SARS-CoV-2: Virological & clinical features and questions

SARS-CoV-2 = virus

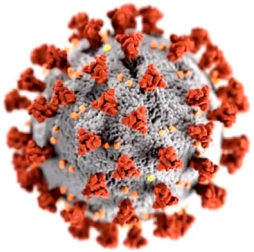
COVID-19 = disease

Dennis Kolson, MD, PhD

Neurology Dept.

University of Pennsylvania

March 12, 2020



Perelman School of Medicine
University of Pennsylvania

Disclosure: Dr. Kolson serves as a consultant to the National NeuroAIDS Tissue Consortium

Authors
Markus Hoffmann, Hannah Kleine-Weber, Simon Schroeder, ..., Marcel A. Müller, Christian Drosten, Stefan Pöhlmann

Correspondence
mhoffmann@dpz.eu (M.H.), spoehlmann@dpz.eu (S.P.)

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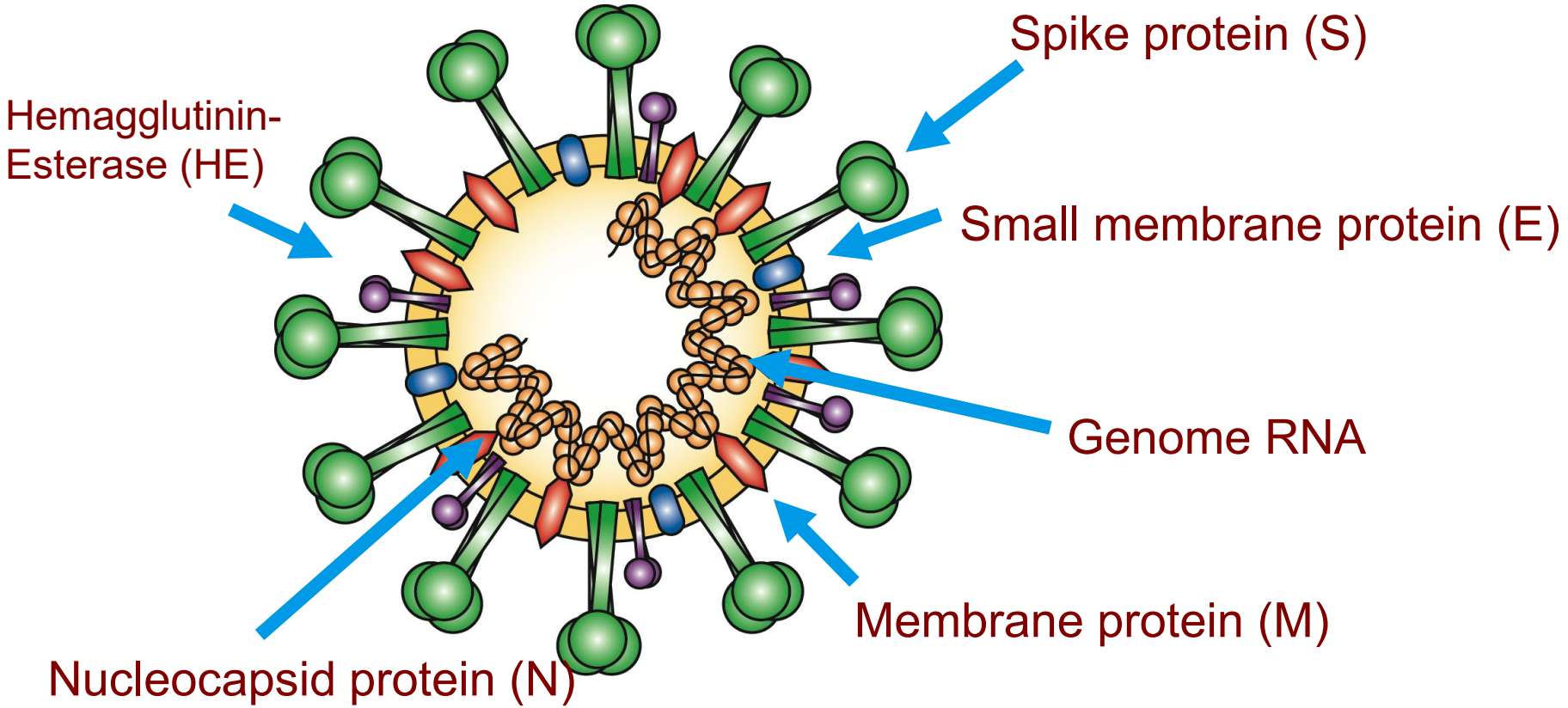
Article

