

# Formulation of Mesoscale Lipid Nanoparticles for Targeted Nucleic Acid Delivery to the Kidneys

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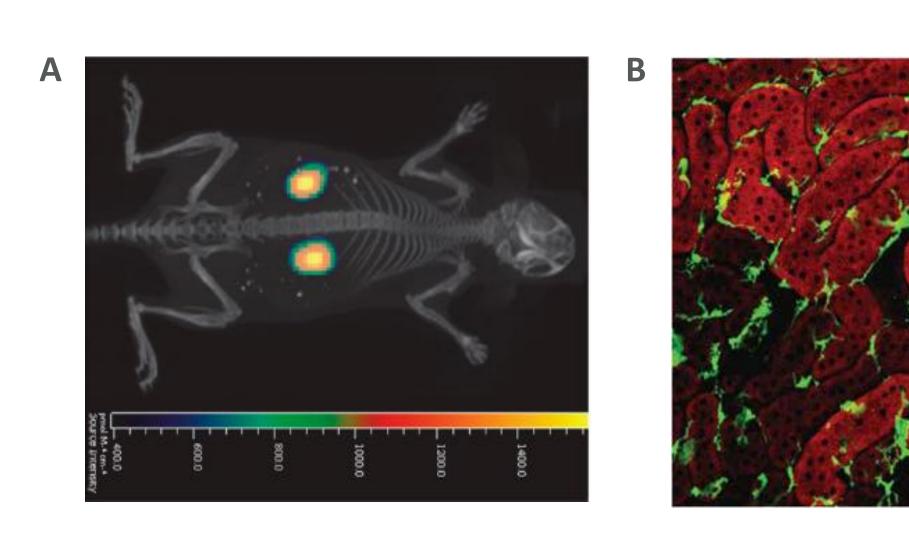
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## Background

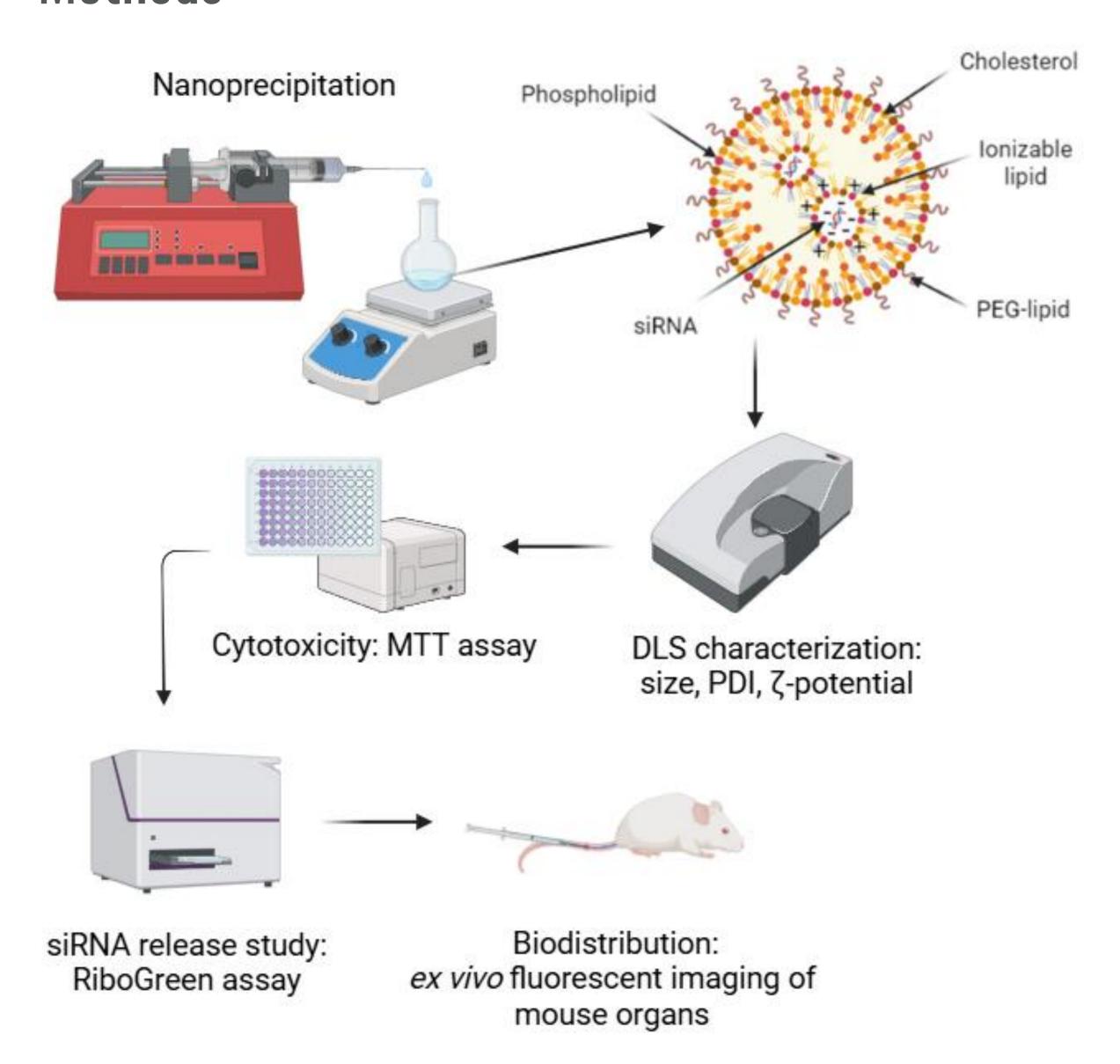
• PEGylated nanoparticles with a size in the mesoscale range (300 – 500 nm) selectively accumulate in renal proximal tubule epithelium 26-fold more than any other organ<sup>[1]</sup>.



