

We are seriously considering developing a handheld device to detect COVID-19 & SARS-CoV-2. Pre-^oof-patent technology has been developed and we are currently testing it. This device can use two-step RT-PCR to detect and differentiate COVID-19 and SARS-CoV-2. The features of the device are described in the brief attached.

I write now because we are unsure if, if we were to produce a COVID-19 detection device, who would deploy, by whom it would be used and who might be willing to purchase it. I would be very grateful if you would be able to speak briefly with me and my colleagues about these open questions. We would be happy to meet with you at your convenience. Your input will be invaluable as we weigh the risks and benefits of pivoting the company's focus to this application.

With best regards,
Gary Schoolnik

Gary Schoolnik, M.D.
Professor of Medicine
Stanford Medical School
Attending Physician (internal medicine)
Visby Medical
Chief Medical Officer

NIH-001879

Linda P. [REDACTED]
Kean and Debra [REDACTED] Professor of [REDACTED]
Professor of [REDACTED]
Mailman School of Public Health
Professor of Medicine, Vagelos College of Physicians and Surgeons
See also [REDACTED]
Columbia University

Hi, Patty -

Executive Director of the National Association of County and City Health Officials (NACCHO) will speak at a [National Conference on Emerging Coronavirus Preparedness](#) on March 12-13, 2020 in Washington, D.C. The conference is organized by the NACCHO and the American Public Health Association (APHA). The conference will bring together public health professionals from across the country to discuss the latest information on COVID-19.

Given the nature of this [conference](#), would you like to receive an invitation and refer to CDC?

Thanks for your input.

5. If someone [REDACTED] (other than the self-isolation time).

Thank you [REDACTED] contribute solutions to this health crisis.

With [REDACTED] regards,

Linda

Linda P. Fried, M.D., M.P.H.

Dean, [REDACTED] School of Public Health

Professor of Epidemiology

Mailman School of Public Health

Professor of Medicine

Senior Vice President for Medical Affairs, Irving Medical Center

Columbia University

- Anne Schuchat will brief on the current situation and public health issues.
- Anthony Fauci will give a brief explanation of our understanding of the virus and development of countermeasures.
- Brig Gen Paul E. Tamm will speak about medical protection.
- Acting Chief of Staff Mulvaney will open the floor for questions and moderate the proceedings. Questions can be submitted via Twitter or stand in here (Eric Ueland or Mike McKenna).

Expected attendees:

Members (confirmed RSVPs thus far)

Senators James Risch

Leader McCarthy

Rep. Kay Granger

Rep. Greg Walden

Rep. Nita Lowey

Briefers

DHS – Alex Zemaitis

CDC – Dr. Anne Schuchat

NIAID – Dr. Anthony Fauci

ASPR – Dr. Bob Kadlec

FDA – Dr. Steve Hahn

DHS – Karen DeSalvo

NSC – Anthony Blinken

NSC – Matt DeMasi

State – Stephen Biegun

DOD – Brig Gen Paul E. Tamm

NIH-001935

NIH-001939

NIH-001941

Draft Agenda

1:30-2:00 pm – Opening Keynote

Dr. Anthony Fauci, MD

Introduction: Dr. Michael O'Leary, Director, Global Health Policy Center

2:00-2:30 pm – Panel Discussion

[The economics/business] John Bellung, Morgan Stanley

[The politics] Michael Green, CSIS Freeman Chair in Chinese Studies (co-chair)

[The foreign politics] Melanie Hart, Center for American Progress (*to be invited*), or Bonnie Glaser, CSIS China Power Project

[The public health] Dr. Jennifer Nuzzo, Johns Hopkins University

Moderator: Matt Pottinger, *to be invited*

Panelists: *to be invited*, Dr. Michael O'Leary, Director, Global Health Policy Center

2:50-3:30 pm – Newsmaker Speech

Matt Pottinger, *to be invited*, Director, Global Health Policy Center

Moderator: Matt Pottinger, Director, Global Health Policy Center

J. Stephen Morrison

Senior Vice President & Director, Global Health Policy Center, Director, Global Health Policy Center

Center for Strategic and International Studies (CSIS) China Power Project

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but not in Vancouver--the ~~Province~~ ~~Health~~ ~~Ministry~~ ~~is~~ ~~not~~ ~~helping~~ ~~us~~ ~~out~~ ~~one~~ ~~pretty~~ ~~quickly~~.

