COVID-19 Vaccines

How They Work & Should We Get One?

Rocky Mountain Chapter of the American Scientific Affiliation (RMASA)
January 5, 2021

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Basics of Immunity

Antigen (SARS Coronavirus 2)
0.05–0.20 µm

B-cells that produce antibodies that match the antigen are activated. The cells proliferate, and each cell ramps up production.

There is not enough DNA in our genome to have a gene for every conceivable antigen. The antibody gene is unique to a given B-cell after having been assembled from fragments from the original genome variable and constant regions.

Antibody (from vast collection produced from B-cells)
0.01 µm

Eukaryotic B-Cell
10 µm (not to scale)
The Central Dogma of Molecular Biology

DNA Polymerase
replication (DNA -> DNA)

RNA Polymerase
transcription (DNA -> RNA)

Ribosome
translation (RNA -> Protein)

DNA
RNA
Protein

Nucleus
Rough Endoplasmic Reticulum (RER)
Ribosome (light blue dots)
DNA Replication / RNA Transcription

Replication

Transcription: DNA unzips, messenger RNA (mRNA) is formed from the opened part of DNA

Protein Synthesis at the Ribosome

1. Transfer RNA is formed—it can bind to both the codon from mRNA as well as the appropriate amino acid.

2. mRNA, tRNA and amino acid meet in the ribosome, peptide forms by condensation reaction.

3. When stop codon arrives, the peptide falls off to go do its thing…
Types of COVID-19 Vaccines

<table>
<thead>
<tr>
<th>Molecular platform</th>
<th>Total number of candidates</th>
<th>Number of candidates in human trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inactivated virus</td>
<td>19</td>
<td>5[^ii]</td>
</tr>
<tr>
<td>Non-replicating viral vector</td>
<td>35</td>
<td>4[^ii]</td>
</tr>
<tr>
<td>RNA-based</td>
<td>36</td>
<td>3[^ii]</td>
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<tr>
<td>Protein subunit</td>
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<td>2[^ii]</td>
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<tr>
<td>DNA-based</td>
<td>23</td>
<td>2[^ii]</td>
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<tr>
<td>Virus-like particle</td>
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<td>1[^i]</td>
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<tr>
<td>Replicating viral vector</td>
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<td>0</td>
</tr>
<tr>
<td>Live attenuated virus</td>
<td>4</td>
<td>0</td>
</tr>
</tbody>
</table>

[^i]: Technologies for dozens of candidates are unannounced or "unknown".[^93]
[^ii]: ^a^ b^c^ d^e^ f One or more candidates in Phase II or Phase II–III trials.
Inactivated COVID-19 Injection

As in many traditional vaccines. An example is the polio vaccine. Intact but inactivated virus is injected. The immune system recognizes the virus as foreign and makes antibodies to the virus, usually cell surface proteins like the SARS-Cov-2 spike protein.

Attenuated (weakened through genetics) vs. killed (heat or formaldehyde treated)

- BBIBP-CorV (China)
- BBV152 (India) Covaxin™
- CoronaVac (China)

More complicated vaccine formulation because of more complex biological material being used; mutations in attenuated virus could lead to return to a more virulent variant.
Spike Protein Injection

The spike protein or fragments/subunits are purified and inject. There is never any exposure to intact virus. Used with hepatitis B and pertussis vaccines.

- NVX-CoV2373
- ZF2001 (China) RBD-Dimer™
**mRNA–lipid nanoparticle Injection**

Embeds in membrane and is detected by antibodies and T-cells

**What Could Go Wrong?**

- Never been done before (shortened trial)
- Does the spike protein do anything surprising when expresses in a human cell?
- Cells expressing spike protein should be destroyed by the immune response
- RNA is short-lived and unstable
- No mechanism to convert RNA to DNA
- Anaphylaxis

**SEQUENCE**

The modRNA sequence is 4,284 nucleotides long, with a molecular weight of approximately 1388 kDa.

**COMPOSITION:** mRNA molecule, lipids (ALC-0315 = ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), ALC-0159 = 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), cholesterol), dibasic sodium phosphate dihydrate, monobasic potassium phosphate, potassium chloride, sodium chloride, sucrose, water for injection
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RNA Polymerase

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Ribosome (light blue dots)

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Nucleus

DNA

RNA

Protein
DNA–chimpanzee Adenovirus Injection

1 – penton capsomers; 2 – hexon capsomers; 3 – linear ds DNA

- Used for gene therapy
- Delivers linear double stranded DNA into the nucleus where it can be transcribed to mRNA which is transported to the cytoplasm and translated into protein.
- The virus has been genetically engineered to remove the genes responsible for virus reproduction and to insert the genes (and their regulators) needed for gene therapy or vaccine function.
- For COVID-19 vaccine the gene present is the SARS-CoV-2 spike protein

- Oxford–AstraZeneca AZD1222
- Ad5-nCoV (China)
- Gam-COVID-Vac (Russia) Sputnik V™
- Janssen/Johnson & Johnson (Belgium)

The AZD1222 vaccine is a replication-deficient simian adenovirus vector, containing the full-length codon-optimized coding sequence of SARS-CoV-2 spike protein along with a tissue plasminogen activator (tPA) leader sequence.

What Could Go Wrong?
- The adenovirus itself is antigenic and will produce an immune response.
- DNA based with a “permanent” presence; theoretical chance of chromosomal insertion.
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**Components of the Cell**
- Nucleus
- Rough Endoplasmic Reticulum (RER)
- Ribosome (light blue dots)
Today’s vaccines use only the ingredients they need to be as safe and effective as possible.

Each ingredient in a vaccine serves a specific purpose:
• provide immunity (protection)
• keep the vaccine safe and long lasting
• for the production of the vaccine

* Thimerosal has a different form of mercury (ethylmercury) than the kind that causes mercury poisoning (methylmercury). It’s safe to use ethylmercury in vaccines because it’s processed differently in the body and it’s less likely to build up in the body — and because it’s used in tiny amounts. Even so, most vaccines do not have any thimerosal in them. Learn more about thimerosal, mercury, and vaccine safety.
Issues

• Getting vaccinated keeps you from getting COVID-19 and helps contribute to “herd immunity”.
• RNA and DNA based vaccines are new technologies and have only been tested for less than a year. No long term trials have occurred.
• Persuasion is better than coercion; conscience and personal liberty must be respected.
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• Getting vaccinated keeps you from getting COVID-19 and helps contribute to "herd immunity".
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• Persuasion is better than coercion; conscience and personal liberty must be respected.
• On the other hand…"The needs of the many outweighs the needs of the few…or the one."
• Normally, use of drugs and medicines is discouraged (via requiring prescriptions and doctor supervision). Even recreational drugs are regulated and sometimes considered vices.
• On the other hand…we put all sorts of strange chemicals into our bodies and do use recreational drugs.
“Shooting Up” and “Popping Pills”

"I believe that many who find that 'nothing happens' when they sit down, or kneel down, to a book of devotion, would find that the heart sings unbidden while they are working their way through a tough bit of theology with a pipe in their teeth and a pencil in their hand."

- C. S. Lewis

Story of aspirin (prevents the pain response)
Vitamin/mineral supplements
Drugs that fix/remediate broken biology

So...WHY NOT?
Extras
4 “letters” (C, G, A, T) can make 64 different 3-letter words (the Genetic Code).

61 of the 64 “words” are used to encode amino acids; the other 3 start and stop the chain.

The image shows a diagram of protein formation, with mRNA binding to ribosomes and tRNAs carrying specific amino acids. The genetic code table is also included, listing the corresponding amino acids for each codon.