2020 Fall CBE Seminar Series

presents:

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Testing Thousands of Nanoparticles In Vivo Using DNA Barcodes

DNA and RNA can manipulate the expression of any gene, making these molecules promising drugs. However, whether the drug is comprised of DNA, siRNA, mRNA, IncRNA, or another nucleic acid, it is limited by one problem: drug delivery. Chemists design thousands of distinct nanoparticles to deliver DNA or RNA to the desired cell type. However, after nanoparticles are synthesized, their ability to deliver drugs is evaluated using in vitro systems devoid of a liver, kidney, spleen, immune system, pulsatile blood flow, and other selection pressures known to affect nanoparticle delivery in vivo.

We have designed a series of increasingly advanced DNA barcoding platforms to quantify how thousands of nanoparticles deliver nucleic acids in vivo. Our goal is to quantify how up to 400 nanoparticles deliver DNA, mRNA, ASOs, or siRNA into up to 30 cell types, all in a single animal. To analyze these large in vivo drug delivery datasets, we have also developed an open source bioinformatics pipeline to iteratively ‘evolve’ nanoparticles that target cells in vivo. Using this high throughput, iterative, in vivo approach, we have identified nanoparticles with tropism to many novel cell types, in many different tissues.

Our data demonstrate that barcoded LNPs can elucidate fundamental questions about in vivo nanoparticle delivery. More generally, the data suggest that it may be feasible to perform very high throughput in vivo studies in the coming years.

Tuesday, Oct. 13, 2020
Lecture at 4:00 p.m.
https://uwmadison.zoom.us/j/91376473708