Hot Topic Discussion

COVID-19: Community and Scientific Innovation

Melodi Anahtar (Bhatia Lab)

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MARBLE CENTER FOR CANCER NANOMEDICINE
Small technologies, BIG impact

KOCH INSTITUTE
for Integrative Cancer Research at MIT

Today's inspiration

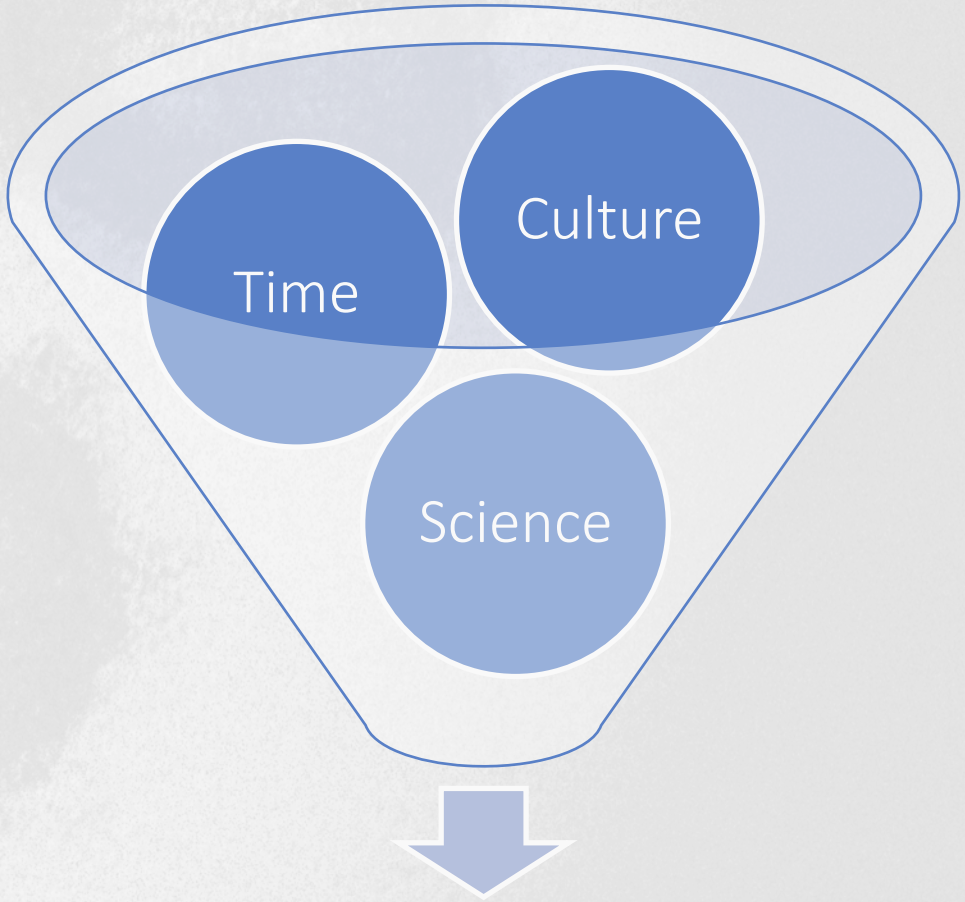
The race against COVID-19

The identification and isolation of individuals with COVID-19 can help to flatten the epidemic curve and win us time to wait for the vaccine development and production, and antiviral drug therapies.

The COVID-19 pandemic concerns people all over the world. It has forced closedown of borders, lockdown of cities, proactive closure of schools/universities/labs in multiple countries, cancellation of events including scientific conferences and triggered a series of chain reactions, harming the global economy.

