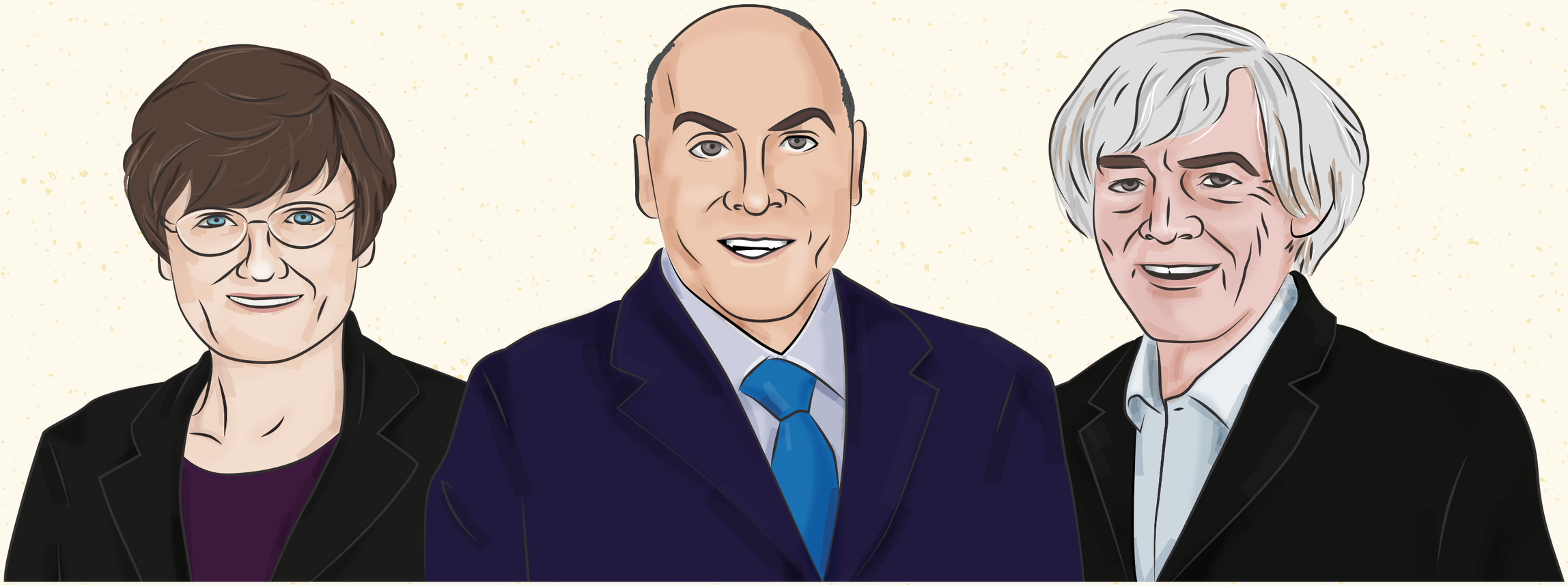
2022 Tang Prize

BIOPHARMACEUTICAL SCIENCE

TANG PRIZE



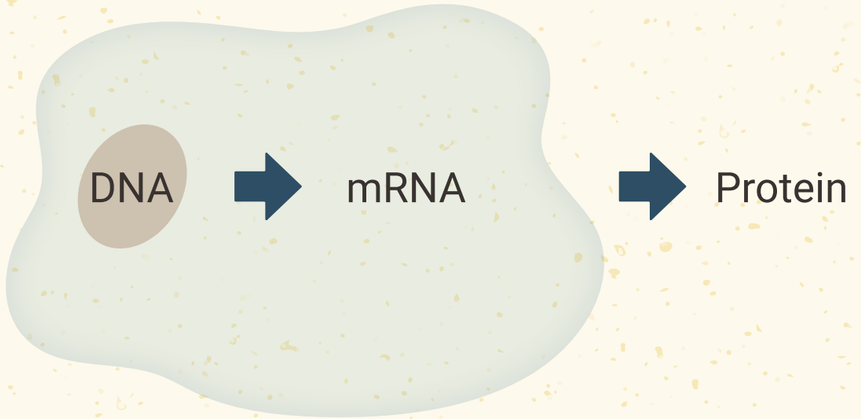
Katalin Kariko

Drew Weissman

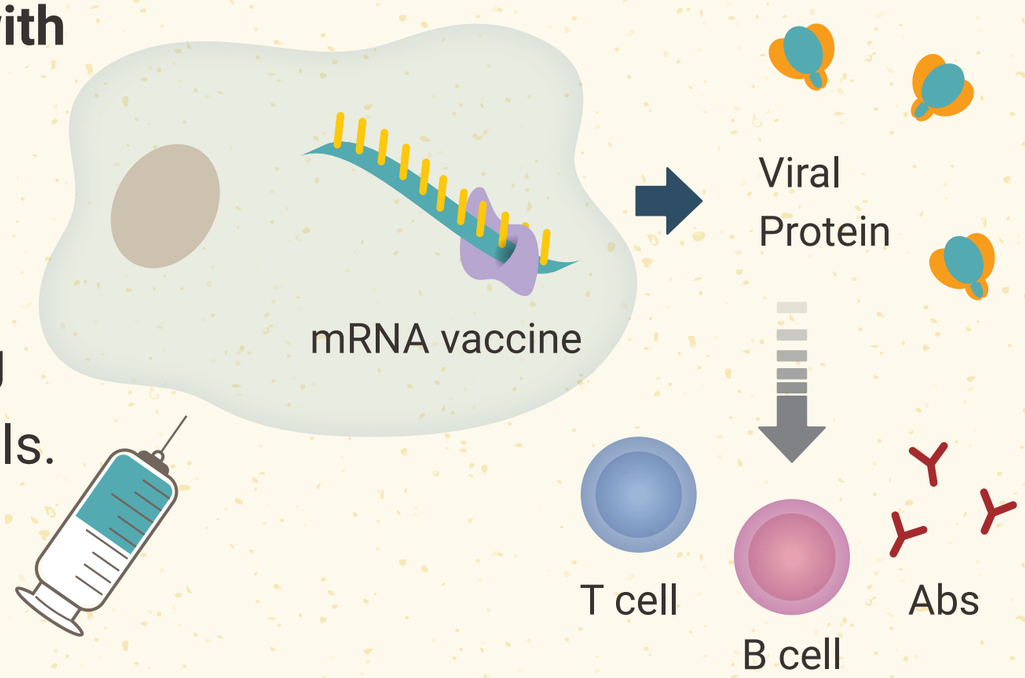
Pieter Cullis

How do mRNA vaccines work?

Human cells are non-stop factories, which can produce specific proteins through a process of **" transcribing DNA into mRNA, then translating mRNA into proteins. "**



COVID-19 mRNA vaccines are **artificial mRNAs with viral sequence**.They are injected to let our cells make **viral proteins that are not pathogenic**.
The proteins can induce adaptive immune responses such as B cells to produce neutralizing antibodies, and T cells to attack virus-infected cells.



How hard it is to develop them?

