Discussion with Jon Cohen on HIV and COVID-19 Vaccine Research

May 13, 2020
### DRAFT landscape of COVID-19 candidate vaccines – 11 April 2020

#### 3 candidate vaccines in clinical evaluation

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#### 67 candidate vaccines in preclinical evaluation

### DRAFT landscape of COVID-19 candidate vaccines – 11 May 2020

#### 130 candidate vaccines in preclinical evaluation

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New vaccines for a safer world

The Coalition for Epidemic Preparedness Innovations (CEPI) is a global alliance financing and coordinating the development of vaccines against emerging infectious diseases.
SARS-CoV-2 Spike Protein
Structure and pre-fusion processing

Because of its location and function, the spike is the target of neutralizing antibodies, and the focus of vaccine design.

- SARS-CoV-2 hooks onto and enters host cells using the Spike (S) protein on its surface.
- Each spike is a trimer with 22 glycosylation sites per subunit, totaling per spike.
- The S protein ectodomain has two major regions:
  - S1: Attaches to host cell receptor (ACE2).
  - S2: Fusion machinery.
- S1/S2 "Priming" cleavage site:
  - Between the S1 and S2 domains.
  - SARS-CoV: Furin recognition site (Polybasic RNN
  - SARS-CoV-2: No furin recognition site (Monobasic R).
- Fusion peptide:
  - Immediately follows the fusion peptide.
  - Transmembrane protease (TMPRSS2) and/or Cathepsin L recognition site.
- Glycosylation sites:
  - 15/22 in S1.
  - 15/22 in S2.

S Protein Trimer
S Protein Trimer Subunit

RBD
- Receptor binding domain. Part of S1.
- SARS-CoV-2 RBD binds host receptor (ACE2) with 10× the affinity of SARS-CoV's RBD.
- Flexible. Some spikes have one subunit with RBD "up" (POD 6VXX), even without ACE2 present.

SARS-CoV-2 Virion

S Protein Processing Required for Fusion

- SARS-CoV-2: The S1/S2 site is cleaved during and after virus assembly.
- SARS-CoV: The S1/S2 site is cleaved on the host cell surface, and within host cell endosomes.

When the S protein is initially translated, the S1 and S2 subunits are noncovalently bonded.

Prior to membrane fusion, the S1/S2 site is cleaved.

S1 and S2 remain noncovalently bound.

S protein must be cleaved again at the S2 site in order to activate the fusion machinery.

After fusion, SARS-CoV-2 delivers its genome into the host cell and begins the process of replication.
Jennifer Haller receives the first administration of an mRNA vaccine, made by the biotech firm Moderna, against the pandemic coronavirus. AP PHOTO/TED S. WARREN

With record-setting speed, vaccinemakers take their first shots at the new coronavirus
Johnson & Johnson is launching a major push to develop a vaccine that can neutralize the new coronavirus.
NATIONAL INSTITUTE OF ALLERGY AND INFECTIONOUS DISEASES/NATIONAL INSTITUTES OF HEALTH

The $1 billion bet: Pharma giant and U.S. government team up in all-out coronavirus vaccine push
Many new vaccines are being tested to thwart the pandemic coronavirus, which infects a human cell (brown) with deadly efficiency to produce new copies (pink). NATIONAL INSTITUTE OF ALLERGY AND INFECTION DISEASES/NATIONAL INSTITUTES OF HEALTH

Speed coronavirus vaccine testing by deliberately infecting volunteers? Not so fast, some scientists warn
People seeking help for pandemic influenza in Brazil in July 2009, when cold weather boosted the spread of the disease. JEFFERSON BERNARDES/A

Why do dozens of diseases wax and wane with the seasons—and will COVID-19?
United States of America

3 days since peak resource use on
April 10, 2020

- All beds needed: 56,831 beds (gap: 3,498 beds)
- ICU beds needed: 15,164 beds (gap: 7,369 beds)
- Invasive ventilators needed: 13,851 ventilators

Graph showing projected resource needs from February 1 to August 1, 2020, with a peak on April 13, 2020.
COVID-19 needs a Manhattan Project

There is an unprecedented race to develop a vaccine against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). With at least 44 vaccines in early-stage development, what outcome can we expect? Will the first vaccine to cross the finish line be the safest and most effective? Or will it be the most well-funded vaccines that first become available, or perhaps those using vaccine technologies with the fewest regulatory hurdles? The answer could be a vaccine that ticks all these boxes. If we want to maximize the chances for success, however, and have enough doses to end the coronavirus disease 2019 (COVID-19) pandemic, current piecemeal efforts won’t be enough. If ever there was a case for a coordinated global vaccine development effort using a “big science” approach, it is now.

There is a strong track record for publicly funded, large-scale scientific endeavors that bring together global expertise and resources toward a common goal. The Manhattan Project brought about nuclear weapons quickly (although with terrible implications for humankind through candidate vaccines are missed. Only then can we start to narrow in on those candidates to be advanced through all clinical trial phases. This shortlist also needs to be based on which candidates can be developed, approved, and manufactured most efficiently.

