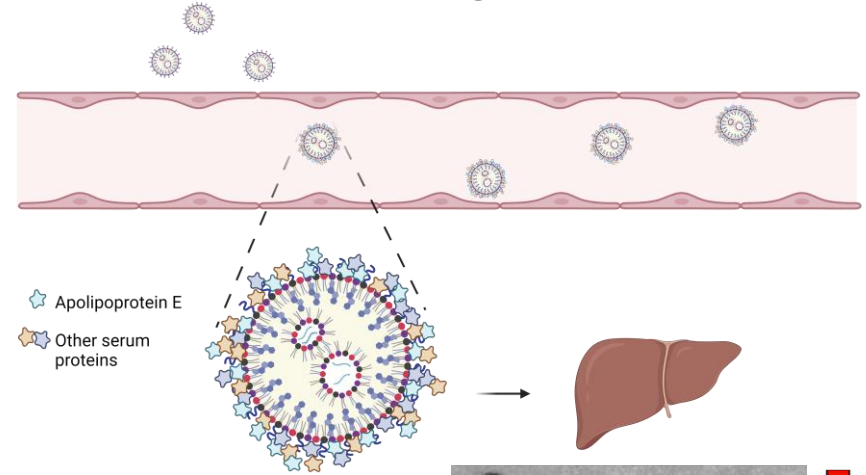
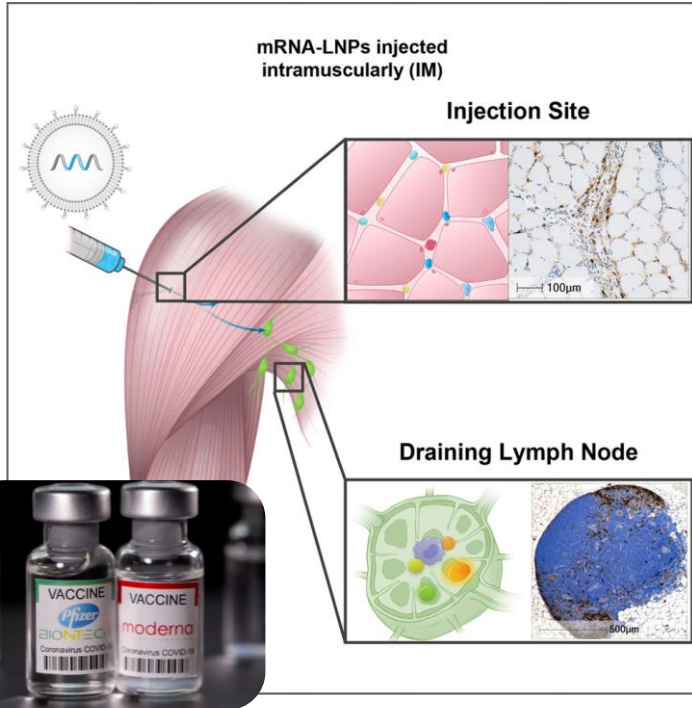


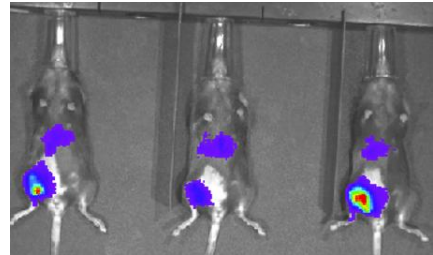
Liver-detargeted aromatic mRNA lipid nanoparticles confer lymph node tropism and robust antigen-specific immunity

Hannah M. Yamagata, Marshall S. Padilla, Michael J. Mitchell
Department of Bioengineering, University of Pennsylvania
July 17th, 2025

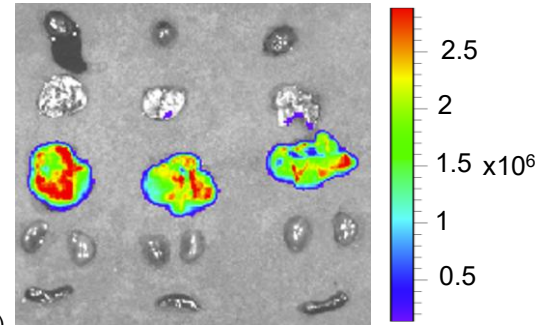
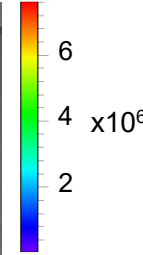
Lipid nanoparticles (LNPs) are ideal vaccine vectors yet tend to accumulate in the liver



IM injection, 6 h



Radiance (p/sec/cm²/sr)



Radiance (p/sec/cm²/sr)

Lipid nanoparticles (LNPs) are ideal vaccine vectors yet tend to accumulate in the liver

[World J Gastroenterol](#). 2022 Dec 28; 28(48): 6791–6810.

