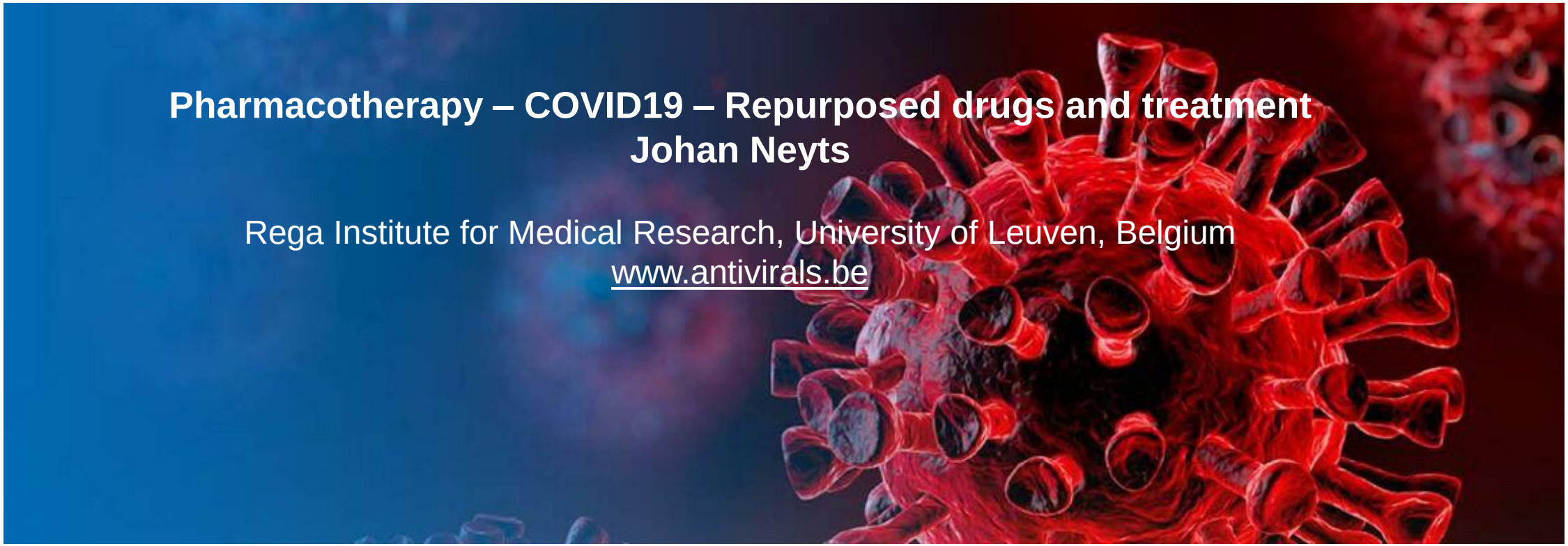

Pharmacotherapy – COVID19 – Repurposed drugs and treatment

Johan Neyts

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www.twitter.com/neyts_johan
www.twitter.com/neytsvirology

Financial disclosure

My laboratory is developing small molecule antivirals either alone or in combination with commercial entities against coronaviruses.

Self assessment questions

1. Antivirals drugs are available against members of most viral families YES/NO
2. Coronavirus have, akin to HIV and HCV a druggable protease YES/NO
3. Phenotypic antiviral screens are the only strategy to indentify novel inhibitors of coronavirus replication YES/NO


第八届武汉现代病毒学国际研讨会
THE 8TH WUHAN INTERNATIONAL SYMPOSIUM ON MODERN VIROLOGY
主办单位
病毒学国家重点实验室
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Hubei Society for Biotechnology
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Wuhan University
Hubei Association for Science and Technology
Wuhan Institute of Virology, CAS
2019. 9. 18-20, 武汉·中国
September 18-20, 2019, Wuhan, China

Menu from Huanan Seafood Wholesale Market in Wuhan

Markets in south-west China's Guilin and southern China's Dongguan are back in business where meats of domesticated animals like cats and dogs are sold.