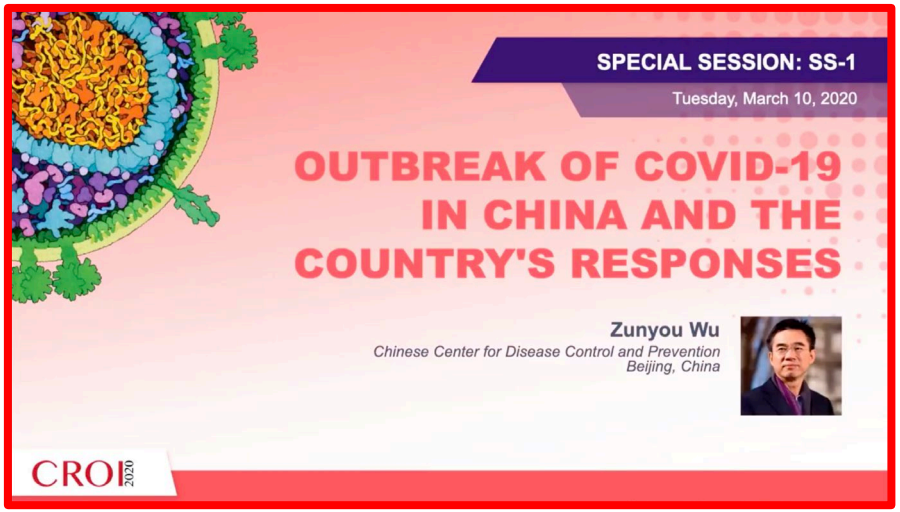
SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor

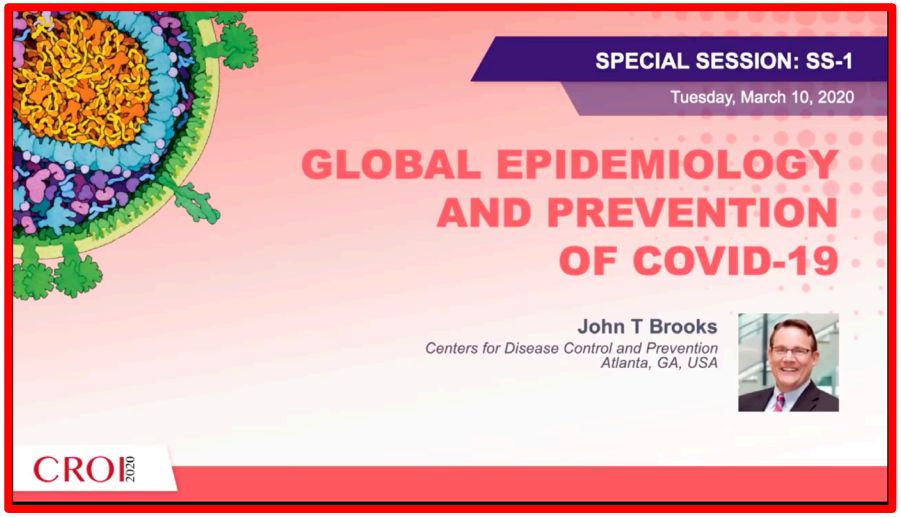
Coronavirus virion

SARS-CoV-2:*Uses human ACE 2 receptor for entry*



SARS-CoV-2: sources of information:
https://special.croi.capitalreach.com/





Susan R. Weiss

Director, Upenn
NIH T32 'Training in Neurovirology'

Director, Office of Biomedical Postdocotoral Programs, University of Pennsylvania

Department: Microbiology

Description of Research Expertise

Research Interests
- Murine coronavirus pathogenesis, central nervous system, liver and lung
- Murine coronavirus antagonism of the OAS-RNase L pathway
- Organ specific virus- host interactions
- Viral and cellular phosphodiesterases
- Middle Eas Respiratory Syndrome Coronavirus pathogenesis
- Role of inflammasome related cytokines in murine coronavirus acute disease and chronic demyelination

Key words: murine coronavirus, human respiratory coronavirus, viral pathogenesis, interferon antagonist.

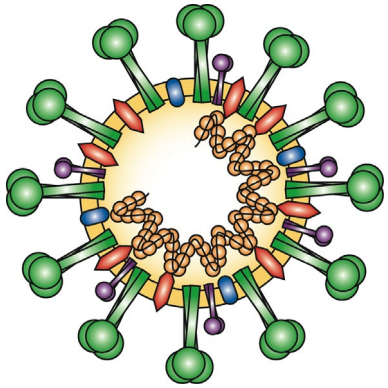
Description of Research

Susan Weiss, Ph.D.

