



HUDSON COLLEGE OF PUBLIC HEALTH  
*The* UNIVERSITY of OKLAHOMA HEALTH SCIENCES CENTER

# **An Intersection between Genetics and COVID-19**

**Aaron M. Wendelboe, PhD**  
**Associate Professor of Epidemiology**  
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# Outline

- Biology review
  - Humans and viruses
- SARS-CoV-2 virus, its cousins, and its animal hosts
- Genetic technology and novel vaccine development
- Epigenetics approach to identifying risk factors for severe COVID-19 disease

# Human Biology Review

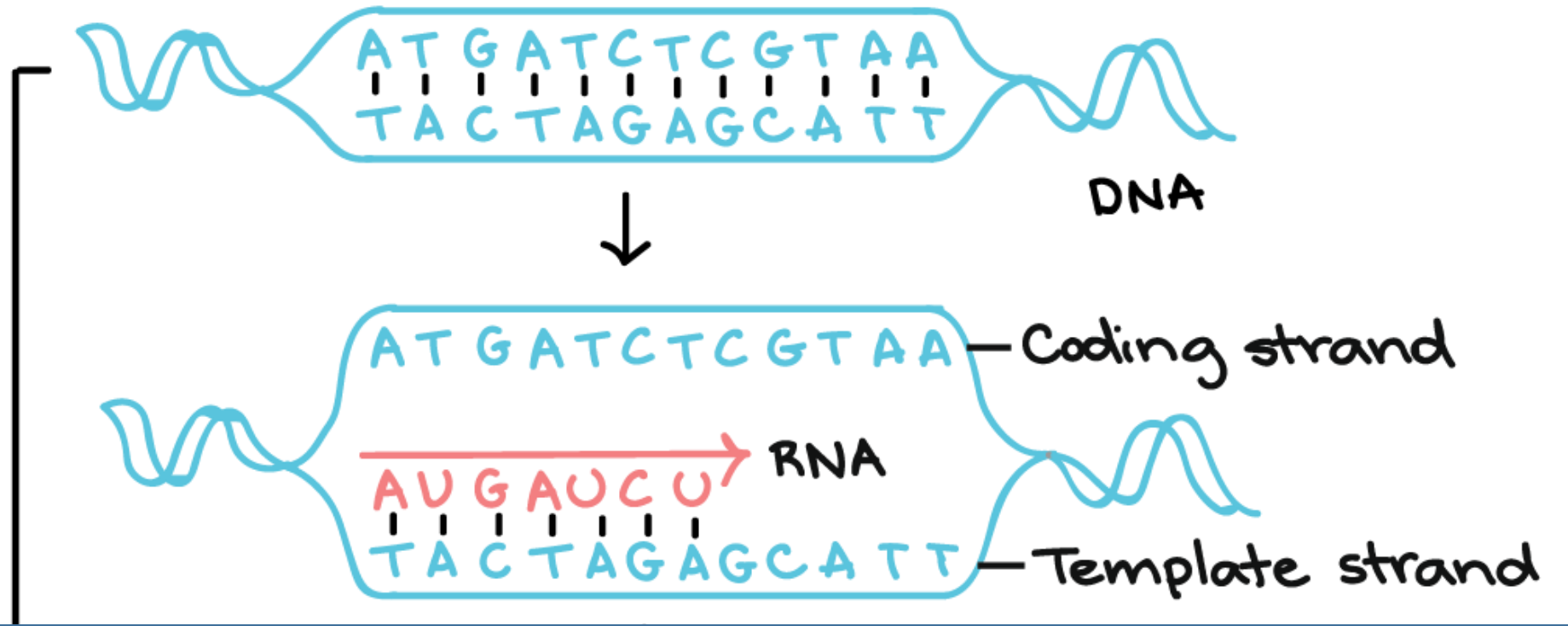
- Chromosomes comprise double-stranded DNA



# Human Biology Review

- Chromosomes comprise double-stranded DNA
- Transcription is process of transcribing DNA to messenger RNA (mRNA)

