ABSTRACT Nanoparticle platforms enable the delivery of therapeutic nucleic acids, such as small interfering RNA or messenger RNA, to tissues and cells for gene therapy to treat diseases. However, the use of these technologies requires overcoming delivery barriers including cell- and tissue-specificity, endosomal escape from intracellular compartments, and off-target toxicity to healthy tissues and cells. In this seminar, I will discuss how stimuli-responsive nanoparticles can be engineered to enable safe and potent nucleic acid delivery for cancer and prenatal medicine applications. I will first discuss how the unique light absorption and surface chemistry of nanoshells, comprised of silica cores and thin gold shells, can be exploited for triggered cancer therapy. Nanoshells coated with Frizzled7 antibodies were used to actively target triple-negative breast cancer cells and inhibit Wnt signaling, which is a driving force behind TNBC progression and metastasis. Further, I will demonstrate how nanoshells coated with small interfering RNA enable triggered gene regulation in response to laser light by releasing the nucleic acids on demand. Lastly, I will present my recent work engineering pH-responsive lipid nanoparticles for mRNA delivery to fetuses in utero. This technology provides the first ionizable lipid platforms for fetal delivery in mice, and may ultimately be applicable for treating prenatal genetic diseases. Thus, the drug delivery tools developed through this research provide stimuli-responsive platforms for nucleic acid delivery with applications in both cancer therapy and prenatal medicine.

BIOGRAPHY Dr. Rachel Riley is an NIH T32 postdoctoral fellow in the Department of Bioengineering at the University of Pennsylvania. She received her B.S. in Civil and Environmental Engineering from Rowan University in 2012 and her Ph.D. in Biomedical Engineering from the University of Delaware in 2018. Dr. Riley’s Ph.D. research focused on the development of gold nanoparticles as tools for multifunctional therapy of triple negative breast cancer. For this work, she was awarded the Best Doctoral Thesis Award in 2018 from the University of Delaware, Women in Engineering travel awards, and the American Dissertation Fellowship from the American Association of University Women. In her postdoctoral research, Dr. Riley is engineering lipid nanoparticles for nucleic acid delivery to fetuses in utero, which can ultimately be used to treat fetal genetic diseases. As a postdoctoral fellow, she received an NIH T32 Multidisciplinary Training Grant in Cardiovascular Biology in 2018.