Perelman School of Medicine
University of Pennsylvania

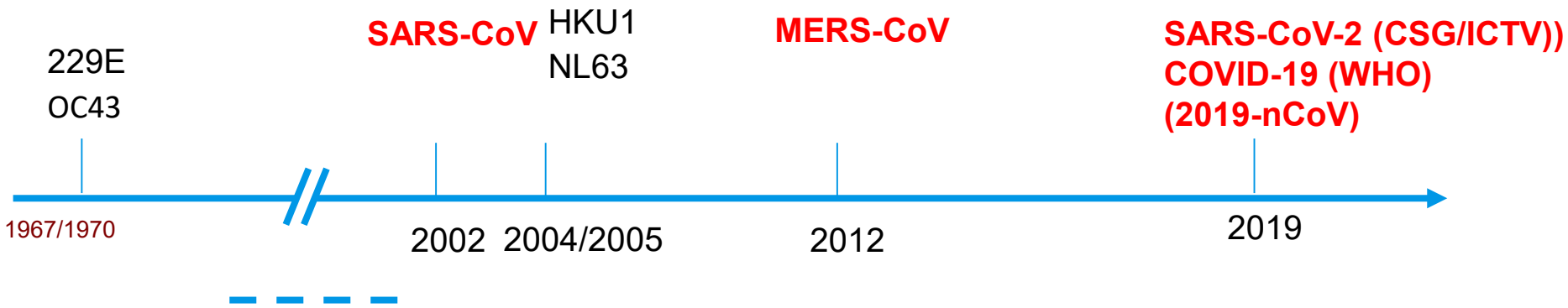
Presented at: 27th annual Conference on Retroviruses and Opportunistic Infections (CROI)
International Meeting (virtual meeting)
March 8-11, 2020

Human coronaviruses: time line



Common cold
OC43 can infect
lower respiratory
track

HKU1; Pneumonia
NL63; Bronchiolitis, croup



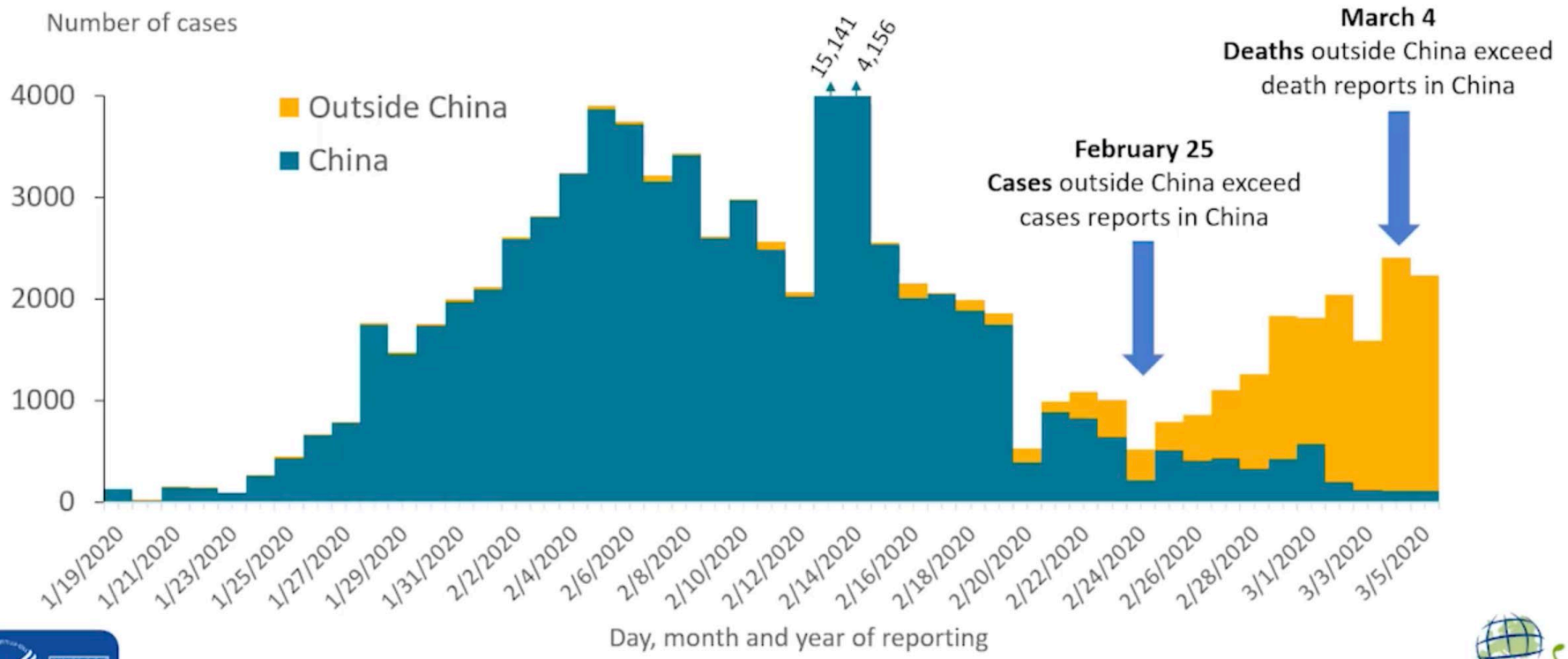
OC43 genome similar to
Bovine coronavirus