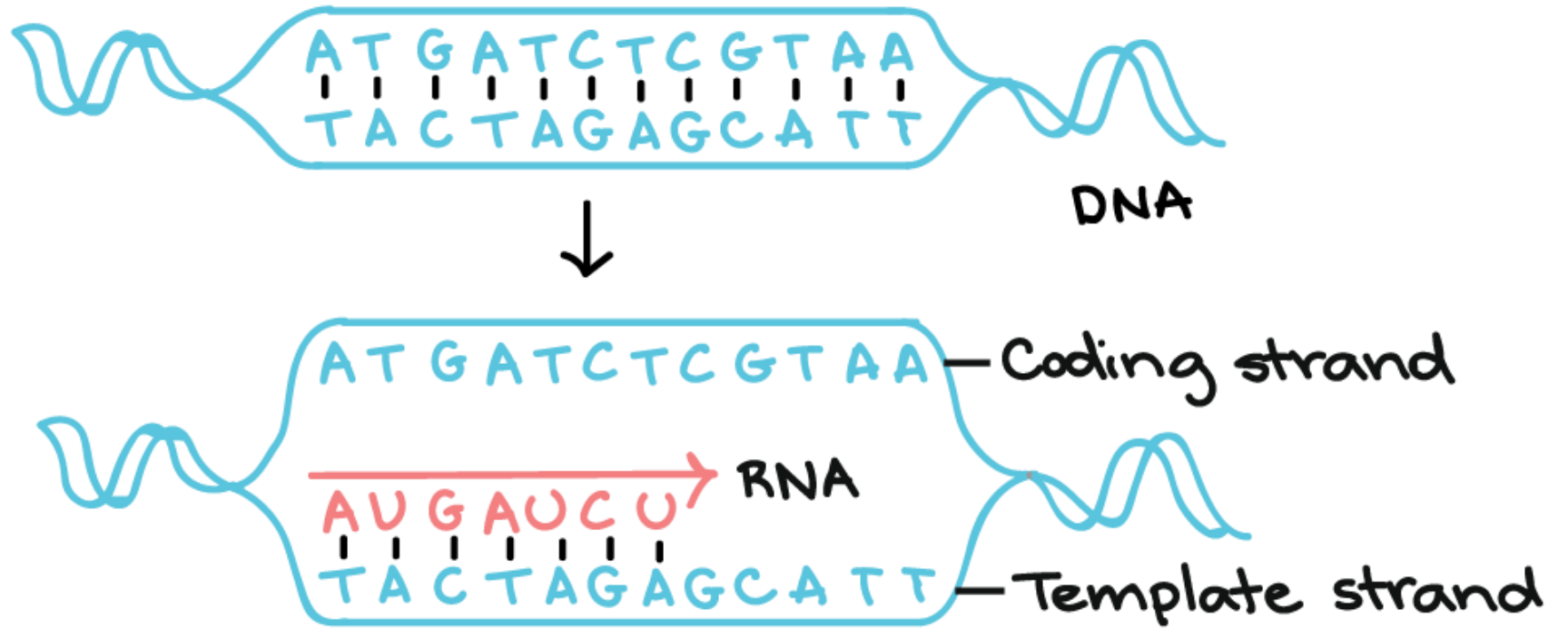
# Transcription



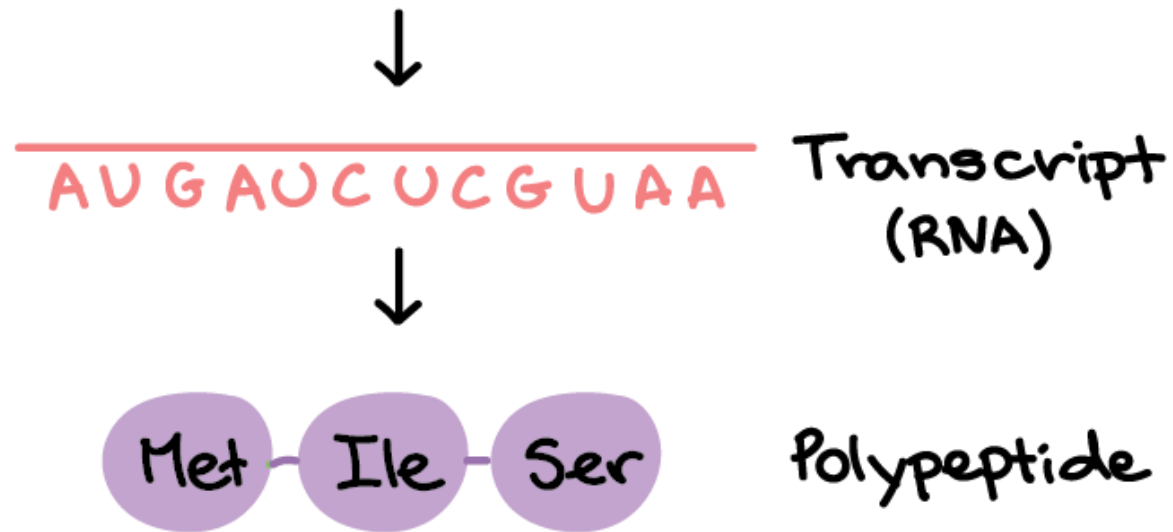
# Human Biology Review

- Chromosomes comprise double-stranded DNA
- Transcription is process of transcribing DNA to messenger RNA (mRNA)
- Translation is process of translating mRNA to proteins via assembling amino acids