Picture : Prof. Linfa Wang

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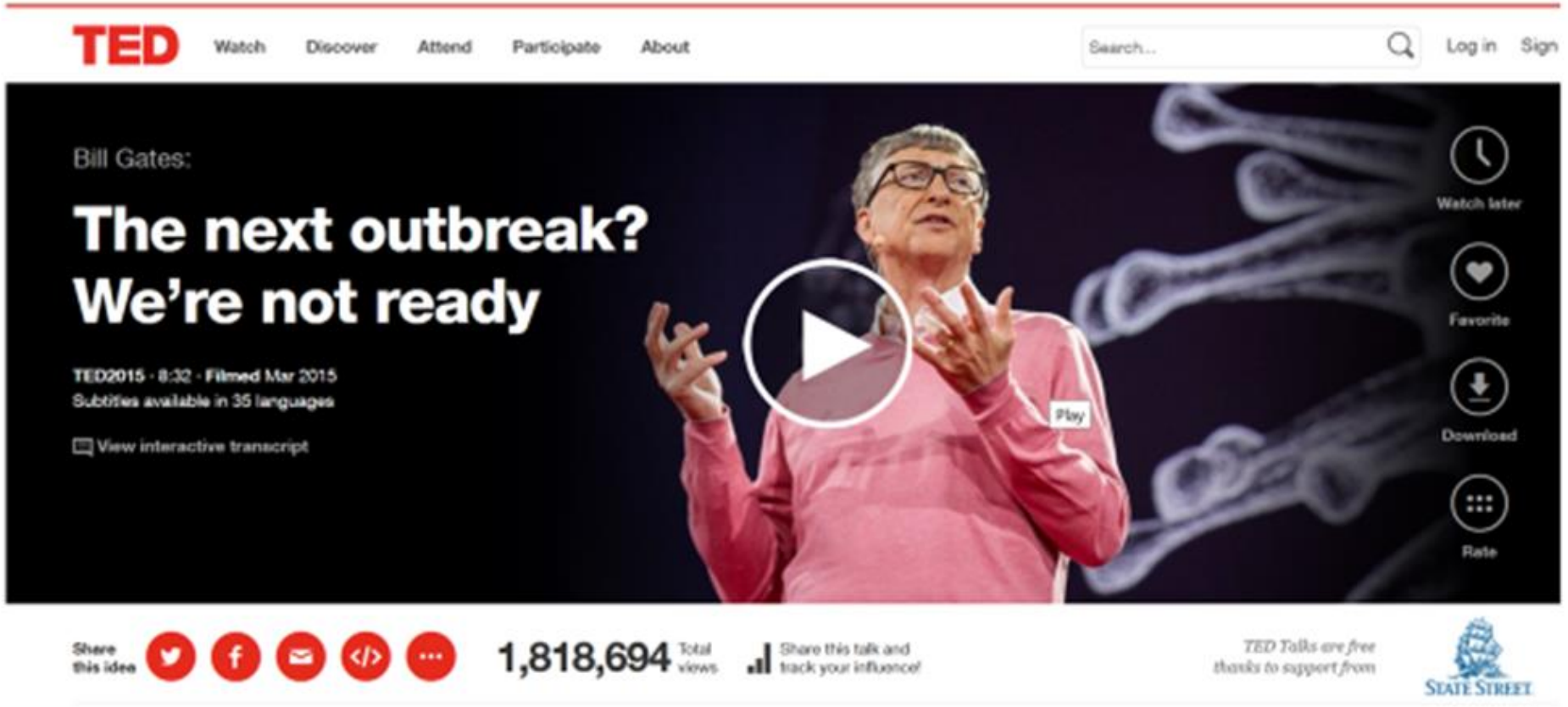
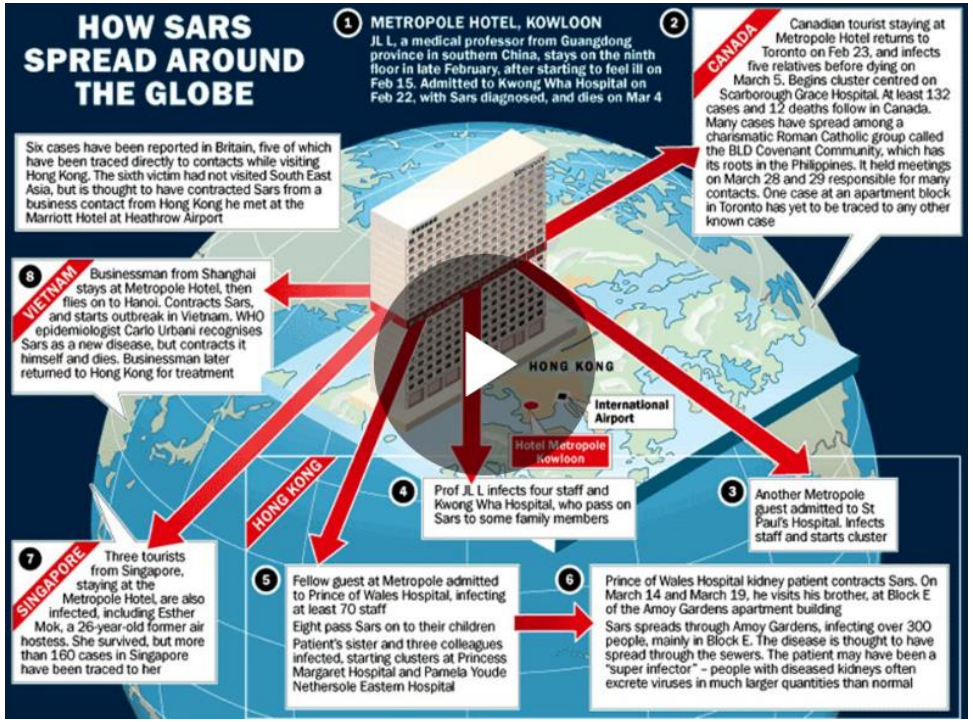
A colony of Angolan free-tailed bats (*left*) lived in this tree in Meliandou, Guinea. (LEFT) JAKOB FAHR; (RIGHT) FABIAN LEENDERTZ, ROBERT KOCH INSTITUTE, BERLIN

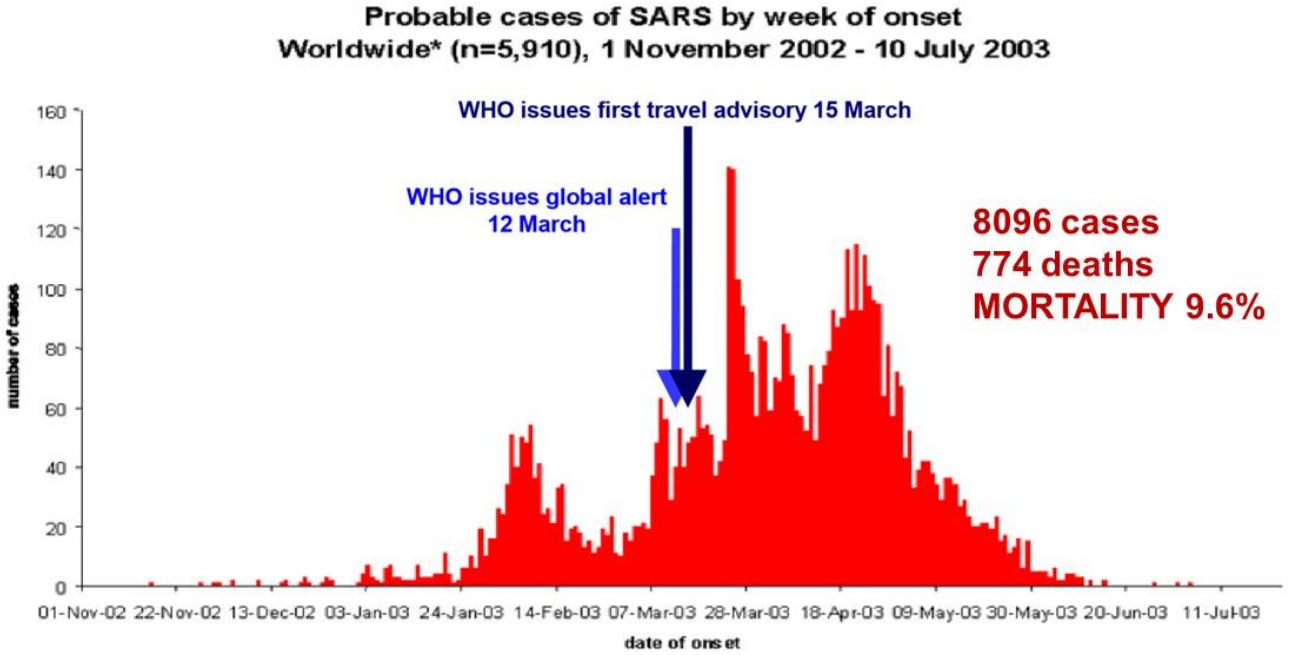
Bat-filled tree may have been ground zero for the Ebola epidemic



If anything kills over 10 million people in the next few decades, it's most likely to be a highly infectious virus rather than a war. Not missiles, but microbes. Now, part of the reason for this is that we've invested a huge amount in nuclear deterrents. But we've actually **invested very little in a system to stop an epidemic**. We're not ready for the next epidemic.

