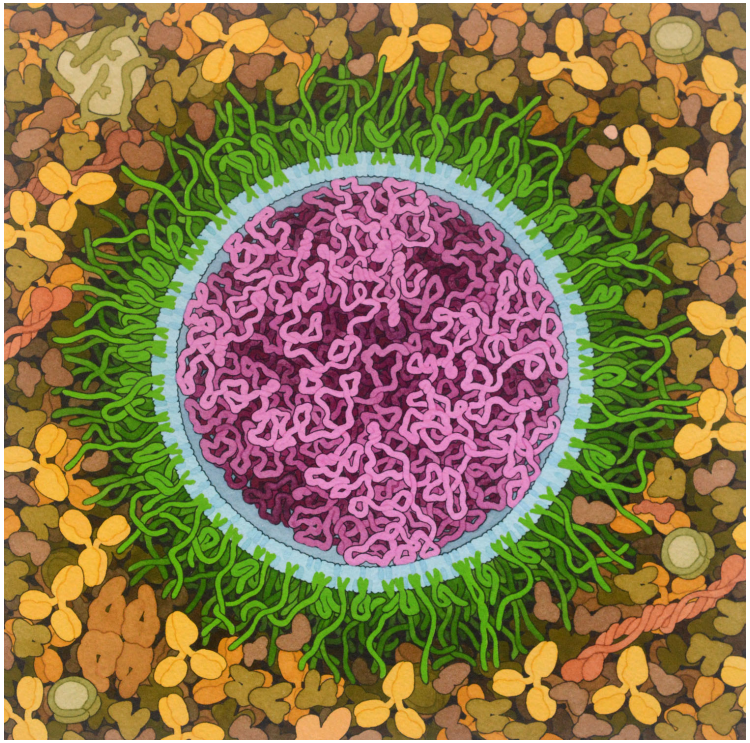
Vaccine Development and Testing

Dr. Robert Seiser

Roosevelt University



ONLINE VACCINATION SCIENCE RESOURCES FOR COVID-19 EDUCATION

Illustration by David S. Goodsell

Module 3, Part 2 – From Trials to Vials

ONLINE VACCINATION SCIENCE RESOURCES FOR COVID-19 EDUCATION

- Vaccines are used to build protective immunity
- Vaccine development pipeline
- Exploratory research: finding a target
- Vaccine design
- Pre-clinical studies and clinical trials
- Regulatory review and approval

Vaccines are used to build protective immunity

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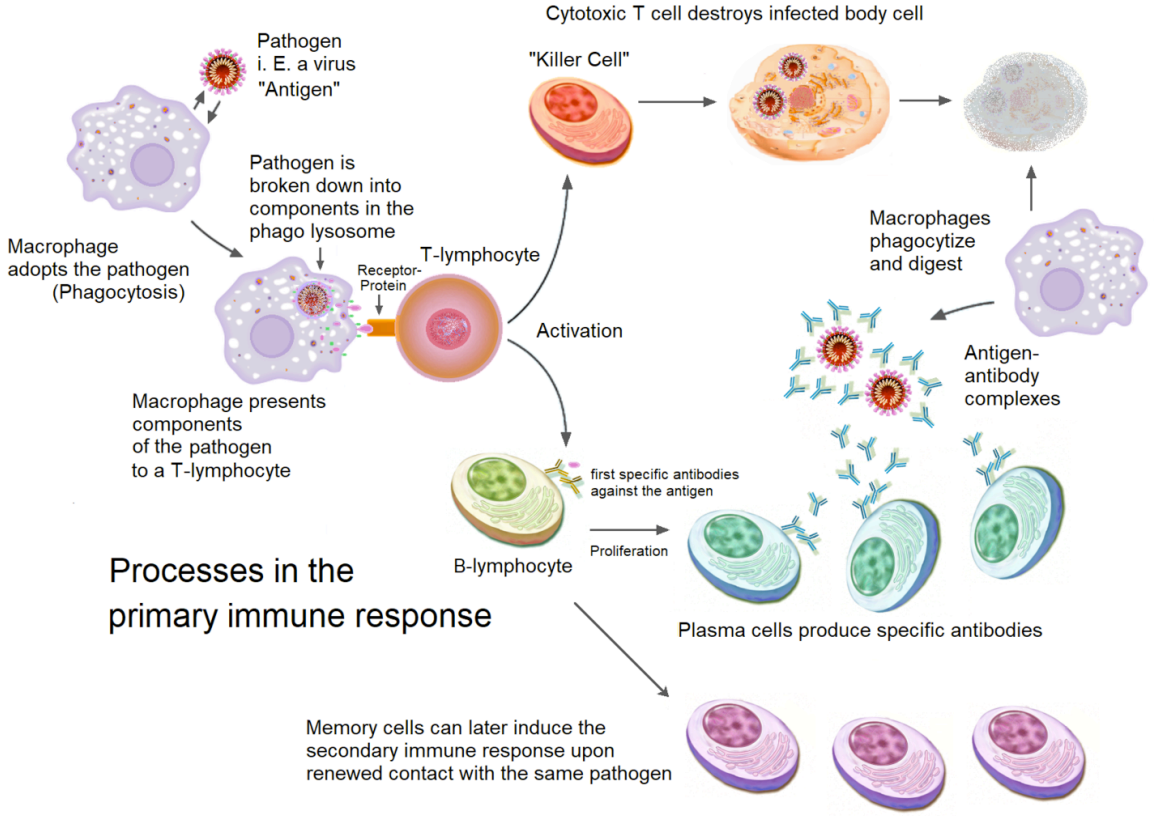
- Infection with a **pathogen** leads to a coordinated response by the immune system
- The system forms **immunological memory** of its interactions with the pathogen and remains prepared for later infections



