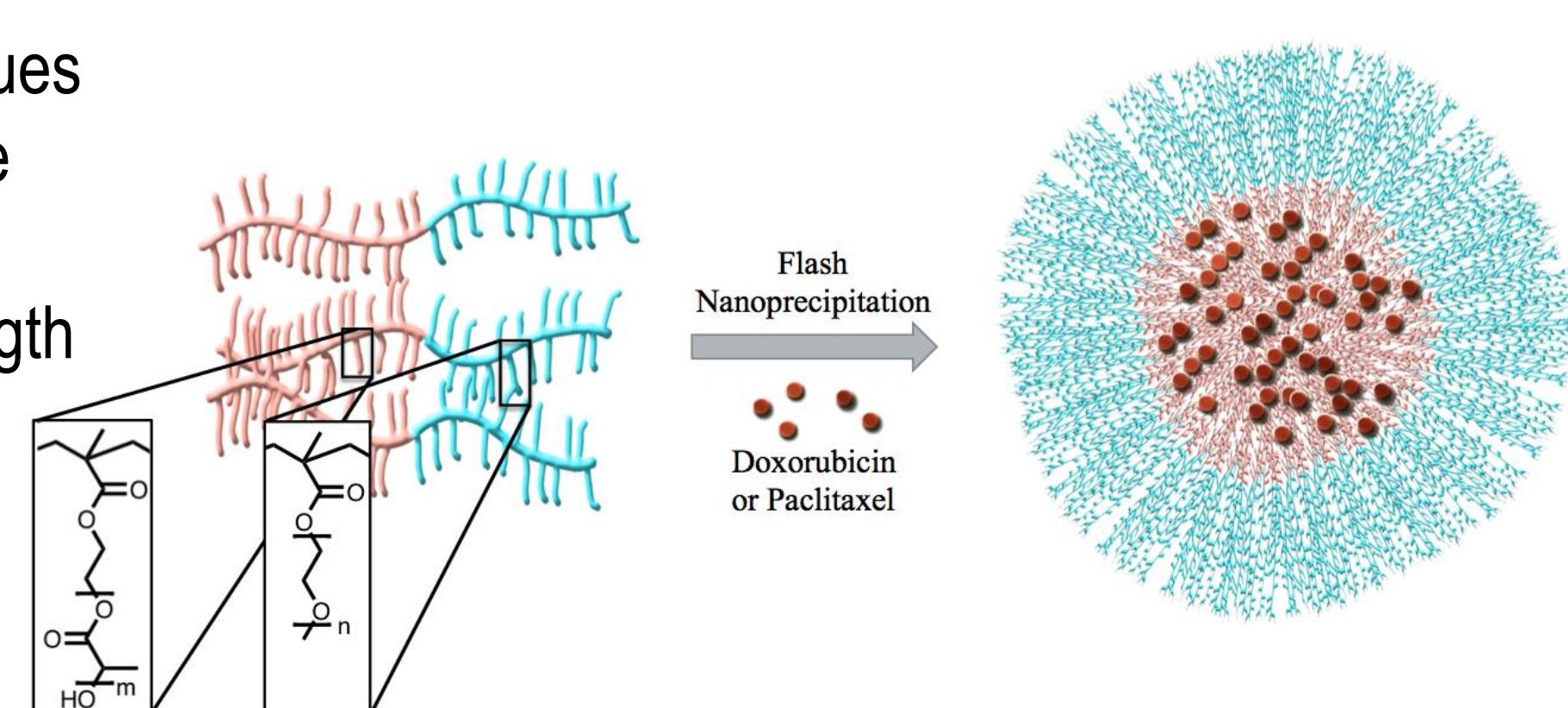




Introduction

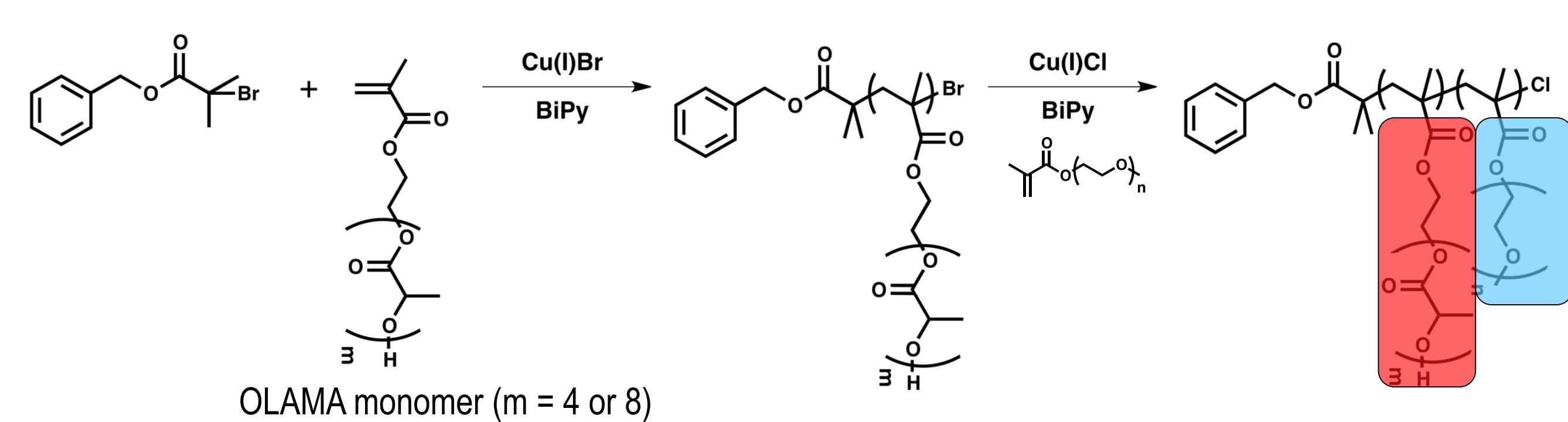
- Nanoparticle based drug delivery confers numerous potential advantages in treating disease
- PL(G)A-PEG based nanoparticle scaffolds have been clinically investigated for the delivery of various chemotherapeutics with promising results
- However, PL(G)A-PEG is limited to end group functionalization and incorporation of functional groups during the step growth polymerization is often challenging
- Brush polymer analogues of PL(G)A-PEG enable greater tunability
 - Tune backbone length
 - Tune brush length
 - Tune backbone chemistry
- Synthesis of scaffold from vinyl monomers enables ease of functional group incorporation within each block using inexpensive and commercially available monomers under standard polymerization conditions



