MESSENGER RNA VACCINES

Tapani Ronni

Welcome!

I am here because I love to give scientific presentations.

You can find me at:
www.polarbearcommunications.com

About the speaker

- PhD in Genetics, University of Helsinki, Finland
- Postdoctoral fellow, University of California, Los Angeles
- Scientific interests: gene therapy, microbiology, immunology
- A full time medical translator since 2007 (English-Finnish)

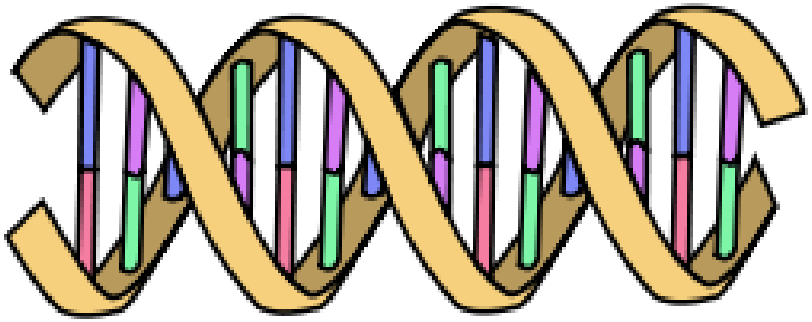
Contents of this talk

- From gene to RNA to protein
- Messenger RNA (mRNA) as a tool
- Chemical modifications
- Nobel 2023
- mRNA for immunization – benefits and drawbacks
- Case study: COVID-19
- Future prospects