Adapted from Wikimedia Commons https://commons.wikimedia.org/wiki/File:Primary_immune_response_1.png

Vaccines are used to build protective immunity

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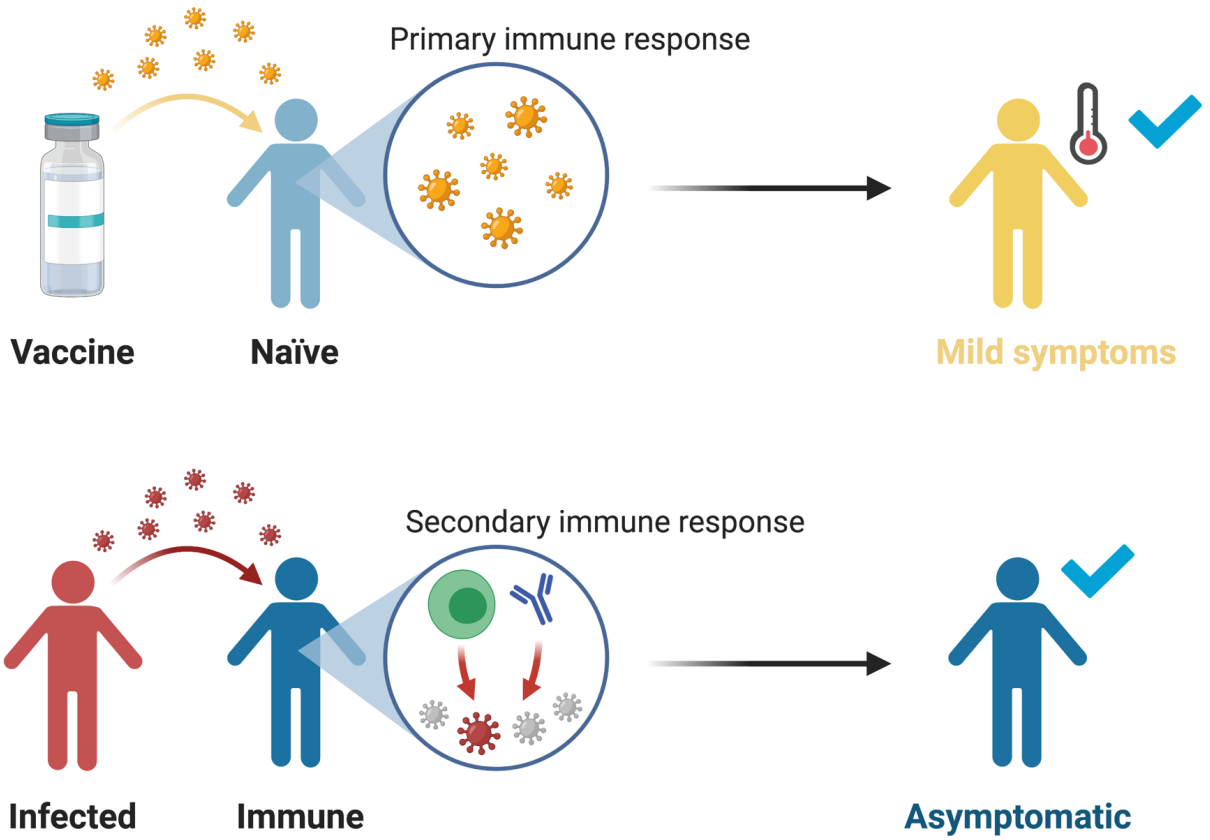
- The goal of a **vaccine** is to stimulate the immune response for protective immunity without the risks of disease