Published online 2022 Dec 28. doi: [10.3748/wjg.v28.i48.6791](#)

COVID-19 vaccination and liver disease

[Sotaro Ozaka](#), [Takashi Kobayashi](#), [Kazuhiro Mizukami](#), and [Kazunari Murakami](#)

Research | [Open access](#) | Published: 13 October 2022

New-onset and relapsed liver diseases following COVID-19 vaccination: a systematic review

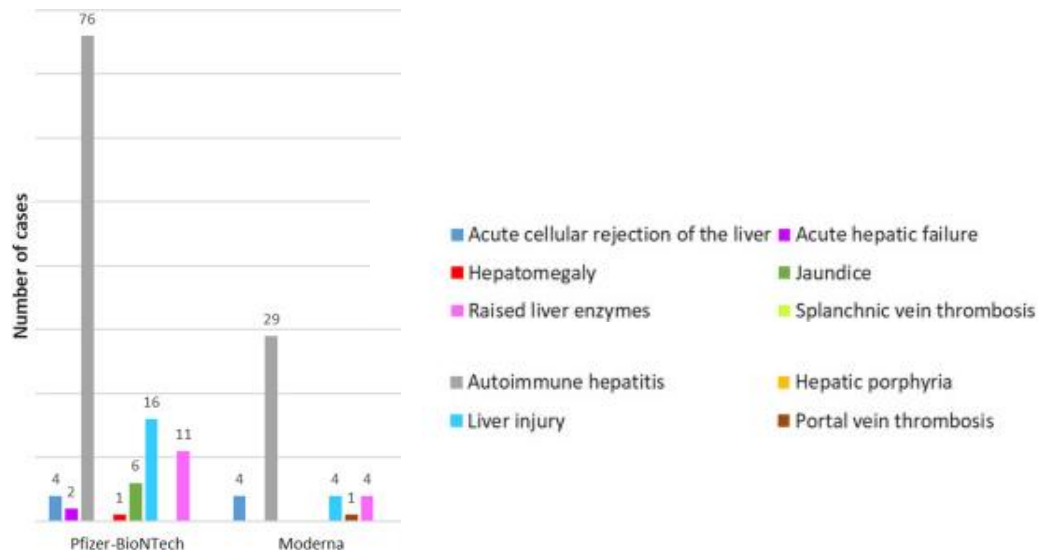
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Impact of COVID-19 vaccines on liver function: A state of the art and challenges for healthcare providers

[Karthikeyan Elumalai](#) ^a , [Sivaneswari Srinivasan](#) ^b, [Anandakumar Shanmugam](#) ^c

Alhumaid et al., *BMC Gastroent...*, 2022

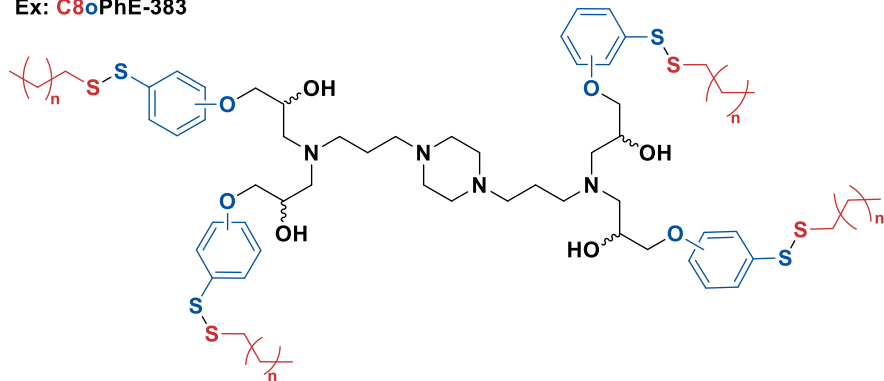


How can we make the next generation of vaccines that generate a strong immune response yet limit hepatic delivery and toxicity?

Novel aromatic ionizable lipids are highly modular

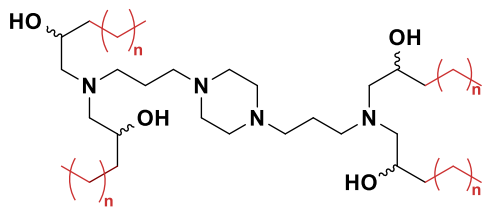
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Ex: C8oPhE-383