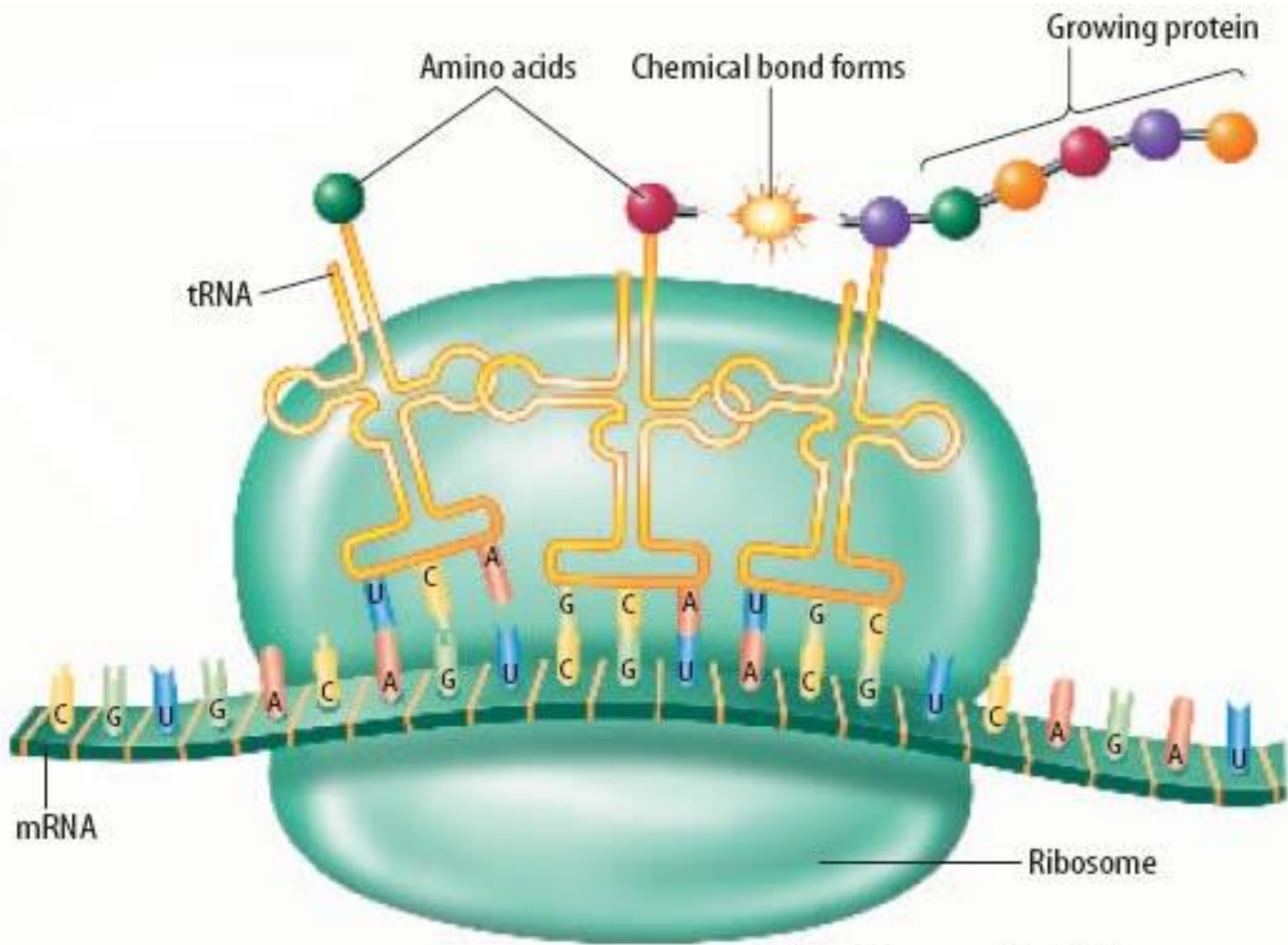
Transcription



Translation



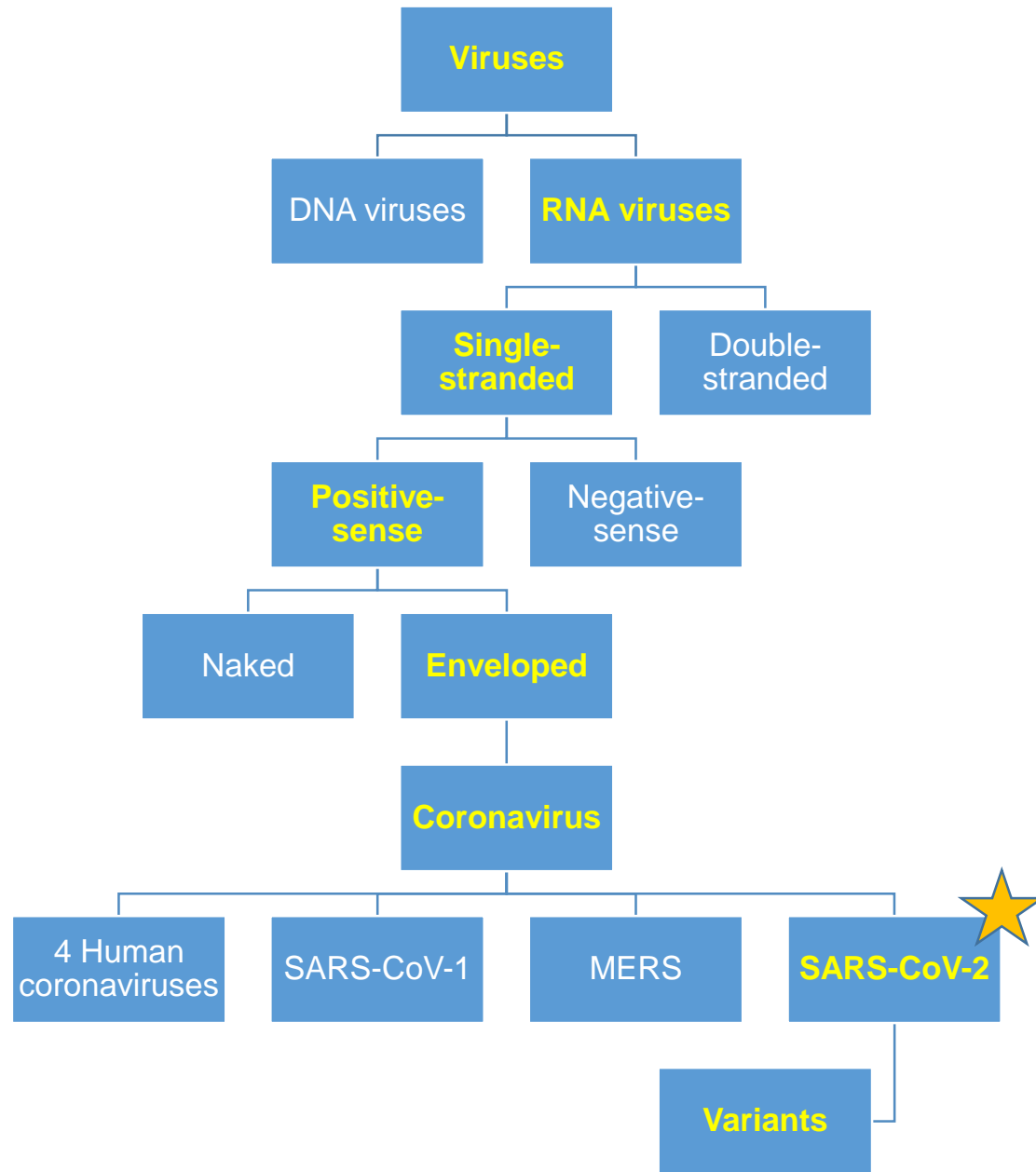




mRNA starts with the 5' end

At the ribosome, the RNA's message is translated into a specific protein.