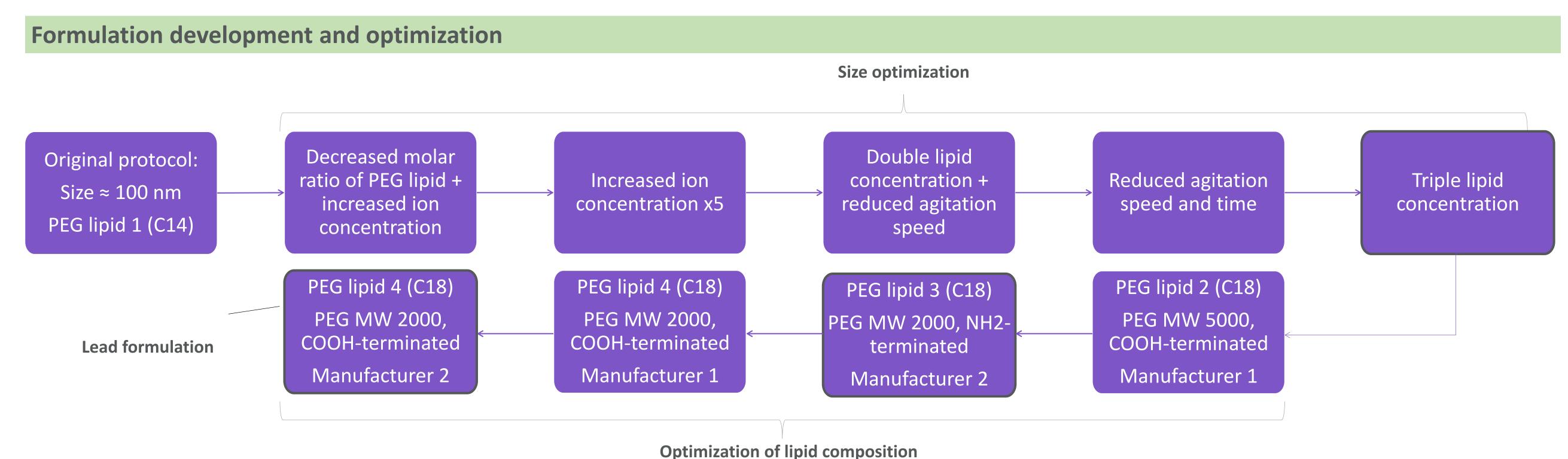
(A) MNP localization to the kidneys in mice<sup>[1]</sup>. (B) Intravital microscopy of MNPs (red) in kidneys of mice with GFP-producing macrophages (green) <sup>[2]</sup>.

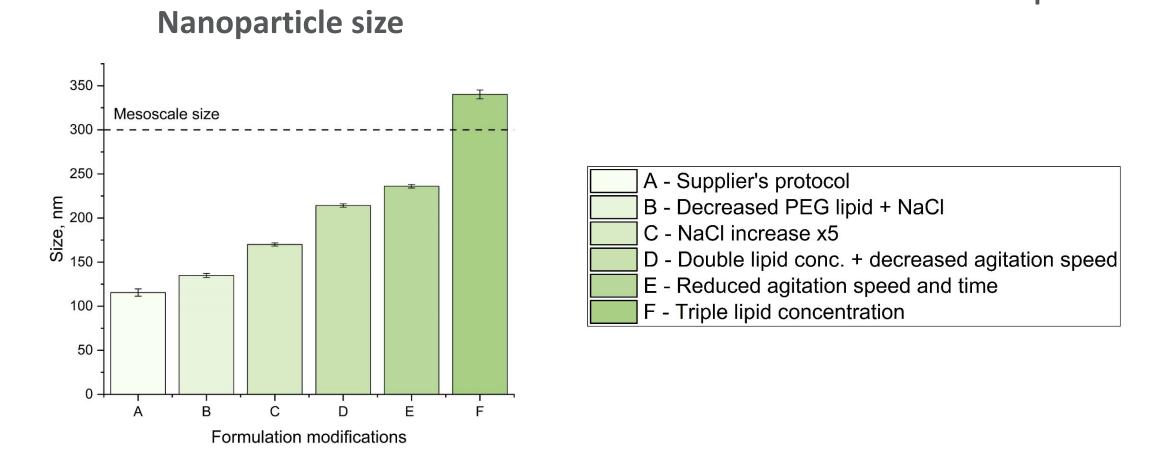
- Mesoscale nanoparticle kidney targeting has so far only been shown with polymeric carriers.
- With the rise of nucleic acid therapies, lipid nanoparticles have proven to be efficient carriers for biological cargo<sup>[3]</sup>.
- Our goal was to develop a lipid-based mesoscale nanoparticle formulation for targeted delivery of nucleic acids to the kidneys.