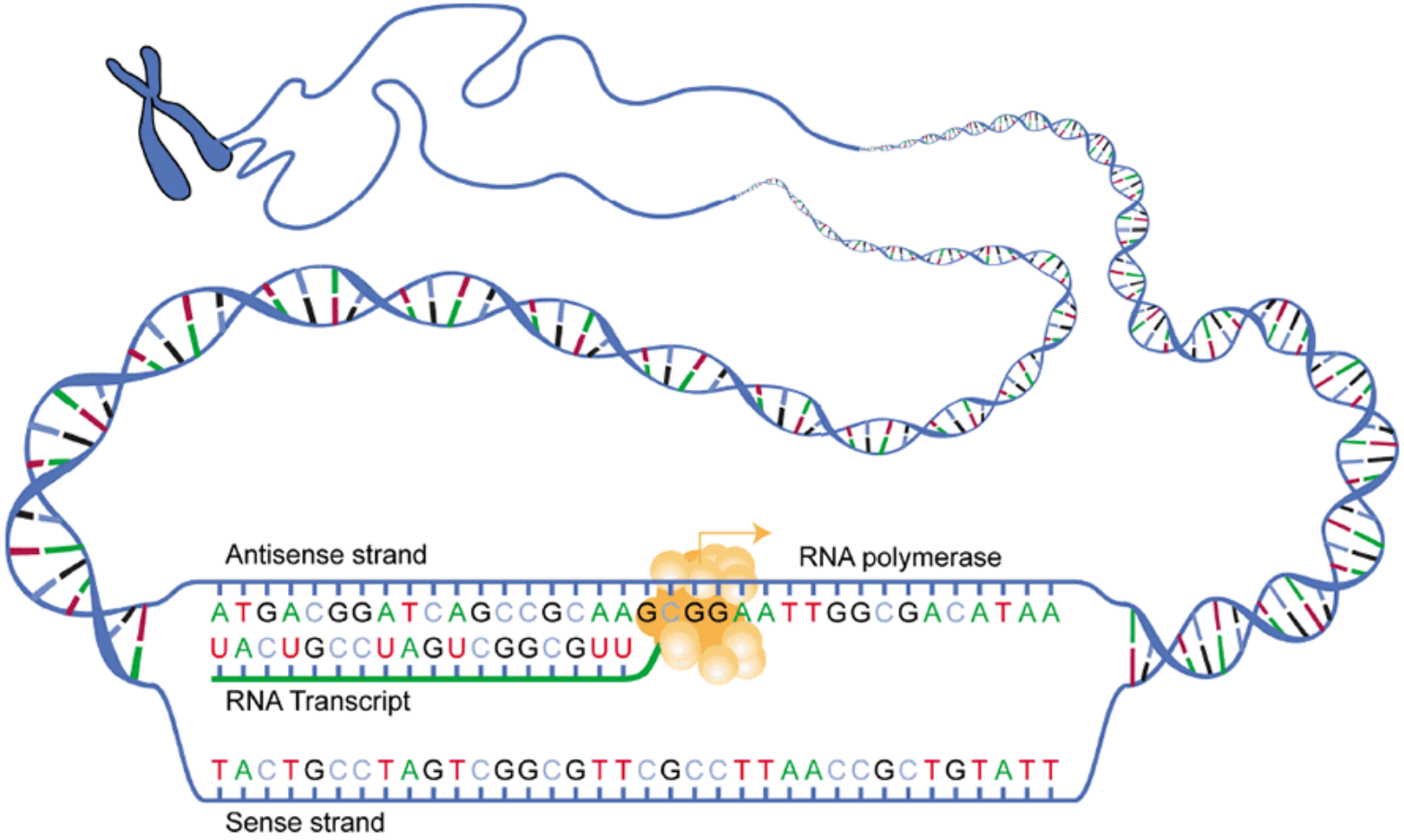
The Double Helix

A schematic view of DNA structure.

Each of the four bases (A, C, G, T) is shown with different color.