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Vaccine Development Pipeline

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Exploratory Research

Pre-clinical Studies

Clinical Trials

Regulatory Approval

Manufacturing

Quality Control

Exploratory research: finding a target

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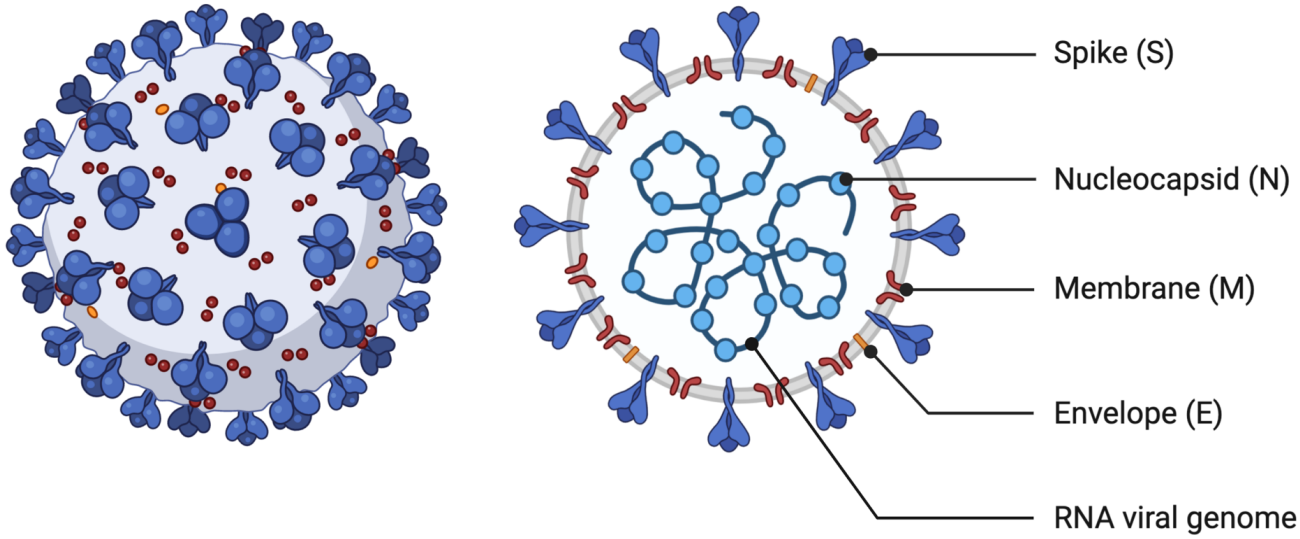
- The **structure** of human coronaviruses has been extensively studied
- The **genome** of SARS-CoV-2 was published soon after the virus was discovered



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Exploratory research: finding a target

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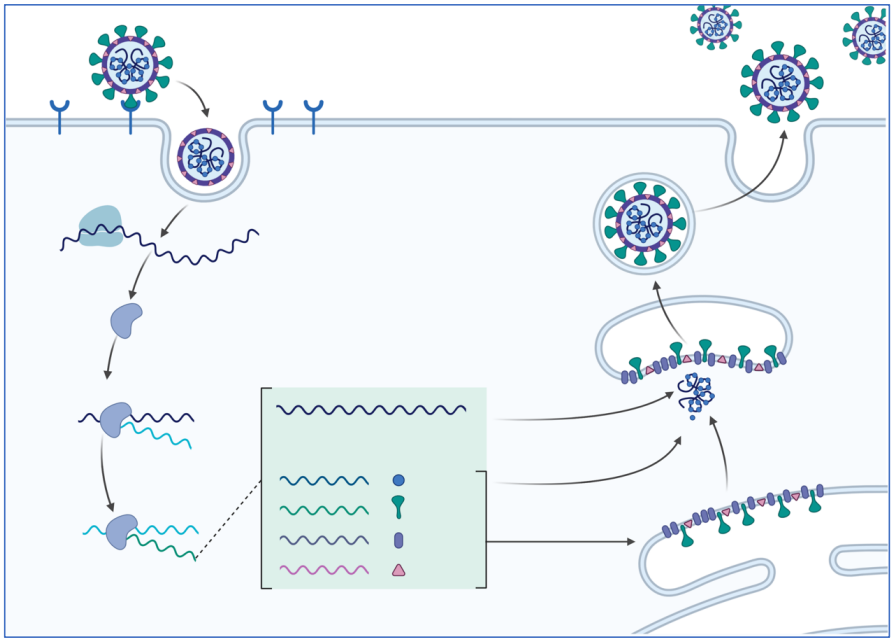
- The **replication cycle** of SARS-CoV-2 and other coronaviruses is also known, based on previous outbreaks
- This information allows researchers to identify parts of the virus that the immune system will recognize and target as **non-self**



