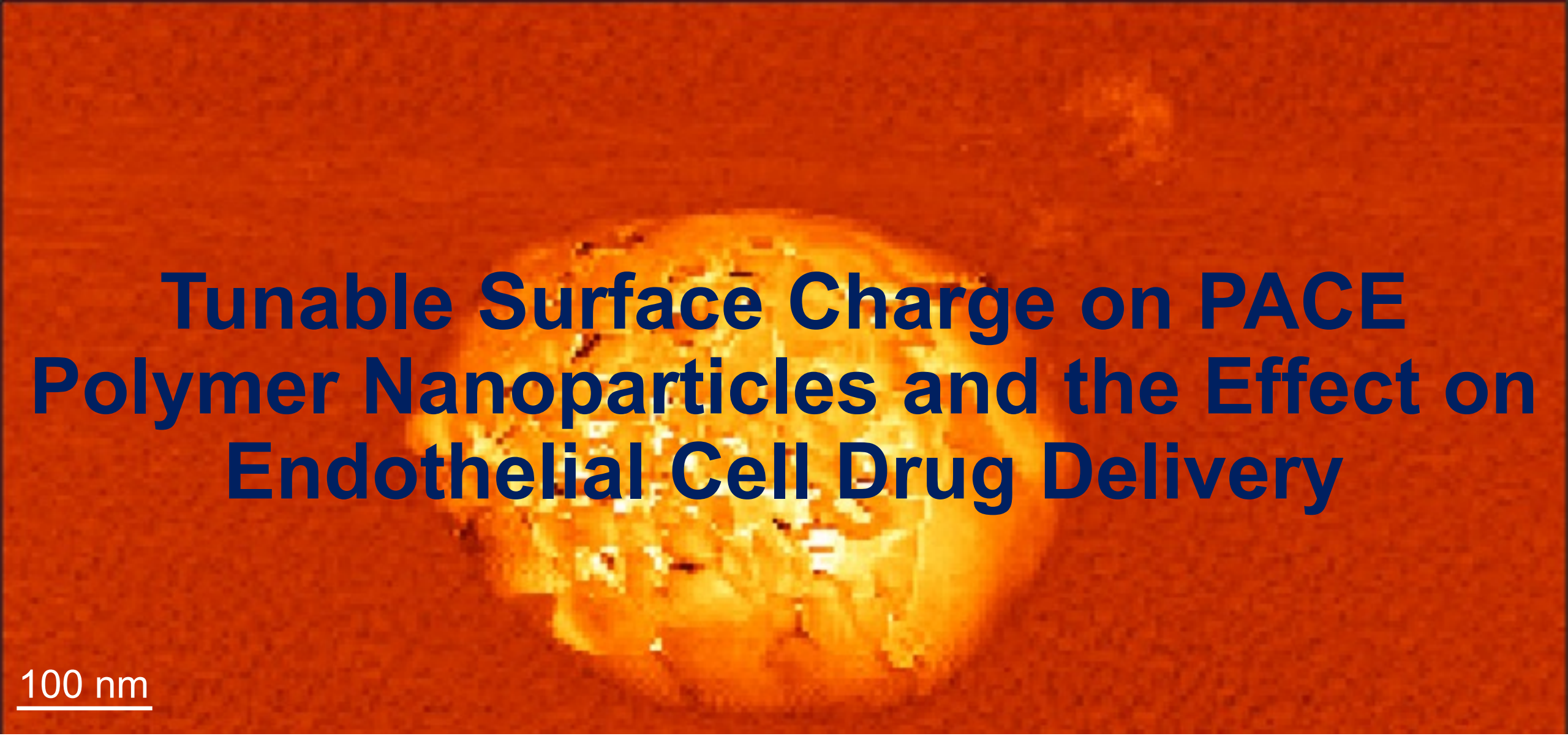
Tunable Surface Charge on PACE Polymer Nanoparticles and the Effect on Endothelial Cell Drug Delivery



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Department of Chemical Engineering and Biological Engineering
Villanova University

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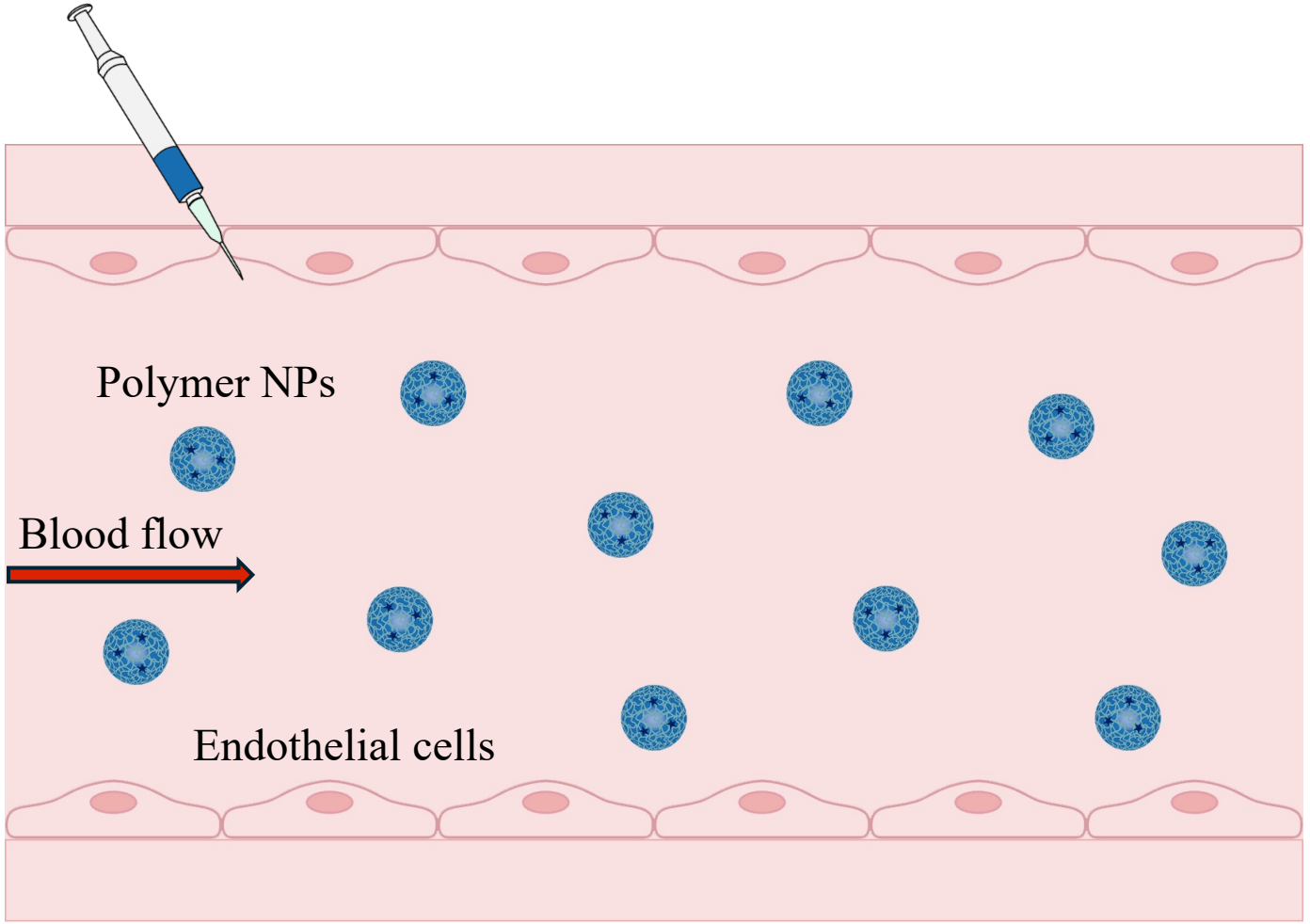
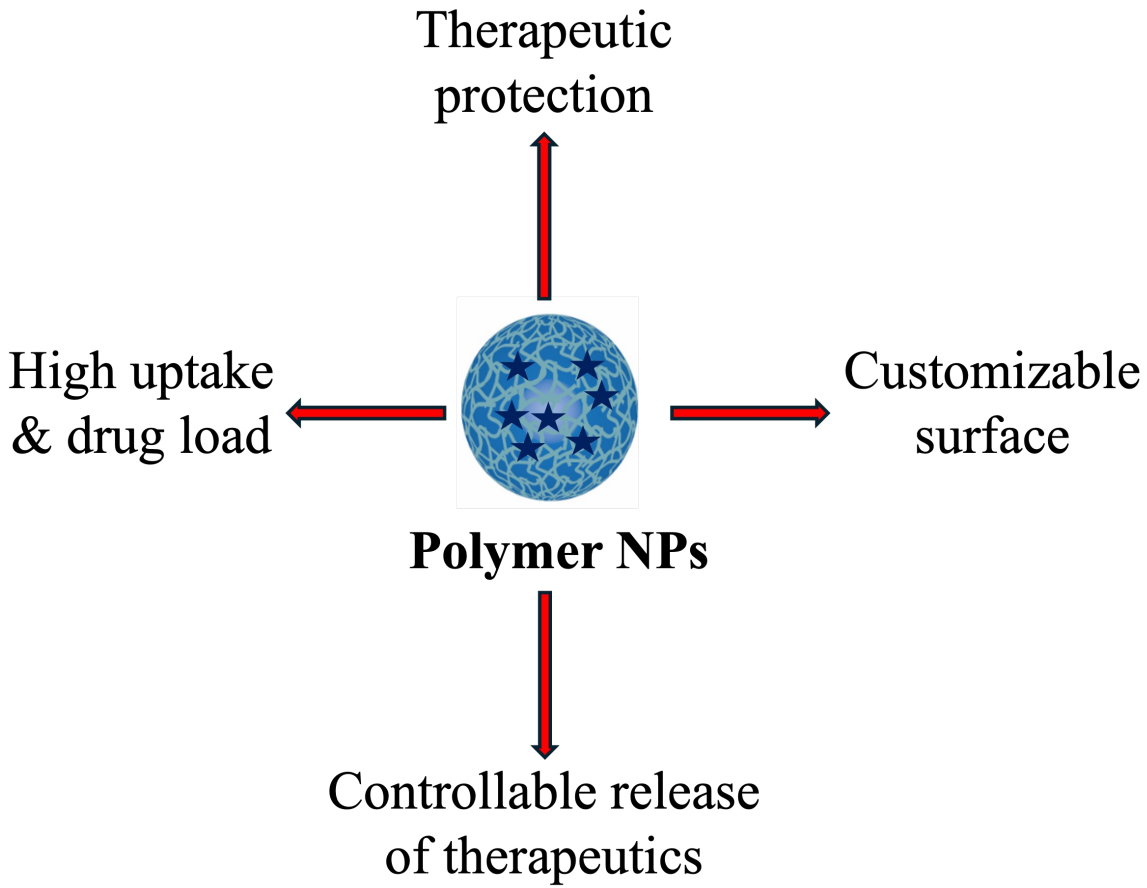
Polymer NP to deliver therapeutics



