Biomarker Identification / Therapeutics Development from Proteomics and Metabolomics Studies of COVID-19 Patients

K. Hun Mok (睦 憲), Ph.D.

Trinity College Dublin.
Trinity Biomedical Sciences Institute (TBSI)
School of Biochemistry and Immunology
Protein Folding and Biomolecular NMR Spectroscopy Lab / TBSI NMR Facility
Dublin 2, Ireland

3rd June 2020 (Wed)

International Trends in Pandemic Quarantine and the Development of Vaccines / Therapeutics

KOFST – KSEAs Online Forum

Seoul - Dublin

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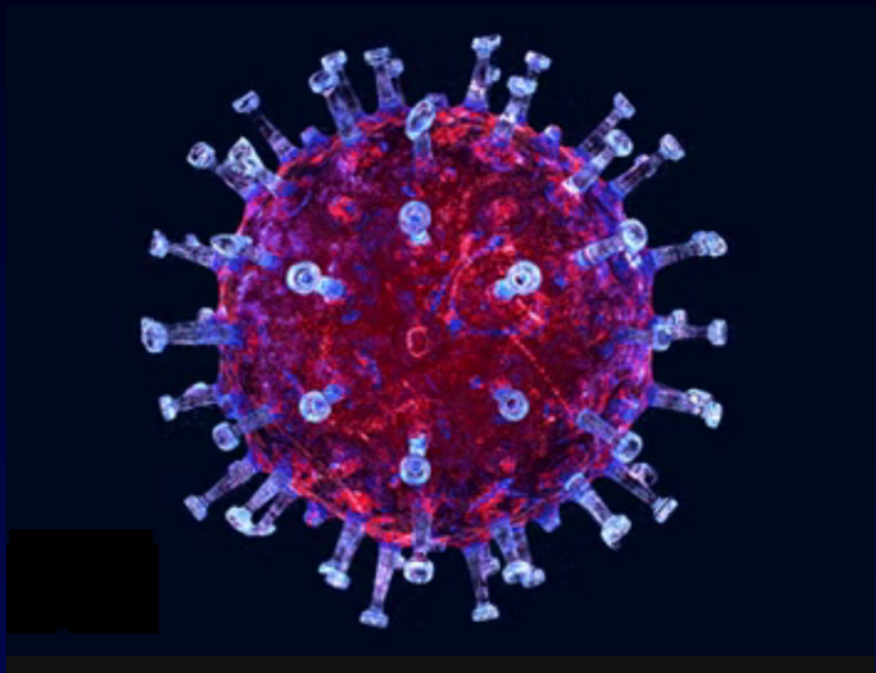

SARS-CoV-2

(The Epidemic: COVID-19)

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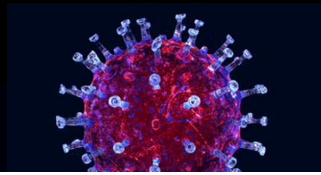
RNA Viruses



Virus Family	Examples (common names)	Capsid naked/enveloped	Capsid Symmetry	Nucleic acid type	Group
1. *Reoviridae*	Reovirus, rotavirus	Naked	Icosahedral	ds	III
2. *Picornaviridae*	Enterovirus, rhinovirus, hepatovirus, cardiovirus, aphthovirus, poliovirus, parechovirus, erbovirus, kobuvirus, teschovirus, coxsackie	Naked	Icosahedral	ss	IV
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4. *Togaviridae*	Eastern equine encephalitis	Enveloped	Icosahedral	ss	IV
5. *Arenaviridae*	Lymphocytic choriomeningitis virus, Lassa fever	Enveloped	Complex	ss(-)	V
6. *Flaviviridae*	Dengue virus, hepatitis C virus, yellow fever virus, Zika virus	Enveloped	Icosahedral	ss	IV
7. *Orthomyxoviridae*	Influenzavirus A, influenzavirus B, influenzavirus C, isavirus, thogotovirus	Enveloped	Helical	ss(-)	V
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11. *Filoviridae*	Ebola virus, Marburg virus	Enveloped	Helical	ss(-)	V
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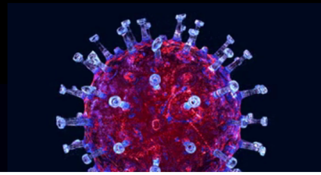
RNA Viruses



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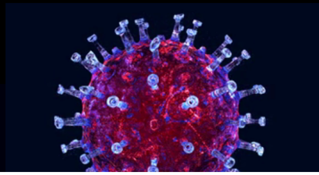

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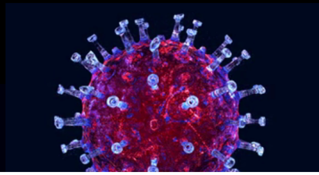

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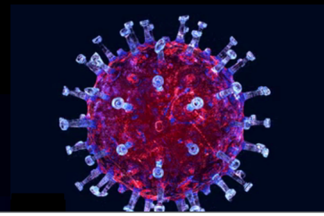
RNA Polymerase

Remdesivir : An Inhibitor of RNA Polymerase



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Remdesivir for the Treatment of Covid-19 — Preliminary 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*

ABSTRACT

BACKGROUND

Although several therapeutic agents have been evaluated for the treatment of coronavirus disease 2019 (Covid-19), none have yet been shown to be efficacious.

