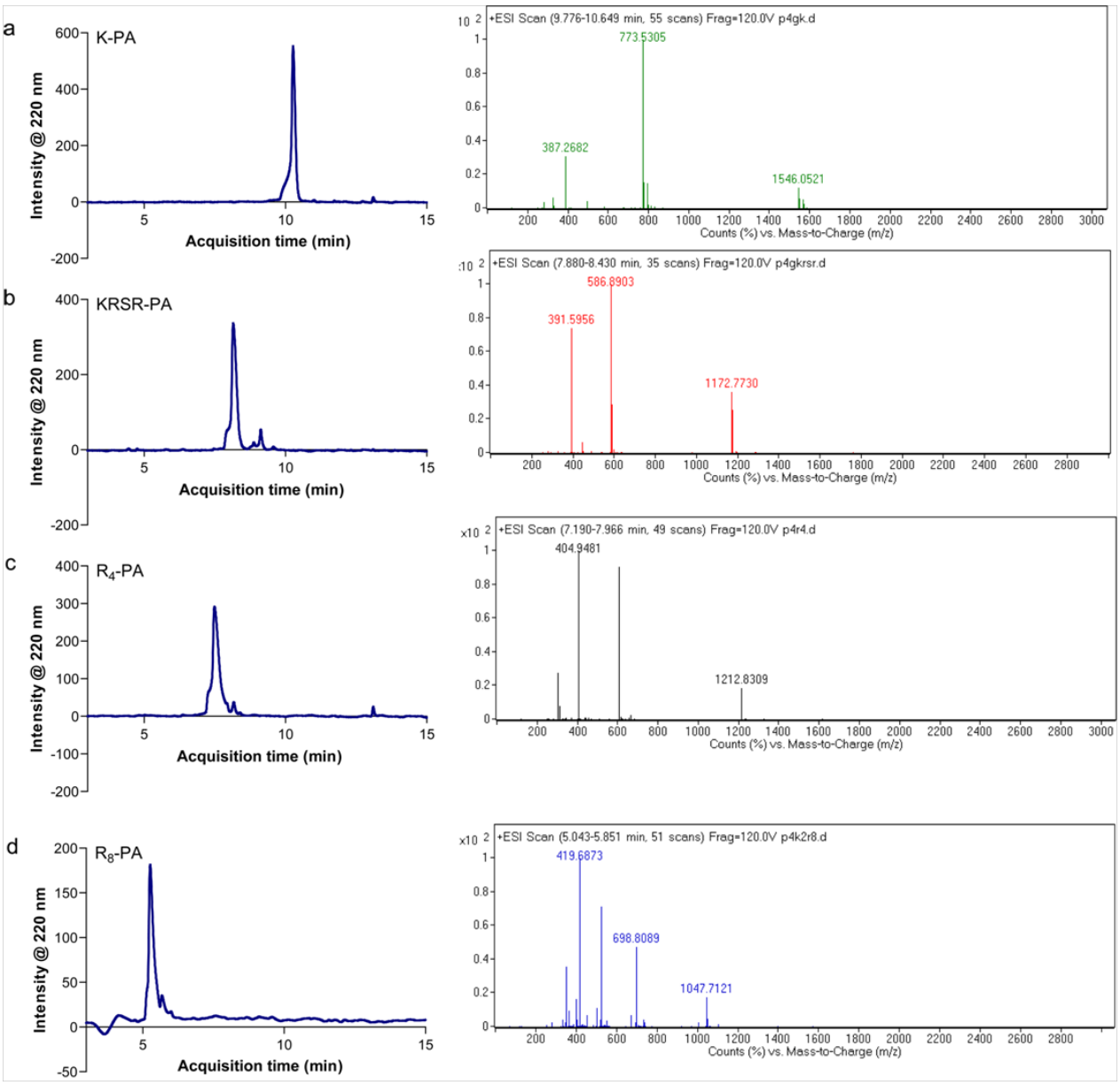

Figure S1. a Liquid chromatogram and mass spectrum of K-PA. Mass data $[M+H]^+$ (calculated): 773.52, $[M+H]^+$ (observed): 773.53, $[2M+H]^+$ (observed): 1546.05, $[M+2H]^{+2}$ *m/z* (observed): 387.27. **b** Liquid chromatogram and mass spectrum of KRSR-PA. Mass data $[M+H]^+$ (calculated): 1172.76, $[M+H]^+$ (observed): 1172.77, $[M+2H]^{+2}$ *m/z* (observed): 586.89, $[M+3H]^{+3}$ *m/z* (observed): 391.59. **c** Liquid chromatogram and mass spectrum of R_4-PA. Mass data $[M+H]^+$ (calculated): 1212.81, $[M+H]^+$ (observed): 1212.83, $[M+3H]^{+3}$ *m/z* (observed): 404.95. **d** Liquid chromatogram and mass spectrum of R_8-PA. Mass data $[M+2H]^{+2}$ *m/z*

(calculated): 1047.71, $[M+3H]^{+2}$ *m/z* (observed): 1047.31 , $[M+3H]^{+3}$ *m/z* (observed): 698.81, $[M+5H]^{+5}$ *m/z* (observed): 419.69.