★ = loaded cargo: drug, nucleic acid….



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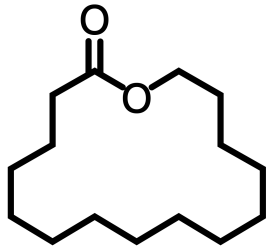
Poly-amine-co-ester (PACE) polymer backbone

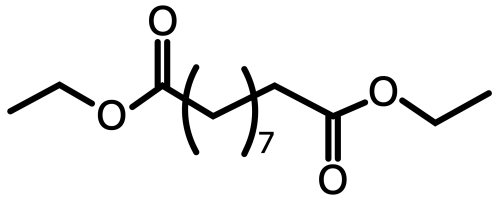
PDL



Lactone

Increase the biocompatibility for the polymer

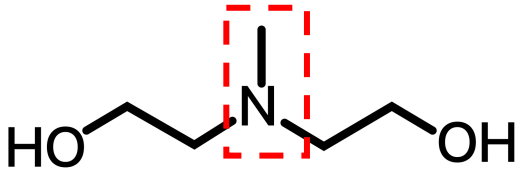
DES



Diester

Provide hydrophobicity to stabilize the polymer structure

MDEA

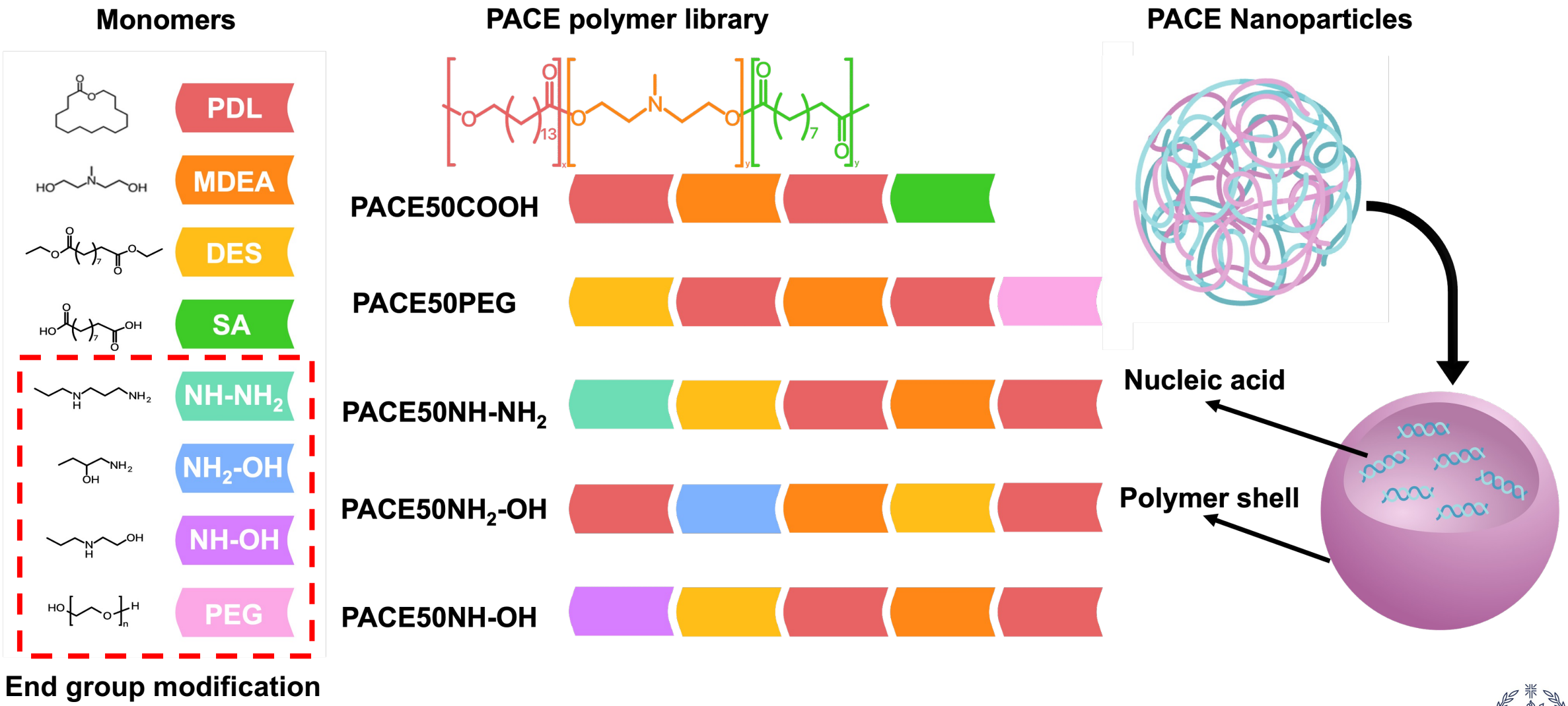


Diethanolamine

(+) positive charged
nucleic acid stabilization & transfection

1. Zhou, Jiangbing, et al. Nature materials, 2012.
2. Kauffman, Amy C., et al. Biomacromolecules, 2018.

PACE NP formulation



1. Jiang, Yuhang, et al. *Nano letters*, 2020.

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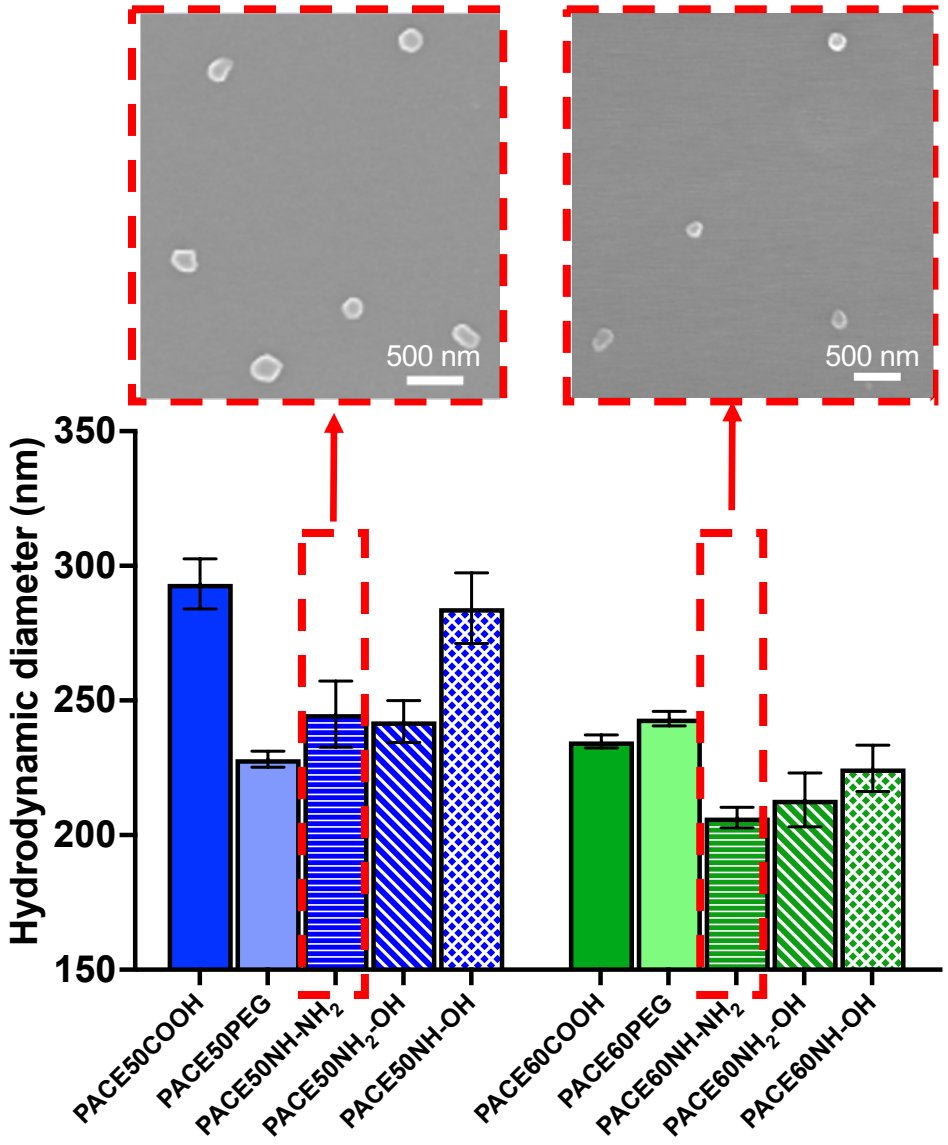
