Johns Hopkins University

Department of Chemical & Biomolecular Engineering

Spring 2023 Seminar Series

Professor Thomas Epps, III
University of Delaware

Date: Thursday, April 6, 2023
Time: 10:30 a.m.
Shaffer Hall 3
Zoom Meeting ID: 919 5918 2879
Passcode: 270887

Title: Responsive polymer nanoplexes - linking in vitro experiments to in vivo outcomes

Abstract: Vascular bypass grafting is a routine treatment for cardiovascular diseases; however, nearly 50% of bypass grafts fail within a few years following surgery due to cellular inflammatory responses at the suture sites – a general concern for wound-healing applications. To overcome this problem, we synthesized novel diblock polymers to deliver nucleic acid therapeutics capable of promoting healing in a spatiotemporal manner. A key component of our design is a monomer containing photocleavable o-nitrobenzyl moieties linking cationic groups to the polymer backbone so that light irradiation can induce polymer hydrolysis and charge reversal. The polymers self-assemble with anionic nucleic acids in solution to form nanoparticle complexes with a PEG "stealth" coating. Application of a photo-stimulus disrupts the electrostatic interactions to trigger the release of bound nucleic acids, such as siRNA, from the nanocomplexes. More significantly, our soft nanoparticles maintained stability in serum, exhibited robust cellular uptake, facilitated nanocarrier imaging, and were capable of photo-responsive on/off control over gene expression. These formulations enabled the knockdown of two key functional genes, IL1β and CDH11, that are implicated in inflammatory responses in human aortic adventitial fibroblasts. The complete knockdown of both genes, in combination, resulted in significant attenuation of TGF-β1-triggered fibroblast proliferation and differentiation into myofibroblasts, two of the primary hallmarks of fibrosis. Further attenuation over clinically relevant time scales was achieved by modulating the polyplex dosing regimen by taking input from a recently developed kinetic model, whose creation was enabled by our polymer design. Finally, we have very recently expanded our kinetic modeling to predict in vivo delivery results from in vitro experiments as confirmed via retrospective analyses, unlocking a potentially streamlined pathway to de novo design.

Bio: Thomas is the Allan & Myra Ferguson Distinguished Professor of Chemical & Biomolecular Engineering at the University of Delaware (UD) with a joint appointment in Materials Science & Engineering. He is Director of the Center for Research in Soft matter & Polymers (CRiSP), Director of the new NSF MRSEC at UD called CHARM (Center for Hybrid, Active, and Responsive Materials) and Deputy Director of the new DOE EFRC at UD called CPI (Center for Plastics Innovation). His research interests include nanostructured assemblies for targeted drug delivery and gene therapy, polymeric materials for bio-separation and ion-conduction membranes, nanostructured soft materials from biobased and plastics waste feedstocks, and polymer films for nanotemplating. He was elected a Fellow of the American Physical Society in 2017, Royal Society of Chemistry (FRSC) in 2018, American Institute for Medical and Biological Engineering in 2021, Polymers Division of the American Chemical Society in 2021, the American Chemical Society in 2021, and the National Academy of Inventors in 2021. Thomas is also co-founder and Chief Scientific Officer of Lignolix, Inc. – a start-up focused on valorization of biomass waste. He has received several honors and awards including: the William W. Grimes Award (AIChE, 2021), Percy L. Julian Award (NOBCChE, 2020); John H. Dillon Medal (APS, 2016); Owens-Corning Early Career Award (AIChE, 2015), among others. Thomas is an associate editor for Science Advances and a member of the DOE Basic Energy Sciences Advisory Committee.