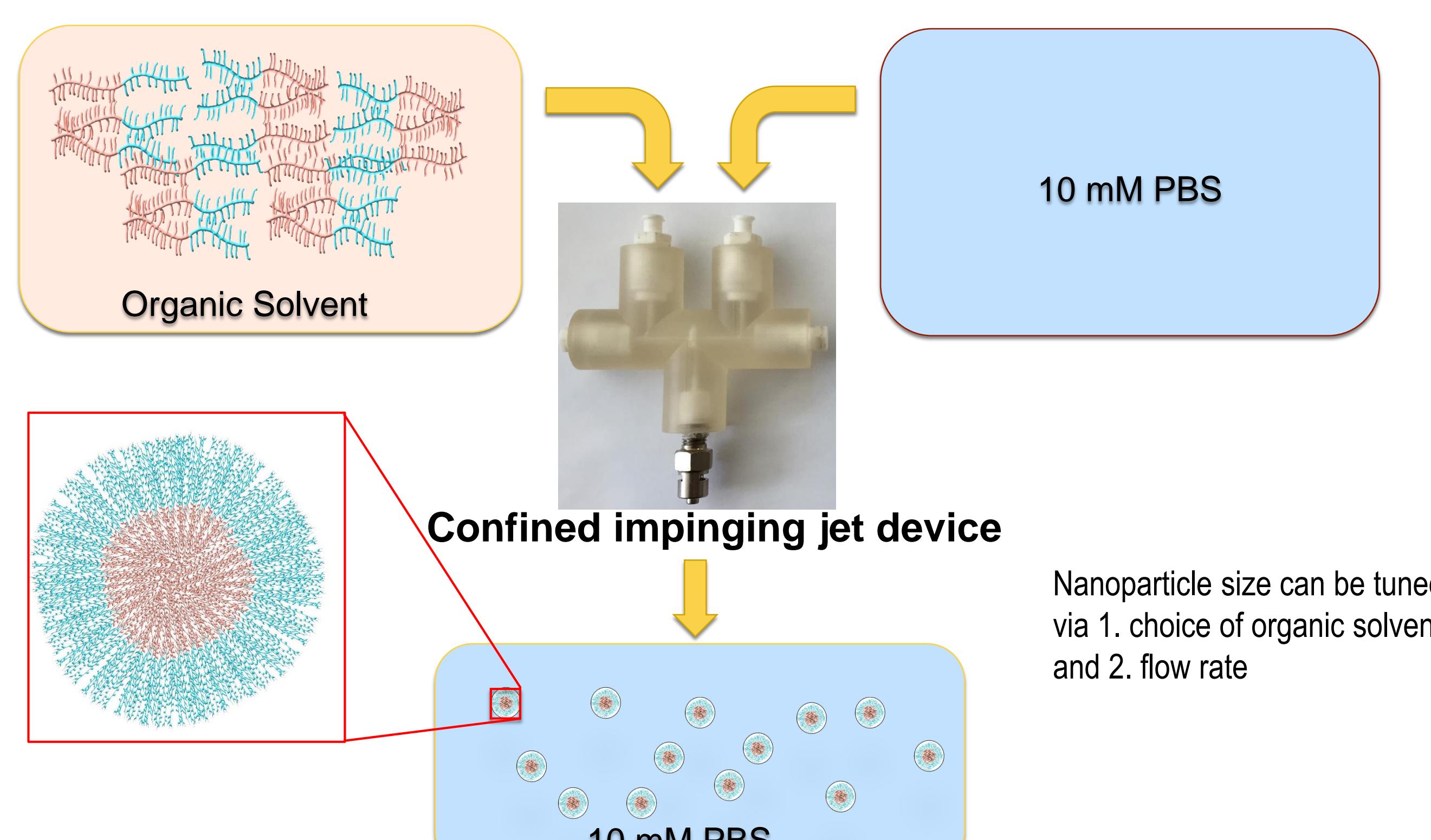
Experimental

Synthesis

- Prepared via controlled living radical polymerization
- Synthetic protocol enables facile incorporation of functionality within each block via incorporation of functional monomer