The 2003 SARS epidemic



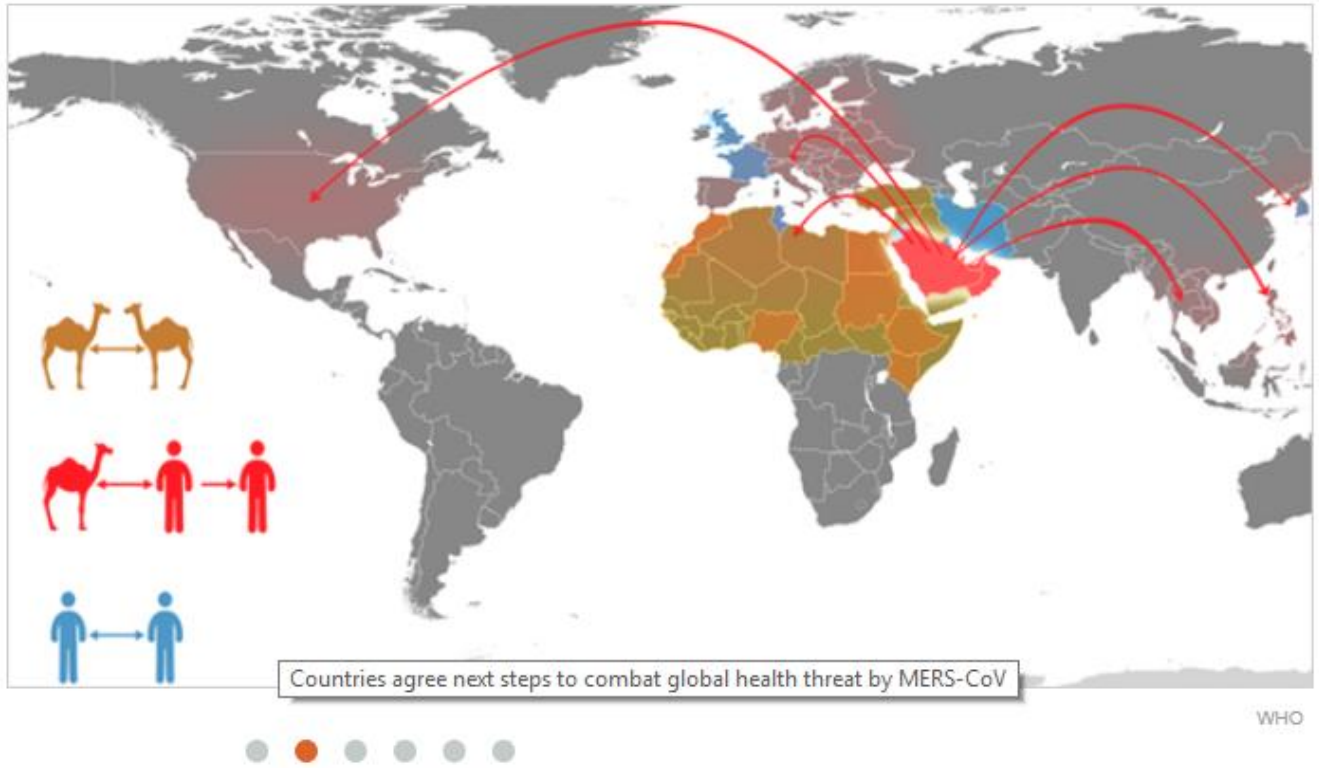


*This graph does not include 2,527 probable cases of SARS (2,521 from Beijing, China), for whom no dates of onset are currently available.

Adapted from World Health Organization. Epidemic curves – Severe Acute Respiratory Disease (SARS) http://www.who.int/csr/sars/epicurve/epiindex/en/index1.html

https://slideplayer.com/slide/5981486/

Middle East Respiratory Syndrome CoV



2 494

Since September 2012, WHO has been notified of 2494 laboratory-confirmed cases of infection with

858

858 MERS-CoV associated deaths have occurred since September 2012.

27

Since September 2012, 27 countries have reported cases of MERS-CoV

Update Dec 2020

MORTALITY 34%

www.who.int

Towards SARS-COV2 therapeutics

www.surplusgezondheid.be

Antivirals available against….