METHODS

We conducted a double-blind, randomized, placebo-controlled trial of intravenous remdesivir in adults hospitalized with Covid-19 with evidence of lower respiratory tract involvement. Patients were randomly assigned to receive either remdesivir (200 mg loading dose on day 1, followed by 100 mg daily for up to 9 additional days) or placebo for up to 10 days. The primary outcome was the time to recovery ... either discharge from the hospital or hospitalization for infect...

... The data and safety monitoring ... on the basis of findings from ... remdesivir group. Pre- ... and 521 to ...

DOI: 10.1056/NEJMoa...
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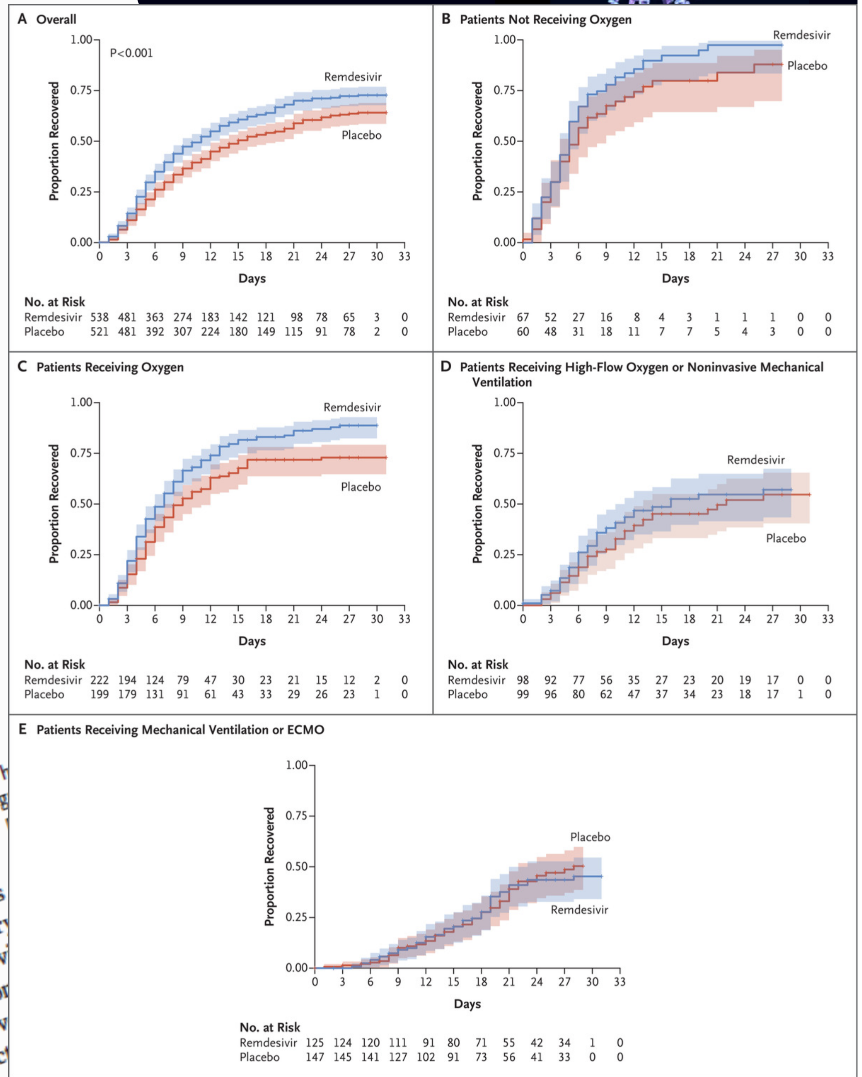