Various biopharmaceutical companies and organizations, such as Moderna/National Institutes of Health (NIH), Medicago, Inovio, Clover/GSK and the Chinese Academy of Military Medical Sciences have announced potential COVID-19 vaccine candidates. More excitingly, Moderna/NIH and the Chinese Academy of Military Medical Sciences have begun their clinical trials. However, health officials estimate that it may still take 1 year to 18 months to achieve the production and distribution of vaccines[1,2]. Repurposing existing antiviral strategies and vaccines could provide a shortcut. Writing in *Nature Nanotechnology*, Hu et al. comment on the fact that chloroquine, which is a US Food and Drug Administration-approved drug for the treatment of malaria, inhibits endocytosis of nanoparticles in the same size range as viruses and discuss the potential of this drug against COVID-19[3]. Indeed, chloroquine has already been put in practice for the treatment of COVID-19 patients in China since 19 February 2020, according to the sixth version of Guideline Over the Diagnosis and Treatment of COVID-19[4]. The guideline was updated on 3 March, still including chloroquine. Chloroquine is not highly efficient but it is beneficial and side effects are minor, according to Chinese health officials[5,6]. The clinical trials in China also suggests favipiravir, the antiviral drug developed by Toyama Chemical to treat flu, shows good clinical efficacy against COVID-19 and is being included into the treatment plan[7]. Doctors in Japan now are also using favipiravir to treat COVID-19 patients with mild to moderate symptoms to inhibit the multiplication of the virus[8]. But the drug does not work that well on people with more severe symptoms, noted a Japanese health ministry source[9].

Investigations and tests of several potential drugs and therapies are also being conducted. Remdesivir, developed by Gilead Sciences, showed promising in vitro and in vivo performance against the coronaviruses that caused Middle East respiratory syndrome (MERS) in 2012 and the coronavirus that caused severe acute respiratory syndrome (SARS) in 2003, and has been described as the "most promising candidate" against COVID-19[10–12]. Results of clinical trials of remdesivir, currently under way in China[13], are expected to be released at the end of April, which hopefully will be followed by the results of clinical trials conducted in the US and other countries[13,14]. Moreover, early clinical trials in China suggest that convalescent plasma therapy, which has previously been used to treat SARS and Ebola infections[15], is effective in



Our future

The race against COVID-19. *Nat. Nanotechnol.* **15,** 239–240 (2020). https://doi.org/10.1038/s41565-020-0680-y

An abbreviated timeline of COVID-19

Dec.
- Dec. 1 – Symptom onset of first patient
- Dec. 12 – Cited in Nature as the start of the epidemic
- Dec. 31 – Chinese government reports a novel virus

Jan.
- Jan. 11 – China reports first death in a 61 YOM
- Jan. 20 – WHO publishes report that confirms cases outside of China
- Jan. 30 – WHO declares a global health emergency

Feb.
- Feb. 2 – First death is reported outside of China (Philippines)
- Feb. 4 – CDC gets EUA for its PCR test
- Feb. 10 – Global death toll surpasses SARS

Mar.
- Mar. 11 – COVID-19 is declared a pandemic
- **Mar. 16 – First clinical trial participant is dosed with mRNA-1273**
- Mar. 18 – WHO launches the Solidarity Trial
- Mar. 23 – MA Stay at home order is put in place