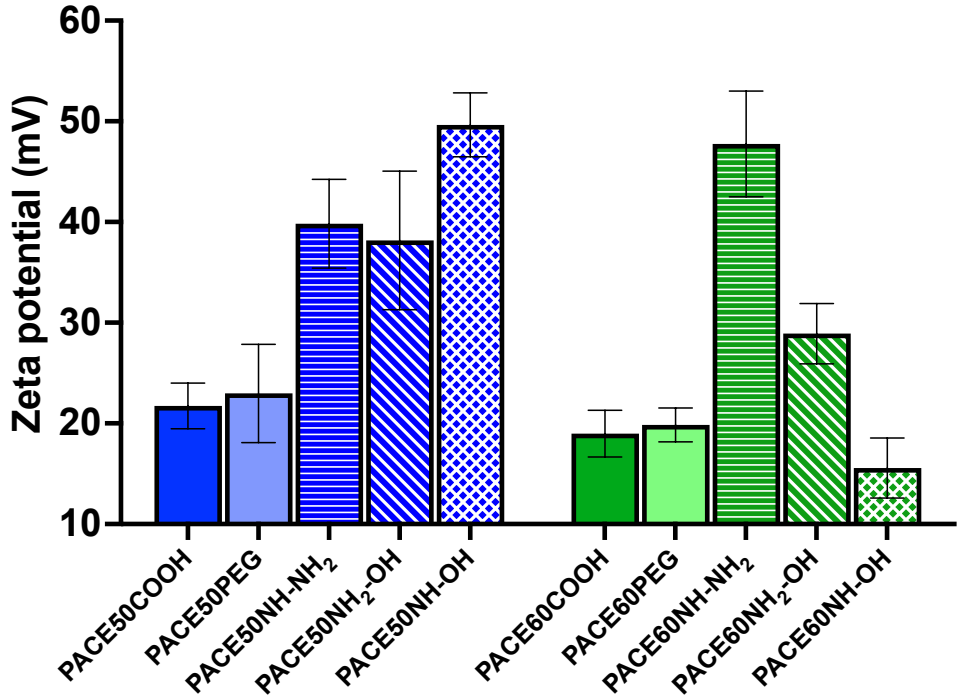
Characterization of PACE NPs



- Average hydrodynamic size: 200 nm – 300 nm
- More amines lead to higher zeta potential
- End groups tune the PACE NP zeta potential



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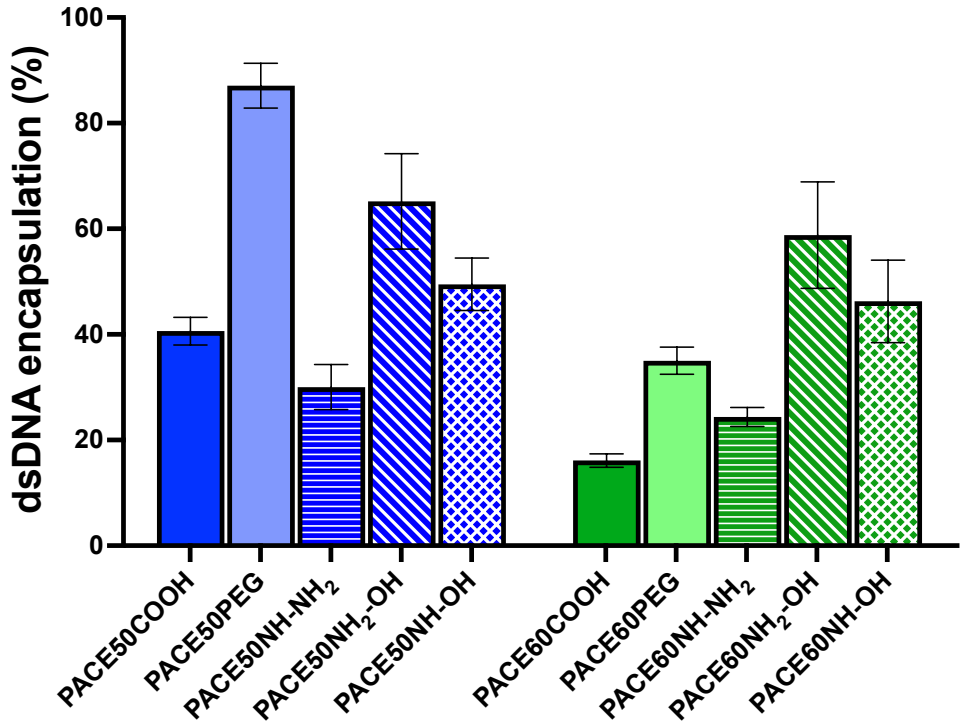
Encapsulation Efficiency of PACE NPs



- The chemical changes for PACE polymer also affect nucleic acid loading
- Increased nucleic acid loading results from the additional amine group incorporation

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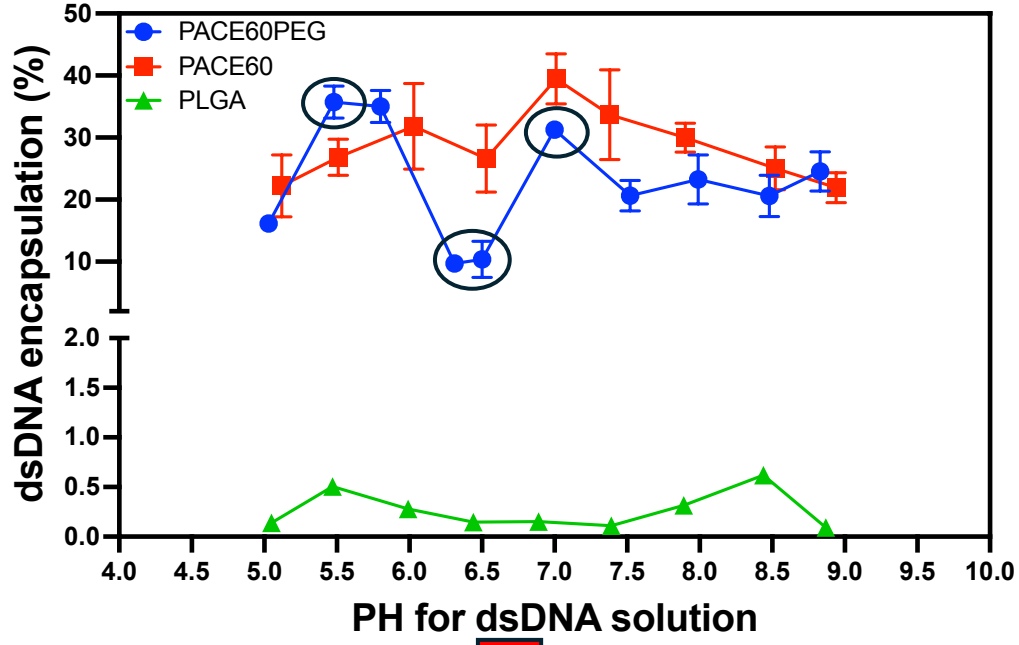
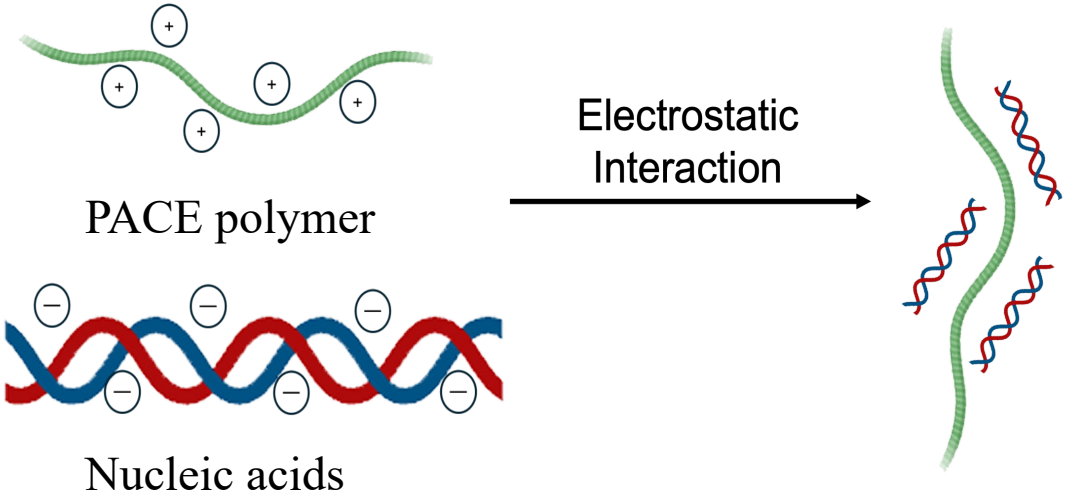
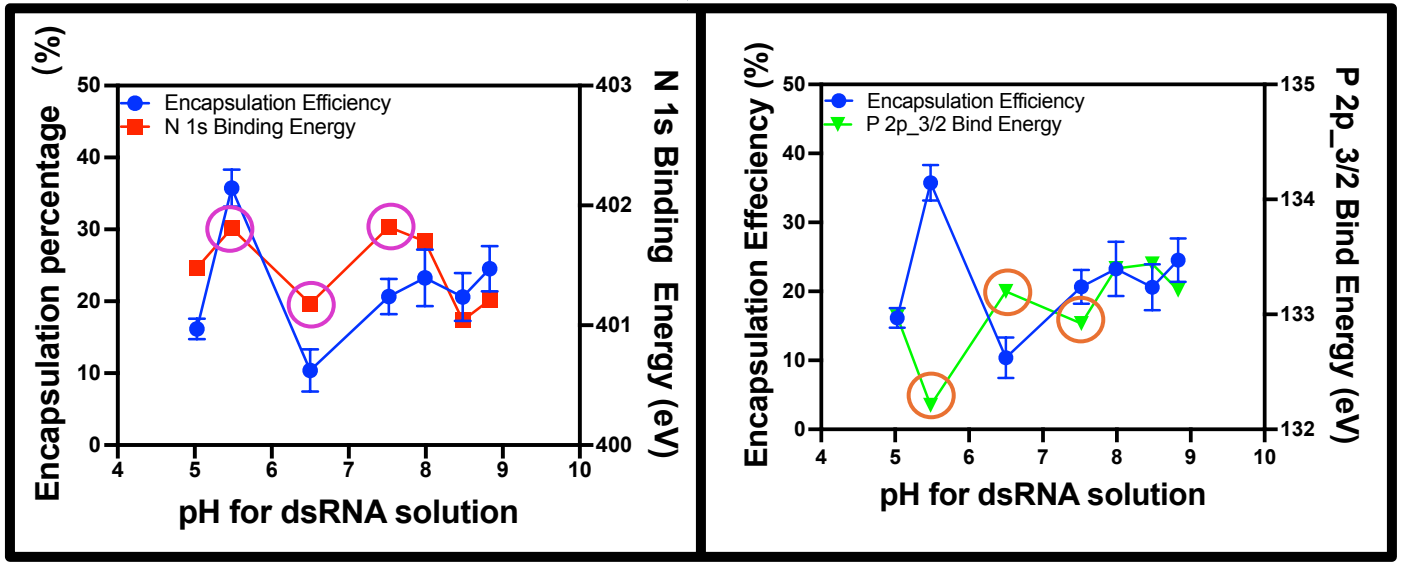
Encapsulation Efficiency of PACE NPs