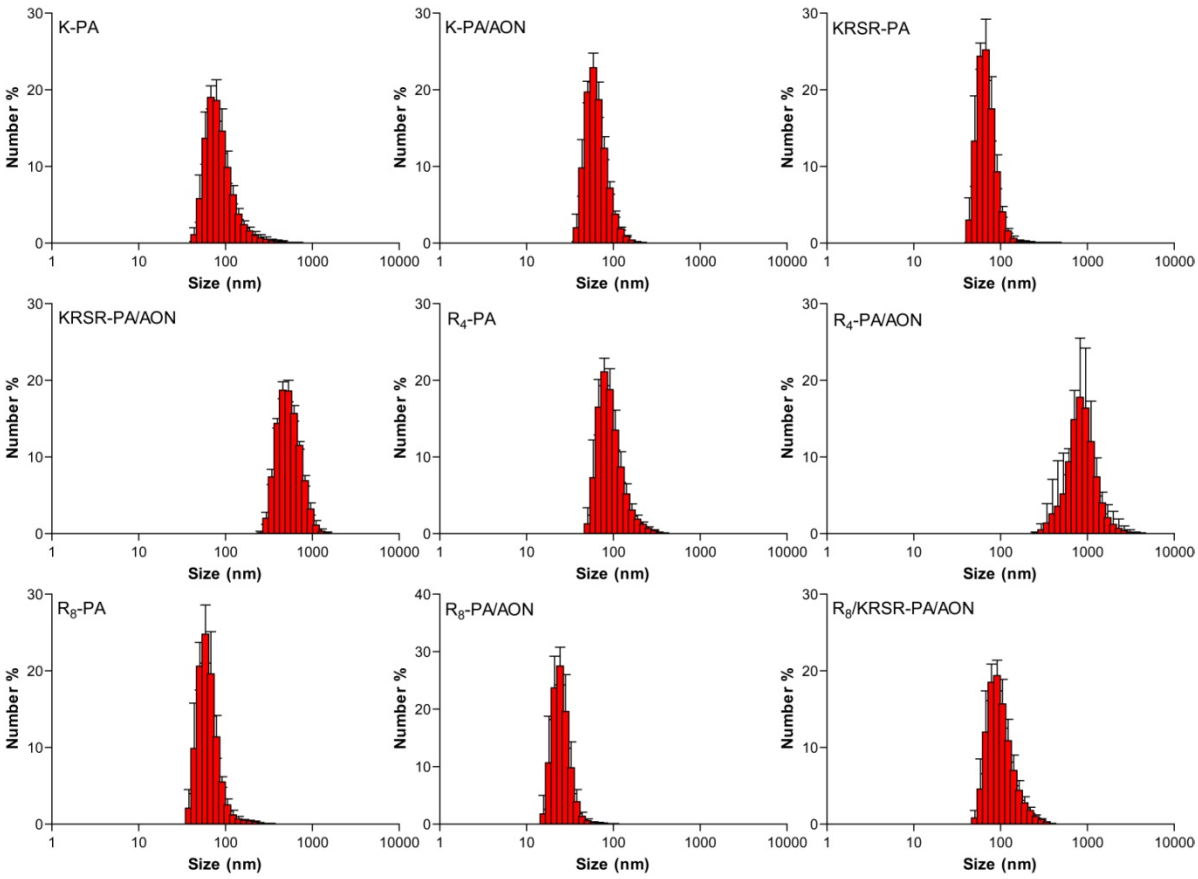

Figure S2. Size distribution of PA and PA/AON nanospheres measured by dynamic light scattering functionality of a Malvern Nano ZS Zetasizer.

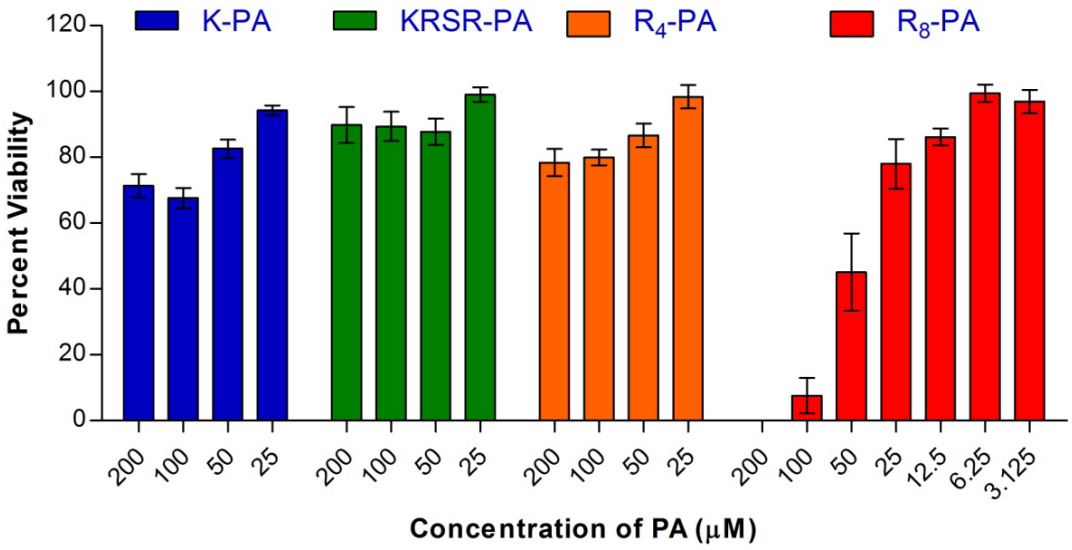

Figure S3. Cytotoxicity of PAs administered to MCF-7 cells for 24 h. (Error bars show SEM, n=4)

Supplementary Tables

Table S1. Zeta potentials of PAs and PA/AON complexes. (n=3)

	Only PA	**30:1 PA/AON**	**100:1 PA/AON**	**300:1 PA/AON**
K-PA	1.1 ± 2.1 mV	(-) 8.1 ± 3.2 mV	(-) 6.3 ± 2.4 mV	(-) 12.8 ± 1.1 mV
KRSR-PA	8.2 ± 1.0 mV	1.4 ± 0.5 mV	9.7 ± 0.2 mV	15.1 ± 0.9 mV
	Only PA	**10:1 PA/AON**	**30:1 PA/AON**	**100:1 PA/AON**
R_4-PA	15.1 ± 0.6 mV	(-)7.1 ± 0.8 mV	2.5 ± 0.2 mV	10.8 ± 0.7 mV
	Only PA	**3:1 PA/AON**	**10:1 PA/AON**	**30:1 PA/AON**
R_8-PA	22.6 ± 3.1 mV	29.1 ± 2.0 mV	31.4 ± 2.4 mV	29.6 ± 3.6 mV

Table S2. Zeta potentials of KRSR-PA/R_8-PA/AON complexes. (n=3)

3:1:1 KRSR/R_8/AON	(-)18.4 ± 0.3 mV
30:10:1 KRSR/R_8/AON	36.1 ± 1.4 mV