5to Panel Virtual

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MEDICAL SCIENCES CAMPUS
Proposed Plan

- Introduction to Coronavirus Family (1’)
- SARS-CoV-2 infectiousness compared with other related infectious diseases and role of the herd immunity (4’)
- Overview of Current Vaccines Candidates (1’)
- Mechanism of protection by mRNA Vaccine (3’)
- Mecanism of Protection by Adenovirus Vaccine (3’)
- The interesting case of BCG (Tuberculosis) Vaccine (5’)
- Challenges to Develop an effective Vaccine (3’)

Human Coronavirus Family

- **Human Coronavirus Types**
  - Human coronaviruses were first identified in the mid-1960s. The seven coronaviruses that can infect people are:

- **Common human coronaviruses**
  - 229E (alpha coronavirus)
  - NL63 (alpha coronavirus)
  - OC43 (beta coronavirus)
  - HKU1 (beta coronavirus)

- **Other human coronaviruses**
  - SARS-CoV (the beta coronavirus that causes severe acute respiratory syndrome, or SARS) (2002-2003)
  - MERS-CoV (the beta coronavirus that causes Middle East Respiratory Syndrome, or MERS) (2012-2013)
  - SARS-CoV-2 (the novel coronavirus that causes coronavirus disease 2019, or COVID-19)

Content source: [National Center for Immunization and Respiratory Diseases (NCIRD), Division of Viral Diseases](https://www.cdc.gov/viral-diseases/index.html)
Human Coronavirus Family

Electron micrograph of Coronavirus, the cause of Severe Acute Respiratory Syndrome (SARS) Scott Camazine/Alamy

https://www.mdpi.com/1999-4915/12/4/372/htm#cite
How infectious can be SARS-Cov-2 and implications for human immunity

$R_0$

Average number of people who will catch a disease from one contagious person

- **Measles**: 11-18
- **2019-nCoV**: 2-3.11
- **Seasonal flu**: 1.3


SOURCES: Travel Medicine, PLOS One, JAMA Pediatrics, MDPI, NCBI, New England Journal of Medicine, “The Spread and Control of Norovirus Outbreaks Among Hospitals in a Region”
How infectious can be SARS-Cov-2 and implications for human immunity

\[ R_0 \]

Average number of people who will catch a disease from one contagious person

\( x \) 10 cycles

\[ 2019-nCoV: \ 2-3.11 \]

\[ \text{Seasonal flu: } 1.3 \]

\[ +59,000 \]

\[ \sim 18 \]


SOURCES: Travel Medicine, PLOS One, JAMA Pediatrics, MDPI, NCBI, New England Journal of Medicine, "The Spread and Control of Norovirus Outbreaks Among Hospitals in a Region"
Herd Immunity and COVID-19

- Herd immunity happens when so many people in a community become immune to an infectious disease that it stops the disease from spreading.
- This can happen in two ways:
  - Many people contract the disease and in time build up an immune response to it (natural immunity).
  - Many people are vaccinated against the disease to achieve immunity.
Many people contract the disease and in time build up an immune response to it (natural immunity).

Many people are vaccinated against the disease to achieve immunity.

Herd Immunity and COVID-19

- Problem
  - $R_0 = 2-2.5$ need 60-66% of total persons infected
    - Ex: PR (~3 M) = 1,2 M
    - USA (~328M) = 196,8 M

- Problem
  - No Vaccine is available....YET
Tools to Combat Covid-19

Healthcare innovations to combat Covid-19

Technological and scientific innovations in diagnostics to help identify positive cases, treatments to alleviate or cure, and vaccines to prevent potential future infections.

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>COUNT</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>DIAGNOSTICS</td>
<td>41</td>
<td>Regulatory authorized diagnostic tests</td>
</tr>
<tr>
<td>TREATMENTS</td>
<td>23</td>
<td>Assets in human clinical trials</td>
</tr>
<tr>
<td>VACCINES</td>
<td>5</td>
<td>Assets in human clinical trials</td>
</tr>
</tbody>
</table>

Source: FDA, WHO, Companies web site.
Taken from [www.visualcapitalism.com](http://www.visualcapitalism.com)
VACCINE CANDIDATES

As April 1, 2020

VACCINES

Vaccine Platform
Mechanism being used for vaccine development

3 DNA
1 Inactivated
1 Live Attenuated Virus (LAV)
5 Non-replicating viral vector
15 Protein subunit
3 Replicating viral vector
7 RNA
1 Virus-like particle (VLP)
5 Unknown

Source: FDA, WHO, company websites, news. Available upon request.

