Unraveling the Impact of Changing Ionizable Lipids on mRNA-LNP Vaccine Pharmacokinetics and Biodistribution

Yuxiang Ren
Drug Delivery, Disposition and Dynamics, Monash Institute of Pharmaceutical Sciences, Monash University, Parkville, VIC, Australia

yuxiang.ren@monash.edu

In the dynamic landscape of vaccine development, mRNA-based vaccines have emerged as pivotal players, revolutionizing the field with their rapid production, cost-effectiveness, and enhanced safety profiles.[1] Despite their numerous advantages, the efficient delivery of mRNA vaccines encounters hurdles such as instability, susceptibility to RNase degradation, and suboptimal uptake by target cells.

Lipid nanoparticles (LNPs) have proven to be promising carriers for mRNA, addressing these challenges and facilitating effective delivery to tissues and cells.[2] However, there remains a crucial gap in understanding how alterations in LNP composition, particularly ionizable lipids, impact pharmacokinetics (PK) and biodistribution.

This presentation will unveil novel results about the influence of changing ionizable lipids within mRNA-LNP formulations on the PK profile and biodistribution of LNP lipids, mRNA, and expressed proteins. Utilizing four distinct ionizable lipids, I formulated four mRNA-LNP which encapsulate nLuc-GFP mRNA as model mRNA. Mouse models were employed to scrutinize plasma PK and tissue biodistribution profiles following intravenous (IV) and subcutaneous (SC) administrations. A comprehensive analysis, involving LC-MS/MS, RT-qPCR, and the In Vivo Imaging System (IVIS), provided precise quantification of lipids and mRNA, offering insights into protein expression in both plasma and tissues.

References

1 Pardi, N., Hogan, M.J., Porter, F.W., and Weissman, D. Nat. Rev. Drug Discov. 2018, 17, 261–279.

2 Evers, M.J.W., Kulkarni, J.A., Van Der Meel, R., Cullis, P.R., Vader, P., and Schiffelers, R.M. Small Methods 2018, 2, 1700375.