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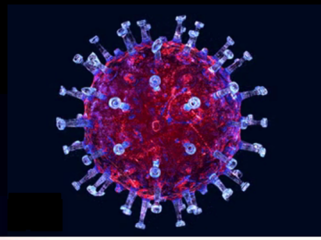
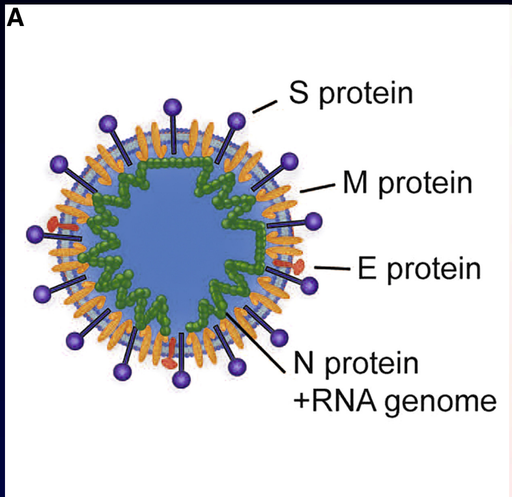
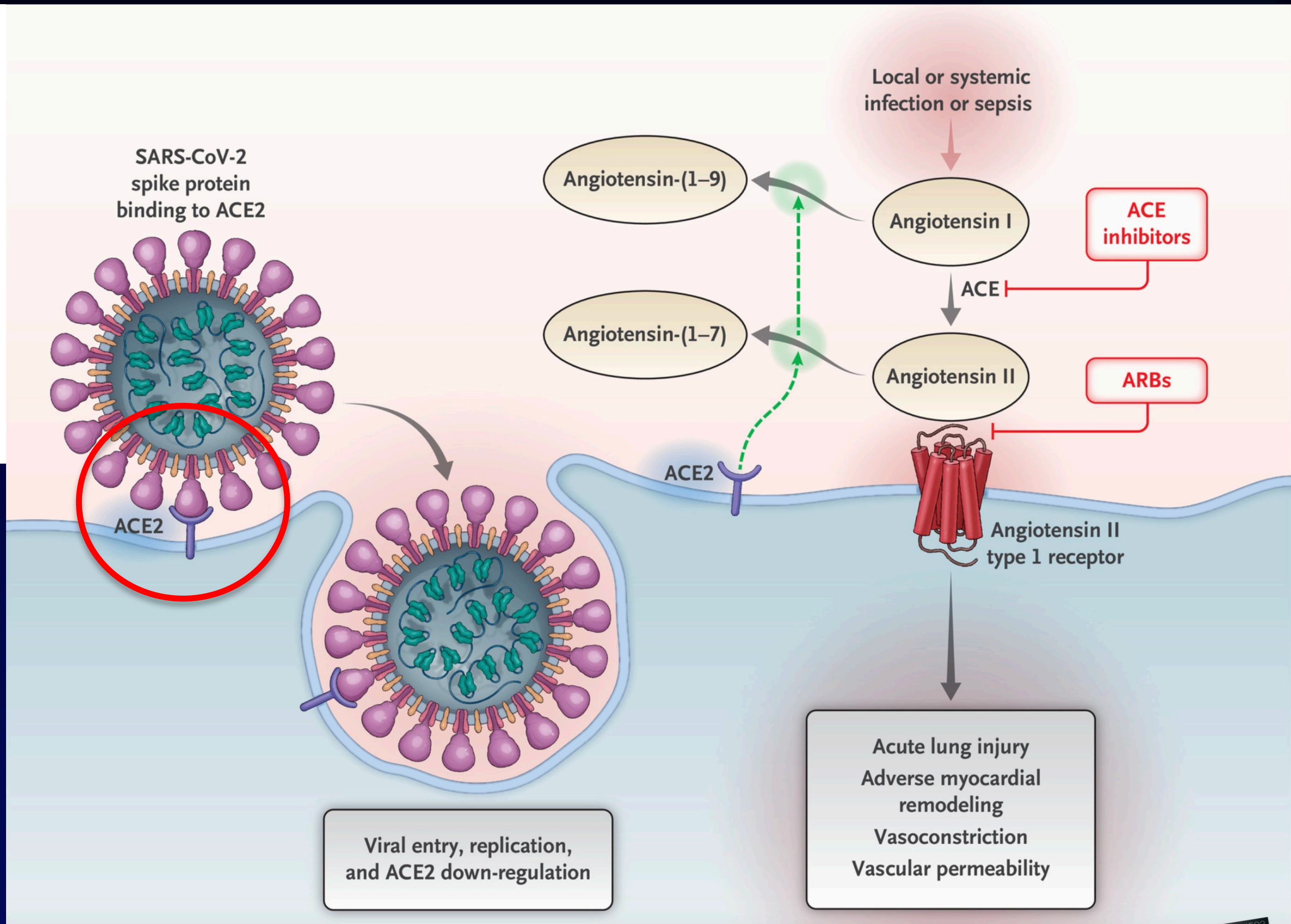
2020.5.22.

The Cellular Entry Path of SARS-CoV-2







- **The S** (Spike) Protein selectively binds to ACE2, then the complex enters via endocytosis
- As a result, ACE2 is unable to carry out its inherent function of vascular relaxation and protection of the heart.

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL REPORT

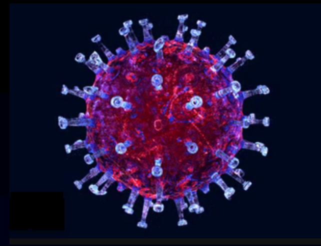
Renin–Angiotensin–Aldosterone System Inhibitors in Patients with Covid-19

Muthiah Vaduganathan, M.D., M.P.H., Orly Vardeny, Pharm.D., Thomas Michel, M.D., Ph.D., John J.V. McMurray, M.D., Marc A. Pfeffer, M.D., Ph.D., and Scott D. Solomon, M.D.