Nanoparticle Fabrication

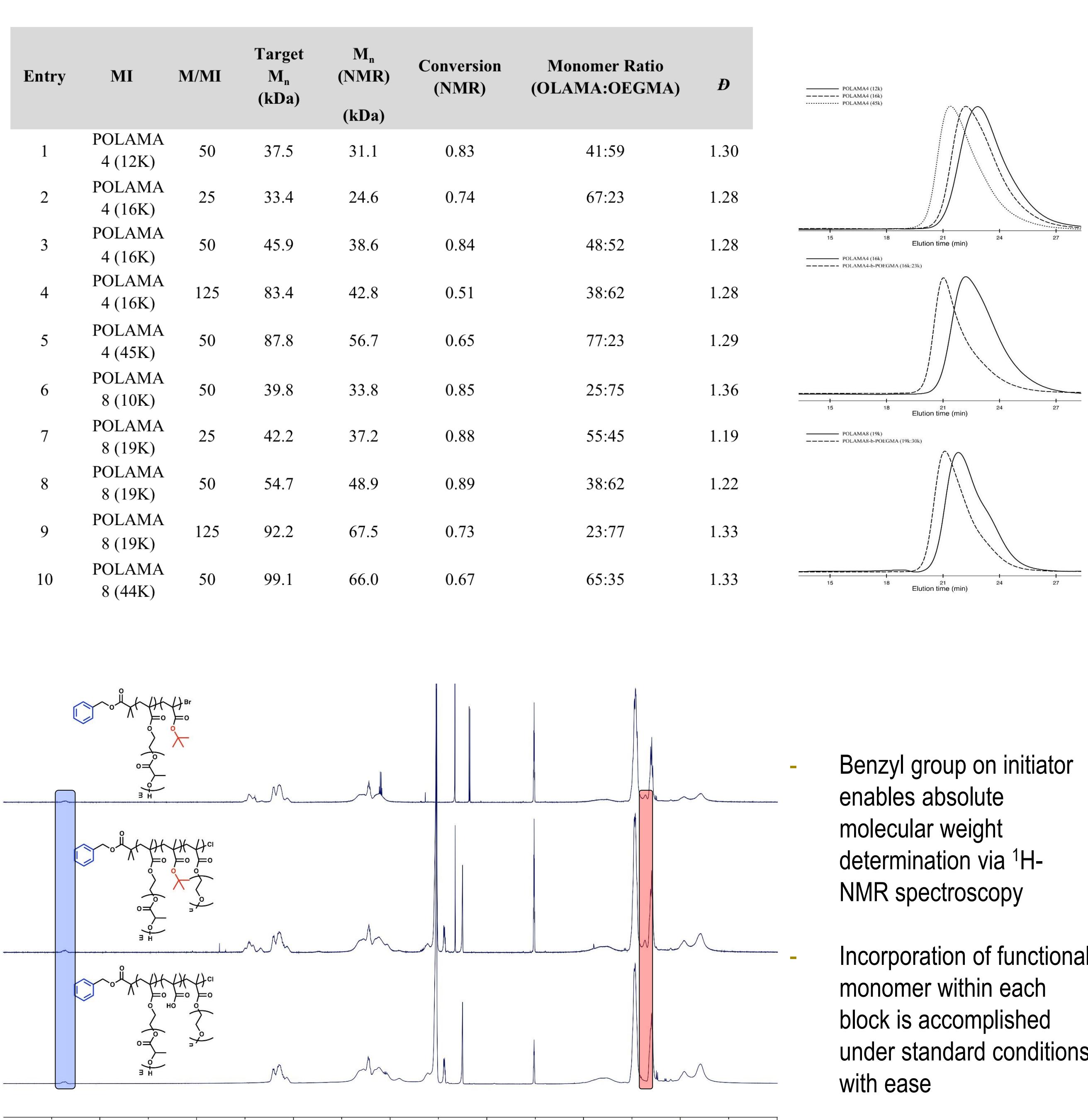


Results

Nanoparticle Properties

Monomer	Entry	M/I	Target M _n (kDa)	M _n (NMR) (kDa)	Conversion (NMR)	GPC		
						M _w (kDa)	D	
OLAMA4	12K	30	12.5	11.7	0.93	15.3	19.5	1.27
	16K	50	20.9	16.5	0.79	18.3	22.9	1.25
	45K	150	62.8	45.0	0.72	25.2	31.5	1.25
OLAMA8	10K	21	14.8	10.0	0.68	16.7	20.5	1.23
	19K	42	29.7	18.8	0.63	22.3	27.1	1.22
	44K	105	74.1	43.8	0.59	25.5	32.2	1.26