Herpesviruses

HIV

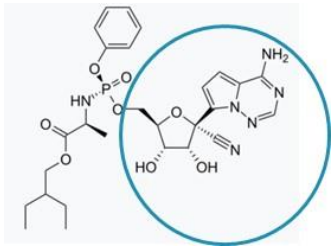
HBV

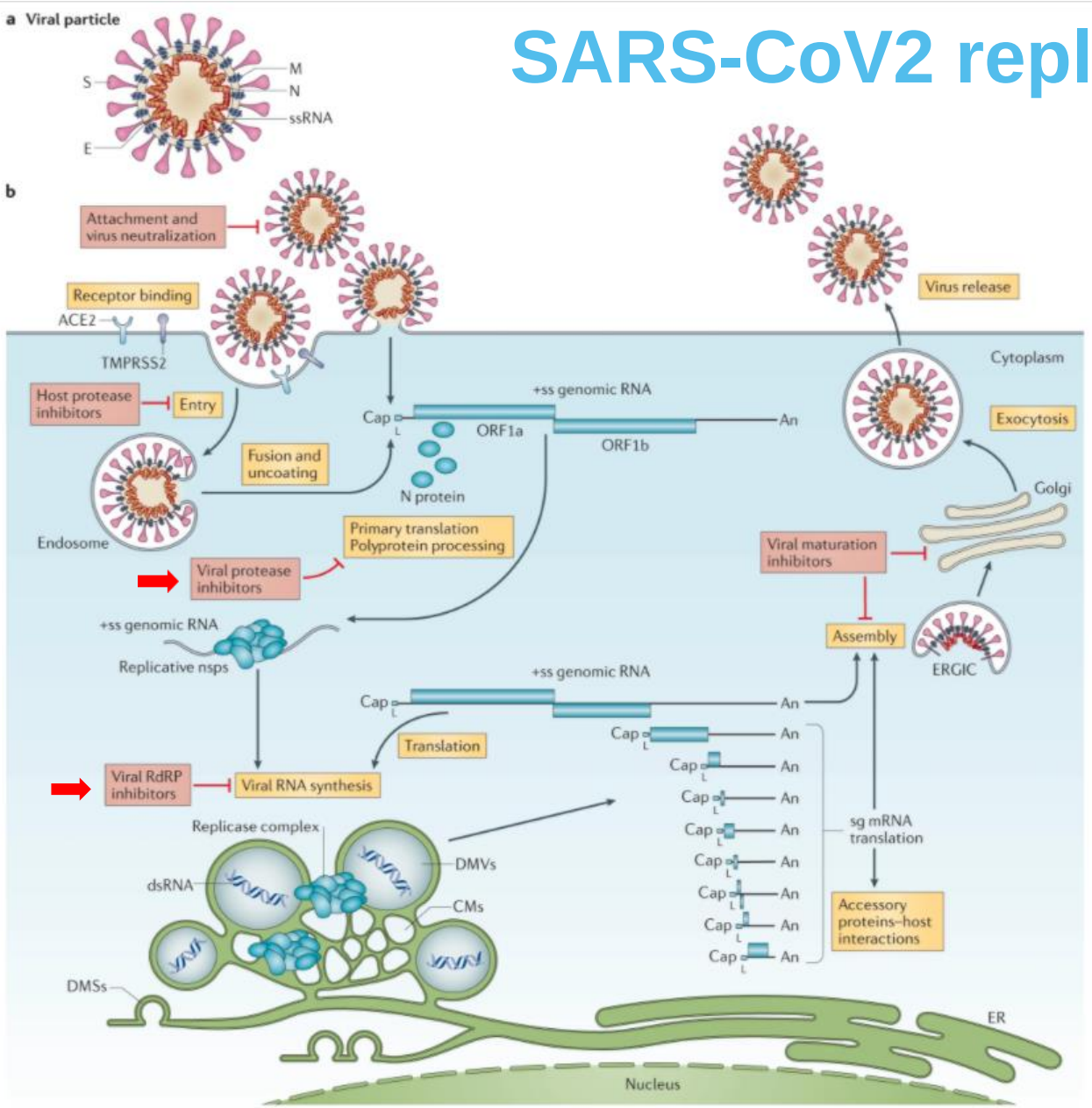
HCV

Influenza

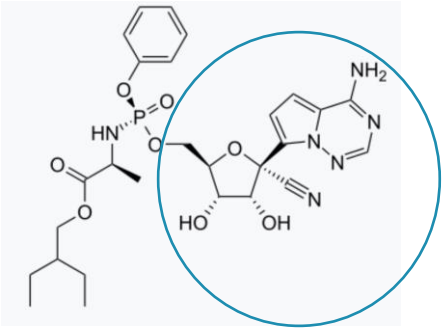
** examples

SARS-CoV2 replication cycle





Remdesivir



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Remdesivir for the Treatment of Covid-19 — Final Report

J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, H.Y. Chu, A. Luetkemeyer, S. Kline, D. Lopez de Castilla, R.W. Finberg, K. Dierberg, V. Tapson, L. Hsieh, T.F. Patterson, R. Paredes, D.A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari, M. Oh, G.M. Ruiz-Palacios, T. Benfield, G. Fätkenheuer, M.G. Kortepeter, R.L. Atmar, C.B. Creech, J. Lundgren, A.G. Babiker, S. Pett, J.D. Neaton, T.H. Burgess, T. Bonnett, M. Green, M. Makowski, A. Osinusi, S. Nayak, and H.C. Lane, for the ACTT-1 Study Group Members*

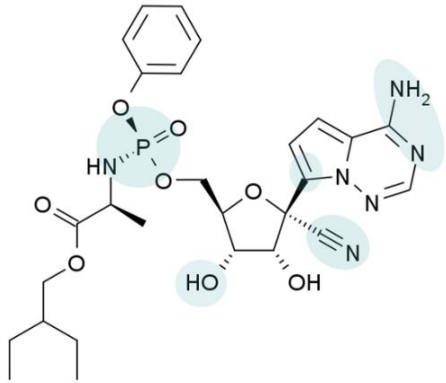
Approved in the EU (July 2020) for use in patients (age >12, BDW >40 kg) with COVID pneumonia requiring 0_2

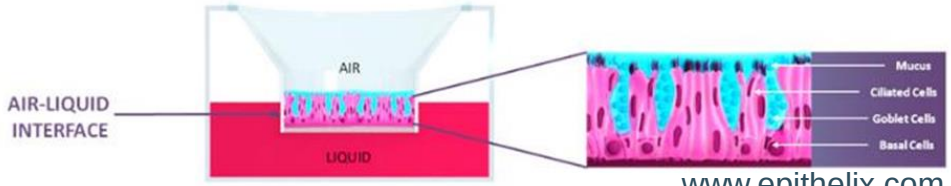
World Health Organization

Solidarity Therapeutics Trial produces conclusive evidence on the effectiveness of repurposed drugs for COVID-19 in record time

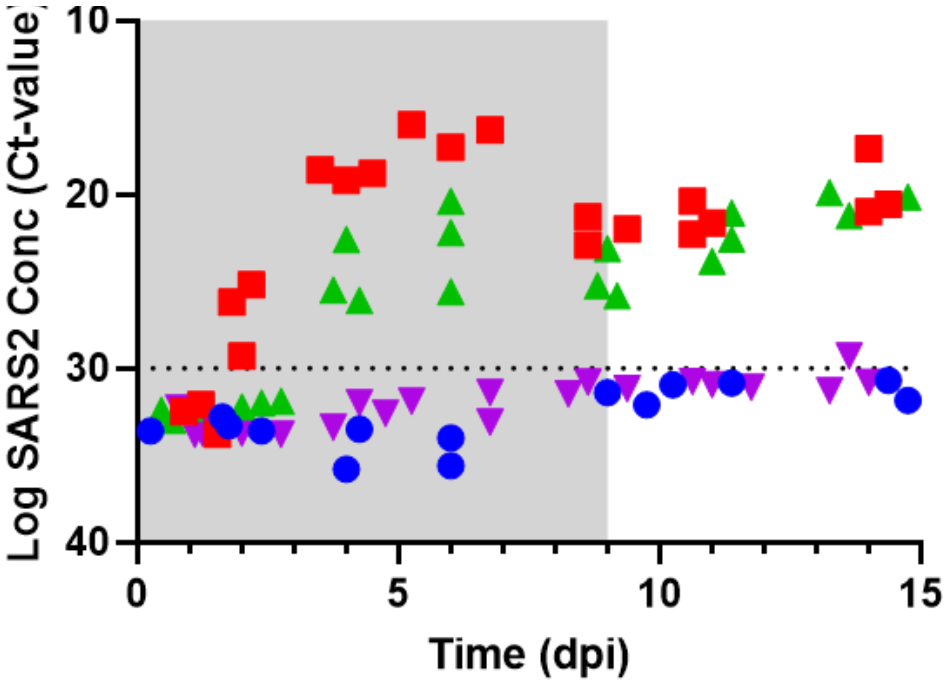
15 October 2020 | News release | Geneva | Reading time: Less than a minute (223 words)

