CHEMICAL ENGINEERING

DISTINGUISHED YOUNG SCHOLARS SERIES

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Precision biomaterial platforms to probe myofibroblast activation

ABSTRACT: Diabetes mellitus is a disease characterized by poor glycemic control which often leads to severe complications including retinopathy, cardiovascular disease, and kidney failure.1 Many diabetic patients must continually monitor their blood sugar and self-administer multiple daily doses of exogenous insulin to combat hyperglycemia. To reduce this patient burden, limit the occurrence of hypoglycemic events, and better mimic native insulin activity, therapies which can self-regulate insulin delivery are an attractive option. 2 Existing technologies, however, are typically insensitive to glucose changes at physiologically relevant concentrations and do not respond on therapeutically relevant timescales.3 This work addresses these limitations by developing new technologies combined with novel in vivo characterization strategies to create a translatable therapy for diabetic patients.

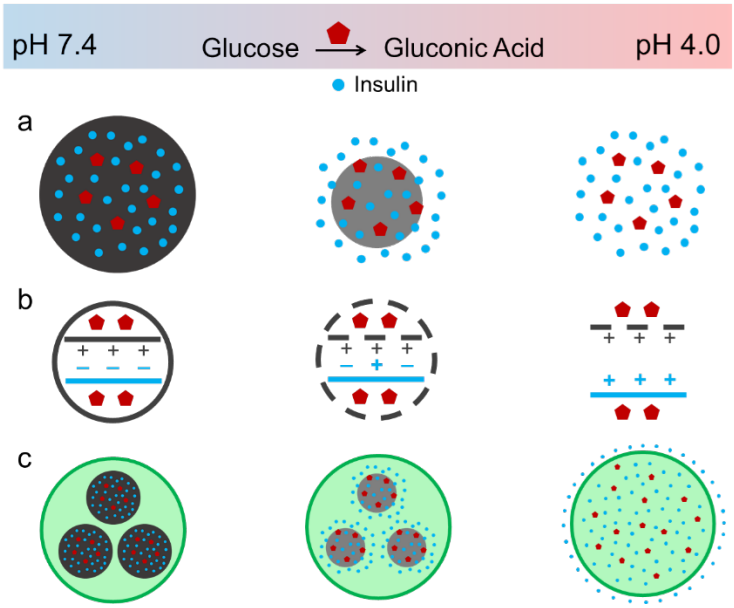

Figure 1. Schematic of glucose-responsive insulin delivery. a) Acetalated-dextran nanoparticle system that degrades in response to glucose. b) Nano-complexes made from insulin and cationic polymers that dissociate at low pH. c) Alginate microgels encapsu

In this seminar, I will discuss three types of glucose-responsive insulin delivery systems that I developed during my PhD. Each system employs the enzyme glucose oxidase as a glucose sensor, which converts glucose to gluconic acid and

reduces the pH of the microenvironment when glucose levels are high. This change in pH acts as a trigger to release insulin on demand. The first system (Fig 1a) uses the pH-responsive polymer acetalated-dextran to formulate nanoparticles that physically encapsulate both insulin and glucose oxidase. The particles rapidly degrade in the presence of acid, making this system a fast acting therapeutic that responds an hour after administration. The second system (Fig. 1b) is based on the electrostatic complexation of insulin to positively charged polymers, such as polyethylenimine and poly(beta-amino esters). When the pH is reduced below the isoelectric point of insulin, the complex dissociates and releases insulin only in response to elevated levels of glucose. These complexes are afforded a prolonged
functional lifetime by decreasing the rate of insulin release under normal glucose concentrations. The final system (Fig 1c) is comprised of alginate microgels that encapsulate nanoparticles to create a depot of insulin for sustained glucose-responsive release in vivo for up to 3 weeks. I will briefly discuss the synthesis, formulation, in vitro characterization, and in vivo results in both a healthy and diabetic mouse model for each of these systems, focusing on their pros and cons. Based on this work, I have received several awards including the grand prize for best presentation at the Society of Women Engineers' Rapid Fire Contest, Graduate Student Research and Design Award, and ALPCO's Young Investigators Award.
Future Perspectives: This seminar focuses on three approaches using pH-responsive materials to create a self-regulated insulin delivery system that can be used to achieve tight glycemic control in diabetic patients and adapted to deliver other therapeutics. As personalized medicine advances, I am interested in better understanding the interaction of responsive biomaterials with their environment to inform the rational design of next generation systems. Based on the techniques developed during my PhD, I aim to create platform delivery systems that respond to a variety of other stimuli to treat a wide range of diseases with the goals of improving patient quality of life and advancing the field of healthcare.

BIOGRAPHY: Lisa R. Volpatti is a Ph.D. candidate in the Anderson and Langer Labs at MIT with research interests in the development of stimuli-responsive materials for biomedical applications. Prior to joining MIT, Lisa received her M.Phil. in the Department of Chemistry at the University of Cambridge, UK and her B.S. in Chemical Engineering from the University of Pittsburgh. Lisa is a NSF Graduate Research Fellow, a Whitaker International Fellow, and a MIT Chemical Engineering Communication Lab Fellow.

LECTURE 4:00 – 5:00 (PAA) A118
Happy Hour in Benson Hall Lobby Following

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1. Nathan, D.M. N. Engl. J. Med. **328,** 1676-1685 (1993). 2. Veiseh, O., et. al. Nat. Rev. Drug Discov. **14**, 45-57 (2015). 3. Yang, J. & Cao, Z. J. Control. Release **263,** 231-239 (2017).