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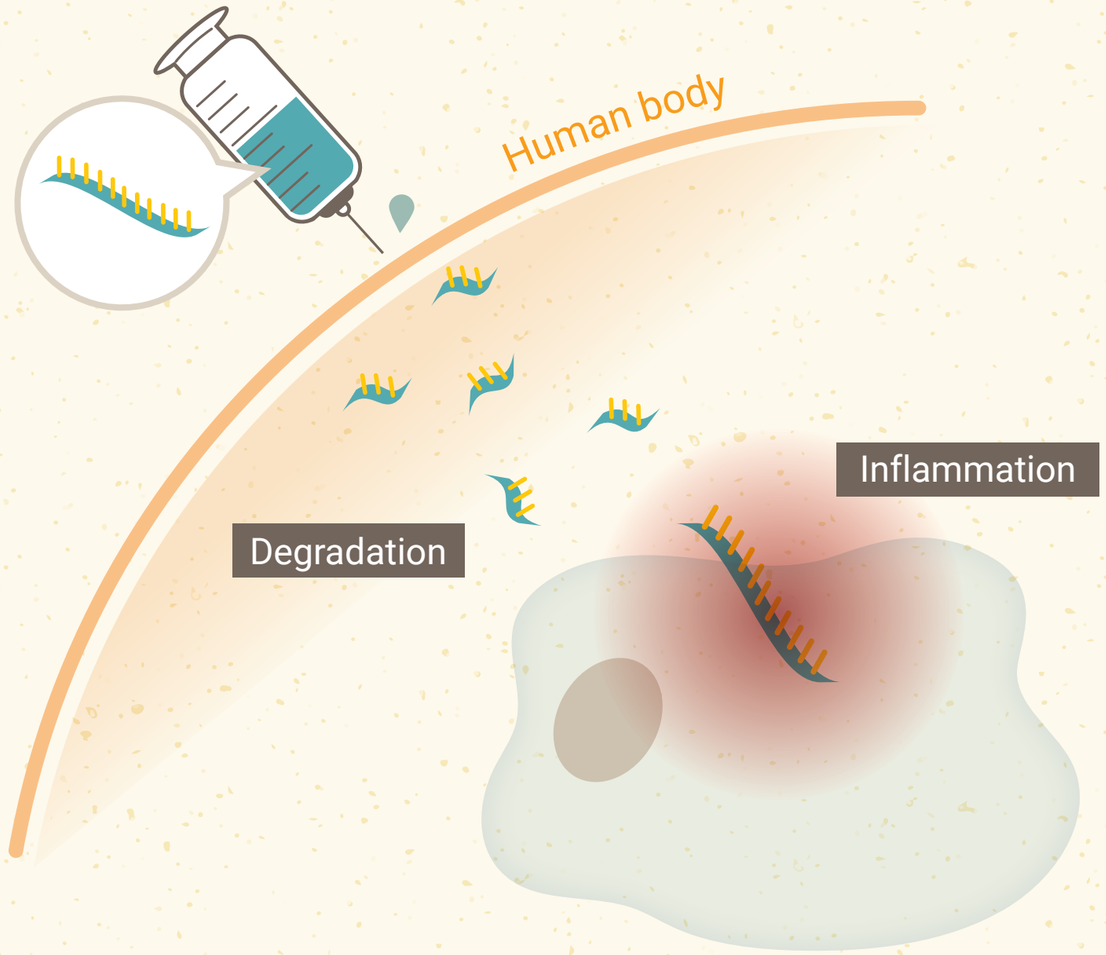
mRNA was discovered in 1961. The origin of mRNA vaccine was in 1993, when mRNA encoded influenza virus was injected into animals and induced T cells successfully. However, over the next two decades, most scientists abandoned this technology with simple concepts but hard to implement.

Two major challenges
in developing mRNA vaccines:

1. Foreign mRNAs trigger innate immune responses, cause severe side effects.

2. mRNAs are degraded rapidly after injection, and are difficult to enter our cells to function.



Their contributions

- **They are awarded the prize for the discovery of key vaccinology concepts and approaches, leading to the successful development of mRNA-based COVID-19 vaccine.**

Katalin Kariko

Drew Weissman

Pieter Cullis

- In early 2020, after obtaining the virus sequence, both Moderna and Pfizer/BioNTech successfully developed the SARS-CoV-2 vaccine within one year.
- The perseverant efforts of the three laureates enabled the world to blunt the advance of the pandemic in time, and have saved millions of lives.

Katalin Kariko & Drew Weissman

Making nucleoside-modified mRNAs

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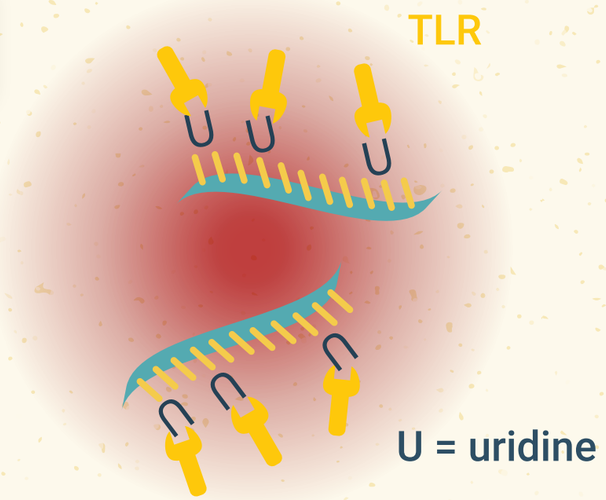
Why doesn’t the immune system attack our own mRNA?