Trials need to be carried out in parallel, not sequentially, using adaptive trial designs, optimized for speed and tested in different populations—rich and developing countries, from children to the elderly—so that we can ultimately protect everyone. Because the virus is spreading quickly, testing will be needed in communities where we can get answers fast—that means running trials anywhere in the world, not just inpreset testing locations. Working with regulators early in the process will increase the likelihood of rapid approvals, and then once approved, a coordinated effort will ensure that sufficient quantities are available to all who need the vaccine, not just to the highest bidder.

All of this will require substantial funding, which is the big ask of big science. Late-stage clinical trials are not cheap, nor is vaccine manufacturing. Although pressures on 

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March 27, 2020
WHO R&D Blueprint

novel Coronavirus

An international randomised trial of candidate vaccines against COVID-19

WHO reference number

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09 April 2020, Geneva

R&D Blueprint

Powering research
to prevent epidemics

ACCESS TO COVID-19 TOOLS (ACT) ACCELERATOR

A Global Collaboration to Accelerate the Development, Production and Equitable Access to New COVID-19 diagnostics, therapeutics and vaccines

24 April 2020

COMMITMENT and CALL TO ACTION

Our Vision and Mission

Grounded in a vision of a planet protected from human suffering and the devastating social and economic consequences of COVID-19, we, an initial group of global health actors (BMGF, CEPI, Gavi, Global Fund, UNITAID, Wellcome Trust, WHO) and private sector partners and other stakeholders, are launching a landmark, global and time-limited collaboration to accelerate the development, production and equitable global access to new COVID-19 essential health technologies.

We know that as long as anyone is at risk from this virus, the entire world is at risk – every single person on the planet needs to be protected from this disease.

We agree that alongside evidence-based public health measures, innovative COVID-19 diagnostics, therapeutics and vaccines are needed – in record time and at record scale and access – to save millions of lives and countless trillions of dollars, and to return the world to a sense of ‘normalcy’.

We recognize the significant amount of critical work, investment and initiatives already ongoing around the world to expedite

Our Mission

Our Mission is not only accelerated development and availability of new COVID-19 tools – it is to accelerate equitable global access to safe, quality, effective, and affordable COVID-19 diagnostics, therapeutics and vaccines, and thus to ensure that in the fight against COVID-19, no one is left behind.

Our Commitment

1. We commit to the shared aim of equitable global access to innovative tools for COVID-19 for all.

2. We commit to an unprecedented level of partnership – proactively engaging stakeholders, aligning and coordinating efforts, building on existing collaborations, collectively devising solutions, and grounding our partnership in transparency, and science.

3. We commit to create a strong unified voice to maximize impact, recognizing this is not about singular decision-making authority, but rather collective problem-solving, interconnectedness and inclusivity, where all stakeholders can connect and benefit from a shared vision and purpose.

April 9, 2020

April 24, 2020
April 29, 2020

Prognosis

Trump’s ‘Operation Warp Speed’ Aims to Rush Coronavirus Vaccine

By Jennifer Jacobs and Drew Armstrong
April 29, 2020, 11:08 AM PDT. Updated on April 29, 2020, 12:18 PM PDT

- Project targets enough doses for most Americans by January
- Fact: A new vaccine will take 12 to 18 months to develop

The Trump administration is looking to the Manhattan Project-style effort to drastically cut the time needed to develop a coronavirus vaccine, with a goal of making enough doses for most Americans by year's end.

April 30, 2020

President Donald Trump speaks during a meeting about the coronavirus response with Gov. Phil Murphy, D-N.J., in the Oval Office of the White House, April 30, in Washington. (AP Photo/Evan Vucci)
World Leaders Pledge $8 Billion in Fight Against Coronavirus, EU Says

By Reuters, Wire Service Content May 4, 2020, at 12:12 p.m.


BRUSSELS (REUTERS) - World leaders promised $8 billion on Monday for the fight against the coronavirus pandemic, European Commission head Ursula von der Leyen said at the end of a pledging event that she chaired.

May 4, 2020

A strategic approach to COVID-19 vaccine R&D

By Laurence Corey1,2, John R. Mascola1, Anthony S. Fauci3, Francis S. Collins1

+ See all authors and affiliations

Science 11 May 2020
edcb53172
DOI: 10.1126/science.edcb53172

Abstract

A public-private partnership and platform for harmonized clinical trials aims to accelerate licensure and distribution.

There is an unprecedented need to manufacture and distribute enough safe and effective vaccine to immunize an extraordinarily large number of individuals in order to protect the entire global community from the continued threat of morbidity and mortality from severe acute respiratory syndrome–coronavirus 2 (SARS-CoV-2). The global need for vaccine and the wide geographic diversity of the pandemic require more than one effective vaccine approach. Collaboration will be essential among biotechnology and pharmaceutical companies, many of which are bringing forward a variety of vaccine approaches (1). The full development pathway for an effective vaccine for SARS-CoV-2 will require that industry, government, and academia collaborate in unprecedented ways, each adding their individual strengths. We discuss one such collaborative program that has recently emerged: the ACTIV (Accelerating COVID-19 Therapeutic Interventions and Vaccines)
Unveiling ‘Warp Speed,’ the White House’s America-first push for a coronavirus vaccine

By Jon Cohen | May 12, 2020, 5:05 PM