To me, one important aspect is the control of respiratory transmission in the hospital, ~~and~~ ~~not~~ ~~allowing~~ ~~extensive~~ ~~use~~ ~~of~~ ~~nebulization/aerosolization~~ ~~in~~ ~~negative~~ ~~pressure~~ ~~rooms~~, as for TB isolation.

(Treating patients with antibiotics would do)

In the community, standard public health quarantine, contact tracing should be sufficient for starters.

As far as the US is concerned, the number of infections is likely much higher. The 41 deaths are the tip of the iceberg of not 800 infections (5% fatality rate). Although the fatality rate is much better, if the mutation in the virus becomes very contagious—then the impact could be enormous. Containment is so important. The government must take action now.

When a new pathogen arrives, children often have mild disease but they are important reservoirs for transmission in the community, reaching high R₀. This is particularly true for SARS-CoV-2. This may also be even more relevant for 2019-nCoV. It is important to keep this in mind in the USA, but it may be less relevant in other countries until this time point comes.

Happy to help, any way that I can. Thank you for all you and NIAID are doing!!!

Best wishes , Marty

- « ... On the rebound, maybe even though they still had ATP exposure to esomeprazole acidified the cytosol and esomeprazole inhibited the acidification... In a similar manner, hprt chronic exposure, which importantly did not have any deleterious effect on epithelial integrity, was linked to decreased TP122A mRNA levels. These results open up the possibility of using PPIs as a new therapeutic approach for treating CF lung disease... » (15)
- « ...We have found that the human homolog of the rat gastric H⁺/K⁺-ATPase, ATP4A mRNA, which translates to around 65% identity in the protein products... » (15)
- « Proton pump inhibitor therapy predisposes to increased risk of developing pneumonia » (16)
- « Na⁺/H⁺ Exchangers Are Required for the Development and Function of Viral Glycoproteins » (17)
- « ATP4a is required for the assembly of the H⁺-ATPase complex... » (18)

Regarding coronaviruses and Golgi complex:

- « ...Coronaviruses... are unique in their ability to hijack the host Golgi network (...). The three major membrane proteins (G, M and E) are synthesized in the ER and move to the ERGIC. Glycosylation occurs there, after the assembly of virus budding from the ERGIC with the viral nucleocapsid (...). Once virions have budded into the lumen of the ERGIC, the ~120 nm particles first move through the host secretory pathway to be released from infected cells. Viruses are believed to follow the constitutive secretory pathway in order to exit the cell by exocytosis, although many questions have to be addressed before release of viruses during infection. A programme of motion control research is currently under way to elucidate the mechanism of release in infection... » (19)
- « ...Weak bases (which disrupt acidification) or v-ATPase inhibitors (which inhibit the generation of a pH activation loop) all block a number of membrane proteins (e.g., V-ATPases). One mechanism for how this might affect vesicle trafficking is to involve a subunit of the membrane sector of the v-ATPase, which has been shown to accumulate in endosomes. This subunit undergoes a conformational change in the presence of H⁺, which may affect the vesicle trafficking machinery leading to subsequent vesicle formation... » (19)
- « ...Pharmacological and other manipulations of the Golgi complex have all been shown to cause slow trafficking or cargo through the Golgi complex and/or substantial changes in Golgi morphology... » (20)
- « ...Similar to M2, the infectious bronchitis virus (IBV) coronavirus E protein mediates membrane disruption, which is hyperexpressed in mammalian cells... » (21)
- « ...The enveloped protein is also important for the assembly and transport of the virus... It plays a significant role in virus assembly and release... » (22)
- « ...Using coronavirus infectious clones, it was shown that the transmissible gastroenteritis virus E protein is essential for infection, and during infection, a virus lacking E protein does not infect... » (23)
- « ...The exact mechanism of coronaviruses exiting the cell after release after budding into the ERGIC and moving through the Golgi compartment is not known... » (24)
- « ...It might be worth investigating whether ion channel inhibitors can block coronaviruses from exiting the cell... » (25)
- « ...CoV release is mediated by viroporin ion channel activity or through FPs with host proteins of the secretory pathway... » (22)
- « ...VAMP2 is also important for transportation of newly synthesized lysosomal hydrolases from Golgi to lysosomes » (24)

