LIPID NANOPARTICLES FOR OVERCOMING BIOLOGICAL BARRIERS TO mRNA DELIVERY
Michael J. Mitchell

Associate Professor of Bioengineering
University of Pennsylvania

Abstract: Recent years have witnessed tremendous developments and breakthroughs in the field of RNA-based therapeutics and vaccines. The distinct mechanisms of exogenous RNAs and analogs, including messenger RNAs, small interfering RNAs, microRNAs, and antisense oligonucleotides, have brought them unprecedented potential to treat a variety of pathological conditions. However, the widespread application of RNA therapeutics and vaccines is hampered by their intrinsic features (e.g., instability, large size, and dense negative charge) and formidable host barriers. Development of safe and efficient vectors is key for successful delivery and translation of RNA therapeutics and vaccines. In this talk, I will discuss our efforts towards the development of lipid nanoparticle (LNP) platforms that enable the delivery of RNA therapeutics and vaccines to a range of target cells and tissues in the body. Furthermore, I will describe new therapeutic strategies utilizing these LNPs including (i) in vivo reprogramming of immune cells for cancer immunotherapy and vaccination, (ii) in utero gene editing for treating disease before birth, and (iii) mRNA prenatal therapeutics for treating pregnancy disorders such as pre-eclampsia.

Bio: Michael J. Mitchell is an Associate Professor of Bioengineering at the University of Pennsylvania, and the Lipid Nanoparticle Delivery Systems Group Leader at the Penn Institute for RNA Innovation. He received a BE in Biomedical Engineering from Stevens Institute of Technology in 2009, a PhD in Biomedical Engineering with Prof. Michael King from Cornell University in 2014. He was a Postdoctoral Fellow in Chemical Engineering with Prof. Robert Langer at MIT from 2014-2017, prior to pursuing his independent career at University of Pennsylvania in 2018. The Mitchell lab’s research broadly lies at the interface of biomaterials science, drug delivery, and cellular and molecular bioengineering to fundamentally
understand and therapeutically target biological barriers. Specifically, his lab engineers new lipid and polymeric nanoparticle platforms for the delivery of different nucleic acid modalities to target cells and tissues across the body. His lab applies their research findings and the technologies developed to a range of human health applications, including the engineering of CAR T cells for cancer immunotherapy, mRNA vaccines, genome editing, cardiovascular disease, and in utero therapeutics to treat disease before birth.

Mitchell has received numerous awards as an independent investigator, including the National Institutes of Health Director’s New Innovator Award, the Rising Star Award from the Biomedical Engineering Society, the Career Award at the Scientific Interface from the Burroughs Wellcome Fund, and the Research Scholar Award from the American Cancer Society. In 2022 Mitchell was named “Emerging Inventor for the Year” by Penn’s for Innovation in recognition for his lipid nanoparticle technologies and received the Young Investigator Award from the Society for Biomaterials, the T. Nagai Award from the Controlled Release Society, the National Science Foundation CAREER Award, and was named a 2023 Young Innovator in Cellular and Molecular Bioengineering. He is a co-founder of Liberate Bio, a biotechnology company focused on developing non-viral delivery technologies for genetic medicines, and serves on Scientific Advisory Board of numerous biotechnology companies.