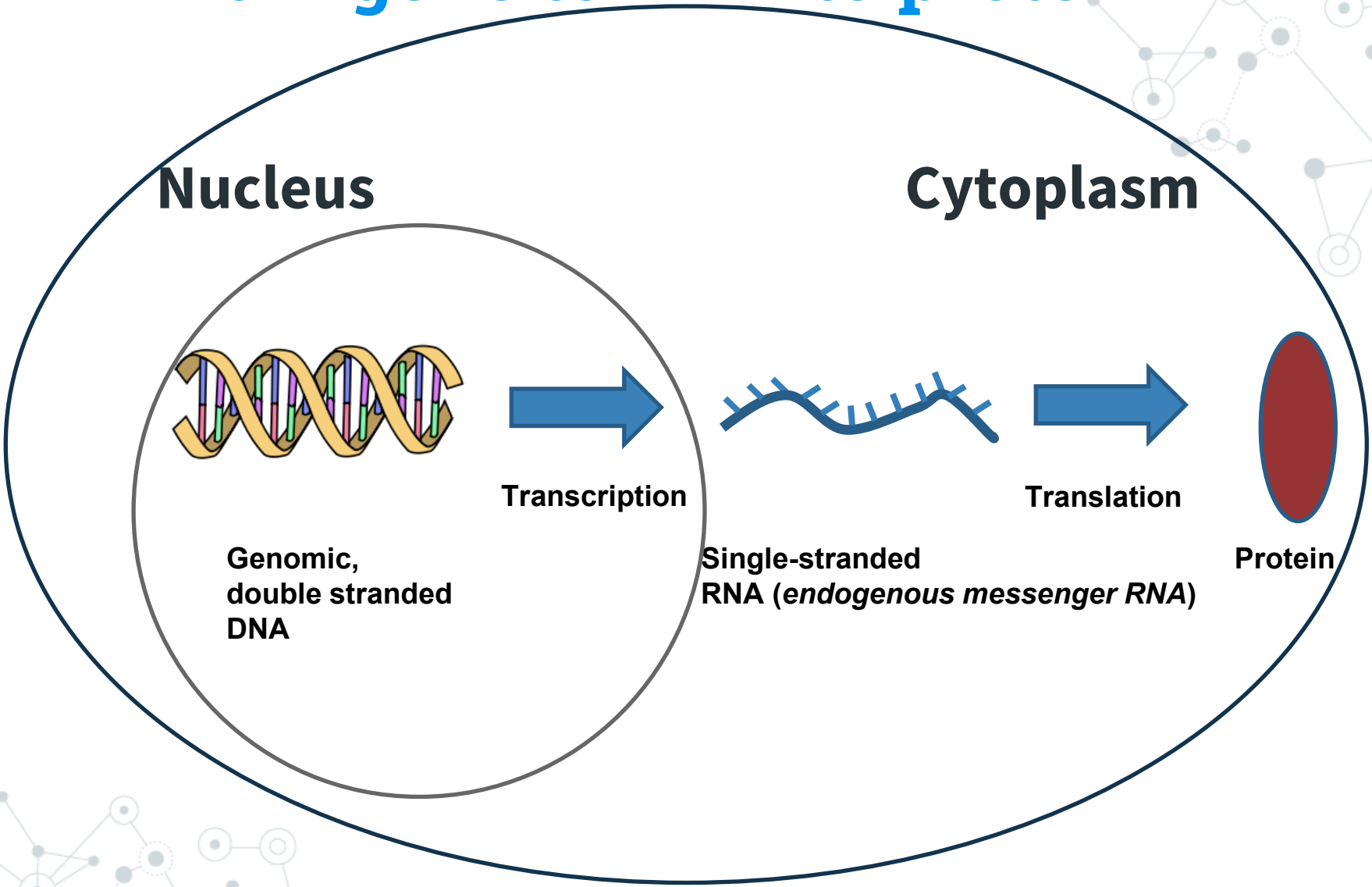


From DNA to RNA (transcription)



National Human Genome Research Institute,
http://www.genome.gov/Images/EdKit/bio2c_large.gif

