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Bioinspired Lipid Nanocarriers x +

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Bioinspired Lipid Nanocarriers for RNA Delivery

Table 1. Overview of Bioinspired Design Strategies for Lipid-Based RNA Carriers (109–112)

Design strategy (with description)	Example schematic
Natural lipid substitution (e.g., substituting traditional ionizable lipids in existing LNP formulation with naturally occurring alkenyl amino alcohol lipids) Image adapted with permission from ref ¹⁰⁸ . Copyright 2016, John Wiley & Sons, Inc.	<p>Naturally Occurring Lipids Alkenyl Amino Alcohol (AAA) Cell Lipid Nanoparticle (LNP)</p> <p>Legend: mRNA (green), DOPE (orange), Cholesterol (yellow), AAA Ionizable lipid (red), PEG-lipid (blue)</p>
Mimicking endogenous molecules (e.g., mimicking HDL by decorating the lipid bilayer membrane of a miRNA carrier with apoA-I, which is highly expressed on the surface of HDLs) Image adapted from ref ¹⁰⁹ . Copyright 2017, American Chemical Society.	<p>phospholipid, cholesterol, sodium cholate, apo A1, anti-miR155, acid-fabrik PEI</p>
Mimicking viruses through virosomes (e.g., incorporating viral proteins, such as influenza hemagglutinin (HA), in lipid bilayer membranes) Image adapted from ref ¹¹⁰ . Copyright 2022, with permission from Elsevier.	<p>Phospholipid bilayer Viral Protein Chol siRNA</p>

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- Paunovska, K.; Loughrey, D.; Dahlman, J. E. Drug delivery systems for RNA therapeutics. Available for everyone to read 265– 280, 0439-4
- Kim, Y.-K. RNA therapy: rich history, various applications and unlimited future prospects. *Experimental & Molecular Medicine* **2022**, *54* (4), 455– 465, DOI: 10.1038/s12276-022-00757-5
- Jackson, L. A.; Anderson, E. J.; Roush, N. G.; Roberts, P. C.; Makhene, M.; Coler, R. N.; McCullough, M. P.; Chappell, J. D.; Denison, M. R.; Stevens, L. J., et al. An mRNA Vaccine against SARS-CoV-2 – Preliminary Report. *New*

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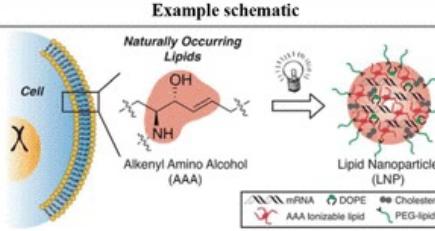
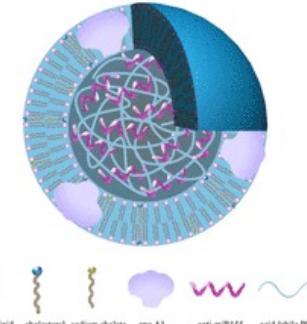
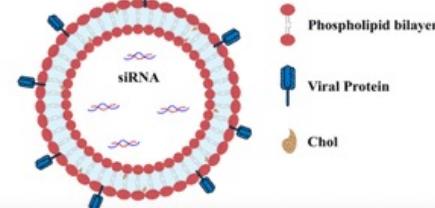
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Natural lipid substitution (e.g., substituting traditional ionizable lipids in existing LNP formulation with naturally occurring alkenyl amino alcohol lipids) <i>Image adapted with permission from ref¹⁰⁸. Copyright 2016, John Wiley & Sons, Inc.</i>	<p>The diagram illustrates the process of substituting natural occurring lipids in a cell membrane with alkenyl amino alcohol (AAA) lipids to create a lipid nanoparticle (LNP). On the left, a cell is shown with its membrane composed of various lipids. An arrow points to the right, where a schematic of an LNP is shown. The LNP contains mRNA, DOPE, Cholesterol, and PEG-lipid. A legend identifies the components: mRNA (black wavy line), DOPE (green oval), Cholesterol (blue circle), and PEG-lipid (red circle).</p>
Mimicking endogenous molecules (e.g., mimicking HDL by decorating the lipid bilayer membrane of a miRNA carrier with apoA-I, which is highly expressed on the surface of HDLs) <i>Image adapted from ref¹⁰⁹. Copyright 2017, American Chemical Society.</i>	<p>The diagram shows a circular miRNA carrier with a complex internal structure. It is surrounded by a lipid bilayer membrane containing various components labeled at the bottom: phospholipid, cholesterol, sodium cholate, apo A1, anti-miR155, and acid-fablic PEI. The apo A1 protein is specifically highlighted on the outer surface of the lipid bilayer.</p>
Mimicking viruses through virosomes (e.g., incorporating viral proteins, such as influenza hemagglutinin (HA), in lipid bilayer membranes) <i>Image adapted from ref¹¹⁰. Copyright 2022, with permission from Elsevier.</i>	<p>The diagram depicts a virosome as a spherical particle. It features a phospholipid bilayer outer layer with viral proteins (blue dots) and cholesterol (brown dot). Inside the bilayer, there is a core containing siRNA (represented by blue and white wavy lines).</p>

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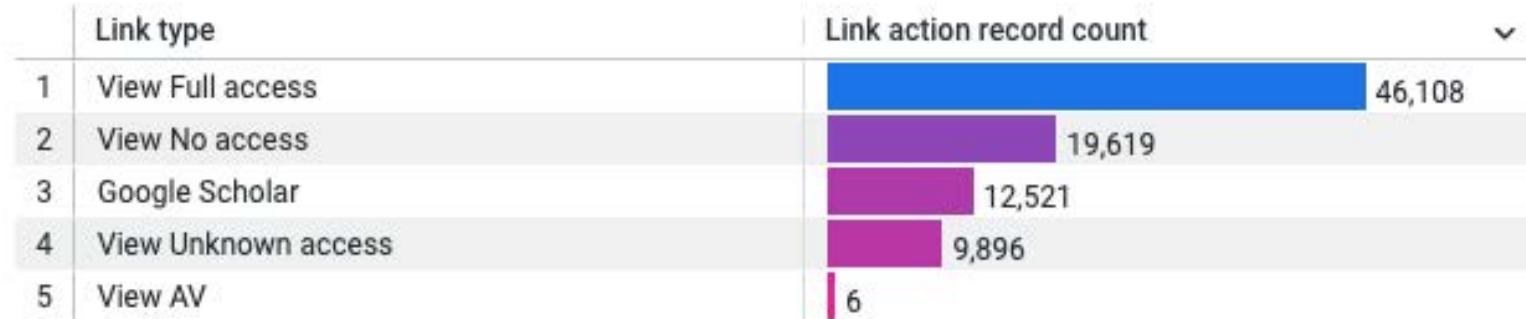
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