Apr.
- Apr. 10 – Global death toll passes 100,000
- Apr. 27 - Today

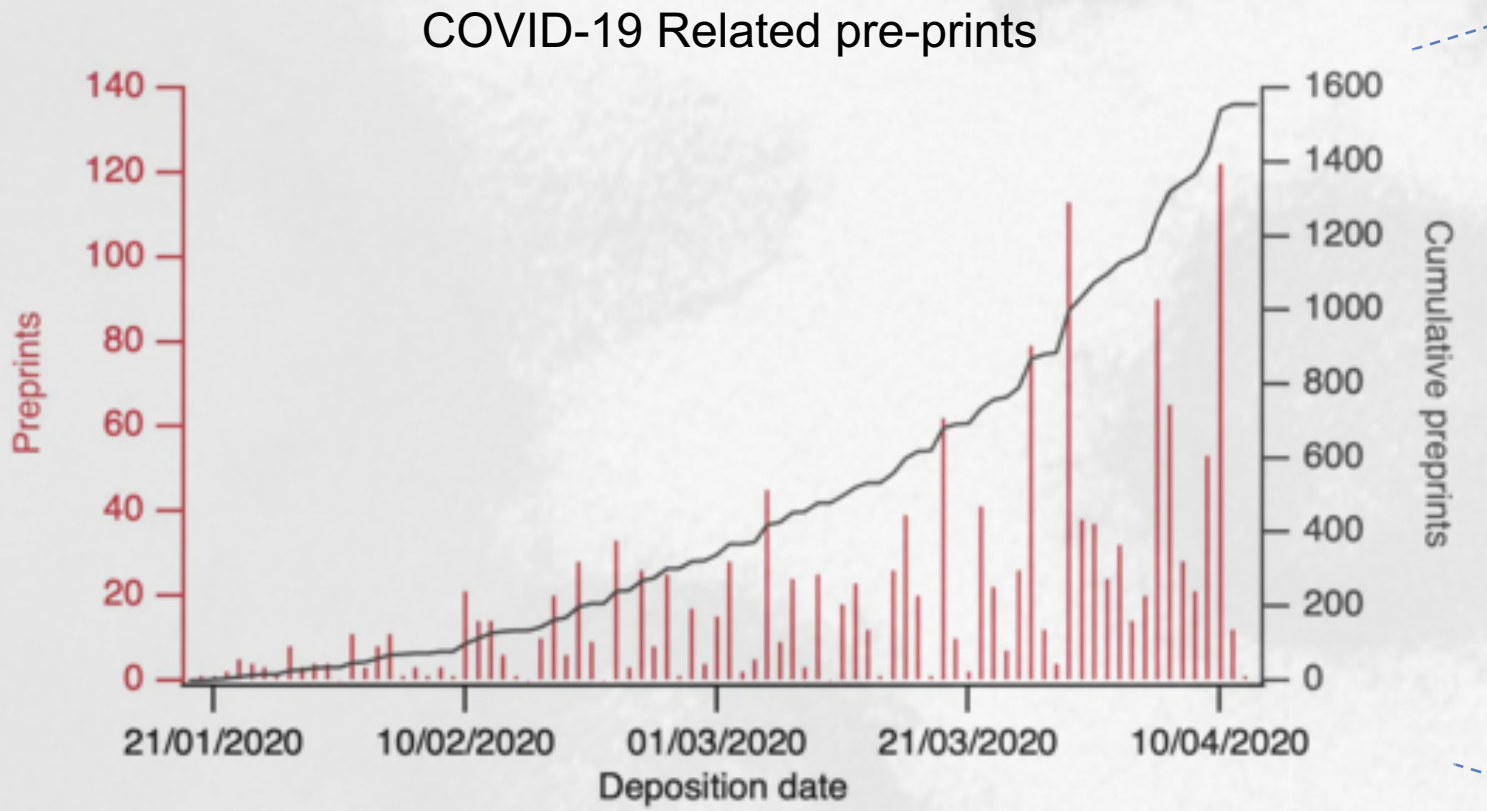
As of 9:30 AM today:

Global cases
2,989,090

US cases
965,933

MA cases
54,938

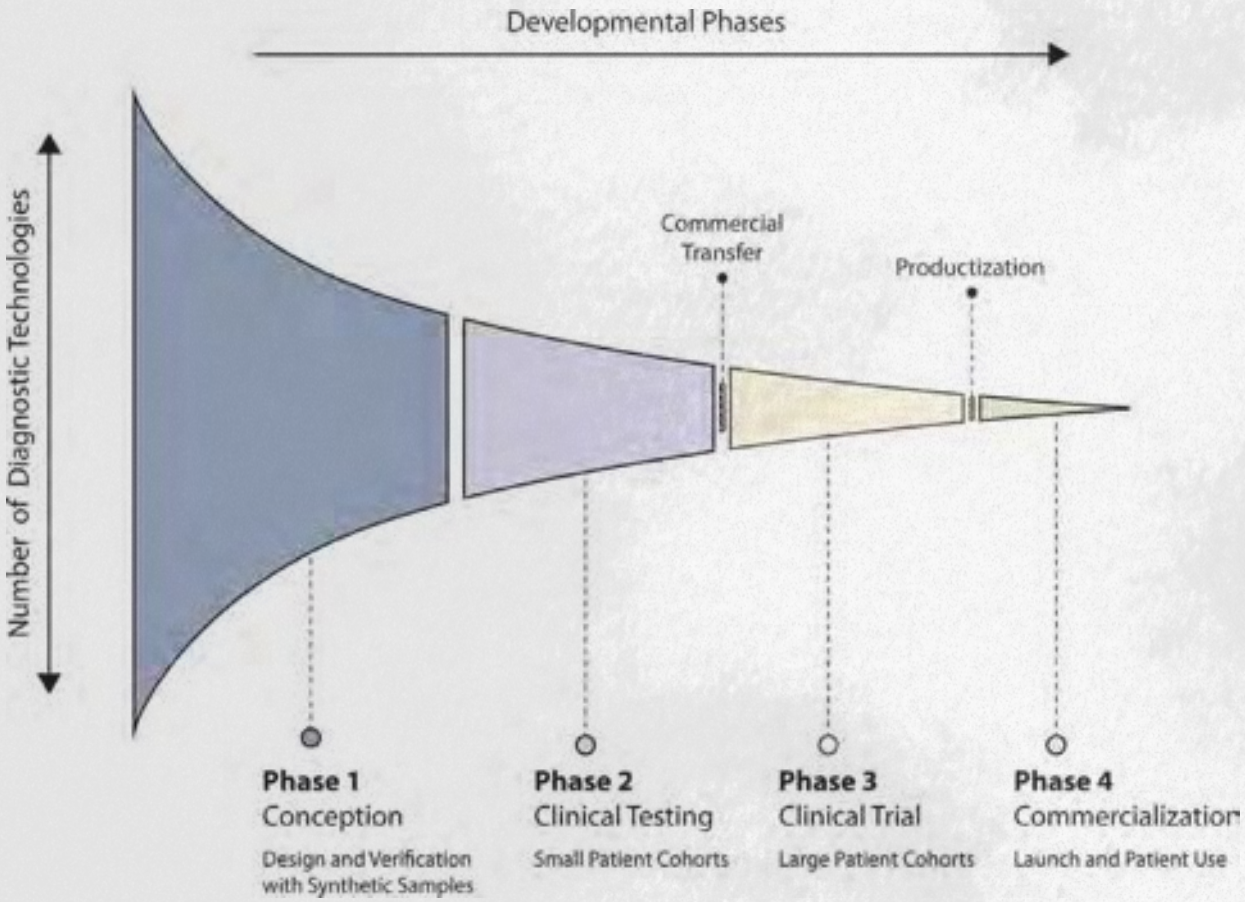
COVID-19 has changed science communication



http://covidpreprints.com/

Biology
Epidemiology
Diagnostics
Therapeutics
Vaccines
Case studies
Modeling

Diagnostic development for SARS-CoV-2



Mammoth Biosciences

Udagama et al., *ACS Nano* (2020) ; Broughton et al., *Nature Biotech* (2020)

Emergency Use Authorizations

Allow unapproved medical products or unapproved uses of approved medical products to be used in an emergency… when there are no adequate, approved, and available alternatives.

70 Diagnostic EUAs:

- 49 test kit manufacturers and commercial labs (e.g. the CDC RT-PCR panel, approved 02/04/20)
- 21 High Complexity Molecular-Based Laboratory Developed Tests (e.g. the MGH qPCR assay, approved 04/03/20)