XPS for PACE60PEG



- The interaction binding energy and indicates the encapsulation efficiency is correlated with amine binding energy but inversely correlated with phosphate binding energy

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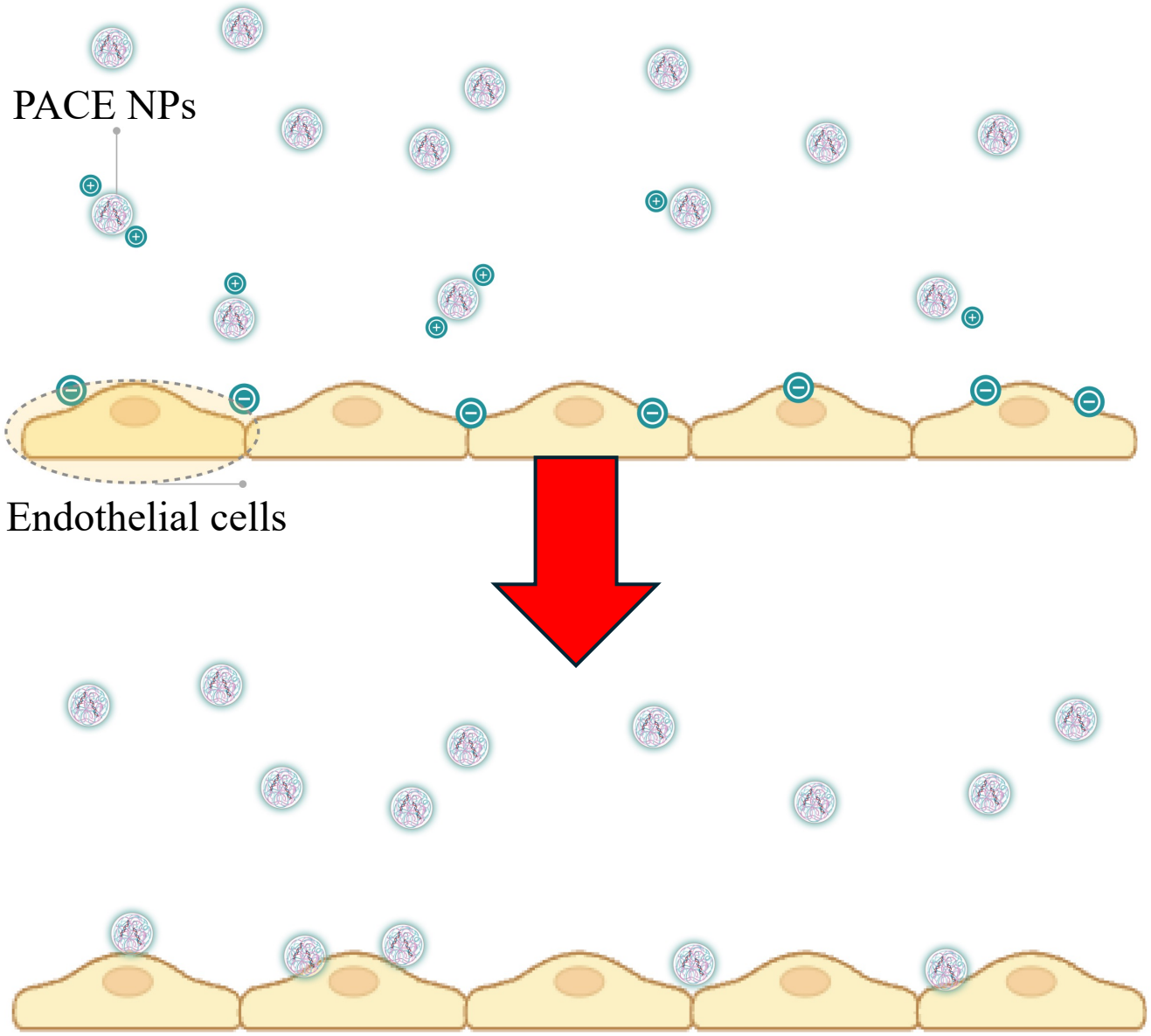
Interaction between PACE NPs and Endothelial Cells



- Increased endothelial cell uptake caused by electrostatic interaction between positively charge NPs and negatively charged cell membrane

- Highly positive charged NPs may cause cytotoxicity to the cells. Tunable surface charge for NPs significantly affect the extent of cellular uptake