From gene to RNA to protein

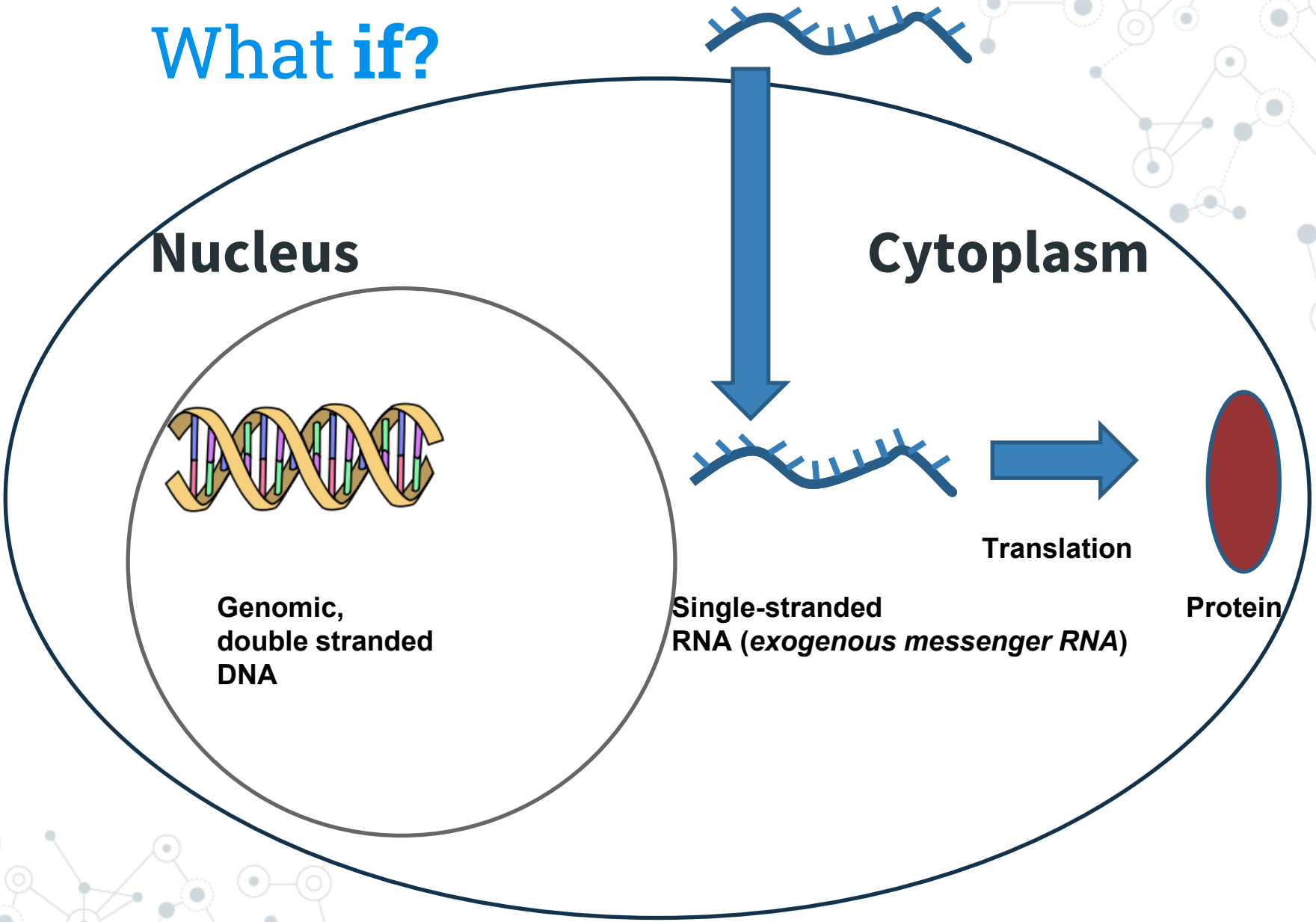


Public Domain image, https://commons.wikimedia.org/w/index.php?curid=7876890

Messenger RNA

- Messenger RNA (mRNA) is produced in the cell nucleus and exported to the cytoplasm
- mRNA is read in the *ribosome*
- Ribosome translates the information into a polypeptide sequence
- The new polypeptide is then folded into a functional protein, such as an enzyme
- Proteins may be exported or stay in the cell

What **if?**



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Messenger RNA (continued)

- ***Endogenous*** **mRNA is short-lived in vivo**
- ***Exogenous*** **mRNAs can be made and introduced to mammalian cells using various vehicles such as lipid nanoparticles**
- **However, they are *fragile* and also cause an immune reaction**

Messenger RNA (continued)

- The idea of exogenous mRNA was compelling
- Clearly, the problem was hard
- A 20-year research project to find a workaround at University of Pennsylvania

