세미나 초록

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발표 주제	항체를 이용한 mRNA-LNP의 표적 전달 기술
발표 내용	Recent advances in mRNA technology have significantly enhanced the potential for therapeutic alteration of gene expression. However, achieving cell specificity and minimizing off-target effects, particularly beyond the liver, remain significant hurdles. While antibody conjugation to LNPs is a promising strategy for targeted drug delivery, successful clinical translation of active targeting approaches requires innovative efforts to simplify the manufacturing process. Conjugating antibodies to LNPs typically uses polyethylene glycol (PEG) lipids and dibenzocyclooctyne, maleimide, or bicyclo[6.1.0]nonyne for stable attachment, but PEG shedding can lead to antibody detachment from the functionalized LNPs. Achieving high conjugation efficiency is challenging due to the complexity of the process. Additionally, there is a significant risk of reduced antibody integrity and misoriented conjugation. Here, "grab antibody" is introduced, which employs apolipoprotein fused to the crystallizable fragment (Fc) domain of a targeting antibody. This allows the antibody to spontaneously display on the surface of mRNA@LNPs, ensuring proper orientation and enhancing the stability and targeting efficiency without modifying the existing LNP process or using complex chemical conjugation techniques. The grab antibody simplifies the production process, ensures the functional integrity and correct orientation of antibodies, and maintains scalability, which are essential for the clinical translation of mRNA therapeutics. We show that various cell types, including cancer cells, dendritic cells, and T cells, can be targeted for the delivery of mRNAs encoding tumor suppressors, vaccine antigens, and chimeric antigen receptors. Our approach holds significant promise for advancing targeted gene therapy, with potential applications extending beyond cancer treatment to other genetic and immunological disorders.