



An Integrated Antibody Discovery and LNP-mRNA Platform for Targeted Gene Delivery

Becky Sadler¹, Ray Hao², Daniel Meng², Ting Song¹, Austin Hammer³, Grace Yu², Bruce Lahn² 1VectorBuilder GmbH, Neu-Isenburg, Germany, 2Yunzhou Biotech, Guangzhou Science City, China, 3VectorBuilder Inc, Chicago, United States

Background: Efficient and precise delivery is critical for advancing mRNA therapeutics beyond their current applications as vaccines. Here, we aim to enable targeted mRNA delivery by integrating human antibody discovery with high-quality lipid nanoparticle (LNP)-mRNA delivery platforms. **Method:** To enable precise, targeted mRNA delivery, we developed a highly efficient LNPmRNA immunization strategy for discovering antibodies against novel and otherwise challenging targets. In parallel, we established a site-specific conjugation technology that enables oriented attachment of antibodies to the LNP surface, including IgG, Fab, scFv, and VHH nanobody formats. To further enhance therapeutic suitability, antibody sequences were optimized through engineering strategies such as humanization and Fc silencing to reduce intrinsic immunogenicity. **Results:** This immunization strategy enables efficient generation of high-quality antibodies against complex multi-subunit targets, representing a significant improvement over conventional single-subunit protein immunization approaches. We demonstrate the robustness of this strategy across multiple animal models, including humanized mice and camelids. As a proof of concept, we show that antibodies generated through this approach can be successfully conjugated to LNPs, enabling targeted mRNA delivery to CD5⁺ cells. Compared with conventional random chemical conjugation, our site-specific antibody conjugation method significantly improves the transfection efficiency of LNP-mRNA in target cells. Additionally, antibody sequence optimization, including humanization and Fc silencing, improves overall safety and therapeutic efficacy of LNP-encapsulated mRNAs. **Conclusion:** Conjugating antibodies to LNPs enables precise and efficient mRNA delivery to desired cell populations. Together, our integrated site-specific LNP conjugation and human antibody discovery platform provides a powerful end-to-end workflow for developing highly targeted and potent mRNA therapeutics