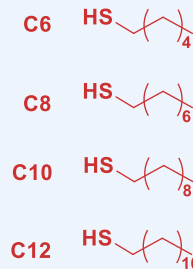


C[n]PhE-383

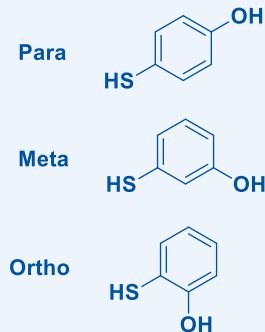
Ex: C8PhE-383



Tails

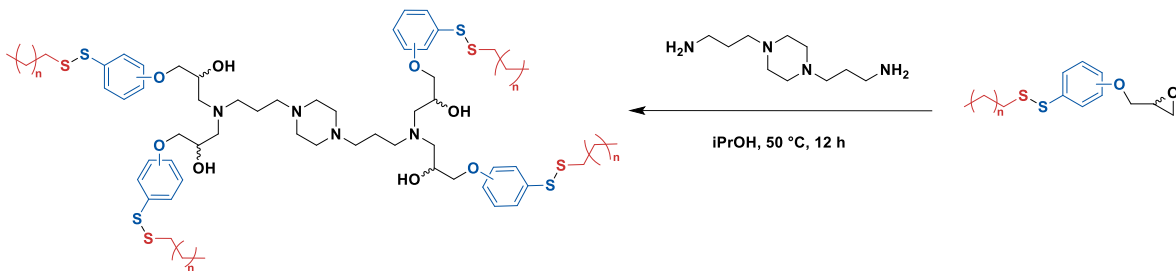


Linkers



CRS 2025
ANNUAL MEETING
& EXPOSITION

**NEXT-GENERATION
DELIVERY INNOVATIONS**



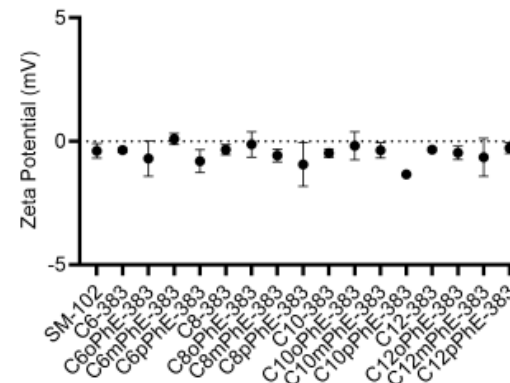
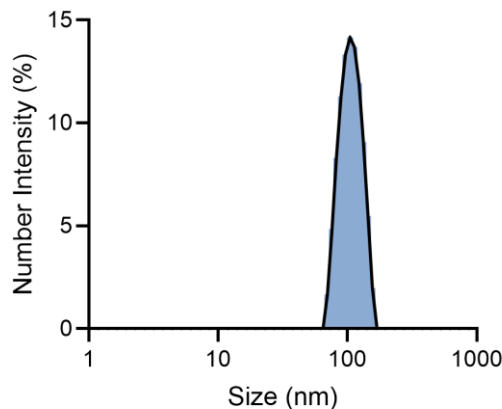
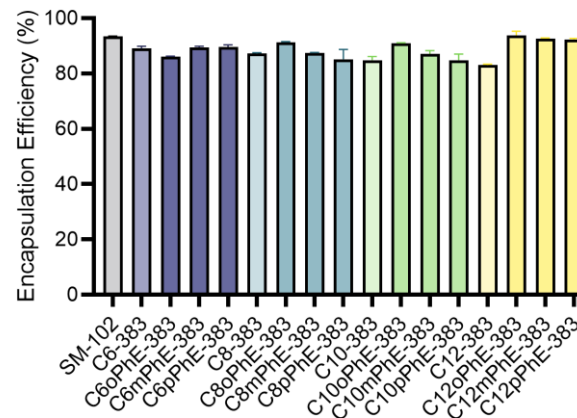
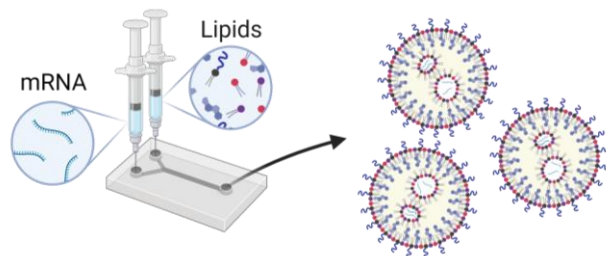
LNP formulation