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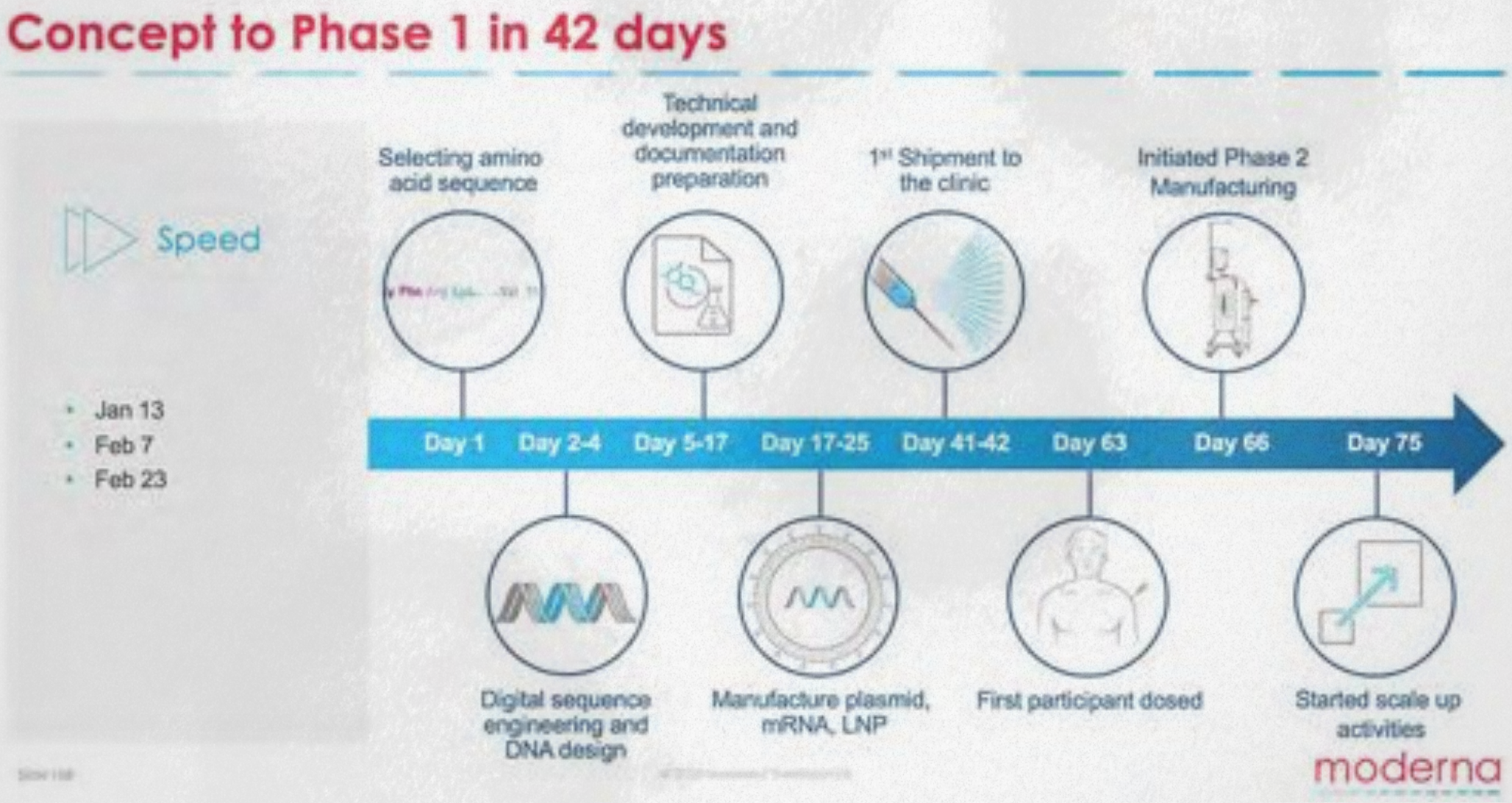
11 Medical Device EUAs:

- CytoSorb (extracorporeal cytokine adsorber)
- Terumo BCT Inc. and Marker Therapeutics AG Extracorporeal Blood Purification (EBP) Devices
- TransAeris Diaphragmatic Pacing Therapy System (DPTS) (Synapse Biomedical, Inc.)
- And others

Moderna's mRNA vaccine candidate



Summary

- New communities of interests are nucleating and driving research innovation.
- Science's success also depends on the support of our ever-adapting social behavior (**social distancing, quarantine policies impact timelines**).
- Innovation does not end with technology; we also need to innovate in the processes that bring these new technologies to patients (Moderna).

What to watch for:

1. Clinical trial outcomes of commercial drugs (favipiravir, chloroquine) and new treatments (remdesivir, plasma therapy)
2. Clinical trial outcomes of vaccines (Moderna, BioNTech/Pfizer, Oxford U.)
3. Emergence of self-diagnostics (home kits)
4. Widespread serological testing (and the challenges that will come with it)

Questions to consider

Community:

- What will we bring back to lab, and what will we leave behind?
- How will our workplace atmosphere change as we ramp up?
- Will publication standards change?
- What would be the effects of centralizing research efforts?

Science:

- How does nanomedicine fit into the EUA paradigm?
- Will this pandemic work in our interest by motivating clinical translation of our research?
- How can we break the mold of current diagnostics? Should we be trying to?