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Exploratory research: SARS-CoV-2 structure

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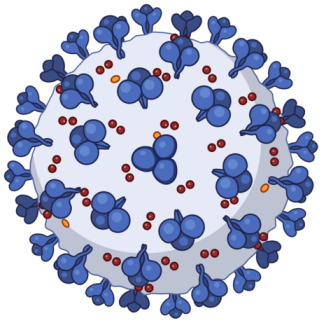
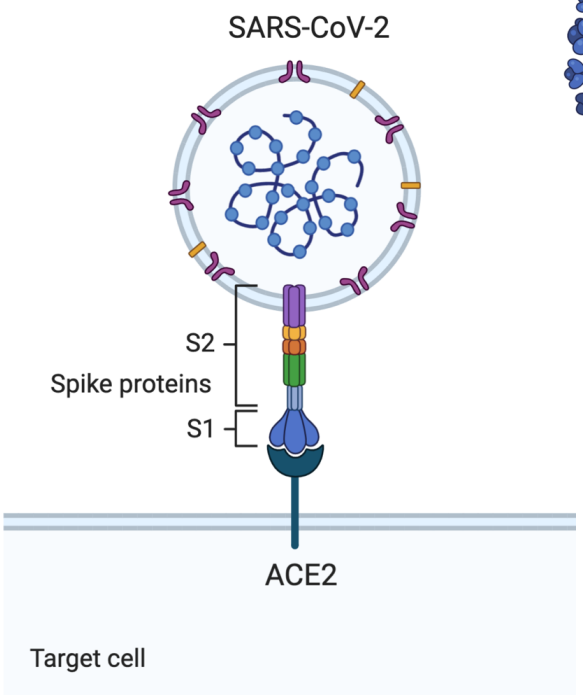
- SARS-CoV-2 first interacts with host cells through its spike proteins
- These became the focus of vaccine research
- Scientists predicted that training the immune system to recognize the spike protein antigen would strengthen the body's ability to make neutralizing antibodies and to kill infected cells





