**ADVANCED
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Supporting Information

Programmable Delivery of Synergistic Cancer Drug Combinations Using Bicompartmental Nanoparticles
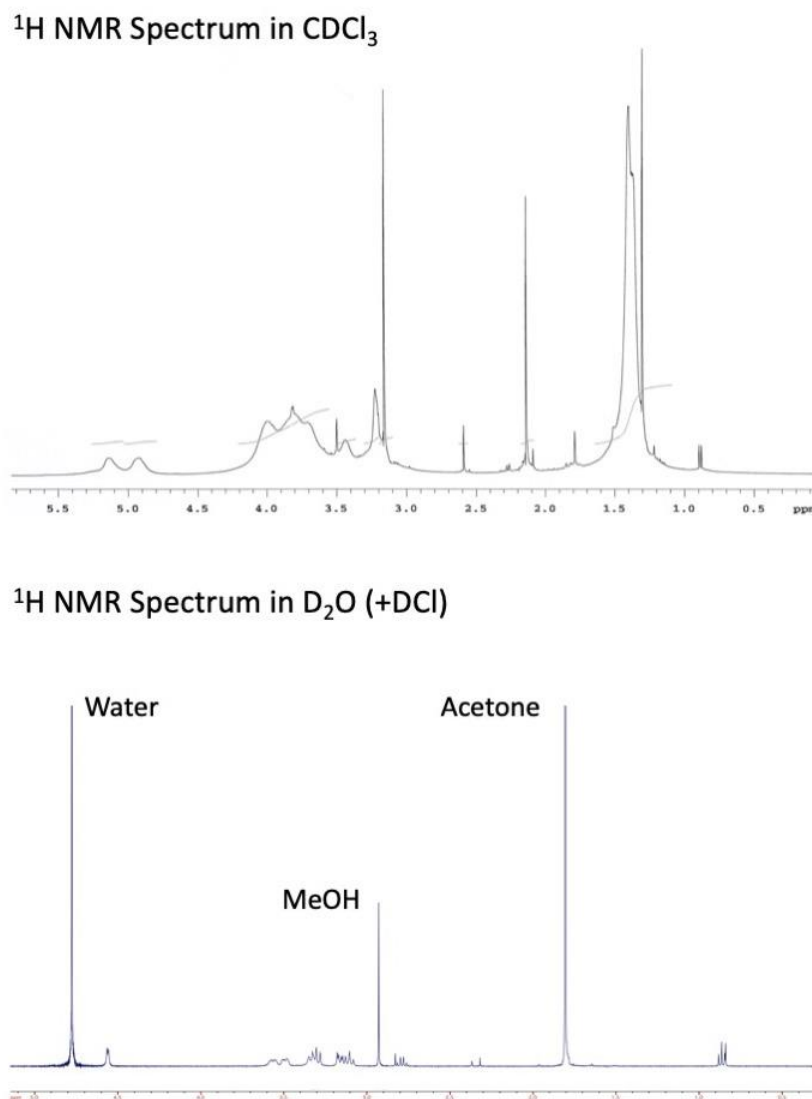
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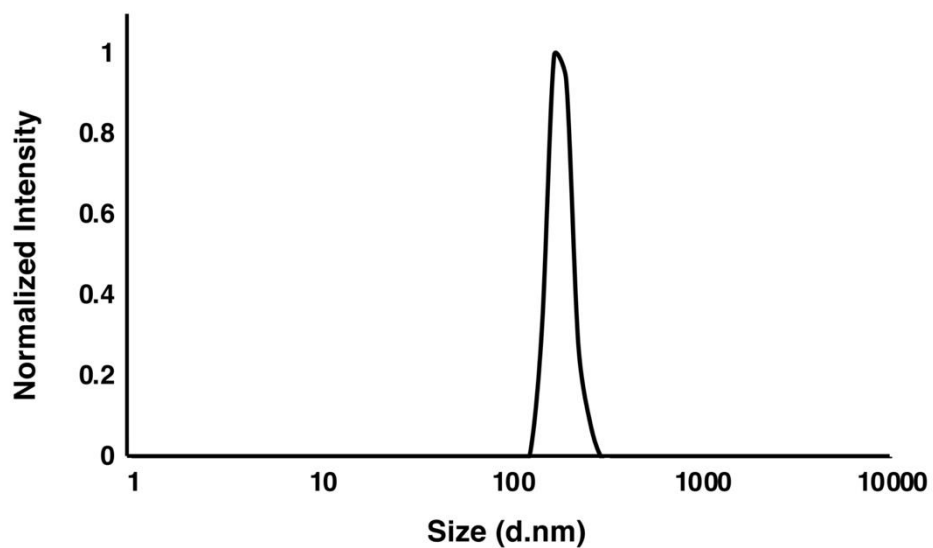
Supporting Information

