Comparative Study on the Circulation and Immune Responses of Different COVID-19 Vaccines in Human Blood

Shiyao Li,^{1,*} Stephen J Kent,² Yi (David) Ju¹

¹Olivia Newton-John Cancer Research Institute, and School of Cancer Medicine, La Trobe University, Heidelberg, Victoria 3084, Australia

²Department of Microbiology and Immunology, Peter Doherty Institute for Infection and Immunity, The University of Melbourne, Melbourne, Victoria 3000, Australia

* Email: Shiyao.Li@onjcri.org.au

SARS-CoV-2 lipid nanoparticle (LNP) mRNA vaccines have been used world-widely in humans. We have recently discovered the boost of poly(ethylene glycol) (PEG)-specific antibodies by SARS-CoV-2 mRNA LNP vaccines in humans.¹ We found that anti-PEG antibodies significantly influence the immune cell interactions of PEGylated nanoparticles in human blood.² Our recent study analyzed the distribution of SARS-CoV-2 LNP mRNA vaccine (Moderna mRNA-1273) in human blood, finding that vaccine components peak within 1-2 days post-administration and exploring factors influencing their pharmacokinetics.³ However, blood circulations and antibody levels boosted by the vaccination of different types of SARS-CoV-2 LNP mRNA vaccines in humans remain poorly understood.

In this study, we compared the pharmacokinetics of three types of intramuscular-delivered mRNA vaccines, i.e., Moderna mRNA-1273.815, Pfizer-BioNTech BNT162b2, and a clinical trial vaccine targeting receptor-binding domain (RBD vaccine) in humans through serially sampling plasma early after vaccination.⁴ We investigated and compared the decay kinetics of SARS-CoV-2 mRNA vaccine components (mRNA and ionizable lipid) and the level of antibodies (ant-PEG antibodies and anti-spike antibodies) boosted by mRNA vaccines in human blood using PCR, mass spectrometry, and ELISA, respectively. We further did correlation studies between the decay kinetics of vaccine components and the antibody levels boosted by the vaccination.

This work defines and compares the pharmacokinetics of lipid nanoparticle mRNA vaccine of different formulations in human blood after intramuscular injection and the factors that influence these processes. These insights should be valuable in improving the future safety and efficacy of lipid nanoparticle mRNA vaccines and therapeutics.

References:

- 1. Ju, Y.; et al. ACS Nano 2022, 16, 11769–11780.
- 2. Ju, Y.; et al. Nat. Rev. Immunol. 2023, 23, 135–136.
- 3. Kent, J.; Li, S.; et al. ACS nano. 2024, 18, 27077–27089.
- 4. T. M. Nolan et al. *EBioMedicine*. **2023**, *98*, 104878.