Source: FDA, WHO, Companies web site. Taken from www.visualcapitalism.com

https://www.who.int/blueprint/priority-diseases/key-action/Novel-Coronavirus_Landscape_nCoV-4april2020.pdf?ua=1
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Company</th>
<th>Platform</th>
<th>Stage</th>
<th>Description</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRNA-1273</td>
<td>Moderna</td>
<td>RNA</td>
<td>Phase I-First Patient Dosed</td>
<td>First to dose a human in the US. Vaccine consists of a synthetic strand of mRNA designed to elicit an immune response to produce antibodies against SARS-CoV-2</td>
<td>🇺🇸</td>
</tr>
</tbody>
</table>

Source: FDA, WHO, Companies web site. Taken from [www.visualcapitalism.com](http://www.visualcapitalism.com)
Moderna Announces Award from U.S. Government Agency BARDA for up to $483 Million to Accelerate Development of mRNA Vaccine (mRNA-1273) Against Novel Coronavirus

April 16, 2020

Award will fund development of mRNA-1273 to FDA licensure

Award will fund manufacturing process scale-up to enable large-scale production in 2020 for pandemic response

NIH-led Phase 1 study of mRNA-1273 has completed enrollment of 3 dose cohorts (25 μg, 100 μg and 250 μg); expanding to an additional 6 cohorts of older adults and elderly adults

Phase 2 study expected to begin in Q2 2020, following safety data from ongoing Phase 1 study

Moderna to hire up to 150 new team members to support efforts

Conference call to be held on Friday, April 17 at 8:00 a.m. ET

CAMBRIDGE, Mass.--(BUSINESS WIRE) -- Apr. 16, 2020-- Moderna, Inc., (Nasdaq: MRNA) a clinical stage biotechnology company pioneering messenger RNA (mRNA) therapeutics and vaccines to create a new generation of transformative medicines for patients, today announced an agreement for a commitment of up to $483 million from the Biomedical Advanced Research and Development Authority (BARDA), a division of the Office of the Assistant Secretary for Preparedness and Response (ASPR) within the U.S. Department of Health and Human Services (HHS), to accelerate development of the Company’s mRNA vaccine candidate (mRNA-1273) against the novel coronavirus (SARS-CoV-2).
How mRNA 1273 Vaccine works

Infected patient with COVID-19 → SARS-CoV-2 virus → Sequencing of genetic information → mRNA vaccine → Protection

https://youtu.be/qJIP91xjvsQ
How mRNA 1273 Vaccine works
How mRNA 1273 Vaccine works

- Genetic information
- Spike (S)
- Envelope (E)
- Nucleocapsid
- Hemagglutinin
- Membrane

Spike protein
How mRNA 1273 Vaccine works
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# VACCINE CANDIDATES

## VACCINES

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<td>Ads-nCoV</td>
<td>CanSino Bio</td>
<td>Non-Replicating Viral Vector</td>
<td>Phase I</td>
<td>Benefits from previous success in the Ebola virus (time to market ~3 years). The vaccine being developed is based on viral vectors (adenoviruses) to deliver antigens to express the SARS-CoV-2 spike protein</td>
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Source: FDA, WHO, Companies web site. Taken from [www.visualcapitalism.com](http://www.visualcapitalism.com)
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<td>ChAdOx1 nCoV-19</td>
<td>University of Oxford</td>
<td>Non-Replicating Viral Vector</td>
<td>Phase I/II</td>
<td>Enrolling 500+ individuals to test its vaccine candidate, which uses a non-replicating virus to deliver RNA into cells.</td>
<td>🇬🇧</td>
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</table>
Recombinant adenoviruses induce balanced immune responses: Antibodies and T cells

- Adenovirus from chimpanzees ‘express antigen’
- Enter Cell
- Antigen presentation
- Protein Production And secretion
- Antibodies
- Virus neutralization
- Killing of Infected cell
- Cytotoxic T cells CTLs

Containing SARS-CoV-2 mRNA
VACCINE CANDIDATES

4. LV-SMENP-DC
   - Shenzhen Geno-Immune Medical Institute
   - Lentiviral
   - Phase I/II

Begun early testing of its vaccine candidate. The vaccine uses a lentiviral vector to deliver Covid-19 minigenes to modify dendritic cells and activate T cells.