SARS-CoV. MERS-CoV, SARS-CoV-2
Severe respiratory disease

coronavirus disease-2019 or COVID-19

Epidemiology: spread from China (apparent control now in China)

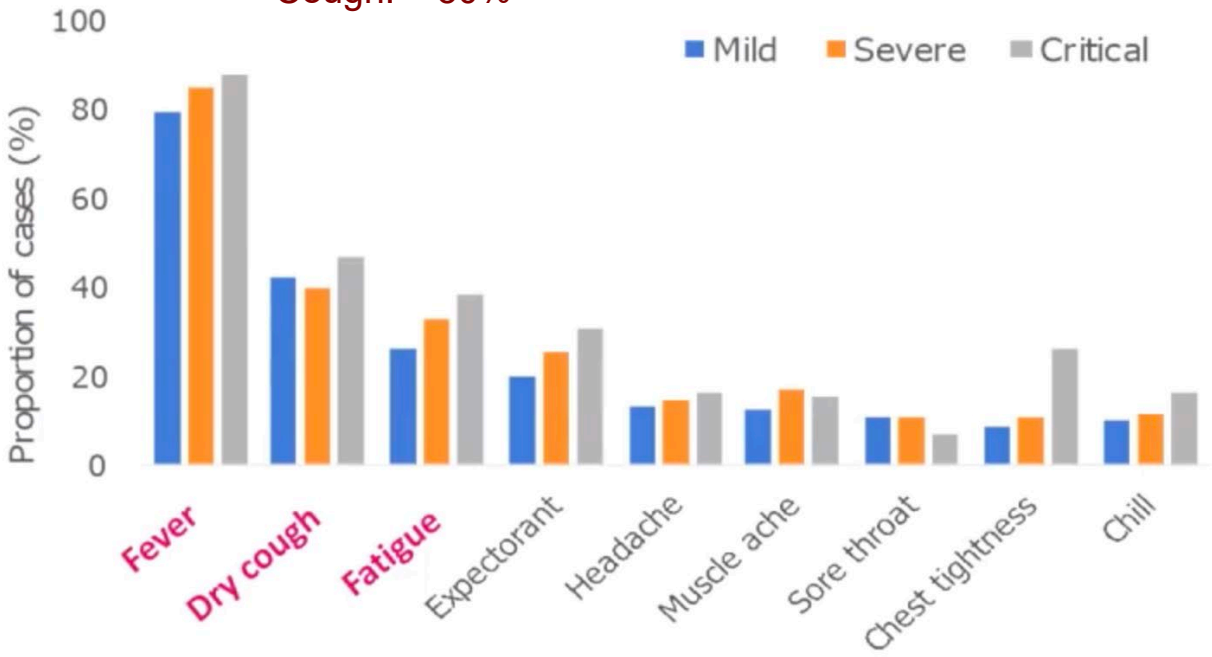
Distribution of COVID-19 cases in accordance with the applied case definitions in the affected countries, as of 05 March 2020



Most common symptoms: fever, dry cough, fatigue

Common Symptoms of COVID-19 in China

Fever: ~ 80%
Cough: ~ 50%



- Median incubation period estimated to be 4-6 days (range 2-14 days)

China CDC/NHC 2020

SARS-CoV-2 can be shed 24-48 hours before symptoms

Key epi/technical insights from China (3 of 3)

3-Virology:

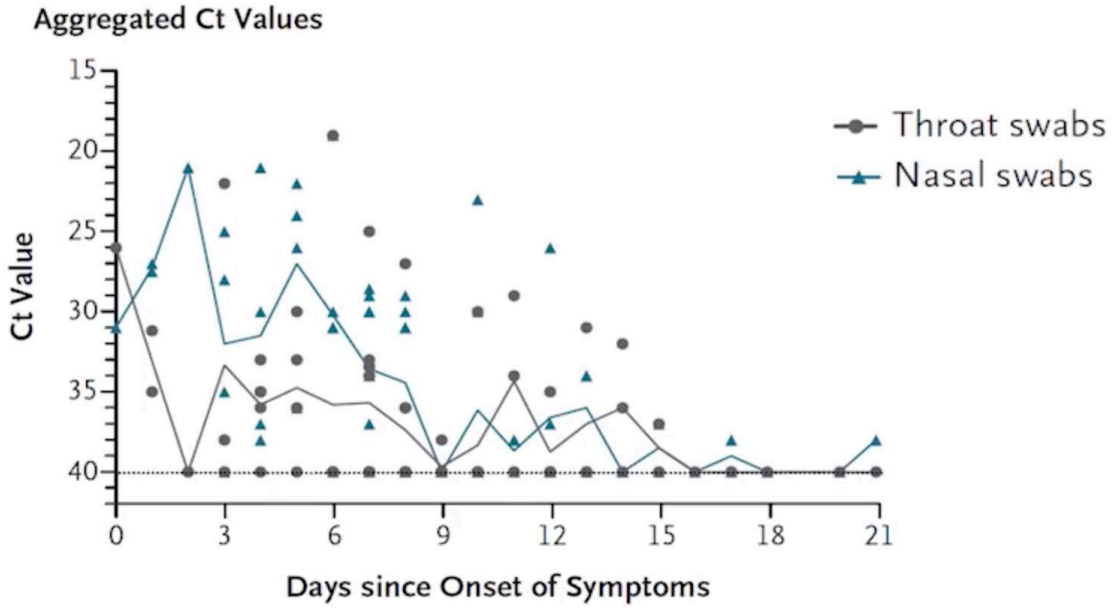
- Virus **shedding** is highest early in the course of disease (vs. SARS shedding, which peaks at least 5 days after onset)
- Virus **shedding** can occur in the 24-48 hours prior to symptom onset
- Virus can be **isolated** from stool but there is no epidemiologic evidence of fecal-oral transmission
- Virus **shedding** usually continues for 7-12 days in mild/moderate cases, and for >2 weeks in severe cases
- Patients who recover can be PCR positive after symptoms resolve

Aylward B et al, WHO-China Mission, 2020

SARS-CoV-2 can be shed 24-48 hours before symptoms

Viral Shedding Greatest At Time Symptoms Start

- SARS-CoV-2 viral loads in 17 symptomatic patients
- No data regarding duration of replication-competent virus shedding (e.g., culture)

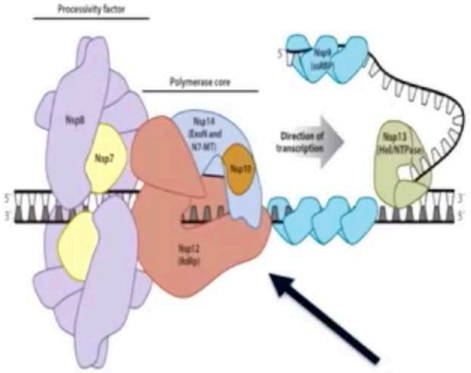


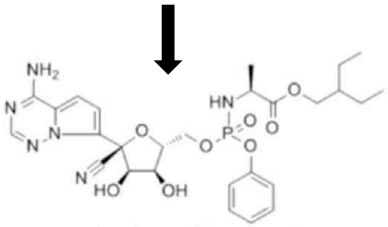
Zou 2020, N Engl J Med; DOI: 10.1056/NEJMc2001737

SARS-CoV-2 Therapeutics

Therapeutic Interventions

- No approved drugs, immune therapeutics and vaccines against any group 2b coronavirus
- Experimental Drugs (nsp12-RdRp target)
  - Remdesivir- *Inhibits RNA-dependent RNA polymerase*





monophosphoramidate prodrug of an adenosine analog, GS-5734

Chain Termination

At least 6 Remdesivir controlled trials planned/currently underway

- Combination lopinavir, ritonavir, and interferon beta tested in China?
- Therapeutic antibodies (MERS, likely soon for SARS-CoV 2)

Sheahan et al., Nature Communications 11, 222 (2020)

Sheahan et al., Sci Transl Med. 2017 Jun 28;9(396).

Many remaining questions

- How extensively will the virus spread ?
- Will it be seasonal?
- How soon will therapeutics (Remdesivir, others) be ready?

Thank you!