GLOBAL HEALTH PRESS

MRNA VACCINES: FROM SEQUENCE TO SHOT

Concept

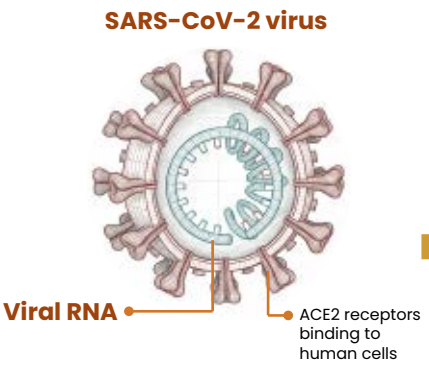
Synthetic mRNA in lipid nanoparticles turns host cells into transient protein-antigen producing factories, inducing robust B and T cell responses without live virus: Human cells are the ultimate vaccine factory.

Upstream: Making the mRNA

1. Antigen design

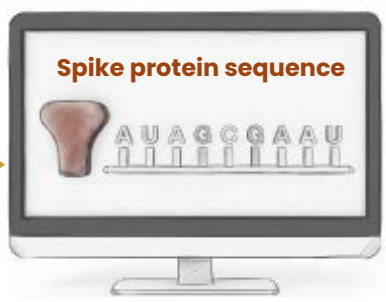
1

- In a pandemic, the genetic code of the threatening new pathogen is deciphered.



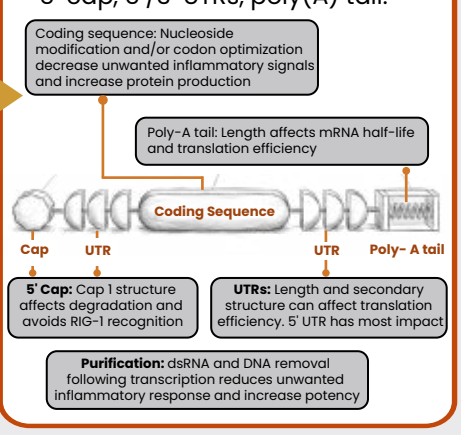
2

- From the code, antigen(s) of the pathogen relevant to induce microbial neutralization (virus) or killing (bacterium) are identified - e.g. receptors attaching to human cells.



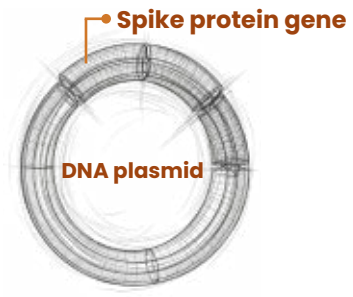
3

- Necessary regulatory elements for messenger RNA are added: 5′ cap, 5′/3′ UTRs, poly(A) tail.



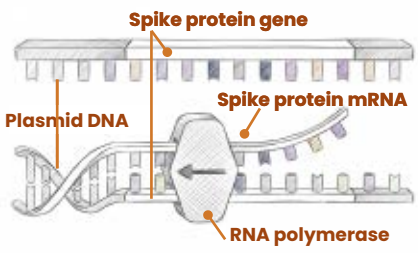
2. DNA template

- DNA-plasmids are now used because they can reliably and rapidly copy the (viral) target gene. Synthesize DNA plasmids containing promoter + antigen ORF + UTRs/poly A signal.
- Linearize plasmid; this is the template for in vitro transcription.



3. In vitro transcription (IVT)

- Produce the antigen-coding mRNA as accomplished in human cells by 1) separation (opening) of the plasmid DNA strands; and 2) by transcribing ("re-writing") DNA into mRNA using the natural enzyme RNA-polymerase.

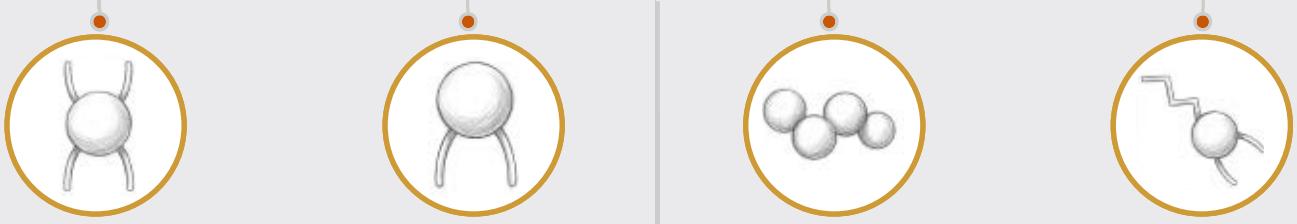


- Incorporate modified nucleosides (e.g., N1 methyl pseudouridine) to reduce innate sensing and increase translation.

4. mRNA polishing

- Cap addition/optimization, poly(A) tail control, and removal of dsRNA and other process-related impurities (chromatography/filtration). Linearize plasmid; this is the template for in vitro transcription.
- Result: highly pure, translation-competent modified mRNA (modRNA)

Formulation: Building the lipid nanoparticle



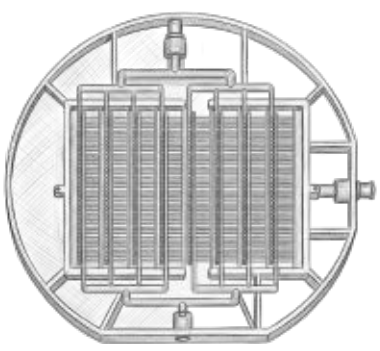
Ionizable cationic lipid: binds mRNA, enables endosomal escape.

Helper phospholipid: supports bilayer structure.

Cholesterol: structural stability.

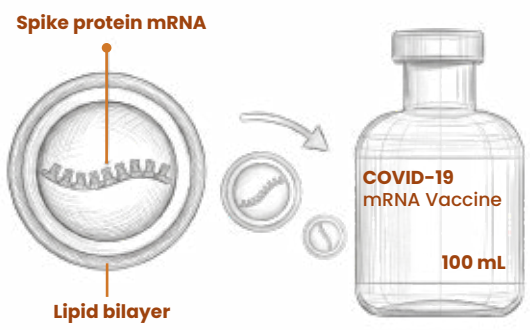
PEG lipid: colloidal stability and size control.

Nano encapsulation



- Rapid mixing of aqueous mRNA with ethanolic lipid phase forms uniform LNPs.
- Target size ~70–100 nm, optimized for uptake by antigen presenting cells.

Formulated drug product



- LNP mRNA in buffered, cryoprotectant containing solution (e.g., PBS/Tris + sucrose), filled into vials under cold chain conditions.Features: Chemical activation and conjugation,

References

Buckland B, Sanyal G, Ranheim T, Pollard D, Searles JA, Behrens S, Pluschkell S, Josefsberg J, Roberts CJ. Vaccine process technology—A decade of progress. Biotechnol Bioeng. 2024;121(9):2604-2635. doi:10.1002/bit.28703

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