Programmable Delivery of Synergistic Cancer Drug Combinations Using Bicompartmental Nanoparticles

Douglas R. Vogus[†], Jason V. Gregory[†], Alexandra Barajas, Melissa A. Cadena, Samir Mitragotri[*], Joerg Lahann[*]
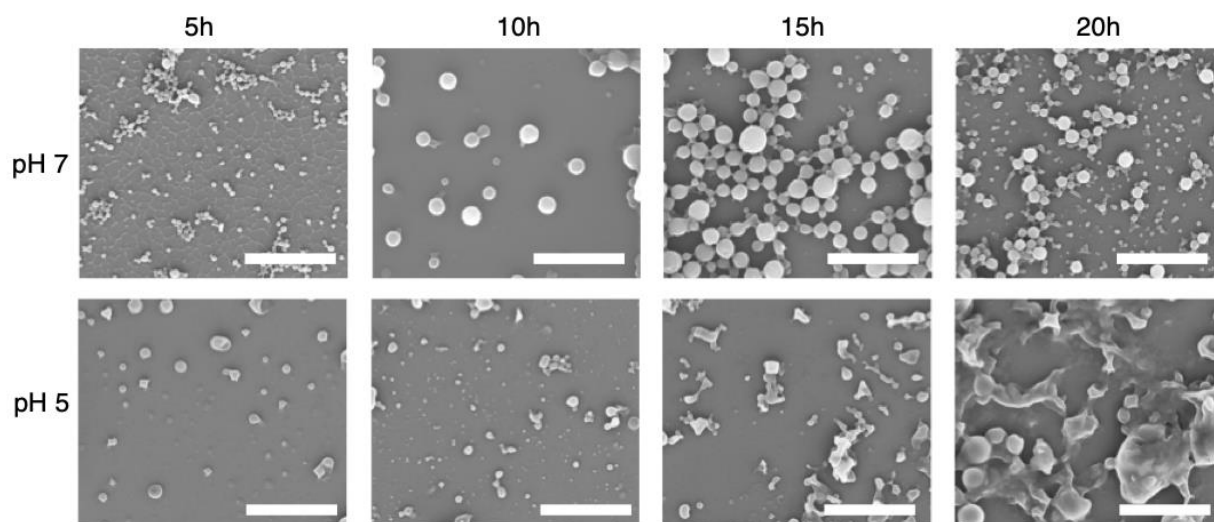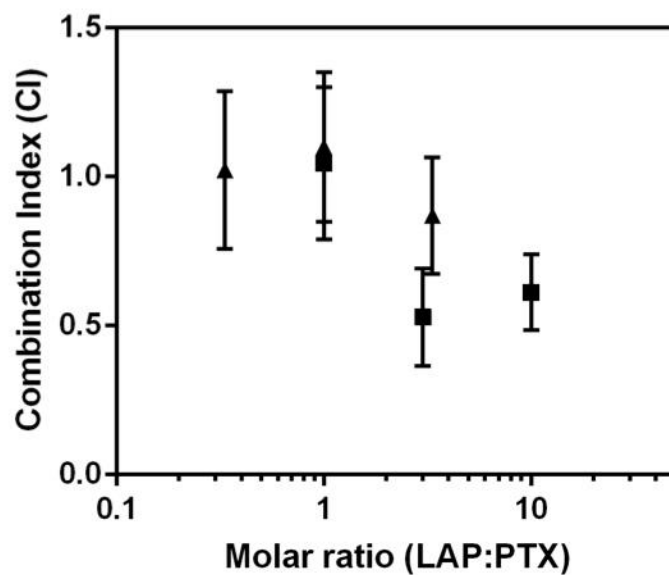
Supplemental Figures:

Figure S1. NMR spectra. (Top) Proton NMR spectra of synthesized 70 kDa AcDex confirms modified chemical structure. ^{1}H NMR (400 MHz, $CDCl_3$, δ): 1.39 (s, br, 23H), 2.15 (s, 1H) 3.25(br, 6H), 3.45 (br, 2H), 3.60-4.20 (br, 14H), 4.93 (br, 1H), 5.15 (br, 1H). (Bottom) Following degradation of synthesized AcDex in D_2O/DCl, deprotection byproduct (methanol and acetone) peaks confirm the degree of protection (71%) and relative ratio of acyclic vs. cyclic (4:1) of hydroxyl protecting groups.
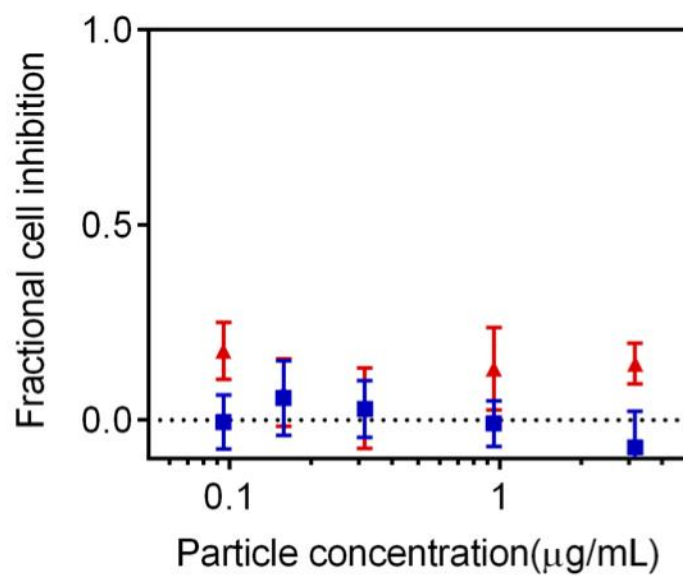
Figure S2. Size distribution post purification via centrifugation. Dynamic light scattering (DLS) size characterization of bicompartmental nanoparticles in PBS following purification via centrifugation. Average diameter = 173 nm, PDI = 0.174.
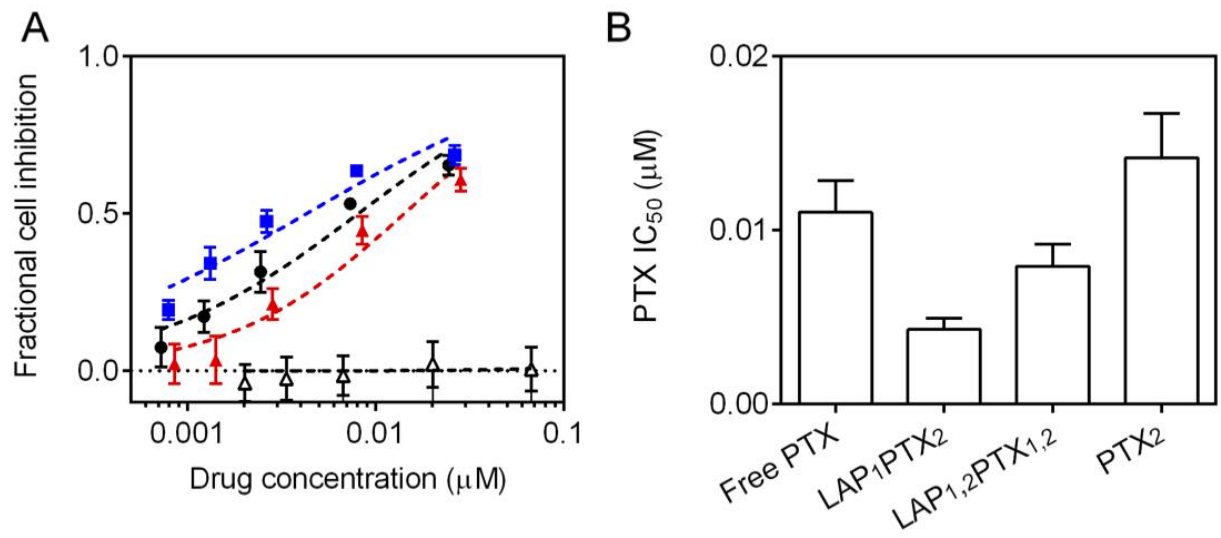
Figure S3. pH dependent particle degradation. Janus nanoparticles consisting of PLGA and PLGA/AcDex compartments undergo distinctly different degradative processes in response to solution pH.