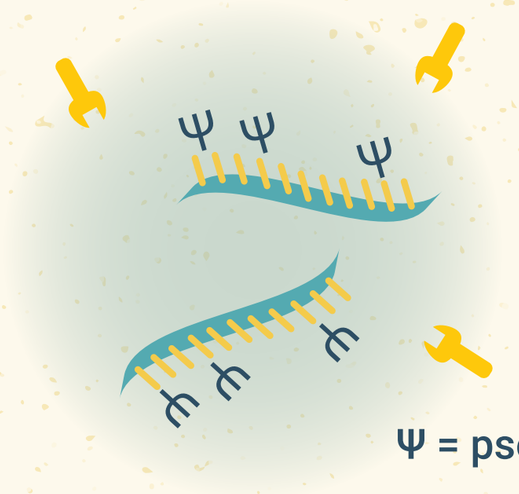
- **Discovered key mechanisms of the immune system attacking foreign mRNA:**

  identified by and cause severe inflammation through **toll-like receptors (TLRs).**



- **Demonstrated that modified mRNAs can reduce immunogenicity:**

  as naturally occurring RNAs, nucleoside-modified mRNAs can escape from immune surveillance. Moreover, modifying **uridine (U)** in the mRNA to “**pseudouridine (Ψ)** ” also helps stabilize the mRNAs and improve protein production.

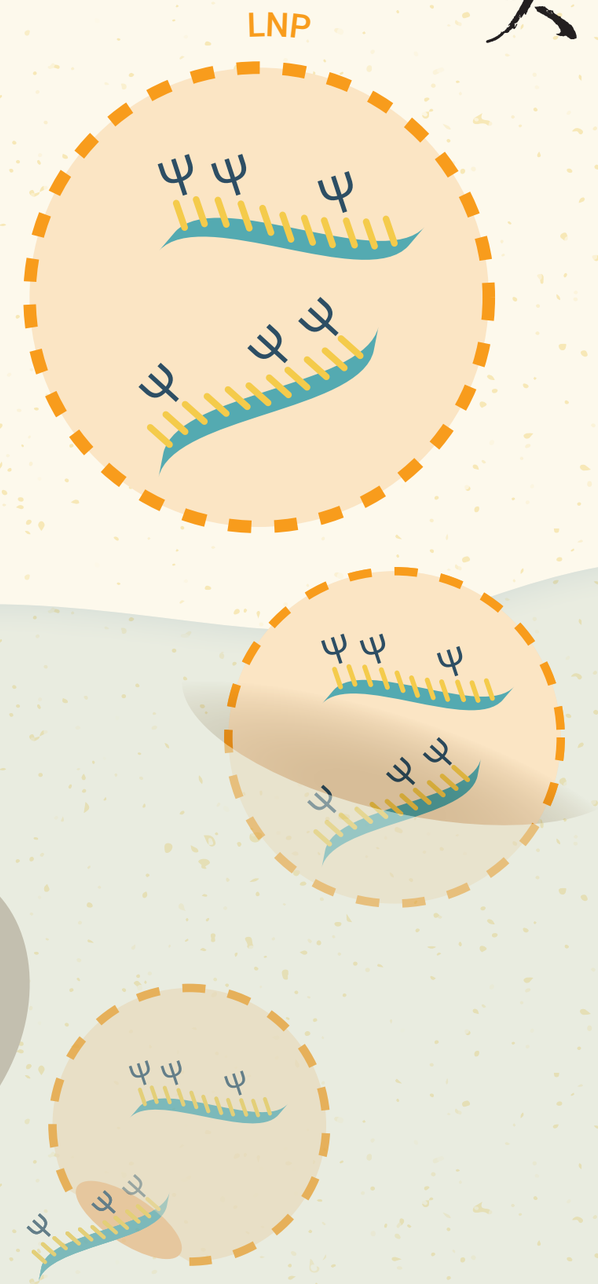


Pieter Cullis

Pioneering the LNP system

mRNA vaccines hardly enter a cell without protection.