Formulated via microfluidic mixing

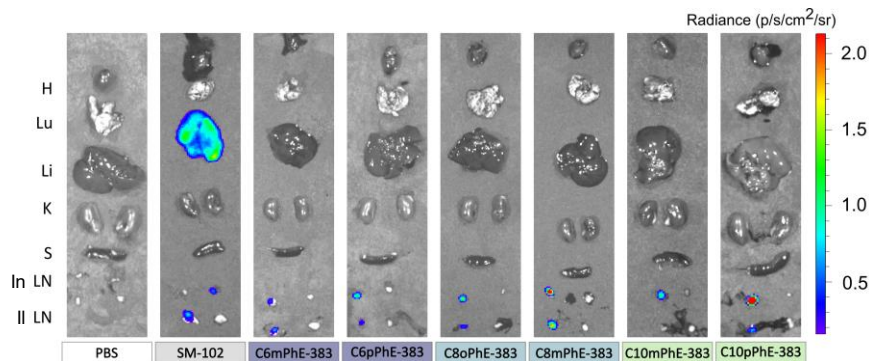
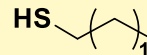
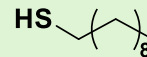
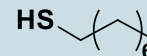
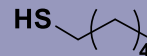
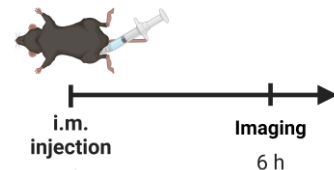
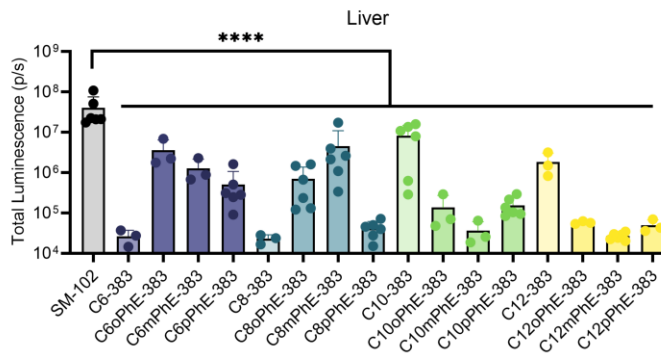
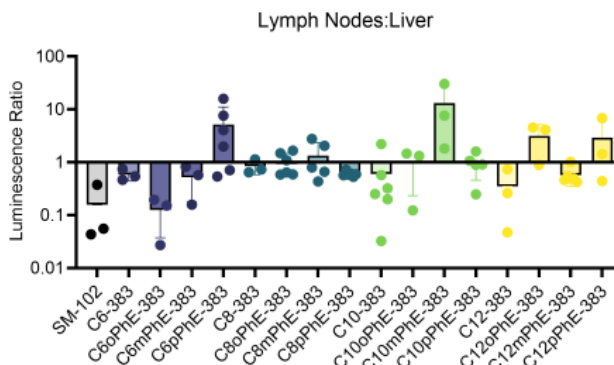
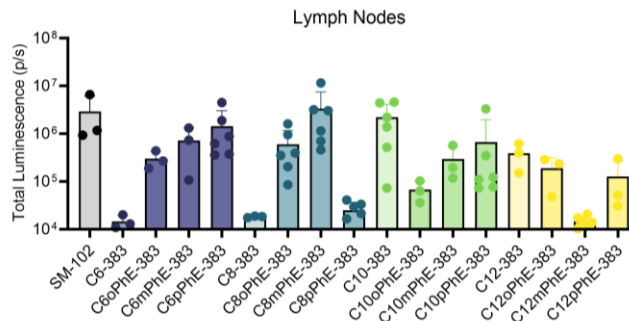
Excipients + molar percentage

- Ionizable lipid: 35%
- DOPE: 16%
- Cholesterol: 46.5%
- C14-PEG2000: 2.5%

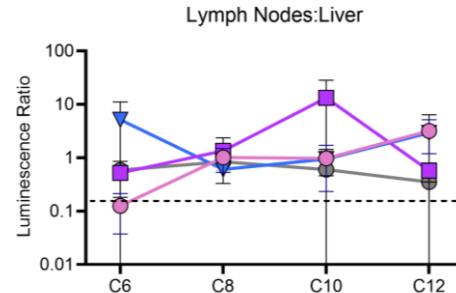
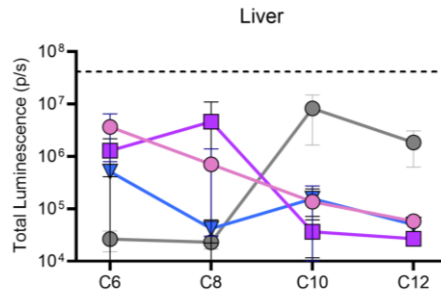
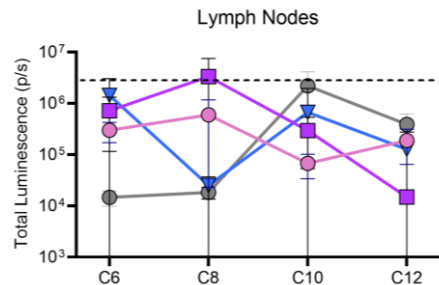
10:1 w/w ionizable lipid:mRNA