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Vaccine design

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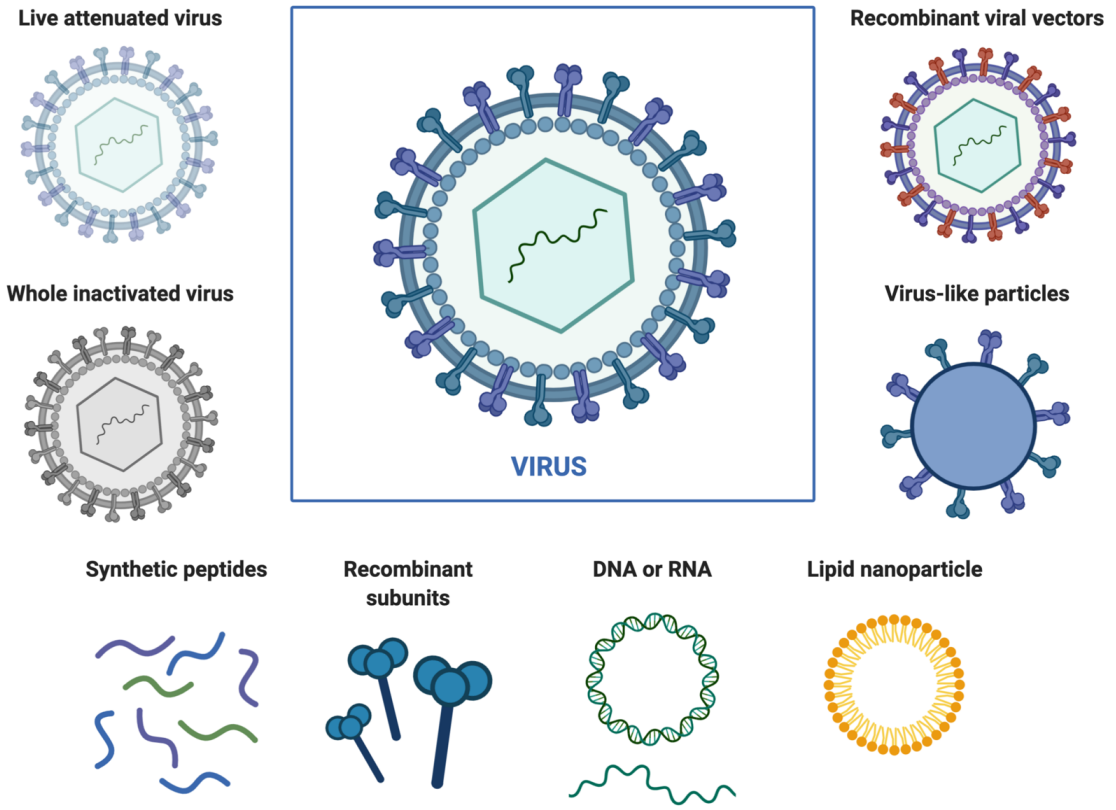
- Conventional, vector-based, and nucleic acid vaccines are the three main types in use today
- Each type of vaccine has its own pros and cons



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Vaccine design

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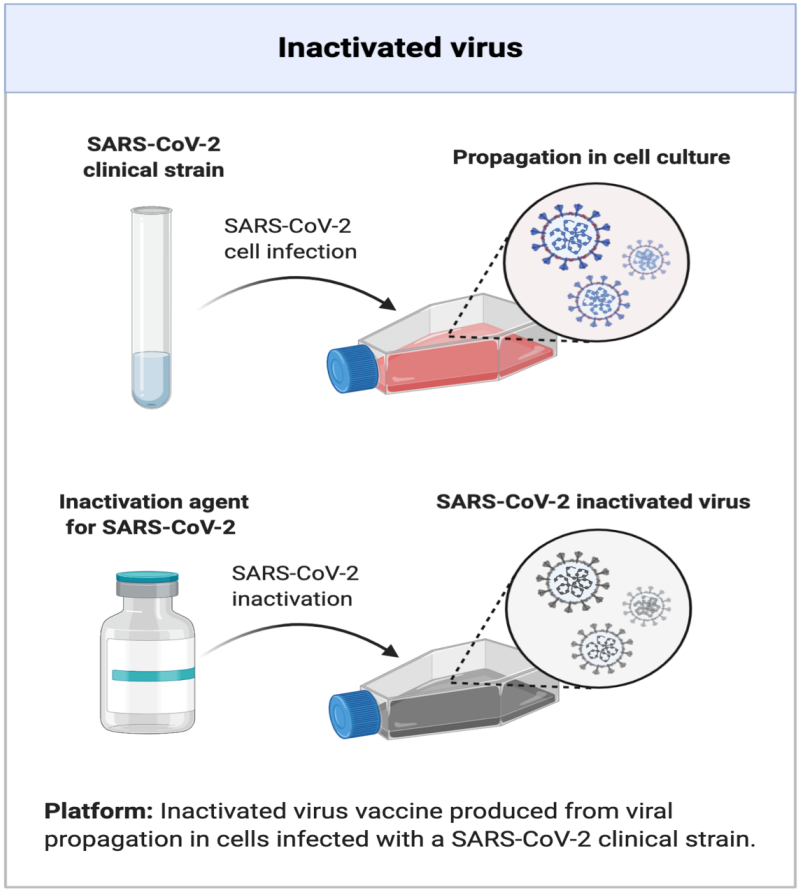
- **Conventional vaccines** use parts of the virus to trigger an immune response
- The vaccine may include a whole, inactivated virus or proteins that were isolated from the virus
- The first vaccines were small doses of live viruses – these are no longer used!
- Conventional vaccines can take a long time to produce in large quantities