The renin–angiotensin–aldosterone system (RAAS) is an elegant cascade of vasoactive peptides that orchestrate key processes in human physiology. Severe acute respiratory syndrome coronavirus 1 (SARS-CoV-1) and SARS-CoV-2, which have been responsible for the SARS epidemic in 2002 to 2004 and for the more recent coronavirus disease 2019 (Covid-19) pandemic, respectively, interface with the RAAS through angiotensin-converting enzyme 2 (ACE2), an enzyme that physiologically counters ...tivation but also functions as a receptor ...iruses.[1,2] The interaction between ...CE2 has been proposed as

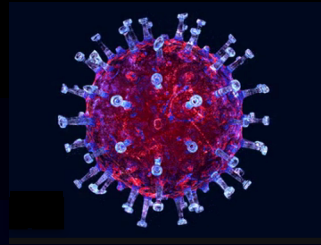
COVID-19 AND OLDER ADULTS WITH COEXISTING CONDITIONS

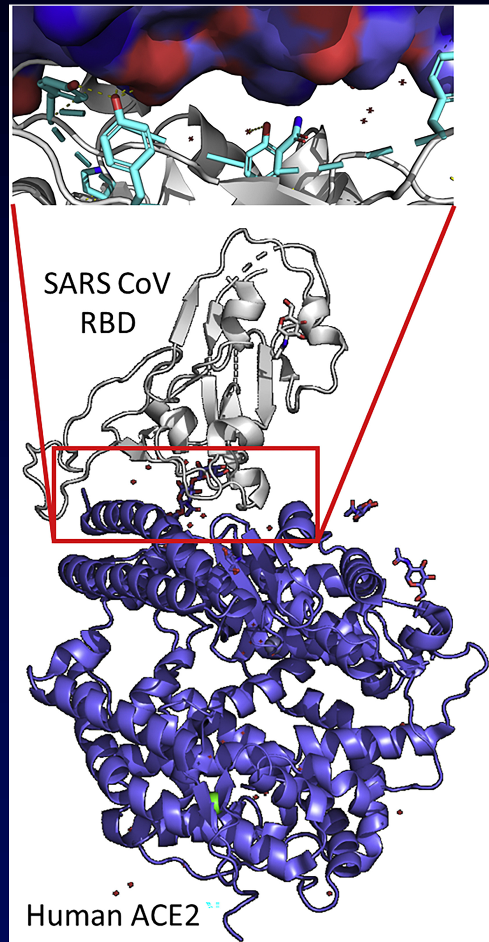
Initial reports[5-8] have called attention to the potential overrepresentation of hypertension among patients with Covid-19. In the largest of several case series from China that have been released during the Covid-19 pandemic (Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org), hypertension was the most frequent coexisting condition in 1099 patients, with an estimated prevalence of 15%[9]; however, this estimate appears to be lower than



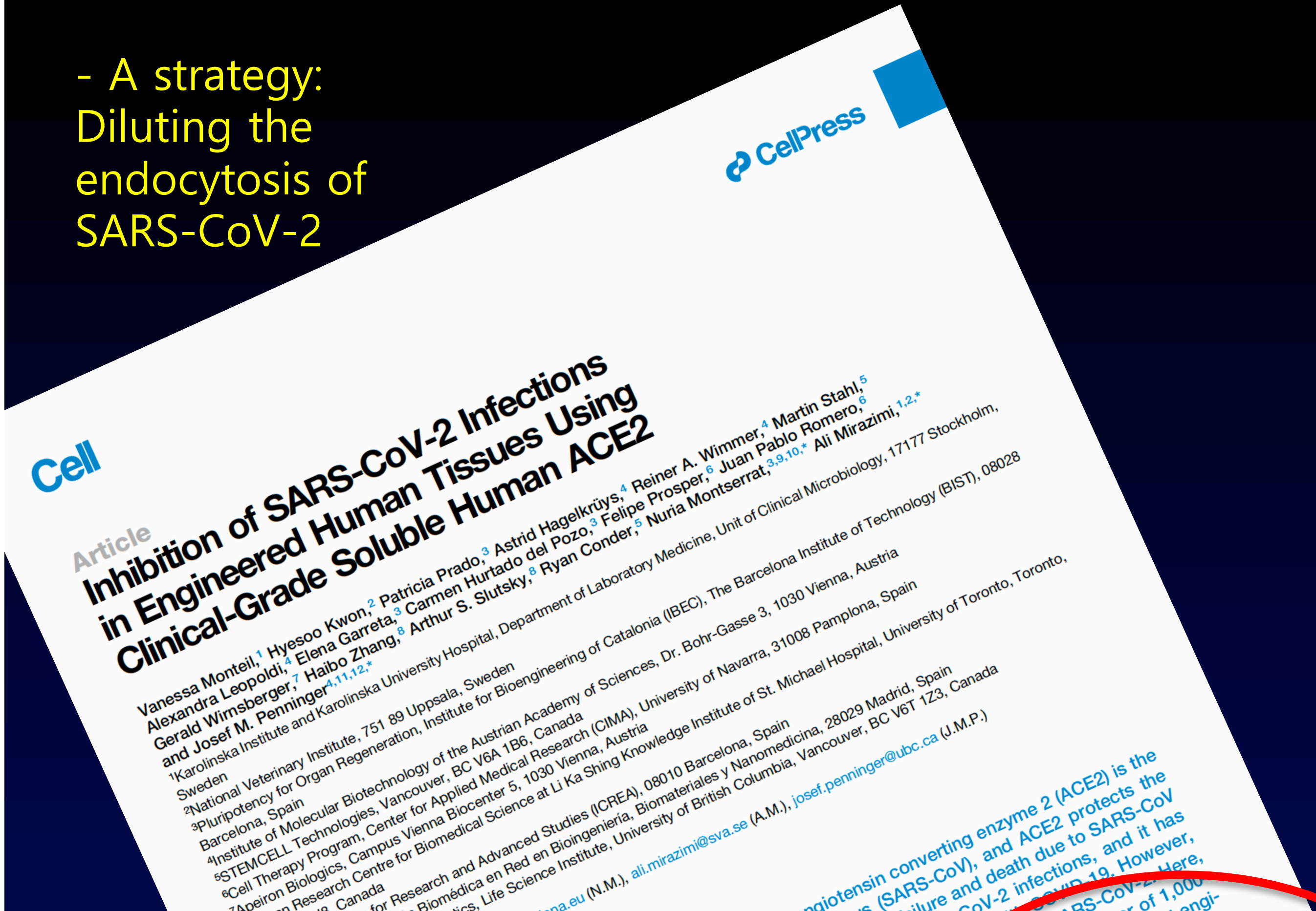
- More dangerous to patients with underlying heart conditions.