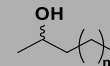
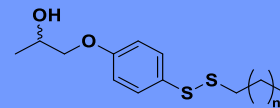
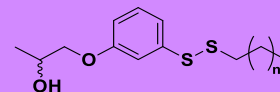
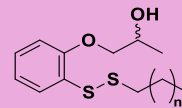
AroLNPs enhance mRNA delivery to lymph nodes with reduced liver transfection



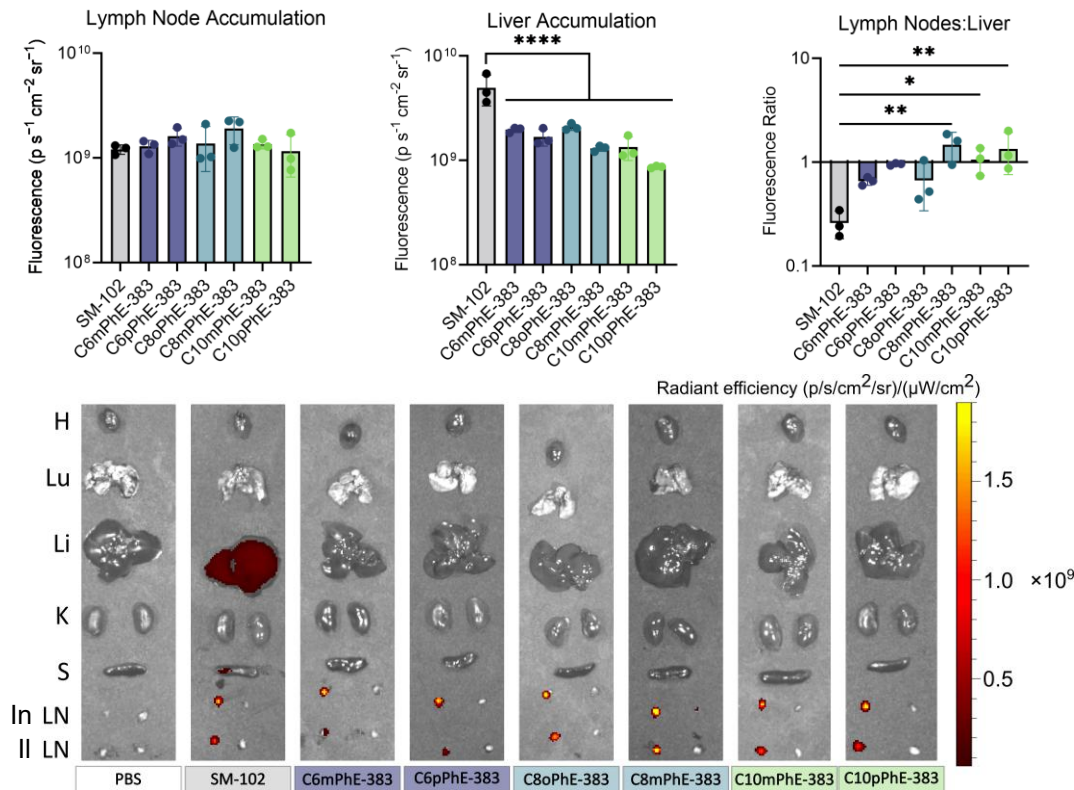
Aromaticity is more beneficial with shorter tail lengths for this library