### Methods



### Results

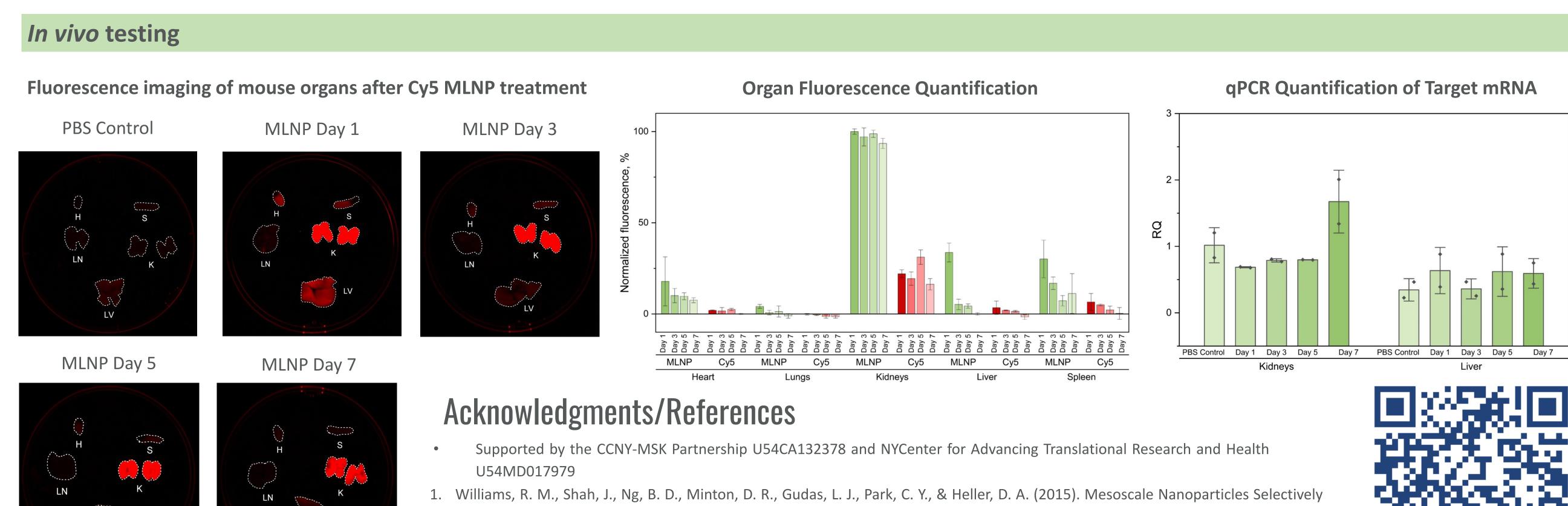




# Viability of HK-2 cells after 48h MLNP treatment PBS at 37°C

# Discussion/Conclusion

- Mesoscale size of lipid nanoparticles has been achieved predominantly through an <u>increase in total lipid concentration</u>, in combination with other modifications.
- Initial formulation was modeled after a liver-targeting nanoparticle, so optimization of lipid composition was performed to achieve <a href="stable-PEGylation">stable-PEGylation</a> essential for kidney targeting.
- Optimized MLNPs demonstrated <u>minimal cytotoxic effect</u> on renal epithelial cells and favorable <u>sustained release</u> properties.
- MLNPs show <u>high kidney selectivity</u> and initial indications of <u>siRNA-induced gene silencing</u> in the target organ (kidneys).
- Thus, we have developed the first, to our knowledge, mesoscale lipid nanoparticle formulation optimized for <u>targeted nucleic acid</u> <u>delivery to the kidneys</u>.
- <u>Future studies</u> will include further *in vitro and in vivo* testing to demonstrate safety and efficacy of nucleic acid delivery by MLNPs.



2. Williams, R. M., Shah, J., Tian, H. S., Chen, X., Geissmann, F., Jaimes, E. A., & Heller, D. A. (2018). Selective Nanoparticle Targeting of

3. Hou, X., Zaks, T., Langer, R., & Dong, Y. (2021). Lipid nanoparticles for mRNA delivery. Nature Reviews Materials, 6(12), 1078–1094.

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