2020.3.30.




SARS CoV
RBD
Human ACE2

- A strategy: Diluting the endocytosis of SARS-CoV-2



Cell

CellPress

Article

Inhibition of SARS-CoV-2 Infections in Engineered Human Tissues Using Clinical-Grade Soluble Human ACE2

Vanessa Monteil,[1] Hyesoo Kwon,[2] Patricia Prado,[3] Astrid Hagelkrüys,[4] Reiner A. Wimmer,[4] Martin Stahl,[5] Alexandra Leopoldi,[4] Elena Garreta,[3] Carmen Hurtado del Pozo,[3] Felipe Prosper,[6] Juan Pablo Romero,[6] Gerald Wirnsberger,[7] Haibo Zhang,[8] Arthur S. Slutsky,[8] Ryan Conder,[5] Nuria Montserrat,[3,9,10,*] Ali Mirazimi,[1,2,*] and Josef M. Penninger[4,11,12,*]

[1]Karolinska Institute and Karolinska University Hospital, Department of Laboratory Medicine, Unit of Clinical Microbiology, 17177 Stockholm, Sweden

[2]National Veterinary Institute, 751 89 Uppsala, Sweden

[3]Pluripotency for Organ Regeneration, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Technology (BIST), 08028 Barcelona, Spain

[4]Institute of Molecular Biotechnology of the Austrian Academy of Sciences, Dr. Bohr-Gasse 3, 1030 Vienna, Austria

[5]STEMCELL Technologies, Vancouver, BC V6A 1B6, Canada

[6]Cell Therapy Program, Center for Applied Medical Research (CIMA), University of Navarra, 31008 Pamplona, Spain

[7]Apeiron Biologics, Campus Vienna Biocenter 5, 1030 Vienna, Austria

[8]Keenan Research Centre for Biomedical Science at Li Ka Shing Knowledge Institute of St. Michael Hospital, University of Toronto, Toronto, ON M5B 1W8, Canada

[9]Catalan Institution for Research and Advanced Studies (ICREA), 08010 Barcelona, Spain

[10]Centro de Investigación Biomédica en Red en Bioingeniería, Biomateriales y Nanomedicina, 28029 Madrid, Spain

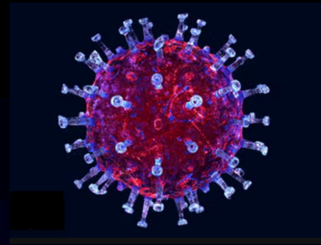
[11]Department of Medical Genetics, Life Science Institute, University of British Columbia, Vancouver, BC V6T 1Z3, Canada