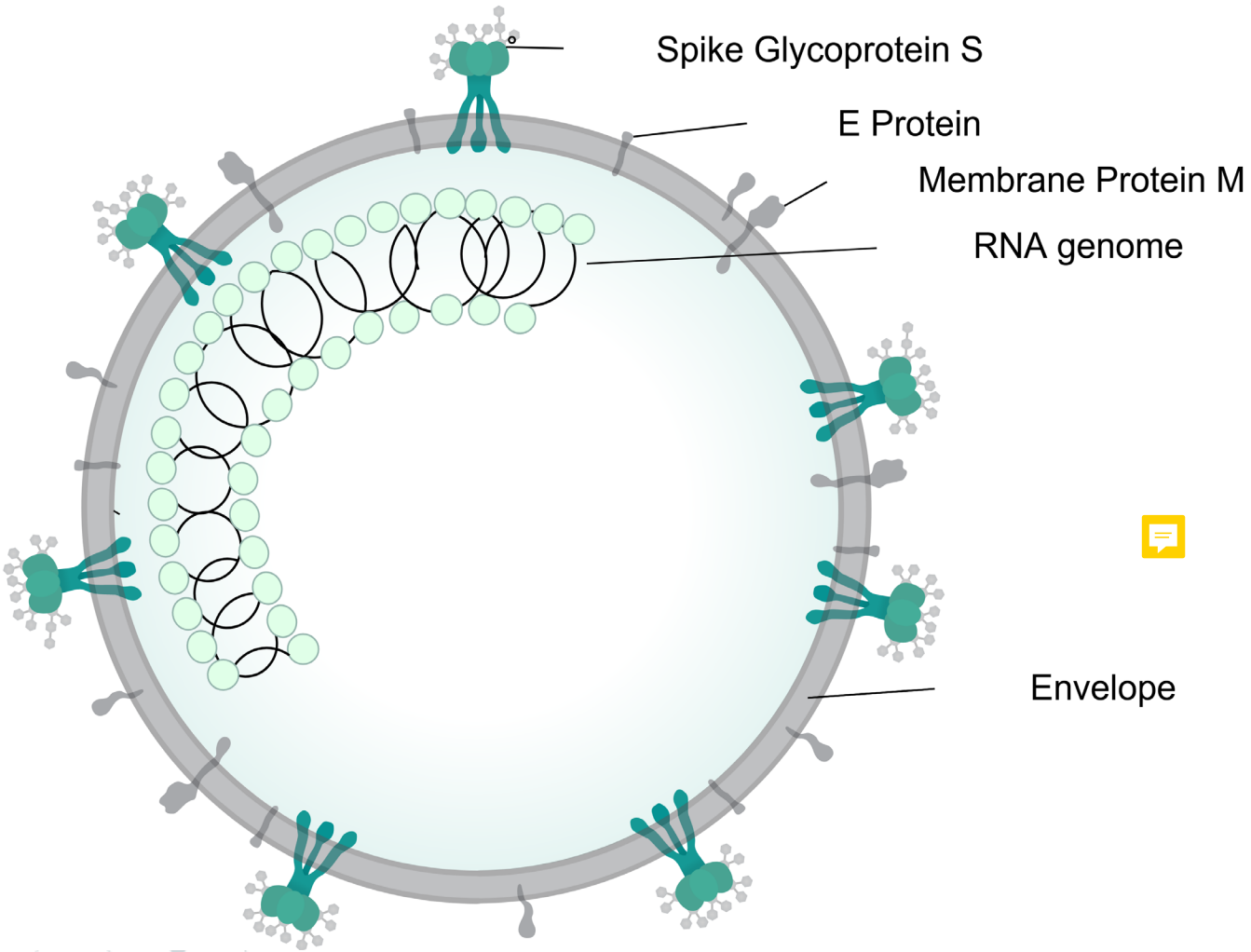
Nobel Prize in Physiology or Medicine, 2023

“To Katalin Karikó and Drew Weissman for their discoveries concerning nucleoside base modifications that enabled the development of effective mRNA vaccines against COVID-19”