Source: FDA, WHO, Companies web site. Taken from www.visualcapitalism.com
# VACCINE CANDIDATES

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<td>5. BCG Vaccine</td>
<td>Research Group, Netherlands</td>
<td>Live Attenuated Virus (LAV)</td>
<td>Phase II/III</td>
<td>Repurposing the BCG vaccine, originally for TB, to fight SARS-CoV-2 in healthcare workers at high risk of infection. 1,000 individuals will be enrolled across 8 hospitals to receive the vaccine or placebo.</td>
</tr>
<tr>
<td>6. BCG Vaccine</td>
<td>Murdoch Children’s Research Institute</td>
<td>Live Attenuated Virus (LAV)</td>
<td>Phase II/III</td>
<td>The BRACE trial will conduct a randomized, multi-center study of the TB vaccine in 4,000 healthcare workers across Australia.</td>
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Could a 100-year-old vaccine protect against COVID-19?

- Jean Antoine Villemin first recognized bovine tuberculosis in 1854.
- In 1882, Robert Koch identified the *Mycobacterium tuberculosis* as the cause of human TB.
- The BCG strain was isolated after subculturing 239 times during 13 years. Developed by Albert Calmette and Camille Guerin (Bacillus Calmette-Guérin, BCG).
- The BCG vaccine was first used in humans in 1921.

Could a 100-year-old vaccine protect against COVID-19?

- BCG vaccination exist in 131 countries;
- 21 countries have no current program of national BCG vaccination;
- Status for 26 countries is unknown.

current universal BCG program
no longer has BCG vaccination program
Country never had BCG vaccination program

Could a 100-year-old vaccine protect against COVID-19?

- As of March 2020, even though the tuberculosis vaccine does not directly protect against COVID-19 it has been thought to boost the immune systems and has been suggested for study. [94][95]

- Spanish, French, German and Dutch research entities are preparing trials using genetically-modified BCG vaccines. [96]

- BCG vaccine is in phase 3 trials in health care workers in Australia and Netherlands. [97]

- The WHO does not recommend its use for prevention as of 13 April 2020. [98]
Tuberculin testing and vaccinating were started in September, 1949, and stopped in May, 1951.

A total of 191,827 children (1-18 y/o) were included in the study population.
The cost **US$0.16 to US$1.11** a dose in the developing world.\[6\][7]
In the United States it costs **US$100 to US$200**
Challenge to develop an effective and secure Vaccine at any time soon.

- No animal model that can recall the diseases like in humans.
  - From mice to humans
  - From Labs to humans
  - Several Preclinical studies in NHP
Challenge to develop an effective and secure Vaccine at any time soon.

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<tr>
<th>Phase</th>
<th>Participants</th>
<th>Time Frame</th>
<th>Description</th>
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<tr>
<td>Preclinical</td>
<td></td>
<td>Months to Years</td>
<td>Laboratory Research Determine if treatment is useful and safe</td>
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<tr>
<td>Phase I</td>
<td>6-10</td>
<td>Several months</td>
<td>Understand effects of treatment in humans</td>
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<tr>
<td>Phase II</td>
<td>20-300</td>
<td>Up to two years</td>
<td>Evaluate safety and efficacy of treatment</td>
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<tr>
<td>Phase III</td>
<td>300-3,000</td>
<td>One (1) to four (4) years</td>
<td>Confirm benefit and safety of treatment</td>
</tr>
<tr>
<td>Phase IV</td>
<td>3,000+</td>
<td>One (1) to several years</td>
<td>Evaluate long-term effects of treatment</td>
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Submit for FDA Approval
Challenge to develop an effective and secure Vaccine at any time soon.

- Manufacture Capabilities

100 Tech Drive, Norwood, Massachusetts
Challenge to develop an effective and secure Vaccine at any time soon.

- SARS-CoV. enhancement was identified by Yang et al. [6] in 2005.
- It was hypothesized as being the reason for such a high mortality rate in China [7].
- At the time, the priming strains were thought to be human coronaviruses known to cause mild infection such as 229E [7].
- Yip et al. [8,9] revealed that anti-Spike protein antibodies were indeed responsible for the infection of immune cells.

**Antibody-Dependent Enhacement (ADE)**

- Antibodies from previous Coronavirus infection OR Vaccine induced??

Challenge to develop an effective and secure Vaccine at any time soon.

Submit for FDA Approval

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