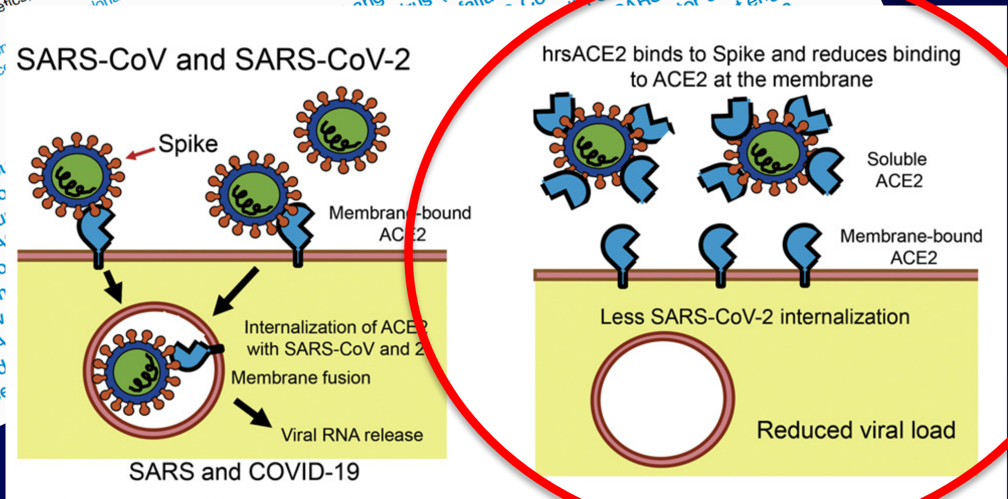
[12]Lead Contact

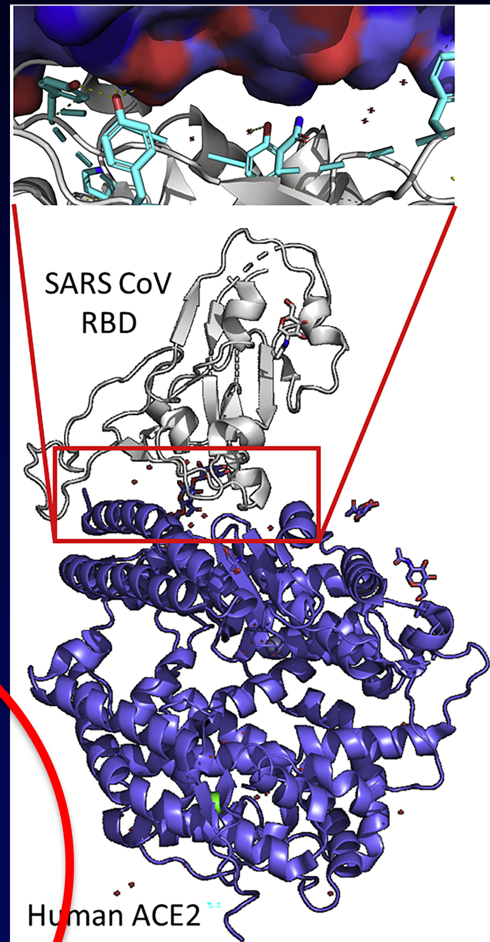
*Correspondence: nmontser... (N.M.), ali.mirazimi@sva.se (A.M.), josef.penninger@ubc.ca (J.M.P.)

https://doi.org/10.1016/j.c...

SUMMARY







2020.5.14.

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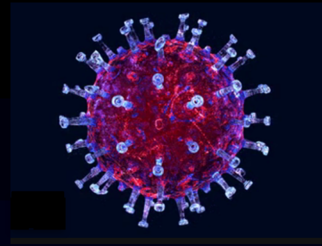
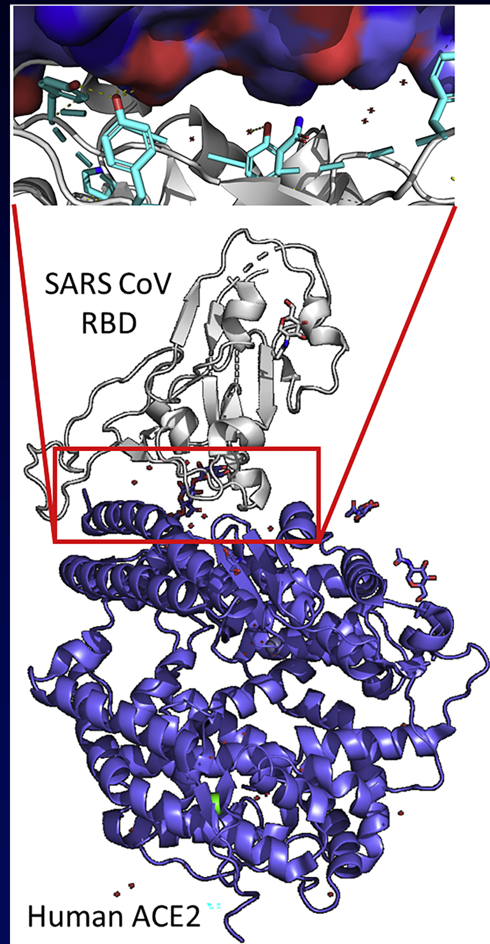
- The ACE2 enzyme's gene is located on the X-chromosome.





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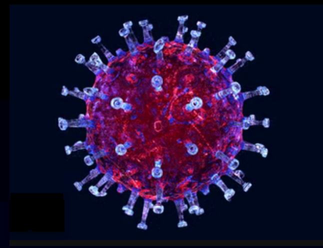

The New York Times

Opinion

Why Are So Many More Men Dying from Coronavirus?

The disproportionate toll this virus is taking on males isn't an anomaly. When it comes to survival, men are the weaker sex.

By Sharon Moalem

Dr. Moalem is a scientist, physician, and the author of the forthcoming "The Better Half: On the Genetic Superiority of Women."