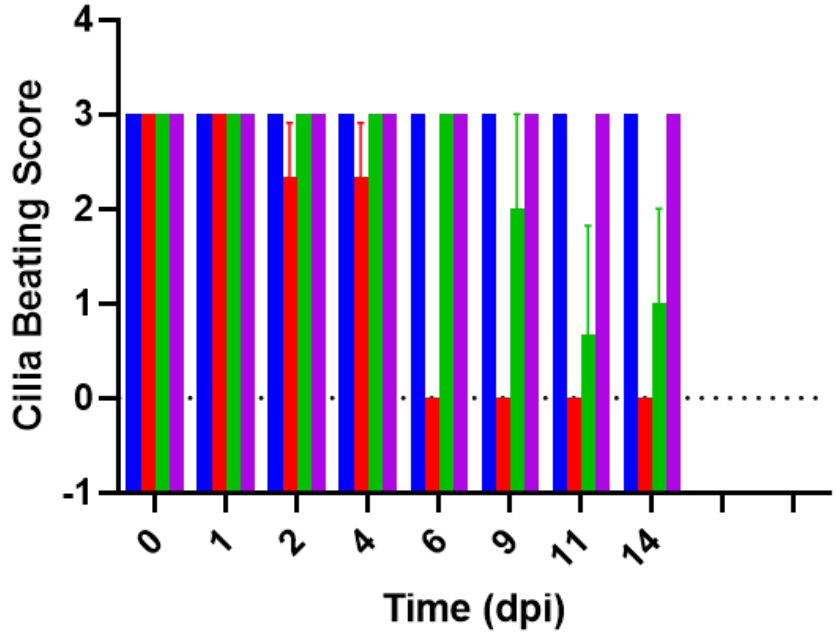
Remdesivir is effective against SARS-CoV2 in human airway epithelial cells





www.epithelix.com





CC
VC
GS-441524 1 uM
GS-441524 10 uM

Jochmans et al., unpublished

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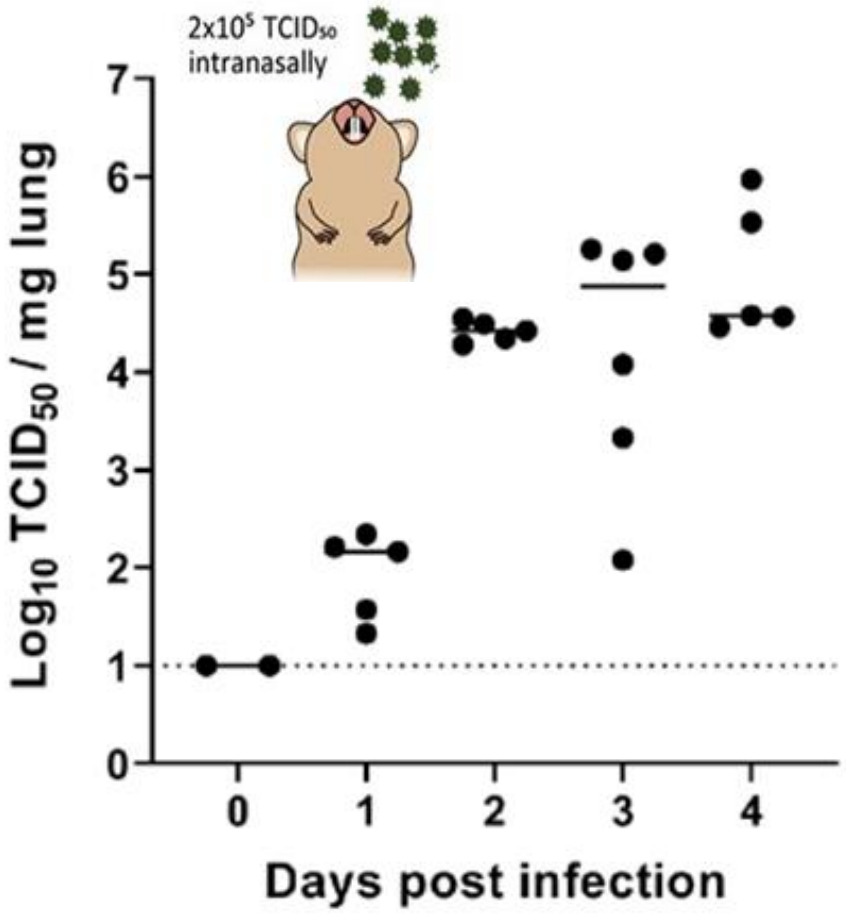
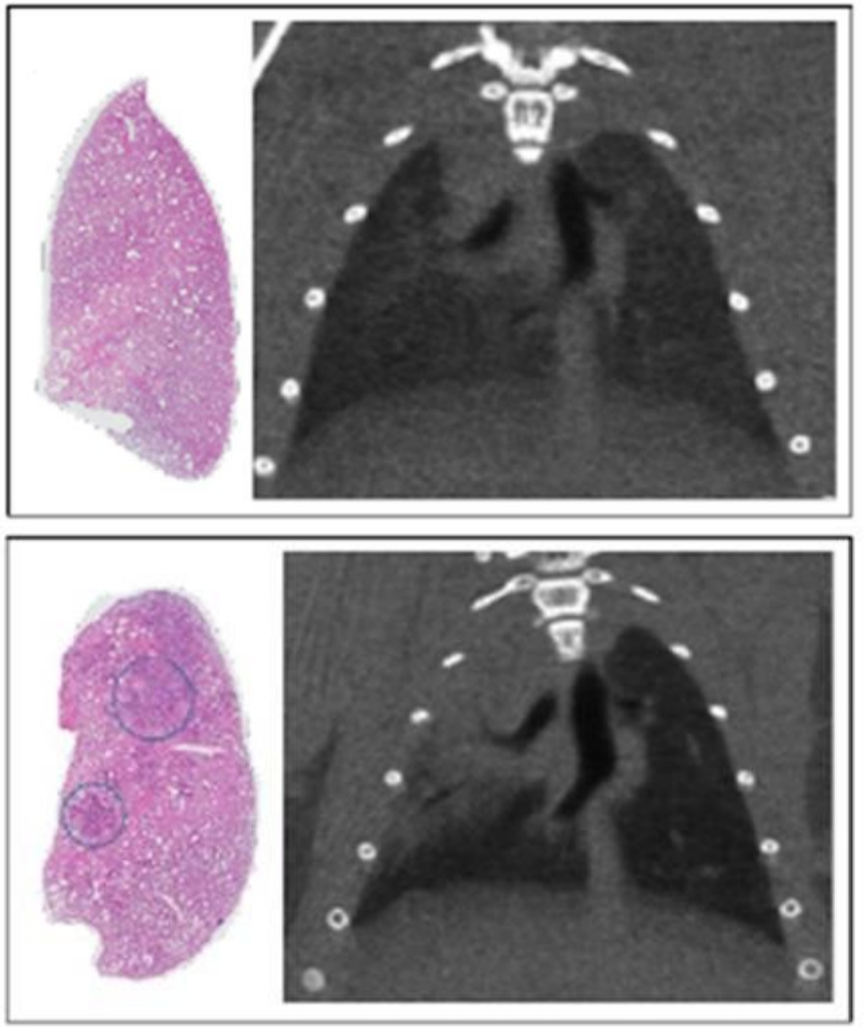
SARS-CoV-2 in hamsters