«...cardiotonic steroids ouabain and digoxin, which are known to inhibit the Na⁺-K⁺-ATPase, inhibited infection of cells by MHV and IAV. When the compounds were present during the early stages of infection, they were shown to inhibit entry of MHV at an early stage, resulting in the formation of vortions close to the cell surface and, as a consequence, in reduced fusion. In agreement with an early block in infection, the inhibition of vortions could be bypassed by low-pI compounds such as captopril. RNA replication was unaffected. The antiviral effect of ouabain could be relieved by the addition of different Src kinase inhibitors, indicating that Src signalling is involved in the entry of MHV and IAV.

In conclusion, in order to verify the possible efficacy of omeprazole and esomeprazole in the treatment of coronaviruses, we must:

The conjugation of the proton pump inhibitor to the S protein of the virus would be the best way to increase its effectiveness. Omeprazole has a pKa of 1.9 and tests in an inactive (ionized) form in vitro. Unlike an in vitro test, the human body is an open system, a dissipative structure. However, the ionized form should not exceed serum concentrations of 500 nM. The active non-ionized form in the absence of active transport.

But the transport of the proton pump inhibitor to the cellular membrane is not a passive reaction. At the cellular level or until the depletion of the transportation capacity from the inactive form to an active form, the concentration of the drug will increase.

As omeprazole can modify or even inhibit the action of the M2 protein of the influenza virus at the cellular level (26), based on a computer simulation, it would also be advisable to check the interaction capabilities of omeprazole with protein E of the coronavirus. Protein E is likely to resemble the protein M2 of the influenza virus.

In the absence of data on the effectiveness of omeprazole against coronaviruses, we can only assume that the absence of data clearly indicates the lack of effectiveness of the drug. It is known that omeprazole after being in contact (at a distance of less than 2 to 3 nm) with the S protein of the virus had the same effect as the S protein of the virus on the cellular membrane. This is due to the similar processes. This is why we can consider omeprazole as a potential drug for the treatment of the immune system a complementary option to defend itself...

Personal experience, using omeprazole in the context of seasonal respiratory viral infections since 2007, reminds me of the indication to divide the daily dose into two daily doses (one morning and one evening). It is usually already effective for aason, especially in children, who have a more pronounced inflammatory state. I associate this with training, continuing education, and self-treatment.

In the context of the COVID-19 pandemic, we can conclude:

- share the maximum impermissible daily dose for omeprazole in divided doses when in contact with people at risk of contamination (not more than 10 mg per day, i.e., 5 mg every 12 hours).
- divide the daily dose of omeprazole into two equal doses when the symptoms appear.
- take the daily dose of omeprazole in two daily doses when the symptoms of severity diminish.
- to resume the daily dose of omeprazole in two daily doses when the symptoms of severity diminish.

The effectiveness of esomeprazole may be greater than omeprazole.

Taking into account the aforementioned, the use of antihistamines containing imidazole will reduce mucus secretion in the respiratory tract. These substances can become negative by modifying the pH, the ciliary mobility and the volume of the mucus (28). Prolonged use, thus promoting the risk of bacterial pneumonia (29). The advantages and disadvantages of these drugs depend on the use of the imidazole ring, which is metabolized by cytochrome P 450 (30).

Best regards

Johannes Hambra

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30. E. N. L. S. H. J. A. P. C. S. V. S. G. Y. T. C. J. A. P. R. J. A. P. R.

Let me kn

Thanks,

Joslyn
Editor
WTOP News
(202) 729-0700

period of [REDACTED] days, I am unable to [REDACTED] the [REDACTED] [REDACTED]
treatment [REDACTED]

I cannot [REDACTED] [REDACTED], [REDACTED] [REDACTED], [REDACTED] [REDACTED],
and [REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED]

Sincerely,

Ching Y. [REDACTED] MD

NIH-001989

Your participation would be greatly appreciated. If you have any questions about the event or your invitation, please do not hesitate to contact me.

Best wishes,

Richard

Richard Fontaine
Executive Director
Trilateral Commission

Jon Pook, M.D.

Jonathan M. Pook, M.D.

Cancer Medical Correspondent
Professor of Medicine

NYU Langone Health

Twitter @DrPook

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