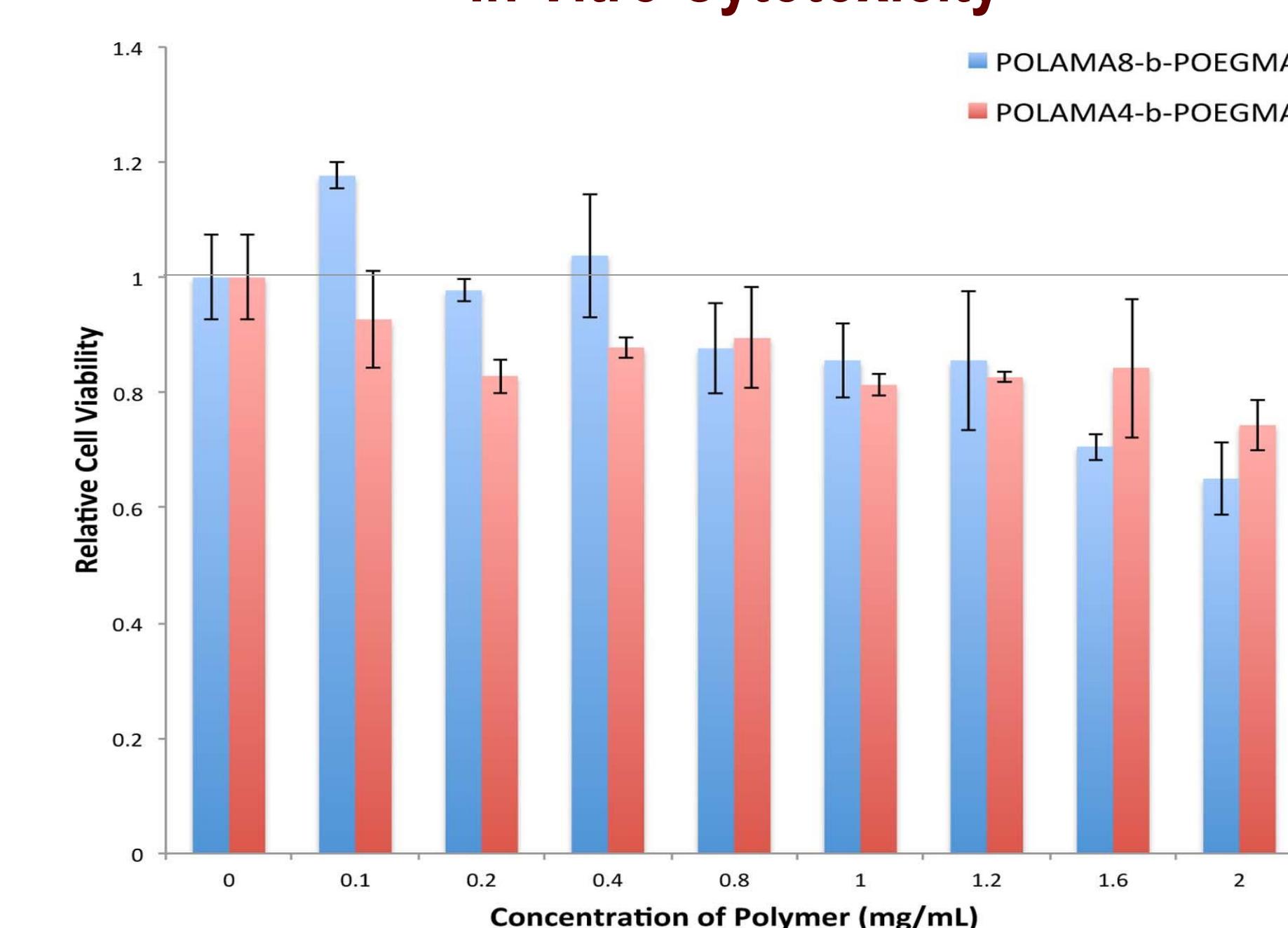
- Polymerization of each block was accomplished using ATRP
- All polymers exhibited a dispersity below 1.4



- Benzyl group on initiator enables absolute molecular weight determination via ¹H-NMR spectroscopy
- Incorporation of functional monomer within each block is accomplished under standard conditions with ease