Uninfected

Infected



Kaptein et al. PNAS (2020)
Boudewijns et al., Nature Communications (2020)

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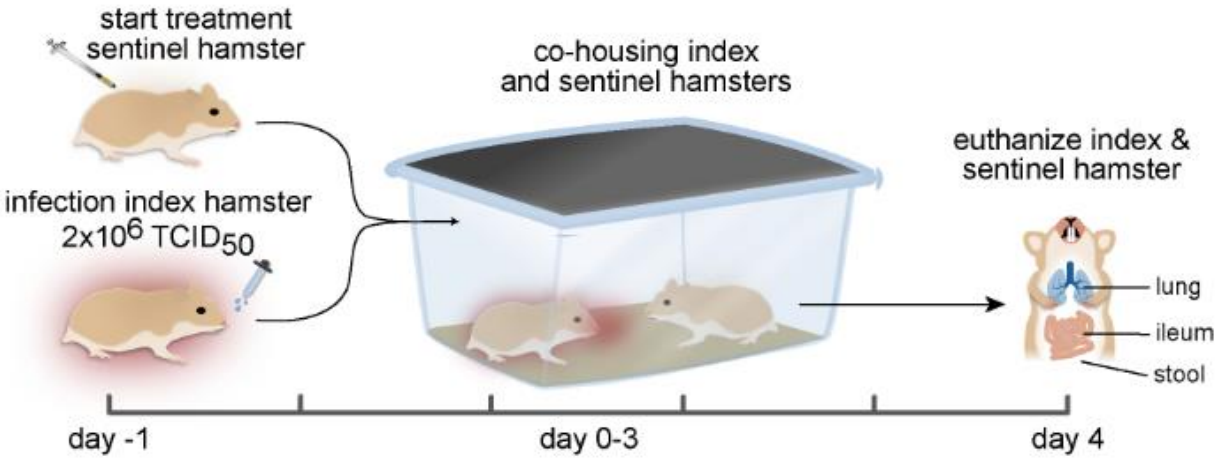
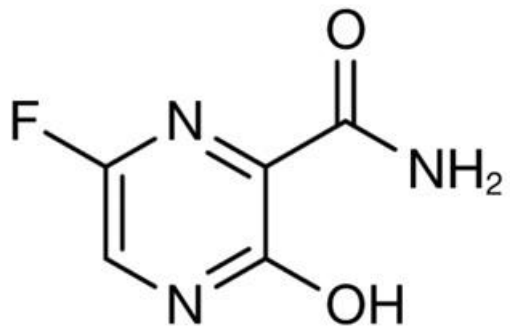
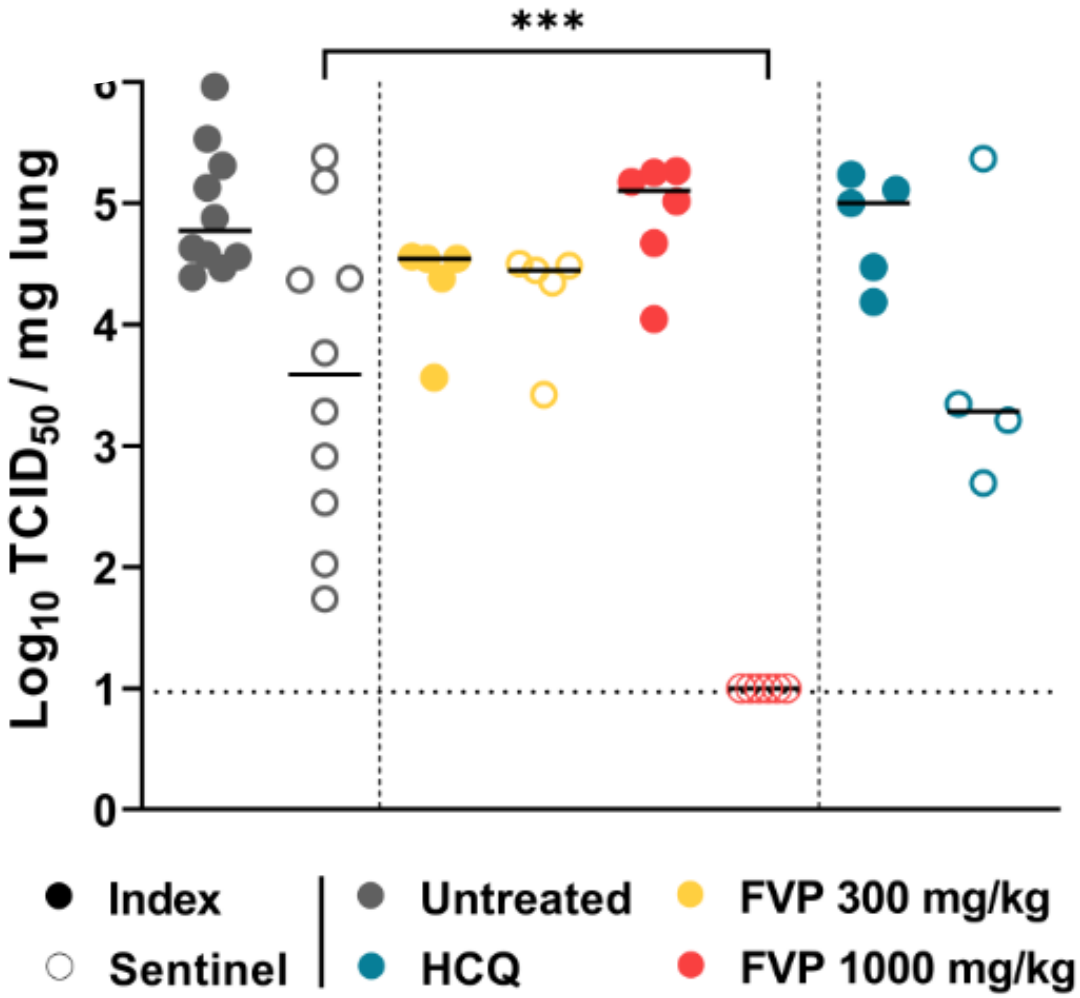
Favipiravir protects against SARS-CoV2 transmission







