Rational Design of Nanoparticle Morphology and Surface Charge to Specify Cellular Uptake

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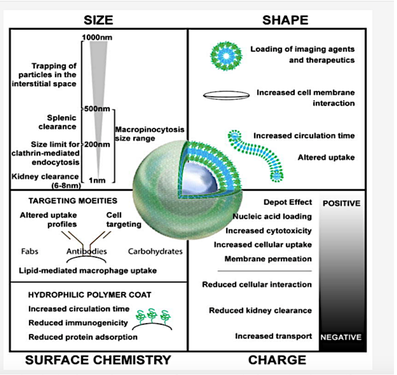
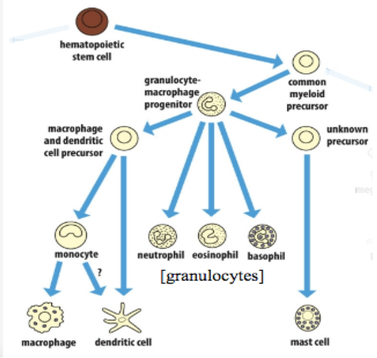
Background and Rationale

Introduction to Nanoparticle-Facilitated Drug Delivery

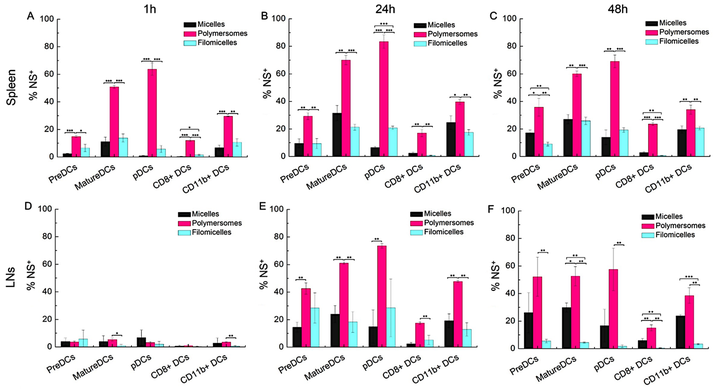


The physicochemical properties of a nanoparticle determine the specific cells it has access to (Allen et al. 2016).



A visual representation of the developmental pathways for cells of the mononuclear phagocyte system(Parham 2014).

Morphology Impacts Nanoparticle Biodistribution

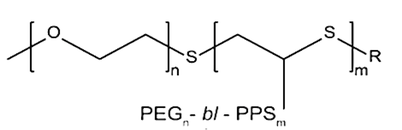


The varying uptake rates of nanoparticles by different immune cells in the spleen and lymph nodes of mice (Yi et al. 2016).

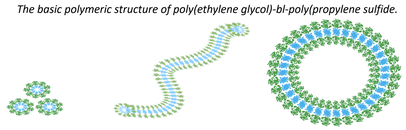
Rationale for Modified Morphology and Surface Charge

- **The surface chemistry of nanoparticles has also been found to impact nanoparticle biodistribution (Gagner et al. 2012).**
- **<u>Purpose</u>: To design nanoparticles <u>with modified morphology and surface charge combinations</u> to explore if multiple nanoparticle physicochemical modifications can synergize to <u>further enhance cell-specific targeting</u>.**

PEG-*bl*-PPS Nanoparticles



The basic polymeric structure of poly(ethylene glycol)-bl-poly(propylene sulfide).