Dr. Drew Weissman and Dr. Katalyn Karikó

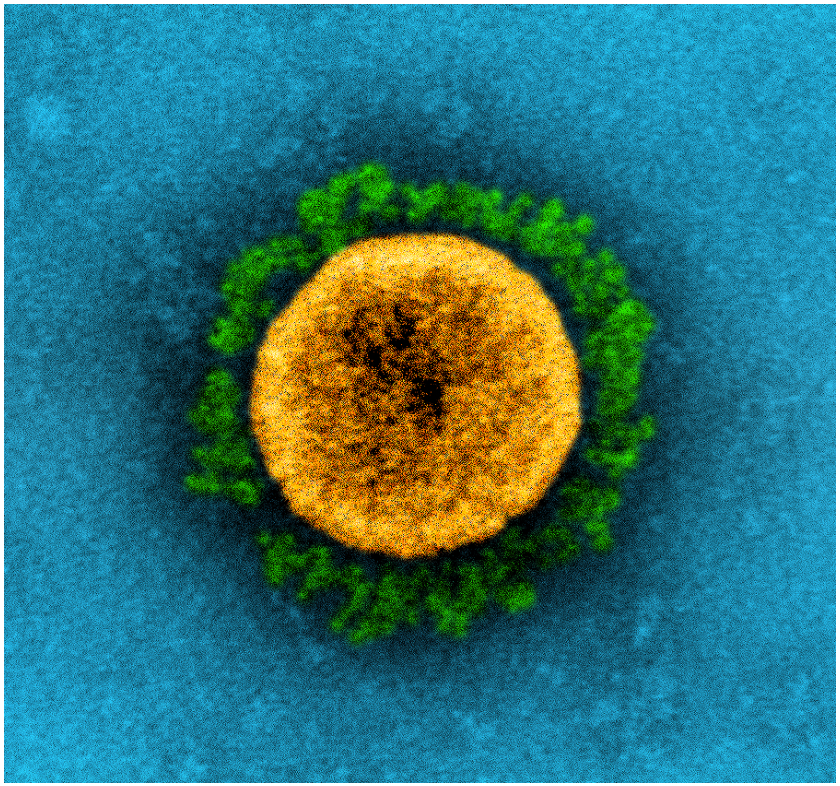
COVID-19 vaccines

Structure of the SARS-CoV-2 (COVID-19) virus



SARS-CoV-2. (2023, October 7). In *Wikipedia*. https://en.wikipedia.org/wiki/SARS-CoV-2

Transmission electron micrograph



60-140 nanometers

Source: NIAID

Benefits of mRNA vaccines against COVID-19

- Fast and easy to produce *in vitro*
- Easy to adapt to match virus evolution
- Safe and effective
- Elicits both B and T cell responses (APC presentation)
- Contains no egg products, mercury, or thimerosal

Benefits of mRNA vaccines against COVID-19 (continued)

- mRNA works in cytoplasm, DNA would need to go to the nucleus
- Self-limiting lifespan
- Highly unlikely to affect the genome in any way
- RNA is itself an adjuvant

Drawbacks of mRNA vaccines

- Current versions require extreme “cold chain” storage (-80 or even -120 Celsius degrees)
- Challenging in the field, e.g. in developing countries
- Lipid nanoparticle – mRNA complex is unstable
- Improvements are required for large-scale applications

Challenges and future trends

- **Rapid mutability of targeted antigens (immune evasion)**
  - **- need to find essential structural antigen targets (such as the HA stalk in the influenza virus)**
  - **Multiple antigens can be targeted in one mRNA vaccine**

- **mRNA as cancer vaccine**

Challenges and future trends

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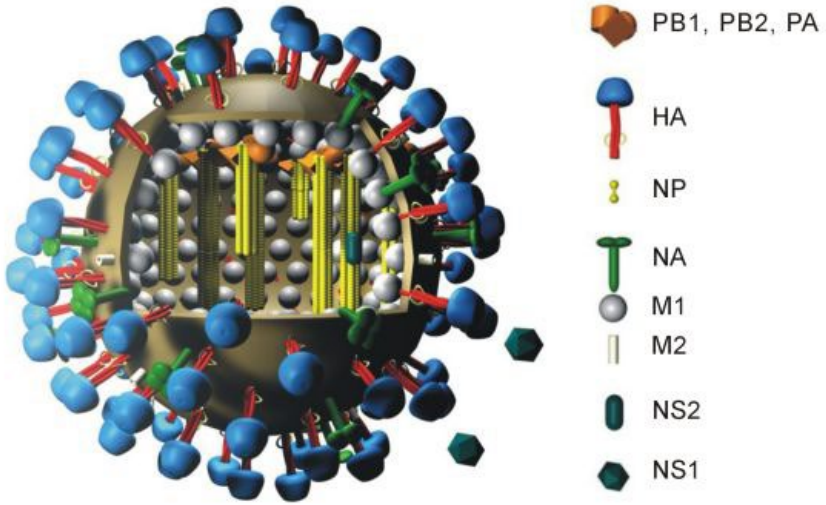

Challenges and future trends

- mRNA as cancer vaccine is a tantalizing idea
  - - antigens? mutations?
  - Personalized to each patient
  - Phase II trial starting for pancreatic cancer
- Customized mRNA, checkpoint inhibitor, and chemotherapy combination, promising results

Summary

- mRNA has proven to work as vaccine against COVID-19
- Promising prospects ahead with infectious diseases
- May be useful against cancer if not too expensive

Thank you!

Any questions?

You can find me at:
tapanironni@yahoo.com

Credits

Special thanks to all the people who made and released this awesome resource for free:

- Presentation template by SlidesCarnival