Kaptein et al. Proc. Natl. Acad. Sci. USA

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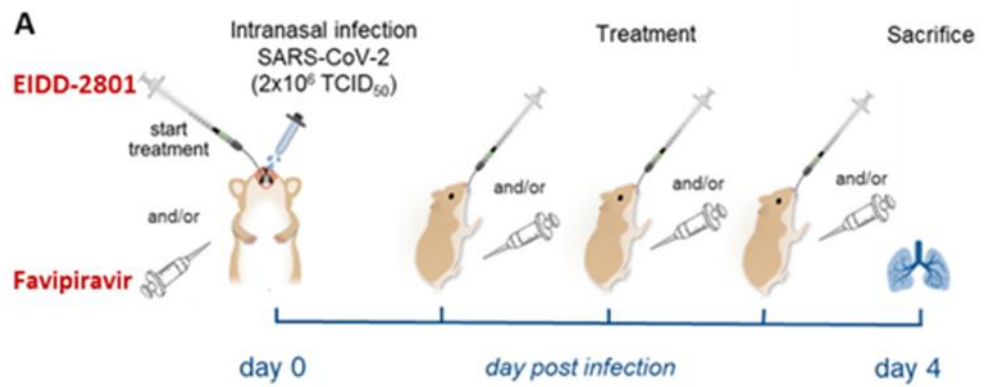
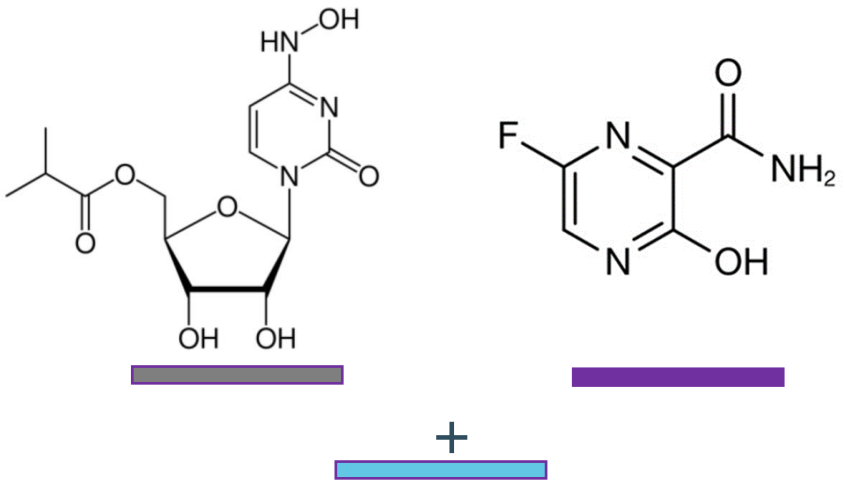
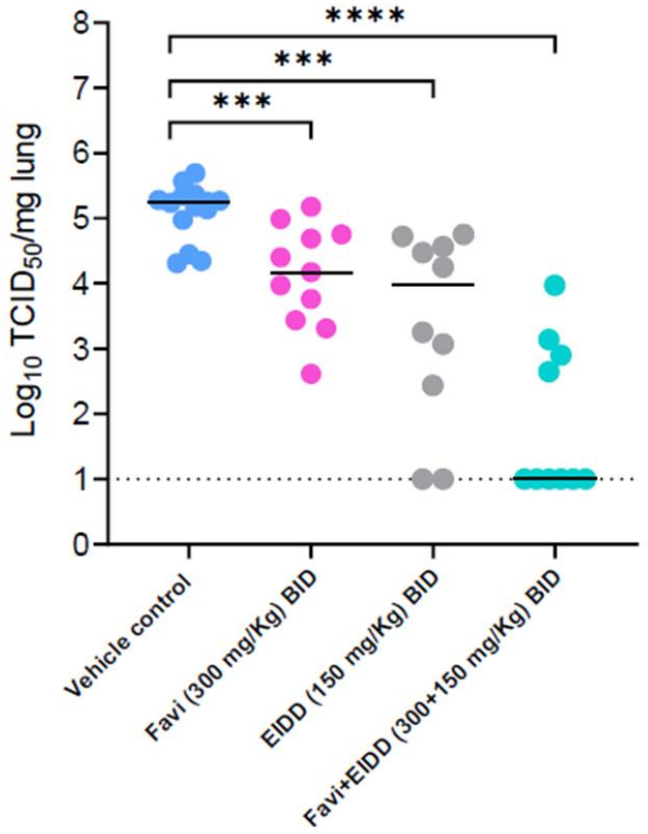
Molnupiravir + favipiravir is synergistic against SARS-CoV2 in hamsters