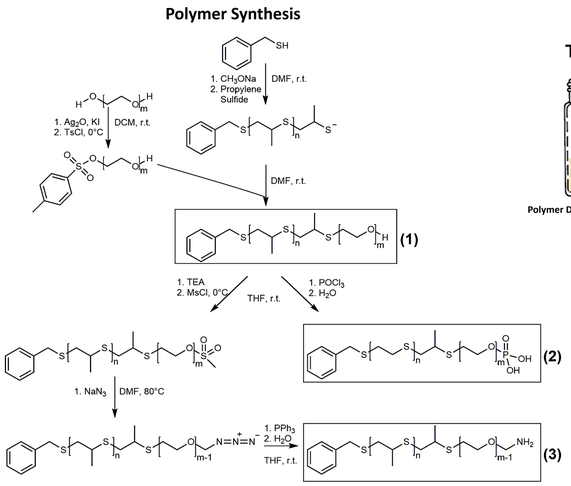
Micelles *fPEG=0.58.* ***Filomicelles*** *fPEG=0.38* ***Polymersomes*** *fPEG=0.31*

The distinct nanostructures/nanoparticles PEG-bl-PPS polymers can form.

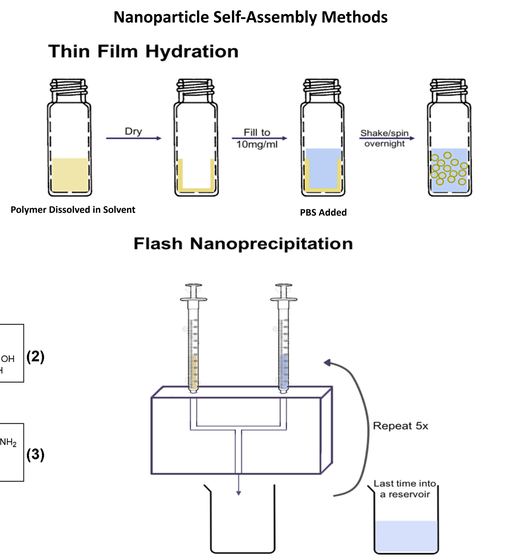
- **Poly(ethylene glycol)-*block*-poly(propylene sulfide) (PEG-*bl*-PPS) are amphiphilic block copolymer (BCP) systems capable of self-assembling into diverse nanostructures.**
- **Control over the hydrophilic mass fraction(fPEG) of BCP systems will determine the specific nanostructures formed.**

Methods

Polymer Synthesis and Nanoparticle Assembly



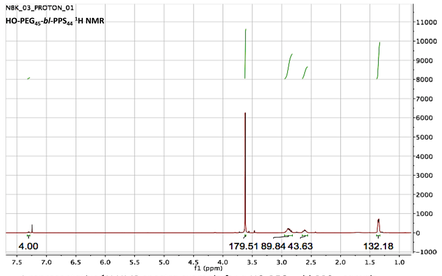
Scheme 1. *Synthesis of HO-PEG-bl-PPS to assemble neutral NP*
Scheme 2. *Synthesis of PO_3-PEG-bl-PPS to assemble anionic NP*
Scheme 3. *Synthesis of NH_2-PEG-bl-PPS to assemble cationic NP*



Results

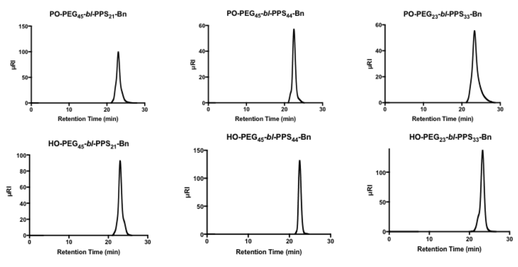
Polymer Characterization

Polymer Chain Length Confirmation via ^{1}H NMR



A representative ^{1}H NMR spectra example for a HO-PEG_{45} -bl-PPS_{44} sample.

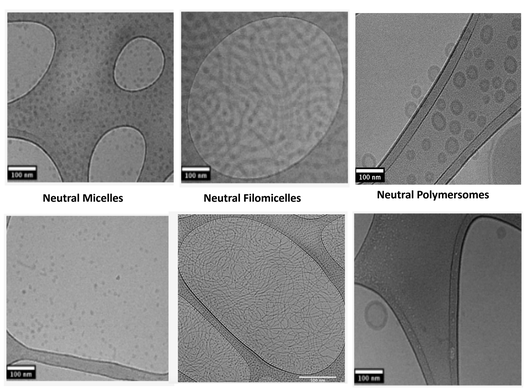
Polymer Product Composition Confirmation via GPC



GPC results for neutral and anionic PEG-bl-PPS polymers to confirm the sufficient removal of side-products in the final polymer product.