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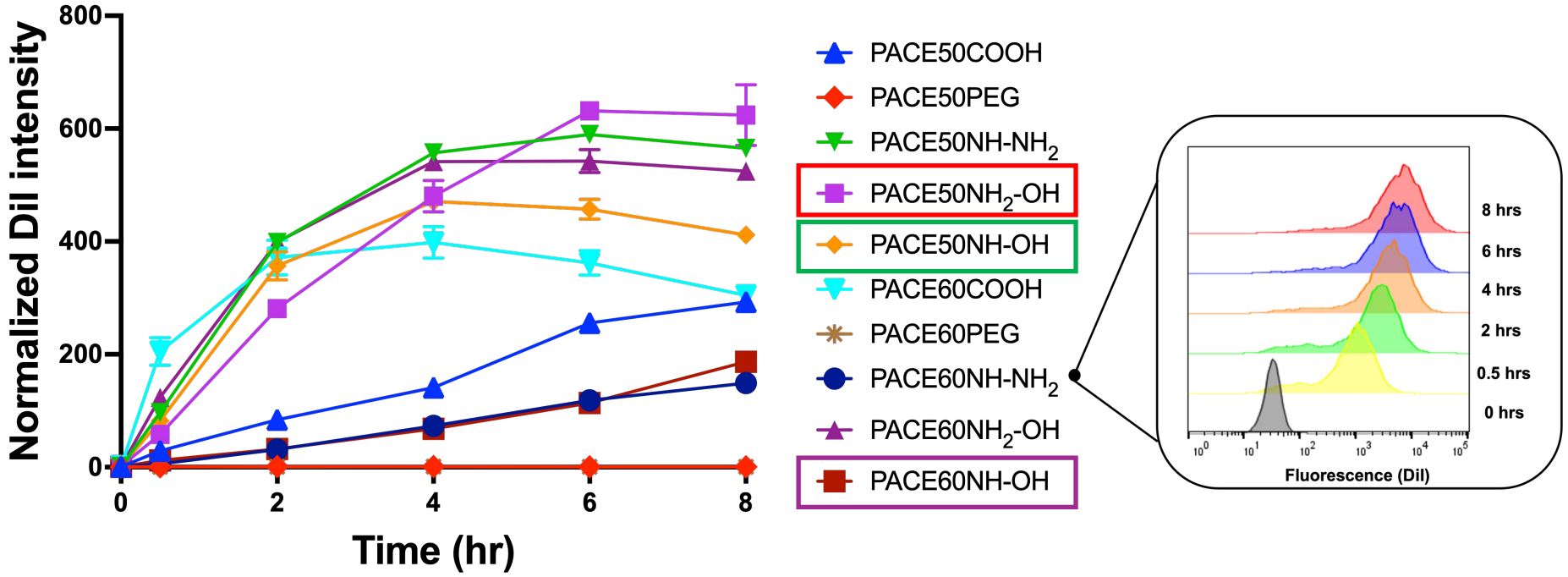
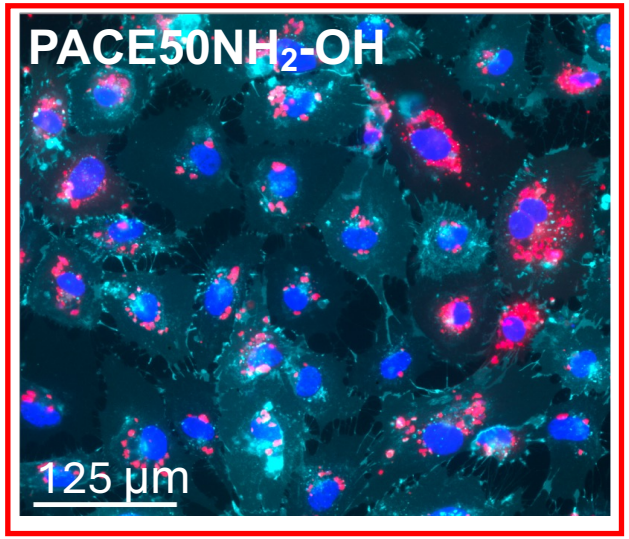
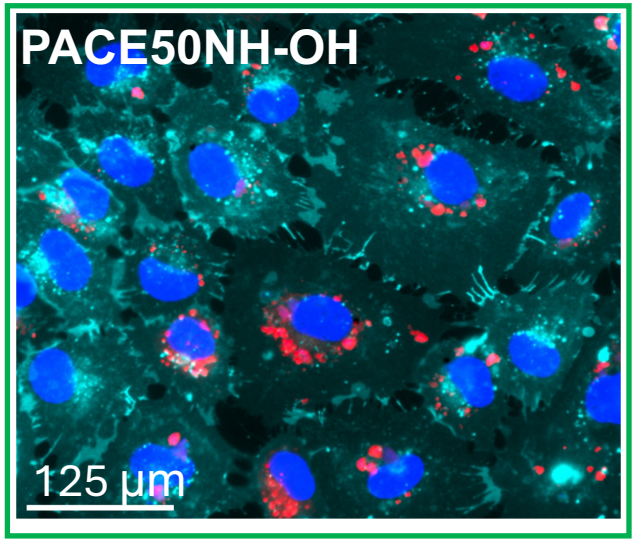
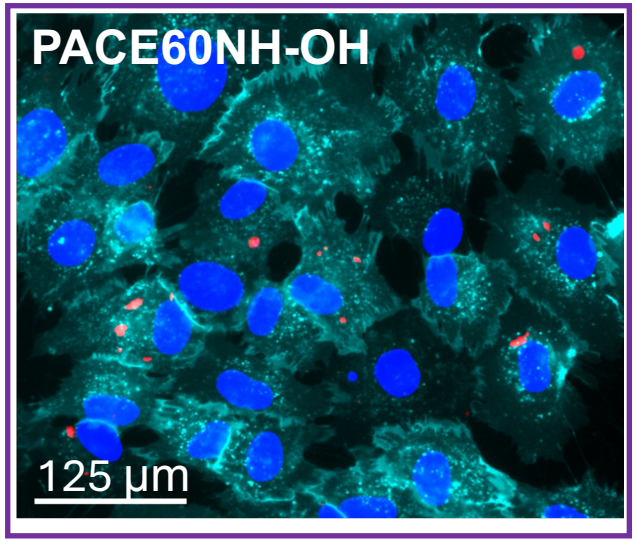
Endothelial Cell uptake by PACE NPs









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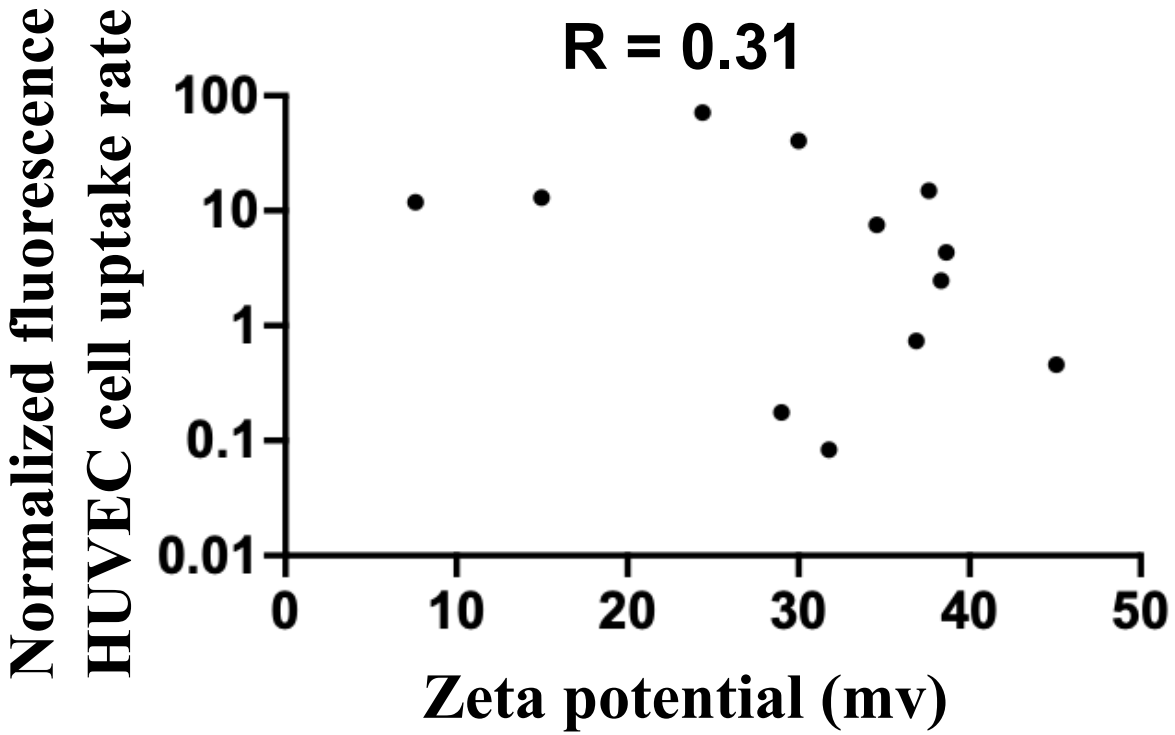
Weak correlation between PACE NP surface charge and endothelial cell uptake



- The correlation with endothelial cell uptake and NP zeta potential is not significant
- NP surface protonation capability is a new direction to demonstrate the relationship with endothelial cell uptake

