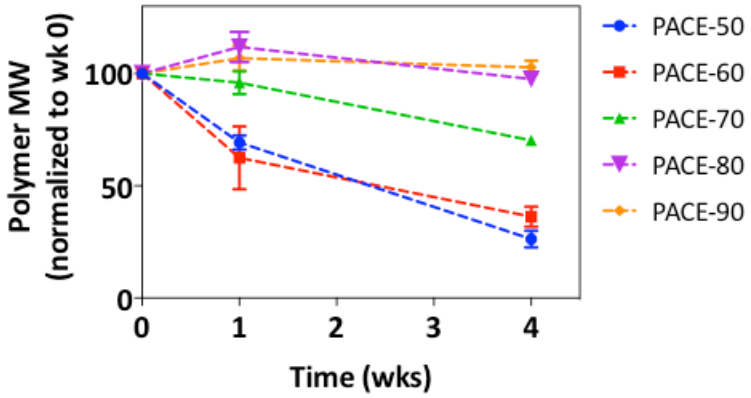
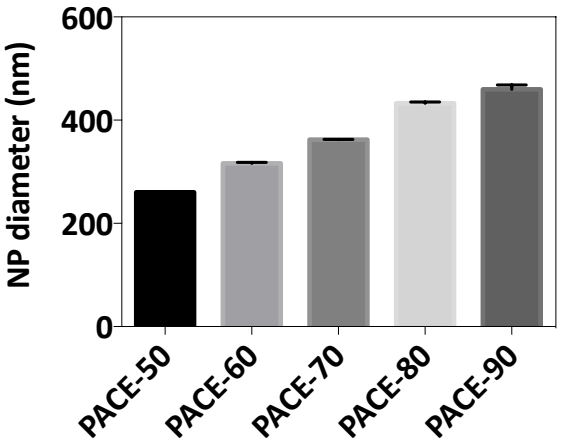
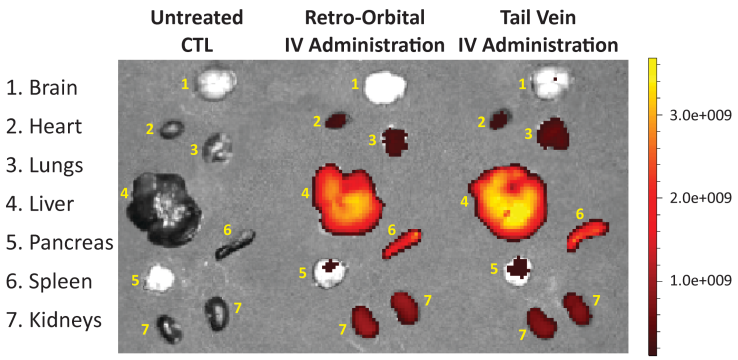
Supplementary Material



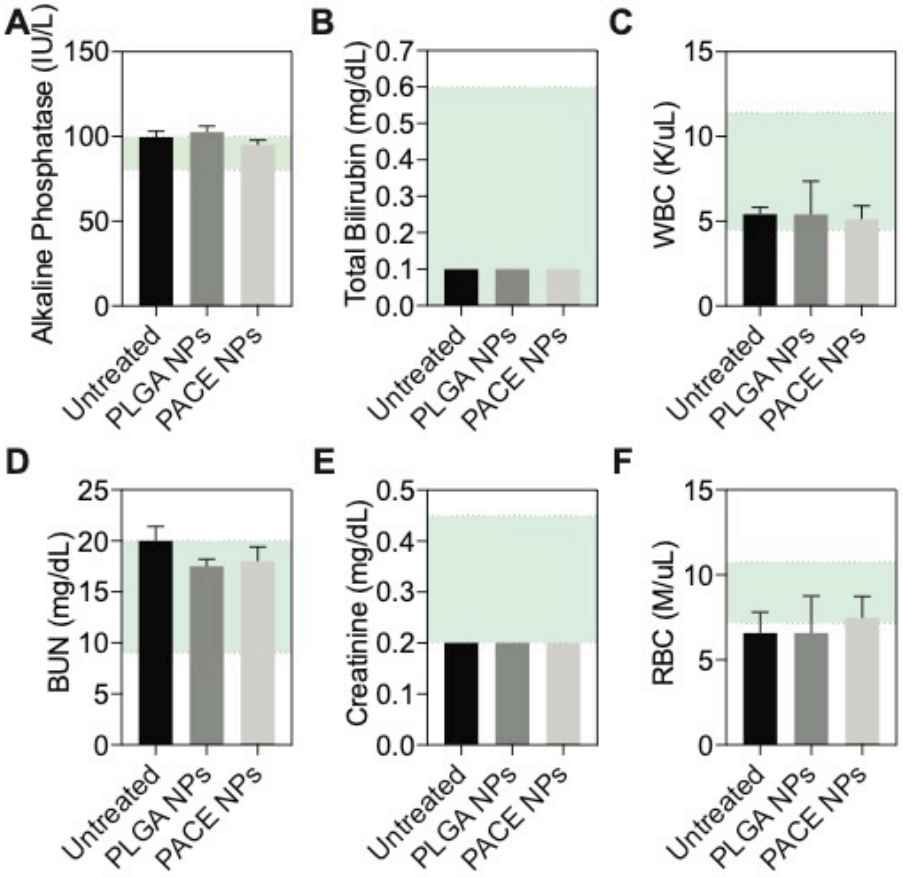
Supplemental Figure 1: PACE polymer degradation in buffer. Polymers were incubated in pH 7.4 Tris-EDTA buffer on a 37°C on a shaker for 1 to 4 weeks. After incubation, polymers were washed and lyophilized for 48 hours. Polymer molecular weight was measured using Gel Permeation Chromatography (GPC).



Supplemental Figure 2: Hydrodynamic diameter of siRNA-loaded PACE NPs. NPs were dissolved in PBS and diameter was measured using dynamic light scattering (Malvern).



Supplemental Figure 3: Nanoparticle biodistribution following retro-orbital and tail vein IV administration. DiD-loaded NPs in PBS were injected intravenously into mice via either retro-orbital or tail vein administration. After 48 hours, organs were harvested and imaged using an IVIS Spectrum In Vivo Imaging System (Perkin Elmer).



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	Untreated	PLGA NPs	PACE NPs
Total Protein (g/dL)	4.8	4.9	5.2
Albumin (g/dL)	2.4	2.5	2.6
Globulin (g/dL)	2.4	2.4	2.6
Phosphorus (mg/dL)	15.0	13.4	14.7
Glucose (mg/dL)	414	356	411
Calcium (mg/dL)	9.7	9.6	9.3
Sodium (mEq/dL)	150	151	148
Potassium (mEq/dL)	11.0	10.9	11.6
Chloride (mEq/dL)	114	115	111
Cholesterol (mg/dL)	100	95	118

Supplemental Figure 4: PACE NPs are non-toxic following *in vivo* IV administration. (A)-(G) Blood serum chemistry analyses from C57BL/6 mice that were either untreated or treated with 1 mg of poly(lactic-co-glycolic acid) (PLGA) NPs or PACE NPs 24 hours after treatment. Green regions in (A)-(F) indicate standard ranges for the C57BL/6 strain, and green text in (G) indicates that the values are in the normal range.