April 2, 2020

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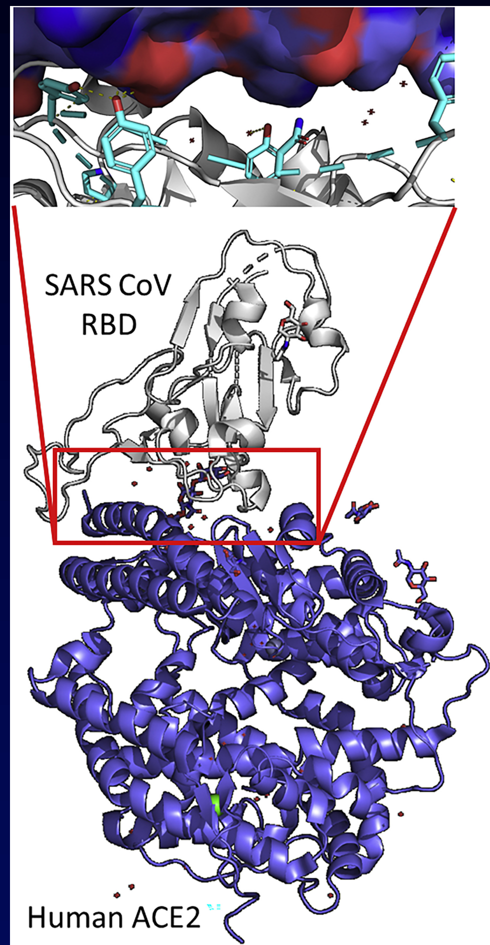

2020.4.2.

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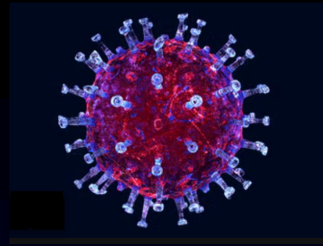
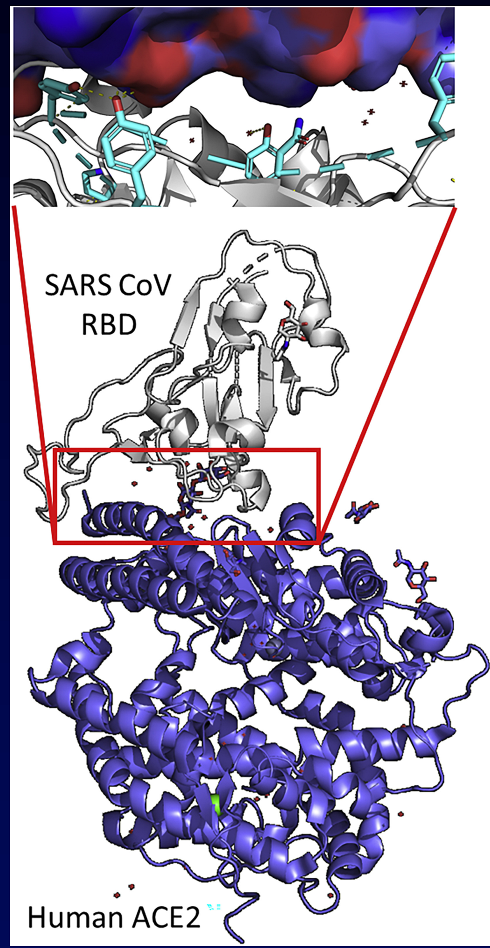
- Another strategy: Hinder the contact surface between the S-protein and the patient's ACE2.





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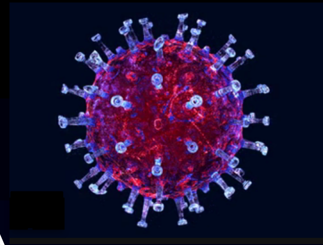
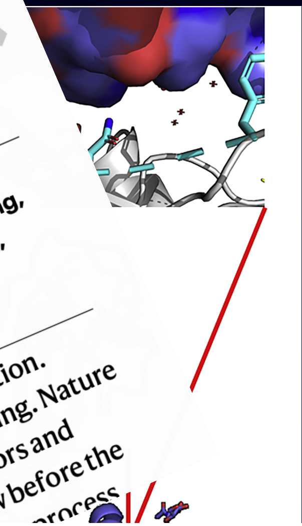




https://doi.org/10.1038/s41586-020-2381-y

nature

Accelerated Article Preview

A human neutralizing antibody targets the receptor binding site of SARS-CoV-2

Rui Shi, Chao Shan, Xiaomin Duan, Zhihai Chen, Peipei Liu, Jinwen Song, Tao Song, Xiaoshan Bi, Chao Han, Lianao Wu, Ge Gao, Xue Hu, Yanan Zhang, Zhou Tong, Weijin Huang, William Jun Liu ...en Wu, Bo Zhang, Lan Wang, Jianxun Qi, Hui Feng, Fu-sheng Wang, Qihui Wang, G... Zhiming Yuan & Jinghua Yan

Received: 2 April 2020

Accepted: 19 May 2020

Accelerated Article Preview Published online 26 May 2020

Cite this article as: Shi, R. et al. A human neutralizing antibody targets the receptor binding site of SARS-CoV-2. Nature https://doi.org/10.1038/s41586-020-2381-y (2020).