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Vaccine design

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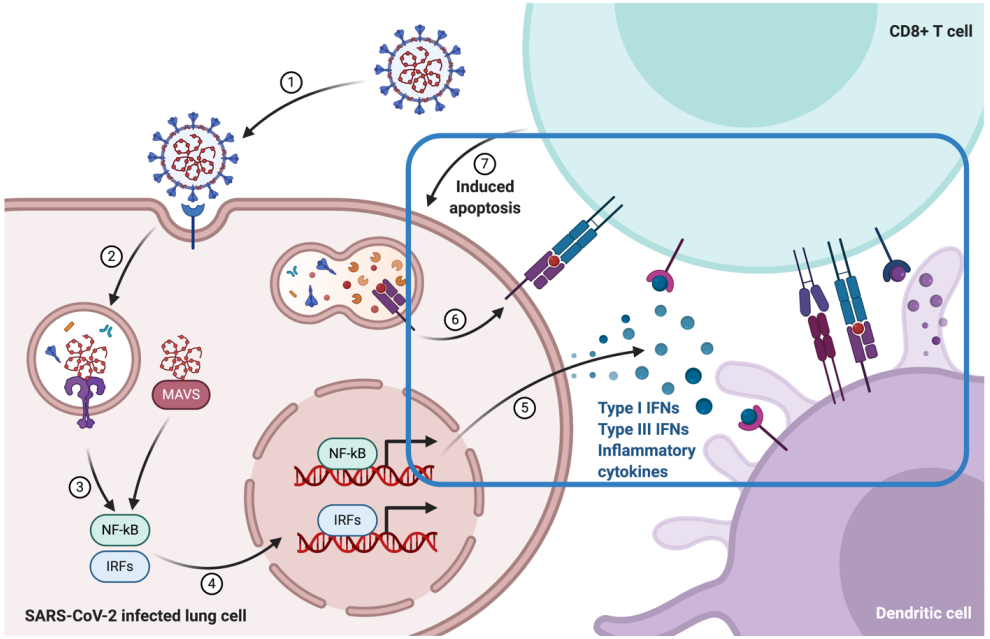
- **Vector-based** and **nucleic acid vaccines** are newer technologies but were proposed decades ago
- Designed for specificity and safety
- They contain only a small set of information about the virus
- The vaccine delivers viral material that the host cell can use to trigger an immune response



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Leading non-conventional vaccine candidates

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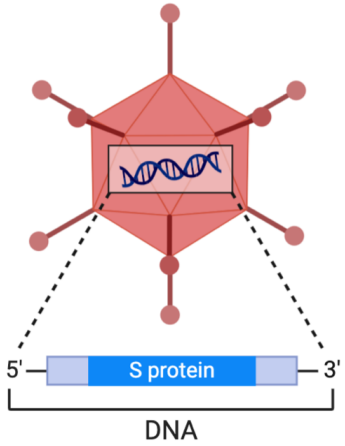
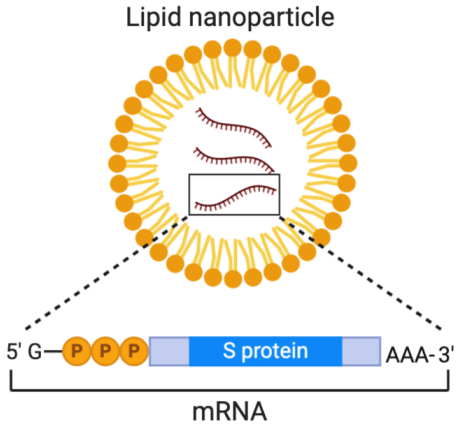
Viral vector



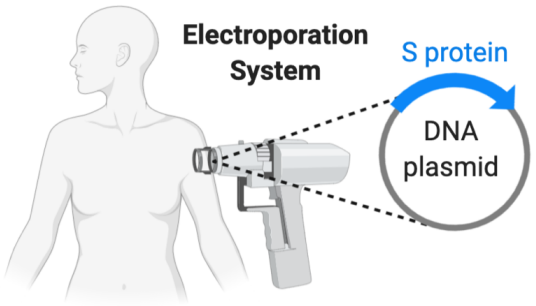
Platform: Adenovirus type 5 vector that expresses S protein.

mRNA vaccine



Platform: LNP-encapsulated mRNA encoding S protein.

DNA vaccine



Platform: Electroporation of DNA plasmid encoding S protein.