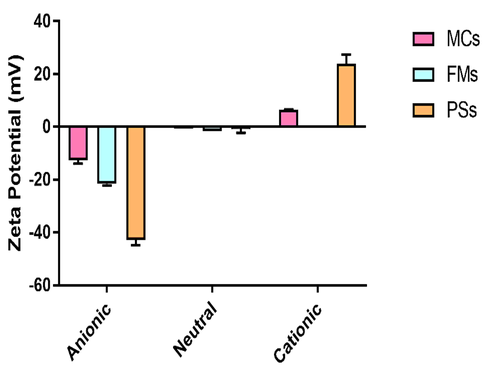
Nanoparticle Characterization

Cryo-TEM Imaging for Structural Confirmation



Images obtained via Cryo-TEM for all of the neutral and anionic PEG-bl-PPS nanoparticle samples.

ELS to Obtain Zeta Values Needed for Charge Confirmation

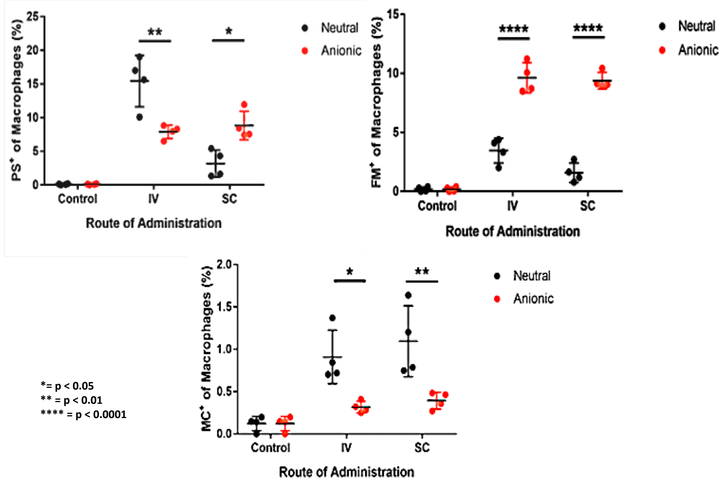


A graphical representation of the zeta potentials for each nanoparticle sample.

Future Direction

In-vitro and *In-vivo* Biodistribution Studies

- **The nanoparticles will be fed to splenocytes *(in-vitro)*—immune cells of the spleen—and also injected into mice *(in-vivo)* for fluorescent imaging studies.**
- **Flow cytometry and confocal microscopy will be used to quantitatively and qualitatively assess the biodistribution.**



Biodistribution results comparing the rate of uptake by macrophages for nanoparticles differing in morphology, surface charge, and route of administration. Nanoparticles with identical morphology but differing surface charges were loaded with different fluorescent dyes. PBS was used as control.

- **The goal is to ultimately determine the <u>morphology and surface charge combination</u> that leads to the most efficient delivery of PEG-*bl*-PPS nanoparticles to <u>dendritic cells</u>, the most effective antigen-presenting cells.**

Acknowledgements

We acknowledge staff and instrumentation support from the Structural Biology Facility at Northwestern University. This work made use of the IMSERC at Northwestern University, which has received support from the NSF (CHE-1048773); Soft and Hybrid Nanotechnology Experimental (SHyNE) Resource (NSF NNCI-1542205); This work was supported by the Northwestern University – Flow Cytometry Core Facility supported by Cancer Center Support Grant (NCI CA060553). The authors acknowledge Jonathan Remis (Structural Biology Facility, NU) for their contribution to cryoTEM image acquisition. This research has been funded by the Undergraduate Summer Research Grant and the Undergraduate Academic Year Research Grant awarded by Northwestern University's Office of Undergraduate Research, as well as the CLP Summer Scholars Fellowship awarded by the Chemistry of Life Processes Institute.

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