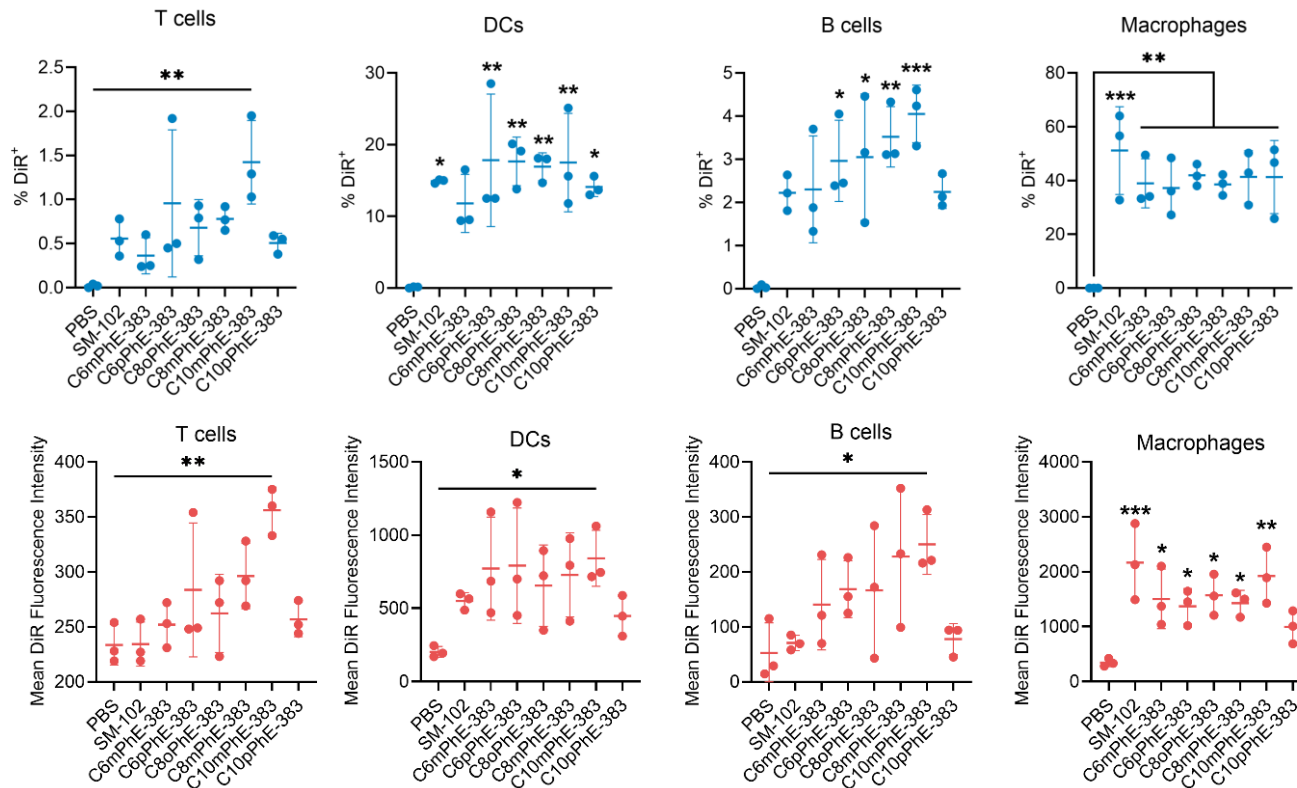
- Ortho
- Meta
- ▼ Para
- Non-aromatic control
- SM-102



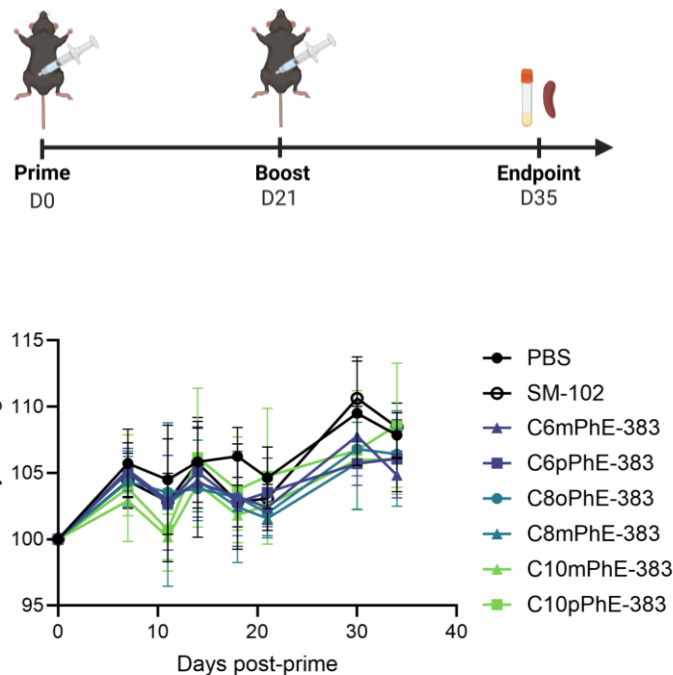
AroLNPs accumulate primarily in the lymph nodes



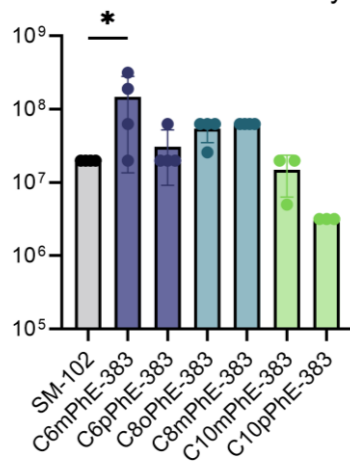
AroLNPs exhibit strong DC, T, & B cell uptake



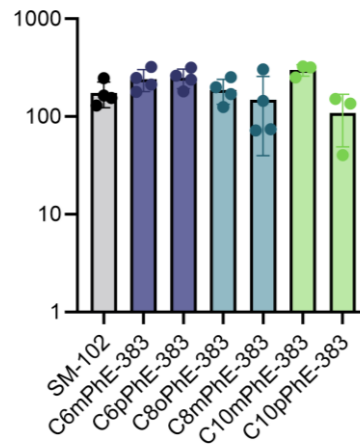
AroLNPs generate a strong prophylactic response in SARS-CoV-2 vaccine model