Results

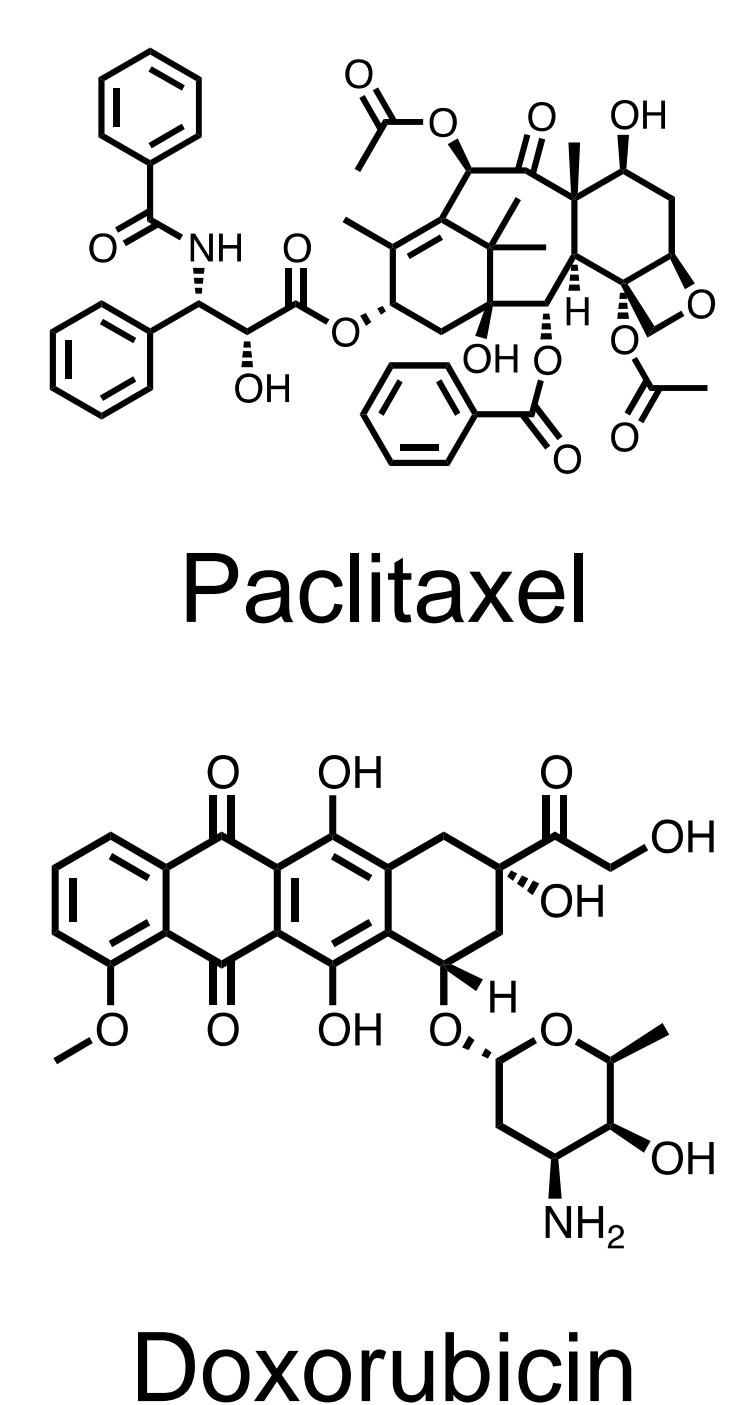
In Vitro Cytotoxicity



- Resazurin assay used to evaluate *in vitro* cytotoxicity
- Both POLAMA4-POEGMA and POLAMA8-POEGMA based nanoparticle scaffolds demonstrate minimal *in vitro* cytotoxicity in 3T3 NIH fibroblasts

Drug Loading

Drug	Solvent	Effective Diameter (nm)	Polydispersity	Loading Efficiency
Paclitaxel	THF	170±3	0.14	>96%
DOX-HCl	DMF	145±9	0.25	41%
DOX	DMF	264±21	0.36	61%



- All drug loading was performed at 10% w/w
- Drug loading quantitative for hydrophobic drugs such as paclitaxel and good for hydrophilic drugs such as DOX

Conclusions

- Amphiphilic block polymers comprised of POLAMA-POEGMA can be prepared via a controlled living radical polymerization
- The POLAMA-POEGMA amphiphilic copolymer can be used to prepare nanoparticles that exhibit excellent stability in PBS at 37 °C
- Nanoparticles prepared from POLAMA-POEGMA demonstrate minimal *in vitro* cytotoxicity
- The nanoparticle platform exhibits excellent drug loading capabilities

Acknowledgements and References

- Hoare, T.; Sadowski, L.P.; Luo, H.; Badv, M. "A Brush Amphiphilic Block Copolymer Enabling Fabrication of Self-Assembled Nanoparticles". U.S. Provisional Patent Application 62/360,615, filed July 11, 2016
- Ishimoto, K.; Arimoto, M.; Okuda, T.; Yamaguchi, S.; Aso, Y.; Ohara, H.; Kobayashi, H.; Ishii, M.; Morita, K.; Yamashita, H.; Yabuuchi, N. *Biomacromolecules*. 2012, 13, 3757
- Han, J.; Zhu, Z.; Qian, H.; Wohl, A.R.; Beaman, C.J.; Hoye, T.R.; Macosko, C.W. *J. Pharm. Sci.* 2012, 101(10), 4018
- Cheng, J.; Teply, B.A.; Sherifi, I.; Sung, J.; Gaurav, L.; Gu, F.X.; Levy-Nissenbaum, E.; Radovic-Moreno, A.F.; Langer, R.; Farokhzad, O.C. *Biomaterials*. 2007, 28(5), 869