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mRNA vaccine

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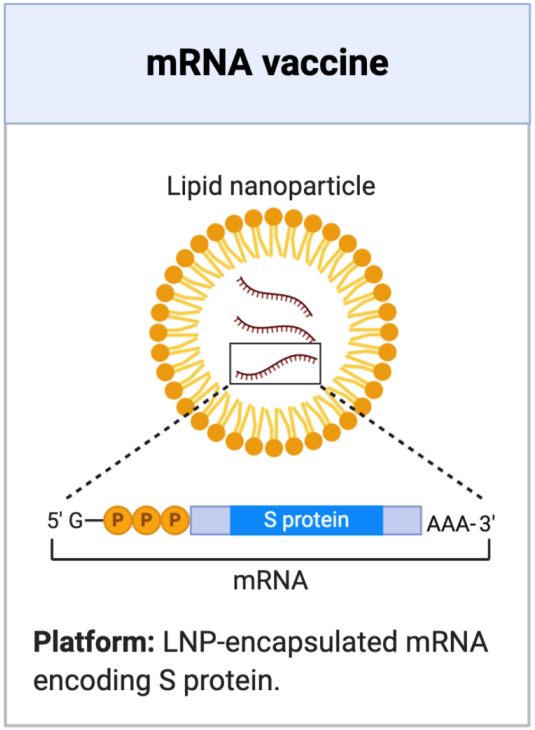
- mRNA vaccines include small pieces of the genetic code from the SARS-CoV-2 virus, enclosed by a fatty coat
- These particles are taken up by our cells and the RNA serves as a template to make a small portion of the viral spike protein
- This protein is recognized as a **pathogen** and stimulates an immune response that will recognize the full protein upon infection with the real virus
- The small piece of RNA inside the particle can't be used to make a virus and won't be combined with human DNA



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Pre-clinical studies

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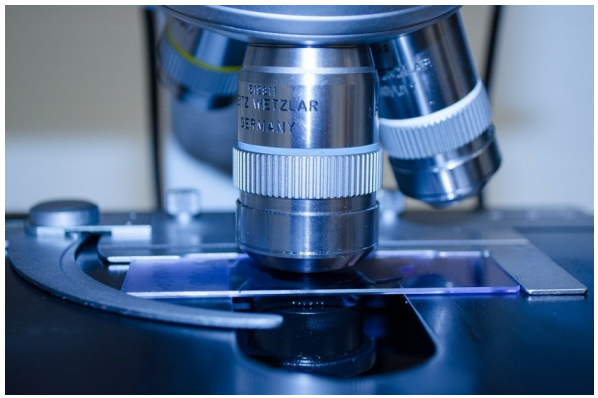
- Researchers work on vaccine development in lab experiments with cell cultures and with animals before testing them on people.
- Pre-clinical studies will ask:
  - Does the vaccine have the desired effect?
  - Do researchers have procedures to make, test and administer the vaccine properly?



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Clinical trials test vaccines on volunteers

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- **Phase 1:** 20-100 healthy volunteers
  - Is it safe to administer?
  - Are there serious side effects?
- **Phase 2:** 100s of volunteers, some at higher risk
  - How do participants' immune systems respond?
  - What are common reactions to immunization?
- **Phase 3:** 1,000s of volunteers from diverse groups at multiple sites
  - How do vaccinated and non-vaccinated people respond to viral exposure?
  - What immunization procedures and doses should be used?
  - How long does immunity last?
  - How do people react to the vaccine based on their age, race, etc.?

