

MIT Chemical Engineering Department

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Lipid-like Materials for RNA Delivery: A How-to Guide for Hacking Gene Expression



Kathryn A. Whitehead, Ph.D.

Assistant Professor

Department of Chemical Engineering
and Biomedical Engineering
Carnegie Mellon University

Friday, September 7, 2018
3:00pm (Reception at 2:45 pm)
66-110

Abstract: Despite the promise of RNA therapeutics, progress towards the clinic has been slowed by the difficulty of delivering RNA drugs, such as short interfering RNA (siRNA) and messenger RNA (mRNA), into cellular targets within the body. RNA therapeutics are large ($10^4 - 10^6$ g/mol) and negatively charged; they do not have favorable biodistribution properties in vivo nor an ability to cross the cellular membrane of target cells. In response to these challenges, our lab has created biodegradable, ionizable lipid-like materials called 'lipidoids' that readily formulate into nanoparticles containing RNA. Lipidoids efficiently manipulate gene expression in a variety of biological systems, including hepatocytes, white blood cells and tumors. This talk will focus on the cell-free prediction of lipidoid efficacy in delivering mRNA to mice. Furthermore, I will describe a new formulation strategy for the synergistic co-delivery of mRNA and siRNA. Together, these data demonstrate the potential of lipidoid materials to robustly manipulate gene expression in vivo.

Kathryn A. Whitehead



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Bio: Kathryn A. Whitehead is an Assistant Professor in the Departments of Chemical Engineering and Biomedical Engineering (courtesy) at Carnegie Mellon University and a member of the McGowan Institute for Regenerative Medicine at the University of Pittsburgh. The interdisciplinary research interests of her lab include the development of RNA and oral protein delivery systems and their application for the treatment of disease. Prof. Whitehead obtained both her B.S. (Univ. of Delaware, 2002) and Ph.D. (UC Santa Barbara, 2007) in chemical engineering. She also completed a postdoc at MIT, where she was an NIH Ruth L. Kirschstein Fellow. Prof. Whitehead is the recipient of numerous awards, including the DARPA Young Faculty Award, the DARPA Director's Fellowship, the George Tallman Ladd Research Award, the CMBE Young Innovator Award, and Kun Li Award for Excellence in Education. Prof. Whitehead was named a Pioneer on the MIT Technology Review's Innovators Under 35 list in 2014 as well as one of the Brilliant Ten by Popular Science in 2015. Her 35+ publications have been cited over 4,000 times, and several of her patents have been licensed and sublicensed for reagent and therapeutic use.

Abstract: Despite the promise of RNA therapeutics, progress towards the clinic has been slowed by difficulty of delivering RNA drugs, such as short interfering RNA (siRNA) and messenger RNA (mRNA), into cellular targets within the body. RNA therapeutics are large ($10^4 - 10^6$ g/mol) and negatively charged; they do not have favorable biodistribution properties in vivo nor an ability to cross the cellular membrane of target cells. In response to these challenges, our lab has created biodegradable, ionizable lipid-like materials called 'lipidoids' that readily formulate into nanoparticles containing RNA. Lipidoids efficiently manipulate gene expression in a variety of biological systems, including hepatocytes, white blood cells and tumors. This talk will focus on cell-free prediction of lipidoid efficacy in delivering mRNA to mice. Furthermore, I will describe a new formulation strategy for the synergistic co-delivery of mRNA and siRNA. Together, these data demonstrate the potential of lipidoid materials to robustly manipulate gene expression in vivo.