Figure S4. Molar ratio dependence and drug synergy. Synergy as a function of LAP:PTX molar ratio when exposing cells to LAP (4 h) → LAP/PTX (68 h). Relative to PTX concentrations of 0.03 µM (triangles) and 0.01 µM (squares). Error bars represent 95% confidence intervals (n ≥ 12 wells)).

Figure S5. PLGA/AcDex nanoparticle toxicity. Fractional cell inhibition of MDA-MB 231 (HER2-, blue) and BT-474 (HER2+, red) cells after 72 h exposure to blank bicompartmental nanoparticles. Error bars represent 95 % CI (n ≥ 6 wells).

Figure S6. Cancer activity of programmable nanoparticles in HER2- cells. (A) Fractional cell inhibition of MDA-MB-231 cells after 72 h exposure to the following bicompartmental particles: $LAP_1 PTX_2$ (blue), and $LAP_{1,2}PTX_{1,2}$ (black) compared to particles containing a single therapeutic, PTX_2 (PTX only, PLGA, red) and LAP_1 (LAP only, AcDex, open triangles). Points are experimental data and lines are best fit median effect model. (B) PTX IC_{50} concentrations for each particle type. Error bars represent 95 % CI (n ≥ 12 wells).

Supplemental Tables

Table S1: Composition of particles synthesized via EHD co-jetting

Particle	PLGA/AcDex Comp	PLGA Comp.	PTX (wt%)	LAP(wt%)
LAP_1PTX_2	LAP	PTX	0.71	1.24
$LAP_{1,2}PTX_{1,2}$	LAP + PTX	LAP + PTX	0.65	1.29
LAP_2PTX_1	PTX	LAP	0.61	1.22
PTX_2	–	PTX	0.76	–
LAP_1	LAP	–	–	1.23
Blank	–	–	–	–

Table S2: PTX IC50 values

	MCF 10a	BT-474	MDA MB 231
Free PTX	4.4 ± 0.7	14 ± 1	11 ± 2
LAP_1PTX_2	1.1 ± 0.1	4.3 ± 0.4	4.3 ± 0.6
$LAP_{1,2}PTX_{1,2}$	3.4 ± 0.4	23 ± 10	8 ± 2
LAP_2PTX_1	1.9 ± 0.4	6.6 ± 0.7	--
PTX_2	3.1 ± 0.4	8.8 ± 1.7	14 ± 2