Clinical trials continue for many vaccines

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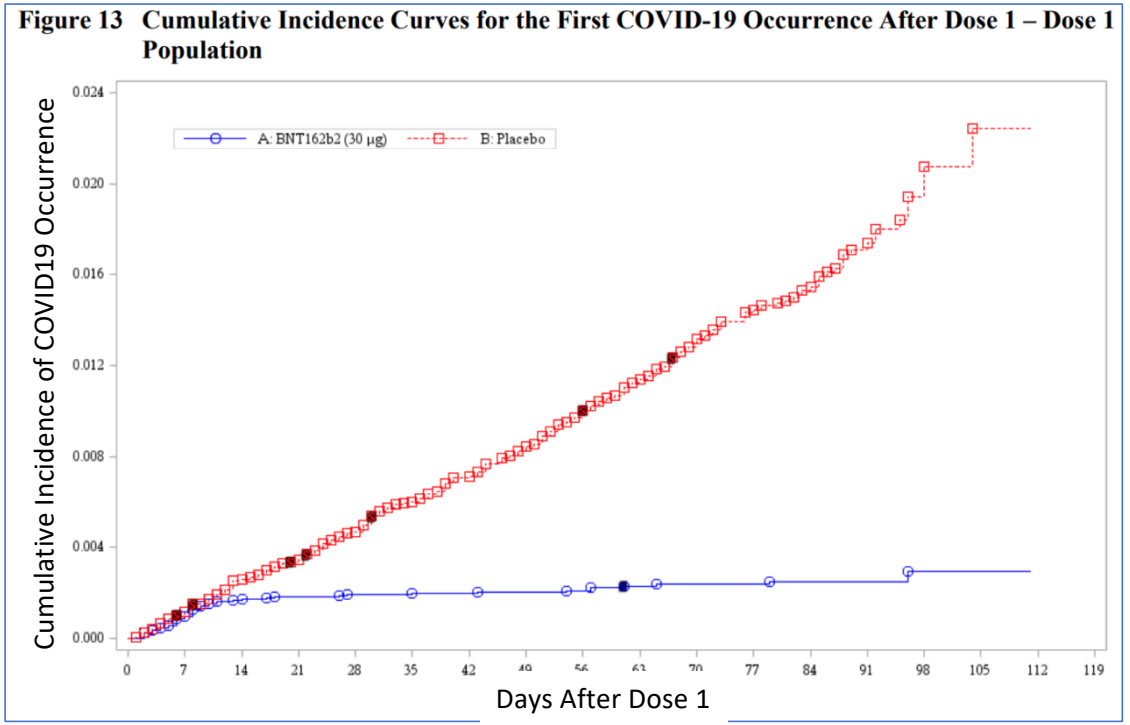
- Moderna & Pfizer/BioNTech: first mRNA vaccines
- Oxford/AstraZeneca: leading adenoviral vector vaccine
- Phase 3 trials report >90% efficacy
  - More than 30,000 volunteers participated in 2020
  - Some participants become COVID-19 positive
  - >90% of COVID-19 positive participants received placebo, not vaccine
  - This is very strong evidence that vaccines confer lasting immunity



Data from Pfizer/BioNTEch provided to US FDA 12/10/20 https://www.fda.gov/media/144246/download

Regulatory review and approval

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- Investigational New Drug application
- Pre-licensure vaccine clinical trials

FDA U.S. FOOD & DRUG ADMINISTRATION

- Presentation of findings to FDA's Vaccines and Related Biological Products Advisory Committee (VRBPAC)
- Biologics License Application (BLA) / Emergency Use Authorization (EUA)
- Inspection of manufacturing facilities
- Usability testing of product labeling

- No steps are being skipped, but most are going faster than they normally would because vaccines are top approval priorities

Regulatory review and approval

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- Companies are gathering more trials data and securing approval to make and distribute vaccines in large quantities.
- Trials are expanding to new groups as well.
- Thanks to an accelerated and successful development process, the first vaccines were distributed in December 2020.
- Widespread vaccine availability for adults is expected by Summer of 2021.

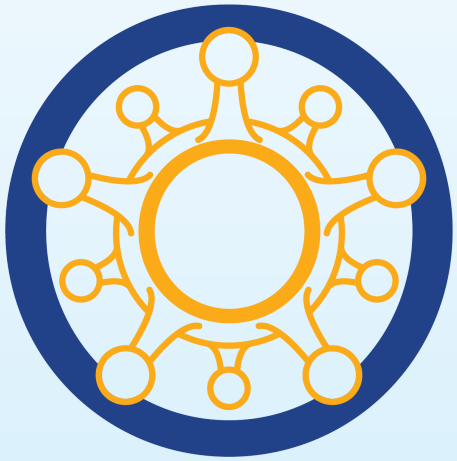
Adapted from Wikimedia Commons https://commons.wikimedia.org/wiki/File:Pfizer-BioNTech_COVID-19_vaccine_(2020)_C_(cropped).jpg

The one-sentence summary

ONLINE VACCINATION SCIENCE RESOURCES FOR COVID-19 EDUCATION

- Scientists have the tools and knowledge to develop safe, effective Covid-19 vaccines

Image adapted from http://tamkeen-jo.org/newsDetails/567/en



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