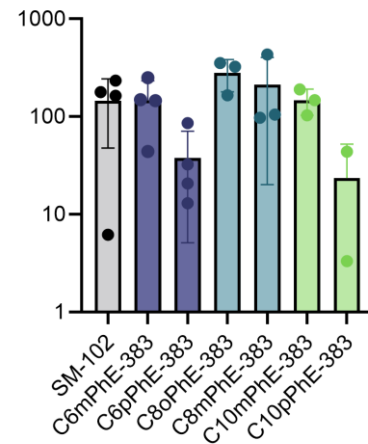
SARS-CoV-2 RBD Antibody Titers



IL-6



IFN-γ



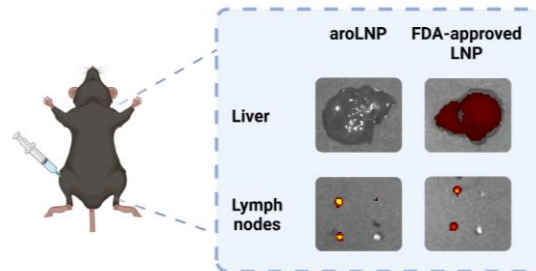
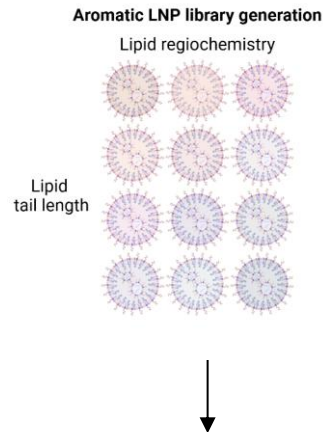
Conclusions + Future Directions

Conclusions

- Regiochemistry and ionizable lipid tail length greatly affect LNP performance and biodistribution
- AroLNPs demonstrate strong tropism to the lymph nodes and highly reduced liver delivery
- AroLNPs facilitate strong vaccine coverage

Future Studies

- Synthesize industry standard ionizable lipids with aromatic rings to determine how they may benefit existing formulations
- Assess the performance of aroLNPs in other vaccine models
- Further probe the mechanistics behind aroLNP tropism



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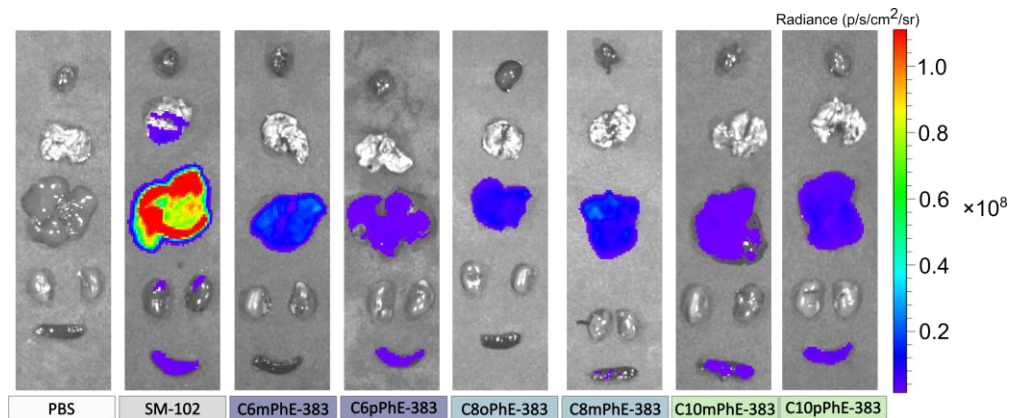
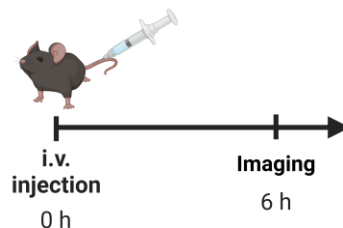
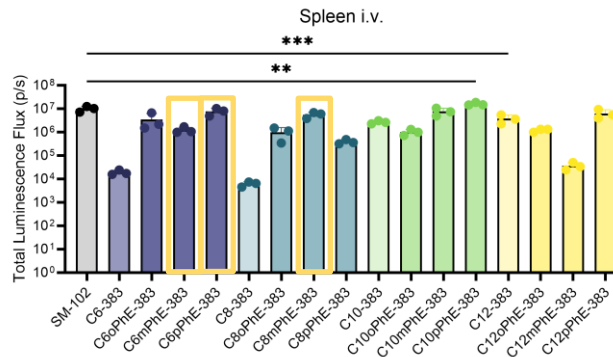
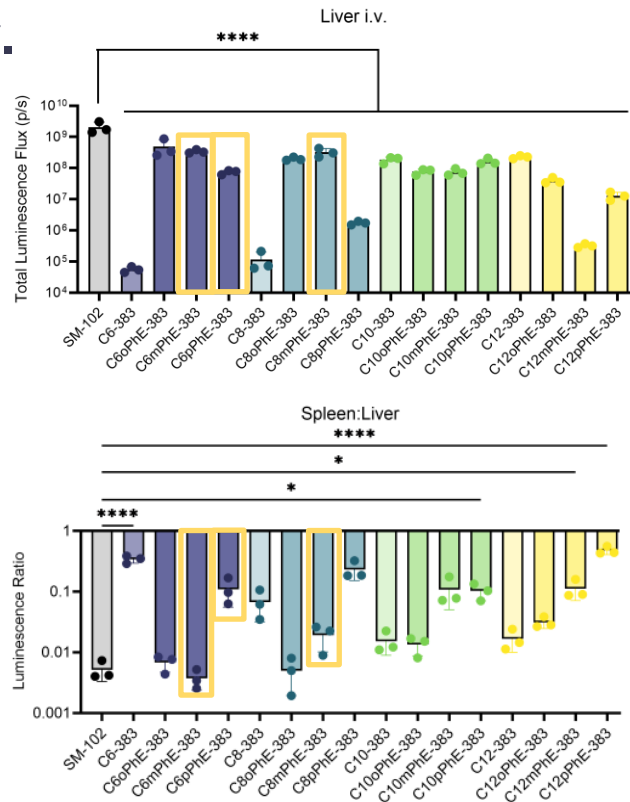