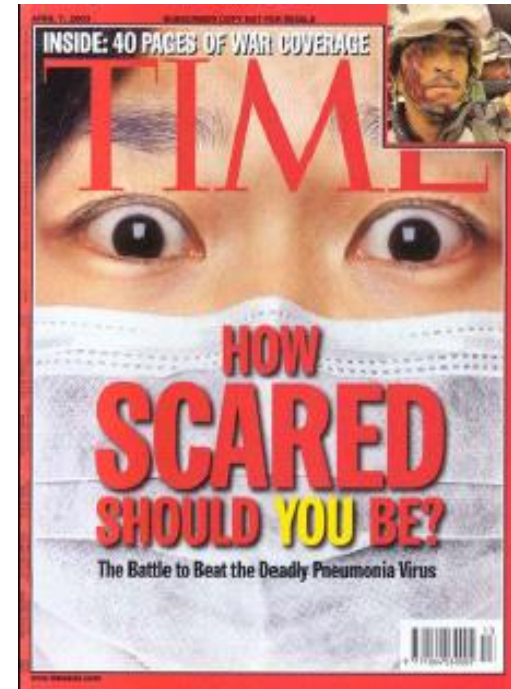
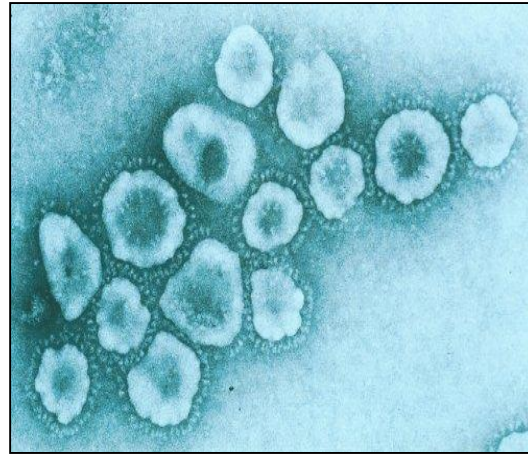
# Virology



# Zoonotic viruses

- Influenza
- West Nile virus
- Rabies
- Dengue fever
- Ebolavirus
  
- HIV
  - Jumped the species barrier at least two independent times

# SARS





# Animals linked to SARS-CoV-1

- Masked palm civet cats
- Raccoon dogs
- Horseshoe bats



<https://news.psu.edu/story/626880/2020/07/28/research/researchers-identify-evolutionary-origins-sars-cov-2>

<https://www.pinterest.com/pin/225180050089265247/>

# Animals linked to SARS-CoV-2

- Pangolin
- Horseshoe bats



- Mink



<https://www.thethirdpole.net/en/nature/pakistan-pangolin-scales/>

<https://www.pbs.org/wgbh/nova/article/mink-covid-virus-mutation/>

# Virus variants

- All viruses change and mutate.
  - Most mutations are not good for the virus.
  - Only small percent of mutations are beneficial to the virus.
  - Because the virus replicates itself billions/trillions/gazillions of times across the globe, those rare times the mutation is beneficial for the virus is enough for it to turn into a new strain or variant.
- More effective strains replace the old, less effective strains.