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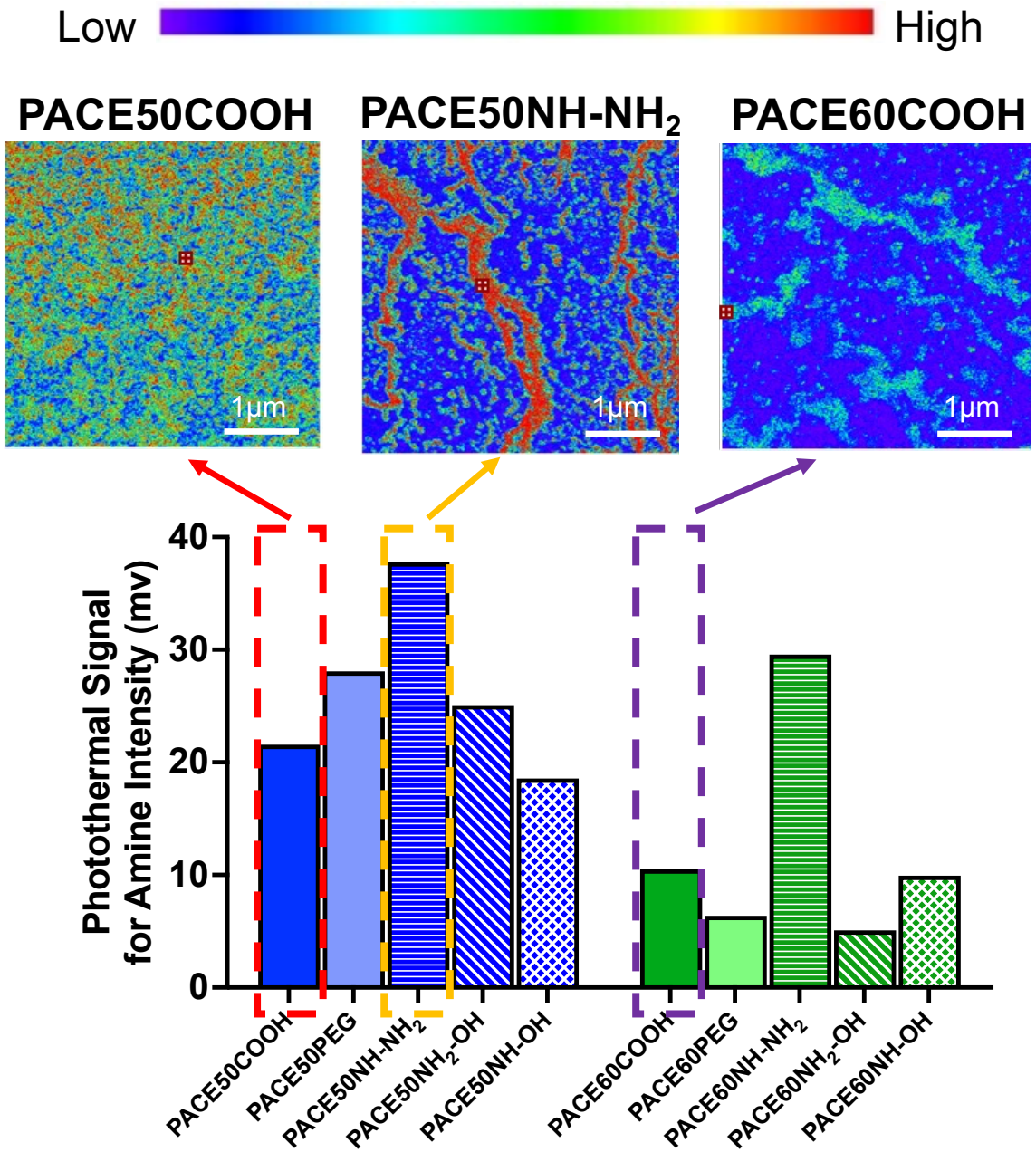
PACE NP amine density



- More redness means higher amine group density on the PACE NP surface
- More amine group content or higher amine density results in higher PACE NP surface protonation capability

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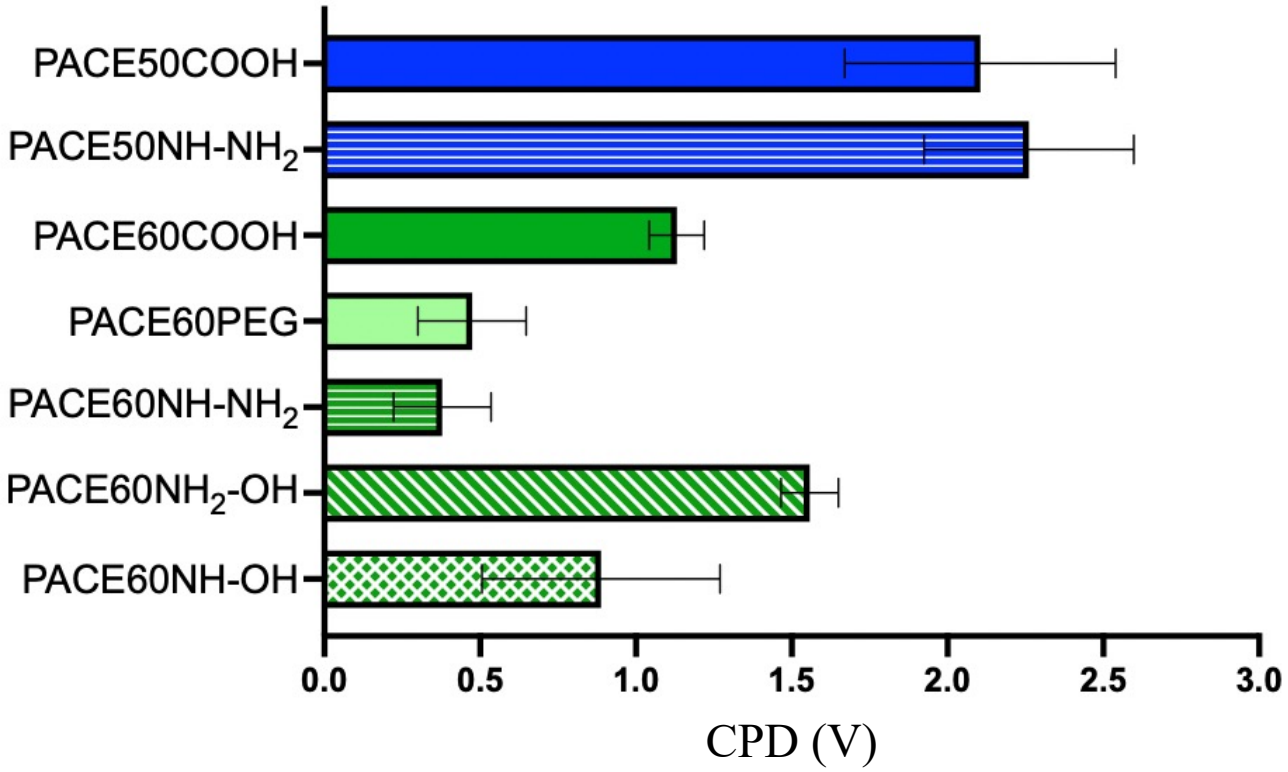
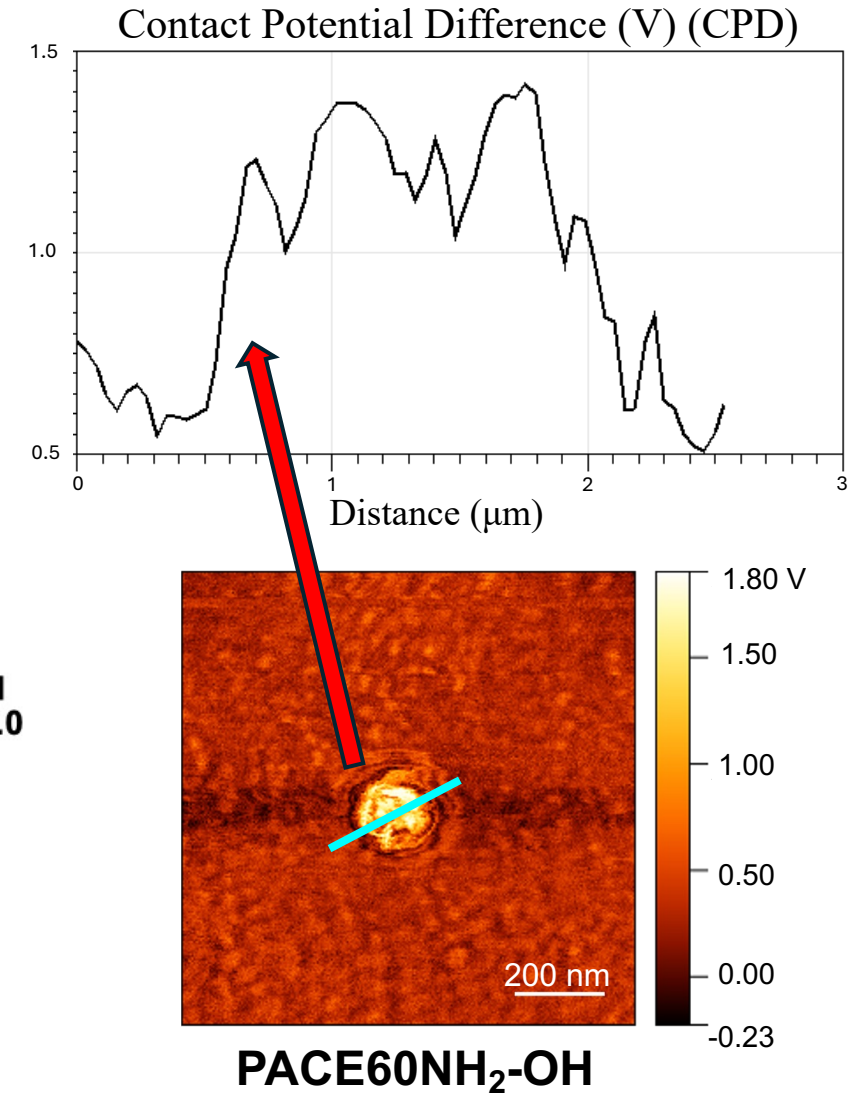
PACE NP surface protonation