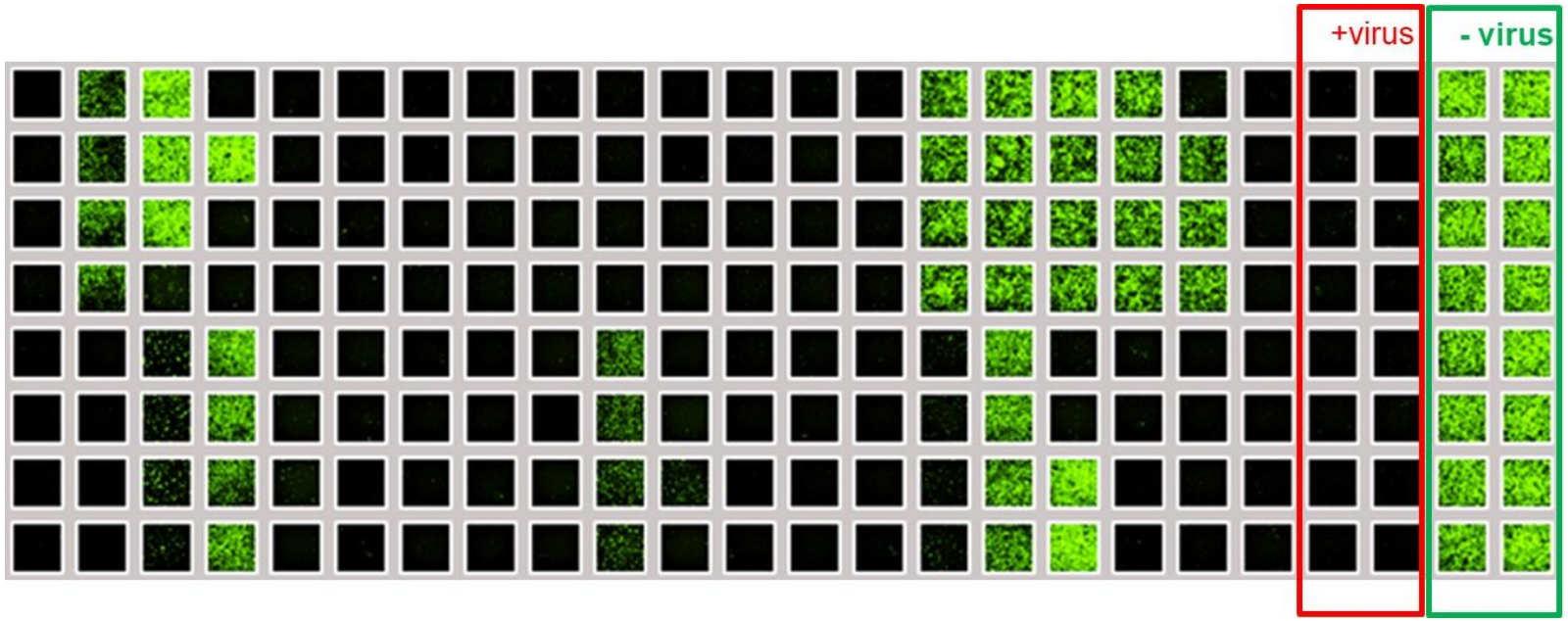


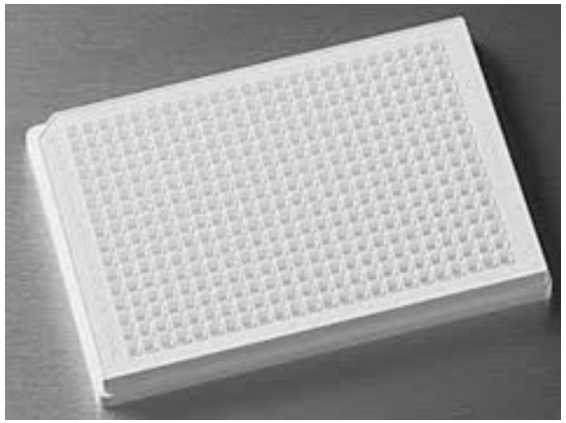
log_{10} reduction	Favipiravir	EIDD-2801	Combo
Infectious virus	1.1	1.3	4.5***

*significance compared to the activity of favipiravir alone

Towards highly potent pan-coronavirus inhibitors

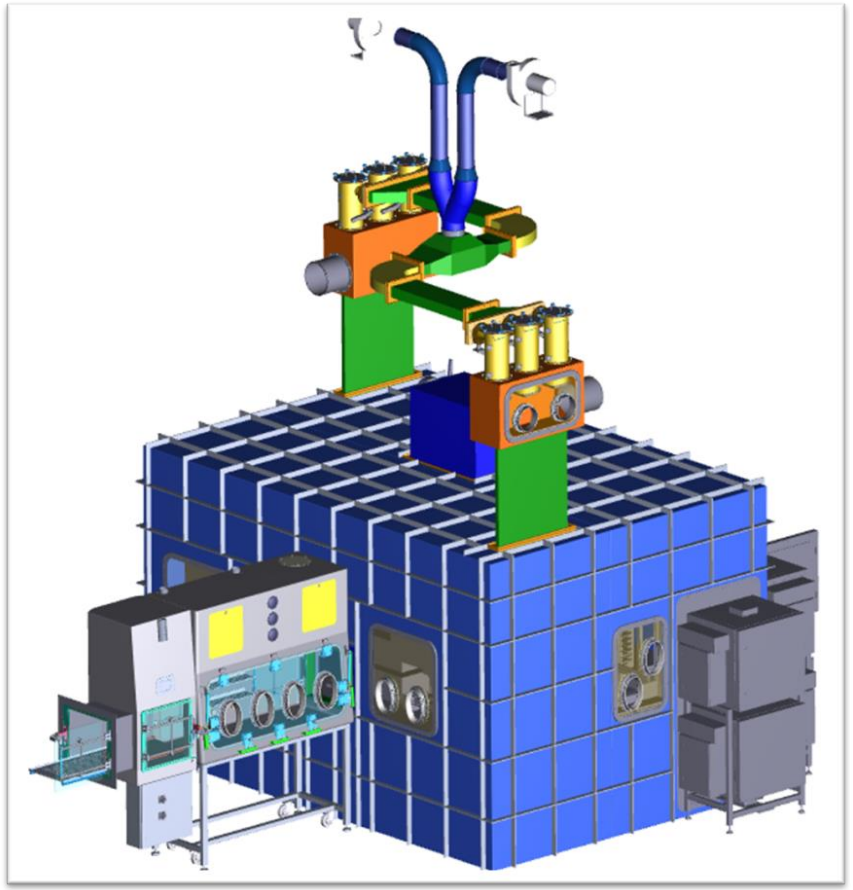
1. Target based drug design (eg protease)
2. Phenotypic screening to identify hits as a starting point for hit/lead optimization)





Towards highly potent pan-coronavirus inhibitors

Caps-It : high-biosafety lab-in-a-box



www.antivirals.be


MBRAUN

Take home messages

1. Antiviral drugs will be an important/essential pilar for the control of the SARS-COV2 pandemic
2. Antiviral drugs will be an important/essential pilar to control future epidemics/pandemics
3. Pan-corona antiviral drugs need to be developed as well as broader-acting antiviral drugs

Acknowledgements

Virology – Rega Institute – KU Leuven
Lorena Sanchez Felipe –Sapna Sharma – Ji Ma – Viktor Lemmens – Robbert Boudewijns- Mahadesh Prasad Arkalagud Javarappa – Laurens Liesenborghs – Suzanne Kaptein – Carolien De Keyzer – Lindsey Bervoets –Sarah Debaveye- Sander Jansen – Michael Bright Yakass – Li-Hsin Li – Xin Zhang – Sebastiaan ter Horst – Niraj Mishra – Lotte Coelmont – Dirk E. Teuwen – Elisabeth Heylen – Dominique Schols –Kai Dallmeier- Johan Neyts and the whole group.

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Corinne Vandermeulen

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