Precise Delivery of mRNA Therapeutics

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mRNA therapeutics are revolutionising our approach to disease management.[1,2] The COVID-19 pandemic demonstrated that lipid nanoparticle (LNP) mRNA formulations are safe, and can be developed more rapidly than conventional therapeutics. While LNPs are an efficient way to encapsulate and protect mRNA, non-specific cellular uptake leads to off-target delivery and limited delivery to specific cells that are important therapeutic targets. Functionalizing LNPs with antibodies is an effective way to achieve targeted mRNA delivery, but antibody modification requires complex conjugation and purification methods, commonly leading to loss of antibody affinity.

Here, we present a simple method for capturing antibodies in their optimal orientation on the surface of LNPs without antibody modification or complex purification. This strategy leads to protein expression levels >1000 times higher than non-targeted LNPs and >10 times higher than conventional antibody functionalization techniques. These precisely targeted LNPs showed highly efficient in vivo targeting to circulating T cells, with minimal binding to other circulating blood cells. This approach enables the rapid development of targeted LNPs and has the potential to broaden the use of mRNA therapies.

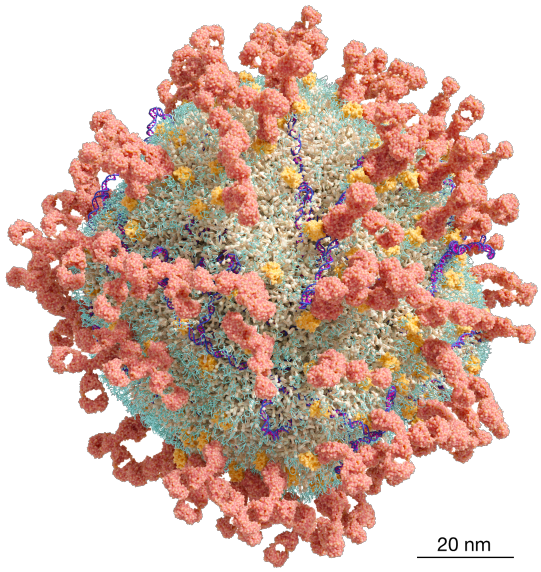

Figure 1: Scale 3D Representation of Targeted Lipid Nanoparticle

References

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[2] Huang, J.; Yuen, D.; Mintern, J. D.; Johnston, A. P. R. *Curr. Opin. Colloid Interface Sci.* **2021**, *55*, 101468.