Increased CPD values correspond to higher endothelial cell uptake

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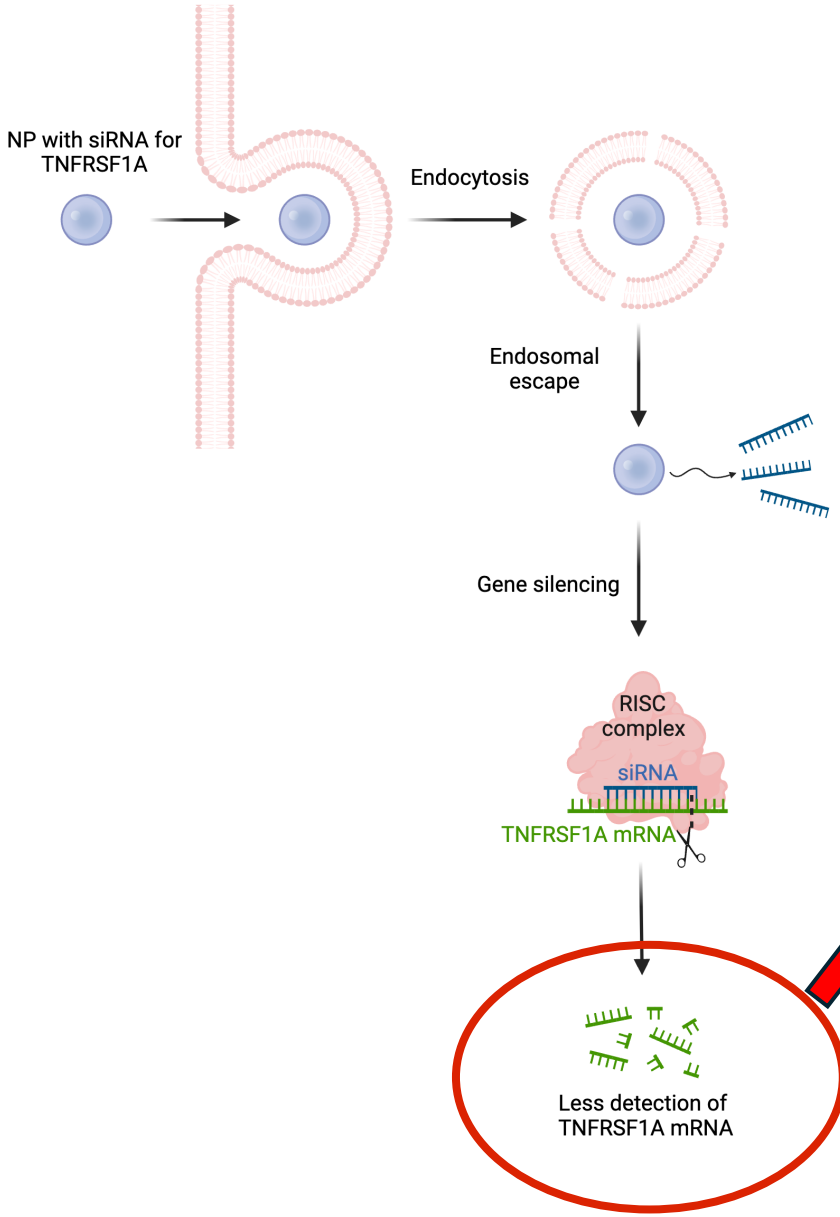
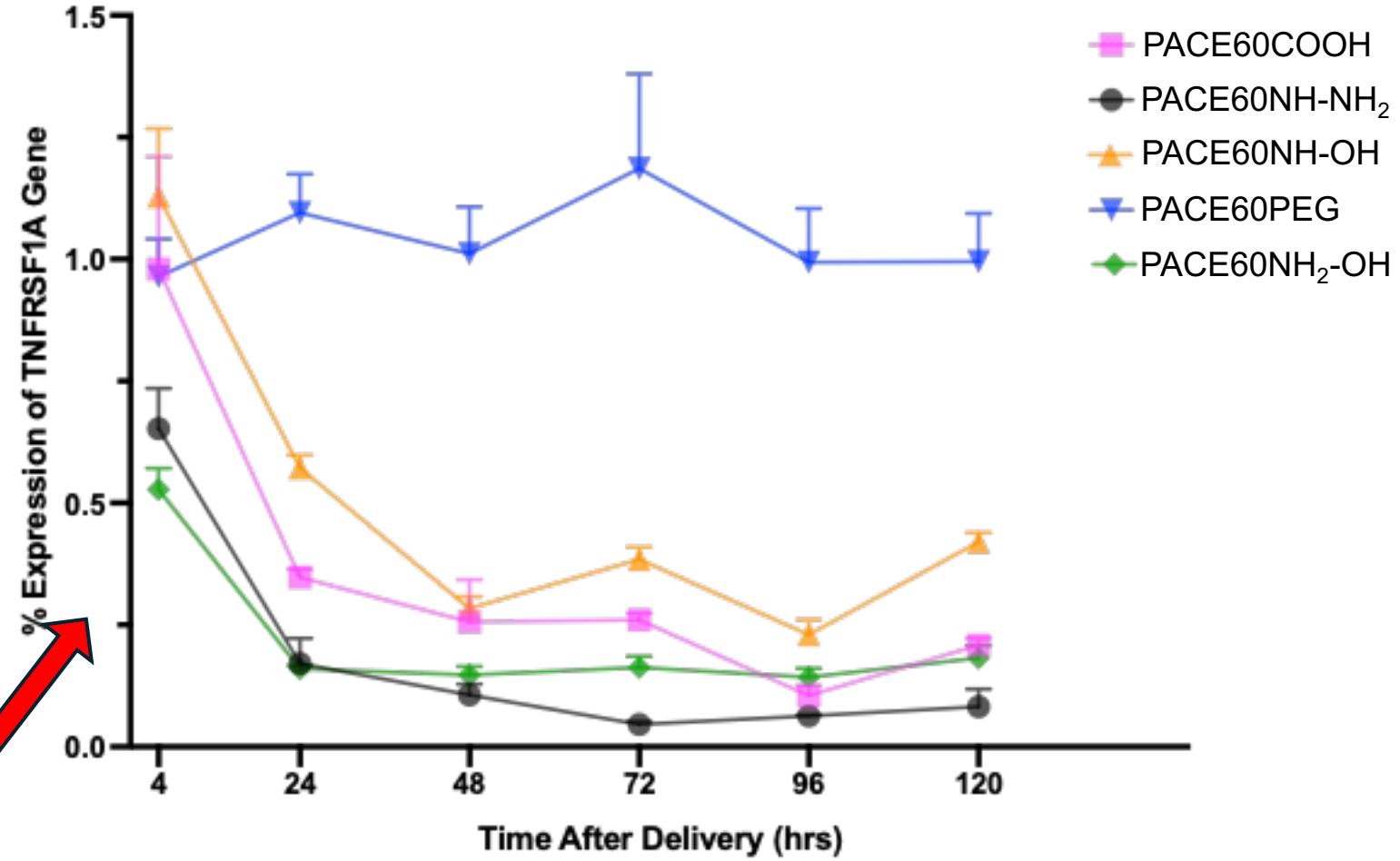
Cellular Uptake of NPs Correlates with Knockdown Activity





Higher cellular uptake also leads to more effective gene therapy delivery

More detail shown in **Poster 171** by Valerie Lallo at **6:30 pm to 7:30pm** on **07/15** in the exhibition hall, **Hall E**.

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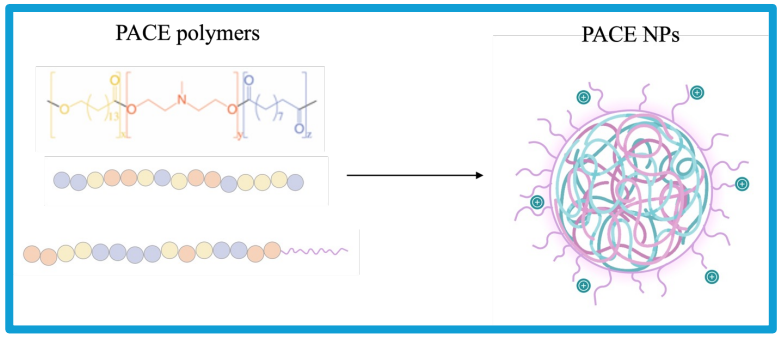
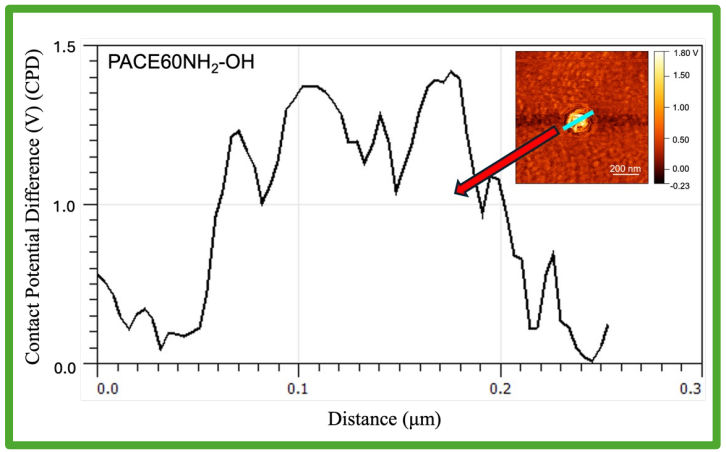
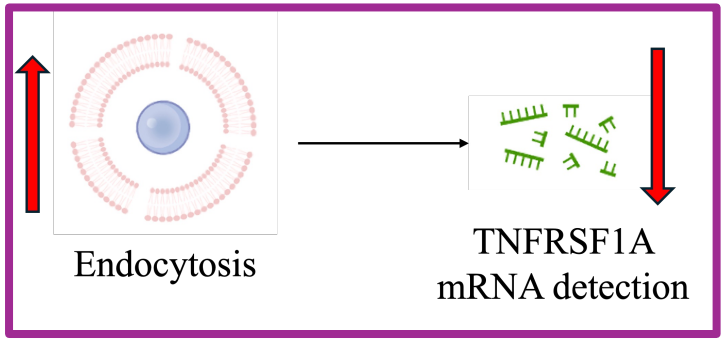
Conclusion



