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Sandia National Laboratories

Imaging *in vivo* Lipid Nanoparticle Delivery

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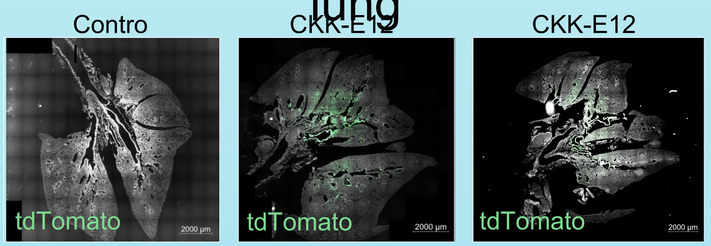
Introduction

Lipid nanoparticles (LNPs) are a powerful new delivery tool brought to the forefront of medical science by the ongoing SARS-CoV-2 pandemic. However, LNPs are still relatively new with untapped potential including an ability to selectively target specific tissues with a wide range of potential cargoes.

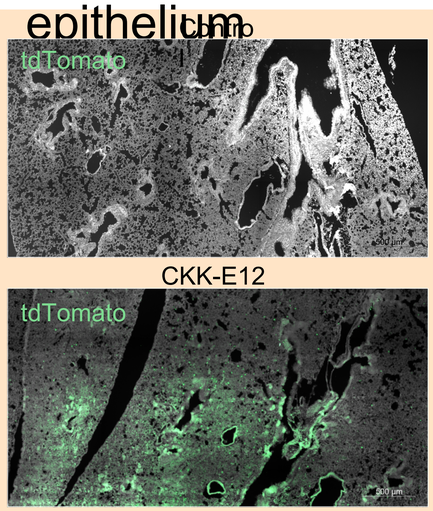
Here, we deliver CKK-E12 LNP encapsulated Cre recombinase mRNA (1350 nt) or β-galactosidase (4320 nt) mRNA in conjunction with reporter systems to visualize LNP delivery in lung and liver tissue.

LNPs delivered to the oropharynx localize to specific areas in the lung



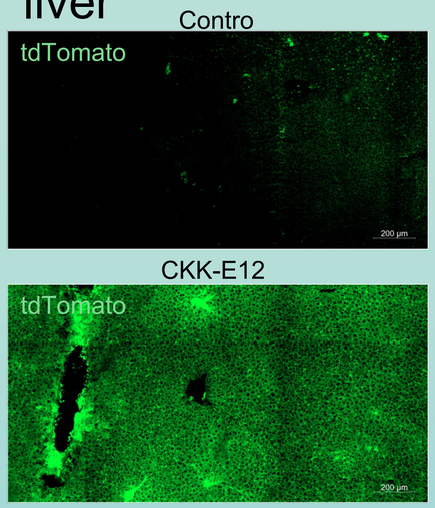
Mouse lungs stained with rabbit RFP antibody, followed by anti-rabbit antibody conjugated to AF488. Stained slides imaged on a Zeiss AxioScan 7 Slide Scanner. Scale bars are 2000 µM.

Cre found in the airway epithelium



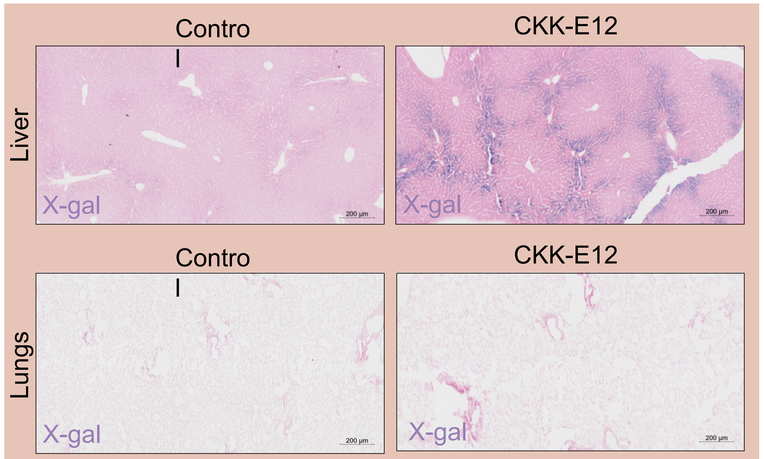
Mouse lungs stained with rabbit RFP antibody, followed by anti-rabbit antibody conjugated to AF488. Stained slides imaged on a Zeiss AxioScan 7 Slide Scanner. Scale bars are 500 µm.

Cre expressed throughout the liver



Mouse liver stained with rabbit RFP antibody, followed by anti-rabbit antibody conjugated to AF488. Stained slides imaged on a Zeiss AxioScan 7 Slide Scanner. Scale bars are 500 µm.

β-gal in the liver is restrictive



Mouse liver and lungs were dissected and stained with X-gal *ex vivo*. Tissues were then fixed, embedded, and sectioned. A eosin counterstain was then performed. Slides imaged on a Zeiss AxioScan 7 Slide Scanner. Scale bars are 200 µm.

Summar

Here we found OPA delivery of Cre mRNA LNPs to the lungs results in a specific focal area with localized epithelium staining. β-gal mRNA OPA delivery did not produce any X-gal stain.

Interestingly, we found 2 different patterns of expression of the liver dependent on the mRNA delivered. Cre mRNA was found throughout the liver and in hepatocytes. β-gal mRNA stained the lobule boundaries near portal triad groupings but was not seen in hepatocytes.

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