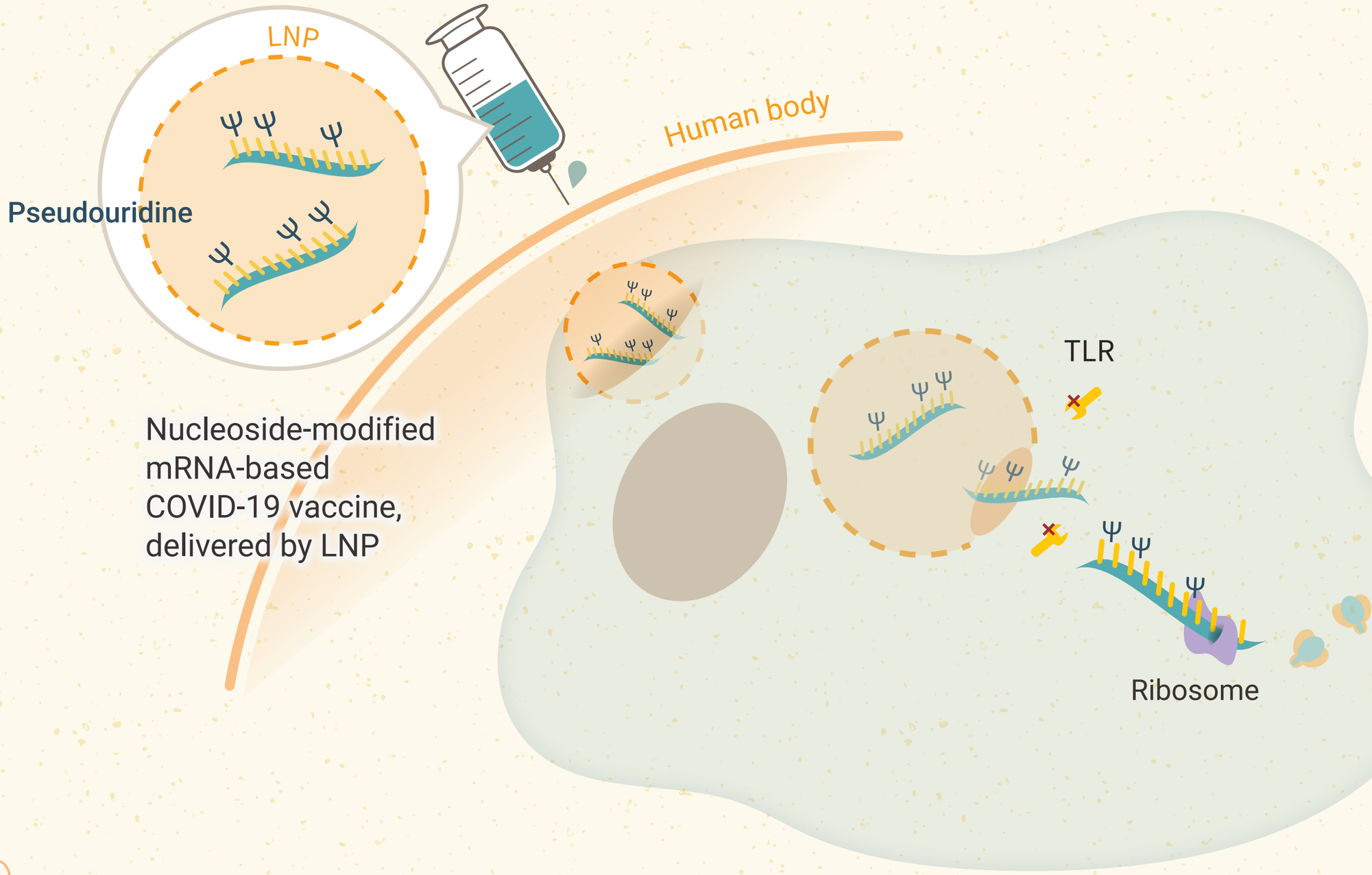
The lipid nanoparticles (LNP) system is a novel drug delivery technology. The nanoscale lipid particles can encapsulate small molecules, making them stay longer in the body and reach the target cells or organs.



- **Established the LNP system after decades of research on lipid delivery systems:**

  composed of **pH-sensitive, cationic lipids with a non-bilayer structure**, which can protect mRNA vaccine be delivered in the body and not released until entering cells.

mRNA-based COVID-19 vaccine



Nucleoside-modified
mRNA-based
COVID-19 vaccine,
delivered by LNP

Broad applications

mRNA vaccines can be developed quickly and more easily to mass-produce, unlike traditional ones. They will thus become an important weapon in the fight against emerging infectious diseases as well as existing diseases without an efficient vaccine or cure.

Cancer Vaccines

Cytokines

ZIKV Vaccines

Hormones

HIV Vaccines

Enzymes

The mRNA vaccine technology platform turns cells into factories where proteins that serve as therapeutics can be produced signals a **paradigm shift in protein therapy**.