Title: Exploring the PEG immunogenicity of SARS-CoV-2 mRNA vaccines in humans

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Abstract: Lipid nanoparticle (LNP) messenger RNA (mRNA) vaccines for coronavirus disease 2019 (COVID-19) have been used world-widely in humans. However, there is limited understanding of factors that influence their PEG immunogenicity. We have recently studied the boost of poly(ethylene glycol) (PEG)-specific antibodies by SARS-CoV-2 mRNA lipid nanoparticle (LNP) vaccines. After studying plasma samples from 130 adults, we discovered that anti-PEG antibodies were significantly boosted by mRNA-1273 vaccine and to a lower extent by BNT162b2 vaccines.[1] We found that anti-PEG antibodies have a significant impact on PEGylated nanoparticle−immune cell interactions in human blood. Our study addresses timely and important questions regarding the anti-PEG antibody responses in healthy adults following SARS-CoV-2 mRNA-LNP vaccination and whether the induced anti-PEG antibody may impact the fate of other PEG-containing nanomedicines.[2] In this talk, our recent human cohort study on PEG immunogenicity of Spikevax bivalent mRNA vaccine will be presented. Our study could prove useful in improving the future safety and efficacy of lipid nanoparticle mRNA vaccines and therapeutics.

References

[1]Ju, Y.; Lee, W. S.; Pilkington, E. H.; Kelly, H. G.; Li, S.; Selva, K. J.; Wragg, K. M.; Subbarao, K.; Nguyen, T. H. O.; Rowntree, L. C.; Allen, L. F.; Bond, K.; Williamson, D. A.; Truong, N. P.; Plebanski, M.; Kedzierska, K.; Mahanty, S.; Chung, A. W.; Caruso, F.; Wheatley, A. K.; Juno, J. A.; Kent, S. J.* Anti-PEG Antibodies Boosted in Humans by SARS-CoV-2 Lipid Nanoparticle mRNA Vaccine. *ACS Nano* **2022**, 16, 11769–11780.

[2]Ju, Y.; Carreño, J. M.; Simon V.; Dawson K.; Krammer F.*; Kent, S. J.* Impact of Anti-PEG Antibodies Induced by SARS-CoV-2 mRNA Vaccines. *Nat. Rev. Immunol.* **2023**, 23, 135–136.