Controlled Release of siRNA from Hydroltically Degradeable Nanomicelles for Potent Gene Knockdown
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INTRODUCTION
Small interfering RNAs (siRNAs) can be used to silence almost any gene in the body, this premise allows siRNA to be utilized as a targeted therapeutic agent against disease[1]. However, intracellular release of siRNA from NPs since they have been internalized is a limiting step in siRNA bioavailability and bioactivity. Therefore, we have developed a vehicle for enhanced siRNA release post-endosomal escape.

RNA Interference
siRNA Release
Cellular Uptake
Gene Knockdown
Conclusions and Future Work
References & Acknowledgements

siRNA Release

Polyplex Composition

RNA interference
siRNA

We employ PEG-shielded, pH-responsive, endosomolytic, micellar nanoparticles (NPs) formed from diblock copolymers for siRNA delivery. The RNA condensing block (orange) will undergo charge reversal in aqueous solution by the hydrolysis of DMAEA to acrylic acid and a benign alcohol[2]. Because of this charge reversal, we posit that hydroltically degradable (HDG) siNPs can release siRNA into cells more effectively than previously established non-HDG NPs[3].

CONCLUSIONS AND FUTURE WORK
HDG siNPs show enhanced siRNA release by charge reversal, and have proven to be a novel, effective platform for improved gene silencing by increasing intracellular bioavailability. The polymer chemistry of our NPs has been optimized for intravenous treatment[4], since we have seen efficient delivery and release in cancer cells with HDG-siNPs, they prove to be an excellent candidate for a therapeutic against metastatic cancers.

Future work will assess cytotoxicity of HDG siNPs, and study the efficacy and bioactivity of siNPs delivered in-vivo.

REFERENCES & ACKNOWLEDGEMENTS
[3] Nelson CE, Kintzing JR et al., In Review
[4] Skylar Haws, Ann Hannah & the Biomaterials research group at Vanderbilt University
[5] National Science Foundation: Research Experience for Undergraduates, Grant DMR-1352333
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CELLULAR UPTAKE

TRANSCRIPTION
TRANSLATION

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