@hannahyamagata

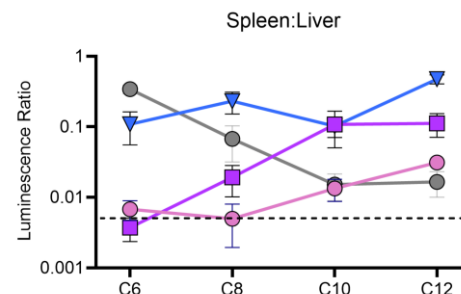
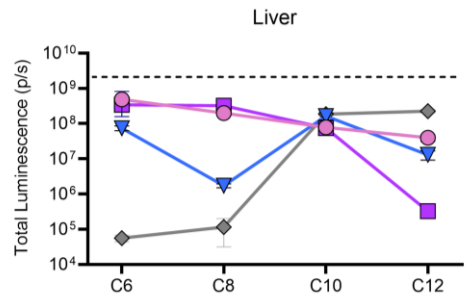
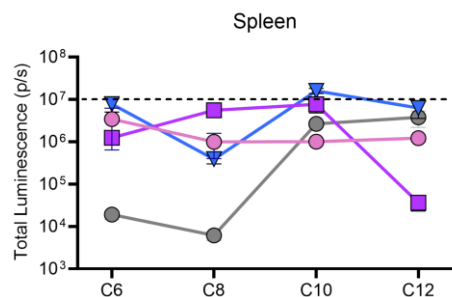
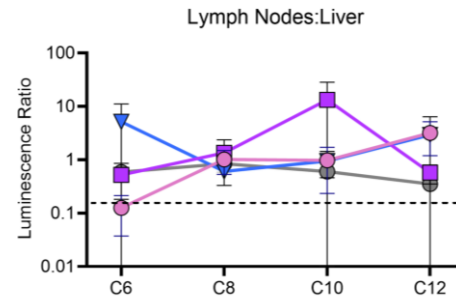
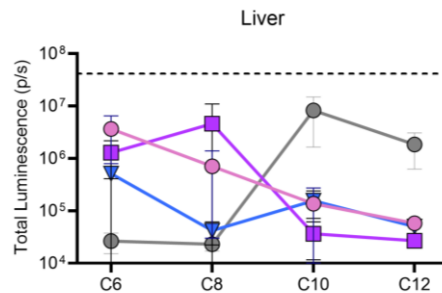
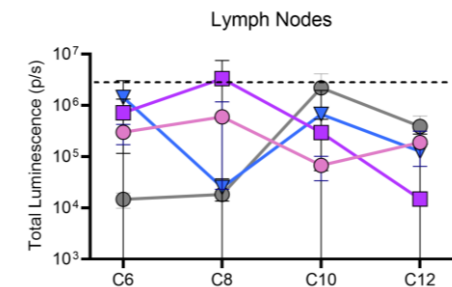


hyama1@seas.upenn.edu

Aromatic LNPs demonstrate reduced liver transfection when delivered i.v.



aroLNP trends



- Ortho
- Meta
- ▼ Para
- Non-aromatic control
- SM-102