Chemical group modifications on PACE NP surface have major impact on endothelial cell uptake rather than nucleic acid loading



Polymer PACE NP surface protonation capability is more crucial to correlate with endothelial cell uptake compared to zeta potential representing the average charge of a whole NP



Higher endothelial cell uptake and higher nucleic acid loading also result in a more effective gene knockdown activity for gene therapy

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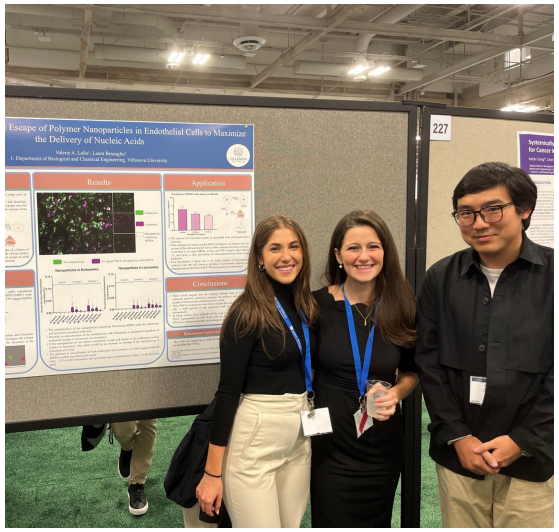
Acknowledgement



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VILLANOVA UNIVERSITY

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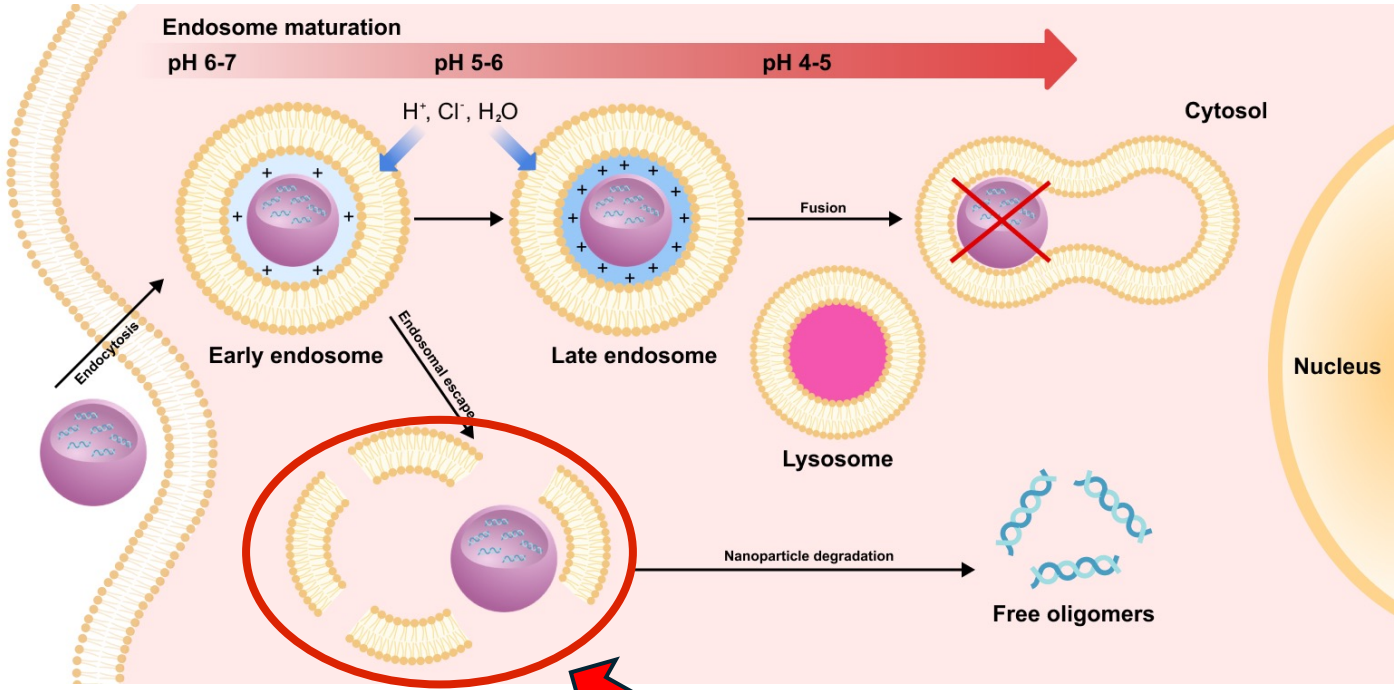
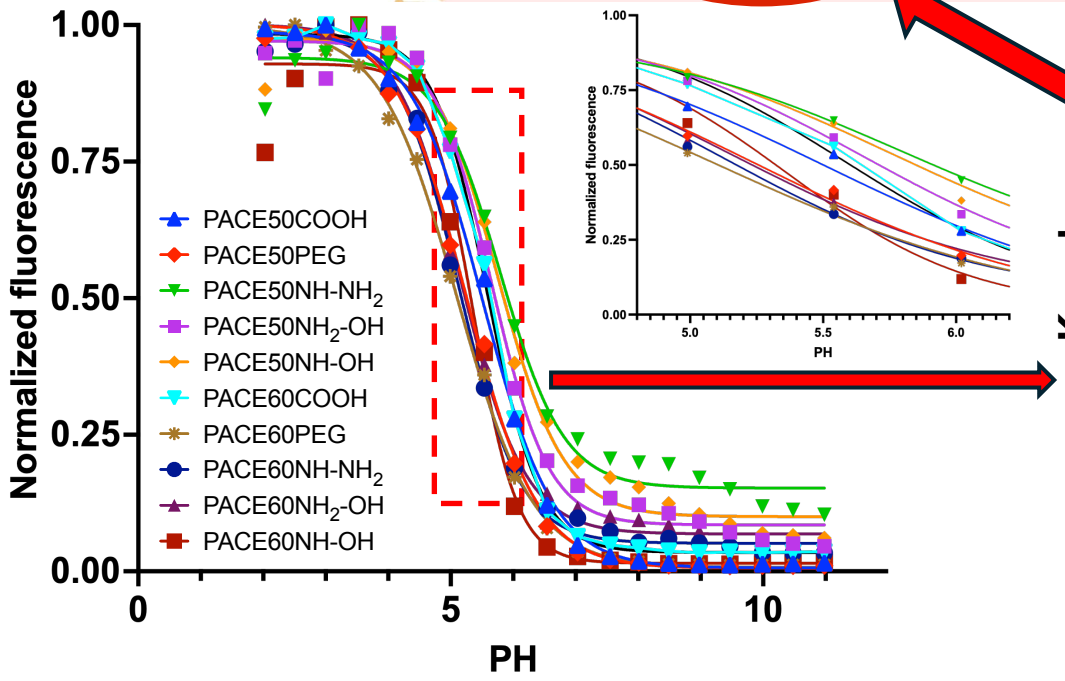
NIH National Heart, Lung, and Blood Institute

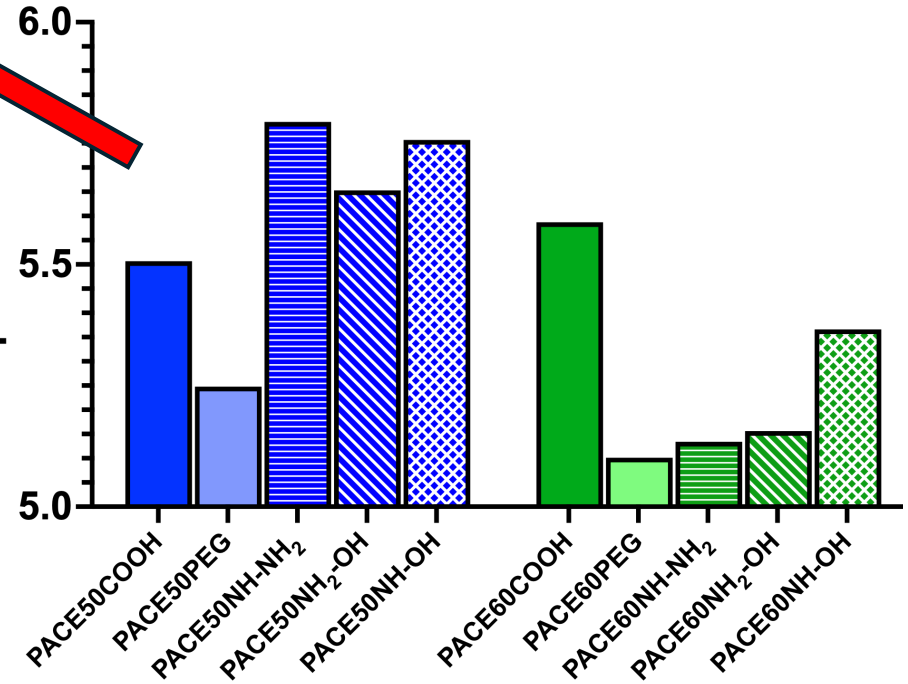
K99/R00 HL157552
PI: Laura Bracaglia

Thank you!

pKa of PACE NPs







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