# Tracking the Variants of COVID-19

## Reported in the US

- P.1 = 5,153
- B.1.1.7 = 84,081
- B.1.351 = 1,147
- B.1.429+B.1.427 = 37,615
- B.1.525 = 642
- B.1.617+ = 325

<https://www.gisaid.org/hcov19-variants/>

## Reported in Oklahoma

- P.1 = 2
- B.1.1.7 = 118
- B.1.351 = 4
- B.1.429+B.1.427 = 17
- B.1.525 = 1
- B.1.617+ = 2

# Vaccine Development

# Brief timeline of synthetic mRNA development

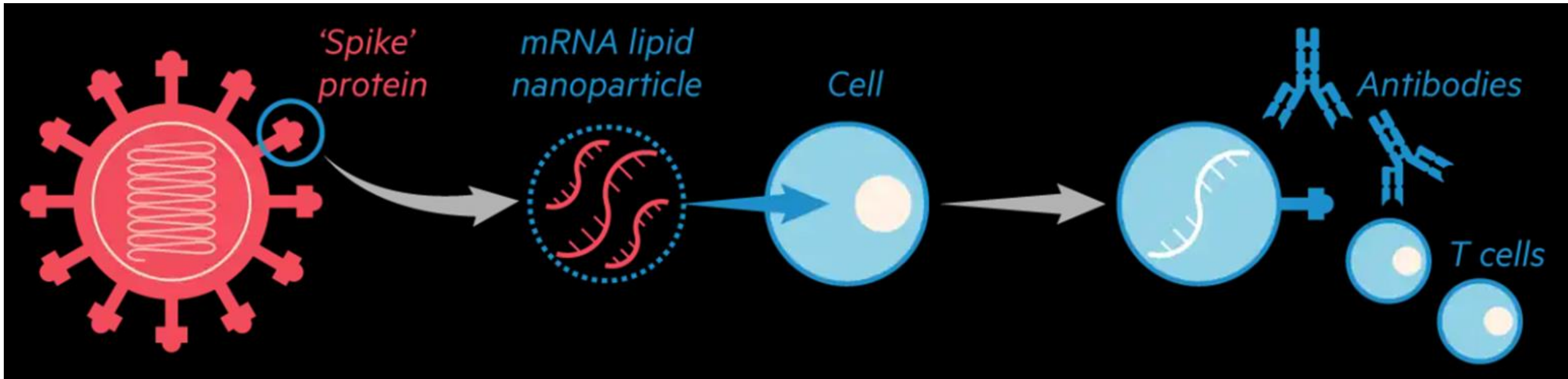
- 1990: researchers at University Wisconsin inject mice with mRNA to express selected genes
- 1989-2005: Dr. Kariko at University of Pennsylvania studying mRNA delivery systems
  - 1989-1995: Failed to obtain research grants
  - 1996-2005: Modest success
- 2005: Dr. Kariko made breakthrough discovery: modified nucleosides that slipped past immune system
- 2009: Dr. Rossi uses synthetic mRNA to develop stem cells
  - No need to use embryos

# Continued timeline of synthetic mRNA development

- 2010: Dr. Rossi co-founds Moderna
- 2013: BioNTech (German company) hires Dr. Kariko as senior VP over mRNA work
  - BioNTech focus on cancer therapy use of mRNA
- Jan 10, 2020: Chinese scientists post SARS-CoV-2 genetic sequence
- Feb 24, 2020: Moderna has first vials of experimental vaccine
  - Computer programming used to develop sequence
- July 28, 2020: Moderna initiated late-stage vaccine trial

# Background on mRNA vaccines: Pfizer and Moderna

mRNA vaccines instruct the immune system to recognize a specific part of the virus



**SARS-2-CoV**

**mRNA that encodes the spike protein is synthesized and packaged inside a lipid coating**

**Cells use the mRNA to make a spike protein that is recognized by the immune system**

# Epigenetics

# Genetics and risk of severe COVID-19 morbidity

- Study of 407 people with confirmed COVID-19
  - Age  $\leq$  61 years
  - Mild disease: 194 patients; Severe disease 213 patients (hospitalized with respiratory support)
- Study population split into prediction and validation cohorts
  - Stratified by disease severity
- 44 CpG sites significantly associated with COVID-19 disease severity
  - Genes associated with immune system and interferon release
- Using validation cohort, epigenetic signature able to predict severe disease with 88.2% specificity and 77.8% sensitivity
- In general population: 13.3% of people have epigenetic signature
  - Approximate percent of population who get severe COVID-19

# Summary

- Genetics and the building blocks of life
  - Viruses mutate and find new hosts for survival
- Synthetic mRNA technology not new, but still in its infancy
- Risk factors for severe COVID-19 disease likely associated with genetic factors



# Questions?