COVID-19 R&D, By The Science: *What is the Objective?*

**TREATMENTS**

- **Antivirals**
  - Polyclonal Antibodies (Convalescent Plasma)
  - ARBs, ACE Inhibitors
  - Targeted Monoclonal Antibodies
  - Stem Cells
  - Gene Therapies (CAR-T)

**VACCINES**

- **Confer Immunity from Previous Host:**
  - Previously infected people have developed molecules that target invaders. Administering to newly sick patients may boost their recovery

- **Inhibit Replication:**
  - The sole mission of a virus is to replicate. Stopping this process halts the spread of infection in the body

- **Mitigate Viral Entry:**
  - SARS-CoV2 enters cells through a well-known pathway. Interacting with this pathway using existing & new therapies may reduce effects

- **Immunomodulation:**
  - In some cases, a person's immune response can be so strong that it causes harm. Reducing this produces better outcomes

- **Direct Host's Immune Response:**
  - Provide the pieces of virus or tools to make pieces. The immune system uses these to build a response, without providing the infection

- **Engineer Targeted Immune Response:**
  - Cutting edge gene manipulation techniques re-program molecules or cells to have new disease fighting functions

**Viral Vector**
- mRNA
- Modified APC
- DNA
- Recombinant Protein
- Attenuated Virus
**Polyclonal Antibodies**
Recovered patients have antibodies in their blood that recognize SARS-CoV2 and signal the immune system to attack it. Injecting these antibodies into sick patients may boost their immune system to better fight the virus.

**Antivirals**
Molecular compounds designed to stop the function of proteins and enzymes necessary for the virus to replicate. The virus cannot spread when it cannot make more copies. These drugs can be intravenous or oral.

**Targeted Monoclonal Antibodies**
Lab-engineered, humanized molecules that directly target SARS-CoV2 proteins (mainly the spike protein) and can initiate an immune response cascade when injected into a patient.

**ARBs, ACE Inhibitors**
Angiotensin receptor blockers and angiotensin converting enzyme inhibitors, respectively. These oral drugs are widely prescribed to alleviate hypertension, but also affect SARS-CoV2’s mechanism of cell entry via the ACE2 receptor. Manipulating this signaling pathway, known as the Renin Angiotensin Aldosterone System (RAAS) may help alleviate acute effects of COVID-19.

**Stem Cells**
Cells that have been carefully re-programmed to behave in a specific way. They can be directed to stop the immune system from overreacting, or to focus on other targets. They can be administered to patients via injection.

**Gene Therapies**
Engineered DNA can be delivered to immune cells, which read the DNA and modify themselves to be able to now recognize and attack SARS-CoV2. These cells are drawn from the patient, engineered, and then transfused back to the patient with new disease fighting properties.
# COVID-19 R&D, By The Science: Vaccines

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<th>Viral Vector</th>
<th>mRNA</th>
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<td>Viruses are better at infecting cells than many available technologies. An efficient way to deliver information to cells is by hijacking a harmless virus, putting specific pieces of SARS-CoV2 into it, and letting it infect cells as it normally would, providing pieces to the immune system that generate a response.</td>
<td>Segments of RNA that code for a piece of SARS-CoV2. They can be engineered or extracted. After injection, the patient uses its own cells to create the viral pieces that the mRNA provide a template for. Then, the patient generates a targeted immune response against those self-manufactured pieces.</td>
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<th>Recombinant Protein</th>
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<td>Composed of specific elements of SARS-CoV2 that have been engineered in a lab. These antigens can be injected into a patient without the pieces that cause coronavirus disease (COVID-19), stimulating an immune response that builds immunity without infection.</td>
<td>Also segments that code for a piece of the virus, but made of DNA rather than mRNA. The aim is the same: provide the patient with instructions to make a viral piece, then let their immune system initiate a targeted response against it. DNA alternatives differ slightly in delivery method and scalability when compared to mRNA.</td>
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<th>Attenuated Virus</th>
<th>Modified APC</th>
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<td>A truncated form of the virus, with reduced infection-causing abilities, is injected into a patient to stimulate an immune response that generates future protection but does not produce robust symptoms. A traditional approach for vaccine development.</td>
<td>Uses similar technology to gene therapies. Engineered DNA tells an antigen presenting cell (APC) how to make pieces that recognize SARS-CoV2. From there, the APC stimulates an immune response that recruits cells to eliminate virus.</td>
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Typically, the R&D process is linear, with the most promising candidates progressing through each stage.

**Basic Research:**
To understand scientific phenomena, without an immediate commercial target.

**Applied Research:**
To solve a problem by developing new, or repurposing earlier, candidate drugs or vaccines.

**Clinical Trials:**
Determine whether the new candidate is safe and effective.

- **Phase 1:** Tests whether the drug is safe
- **Phase 2:** Tests whether the drug is effective
- **Phase 3:** Tests safety & efficacy in a large & diverse group

**Approval:**
To determine whether the benefits of the drug outweigh the risks.

**Phase 4:** Ongoing monitoring

**Production:**
Manufacturing & distribution

Now, in the race to safely develop treatments and a vaccine for SARS-CoV-2, research institutions, federal agencies, and private companies are working collaboratively to share data and finding innovative ways to compress the R&D timeframe.

Basic research is ongoing, exploring fundamental questions of how SARS-CoV-2 spreads and causes disease.

The early release of the SARS-CoV-2 genome, paired with robust computational approaches to identifying potential molecular targets for SARS-CoV-2, jump-started research. This approach allows researchers to build on previous R&D by repurposing existing drugs and developing new vaccine candidates. These products can quickly move into the applied research and clinical testing phases.

Some manufacturers are combining phase 1 & phase 2 trials, starting with a small group of healthy volunteers and scaling to test drug candidates in larger and more diverse cohorts.

Manufacturers are developing master protocols for umbrella trials, allowing them to conduct test multiple candidates against a single control group at the same time.

The FDA is using its regulatory tools such as compassionate use and emergency use authorizations to make quickly make new drugs available when there are no adequate and approved alternatives.

To ensure a vaccine or drug is available to the public as soon as it is approved, manufacturers are beginning to ramp up production as they conduct clinical trials.