This is a P... ...t has been accepted for publication. Althoug... ...o preliminary formatting. Nature is prov... ...ice to our authors and reade... ...review before the pap... ...process

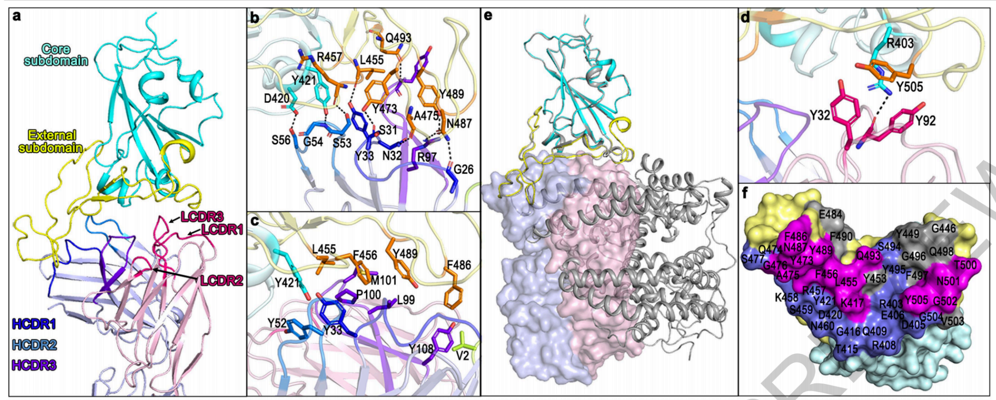


Fig. 4 | The crystal structure of CB6 and SARS-CoV-2-RBD complex and the competitive binding of CB6 and hACE2 with SARS-CoV-2-RBD. a, The complex structure of CB6 bound to SARS-CoV-2-RBD. The SARS-CoV-2-RBD is colored in cyan (core subdomain) and yellow (external subdomain). The variable fragment of CB6 is shown with HCDR1, HCDR2, and HCDR3 loops from the V_H domain (purple) colored in blue, marine and purple, while the LCDR1, LCDR2 and LCDR3 loop from the V_L domain (pink) are colored in hot-pink, respectively. **b-c**, Both hydrophilic interactions (b) and hydrophobic interactions (c) between CB6 heavy chain and SARS-CoV-2-RBD are displayed. **d**, The binding details between CB6 light chain and SARS-CoV-2-RBD are also presented. The hydrogen bonds are shown as dashed black lines. **e**, Superimposition of CB6/SARS-CoV-2-RBD complex and hACE2/SARS-CoV-2-RBD (PDB code: 6LZG) revealed the steric competition between CB6 and hACE2 for RBD binding. CB6/SARS-CoV-2-RBD structure was superimposed on hACE2/SARS-CoV-2-RBD to demonstrate steric hindrance. hACE2 is shown as cartoon (gray). **f**, Competitive binding surfaces of CB6 with hACE2 on SARS-CoV-2-RBD. The SARS-CoV-2-RBD binding surface to ACE2 and CB6 is shown. The residues bound by both CB6 and hACE2 are colored in magenta. The residues in contact with hACE2 alone are colored in gray while the residues in contact with CB6 alone are colored in blue. The amino acids on SARS-CoV-2-RBD interface contacting CB6 or ACE2 are labeled.

2020.5.26.

- **Using monoclonal antibodies**

Current Status of Vaccine Development

CellPress

Cell Host & Microbe

Forum

The Challenges of Vaccine Development against a New Virus during a Pandemic

Michael S. Diamond[1,2,3,4,*] and Theodore C. Pierson[5,*]

[1]Department of Medicine, Washington University School of Medicine, St. Louis, MO 63110, USA
[2]Department of Molecular Microbiology, Washington University School of Medicine, St. Louis, MO 63110, USA
[3]Department of Pathology & Immunology, Washington University School of Medicine, St. Louis, MO 63110, USA
[4]Center for Human Immunology and Immunotherapy Programs, Washington University School of Medicine, St. Louis, MO 63110, USA
[5]Laboratory of Viral Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892, USA
*Correspondence: diamond@wusm.wustl.edu (M.S.D.), piersontc@mail.nih.gov (T.C.P.)

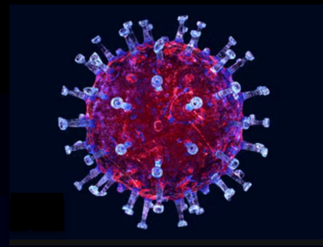
https://doi.org/10.1016/j.chom.2020.04.021

The rapid emergence of a highly pathogenic, readily transmissible coronavirus has resulted in a global pandemic, affecting millions and destabilizing economies. This catastrophe triggered a clarion call for the immediate deployment of a protective vaccine. We describe the unique challenges of developing a vaccine against SARS-CoV-2 in a pandemic setting.

Historically, human coronaviruses have received limited attention from the research and medical communities. Although infections by human coronaviruses (e.g., HCoV-229E and HCoV-OC43) frequently cause common cold symptoms in healthy individuals, severe clinical illness is relatively rare even in immunocompromised individuals, infants, and the elderly. Considerably zations, limited transmission and human disease. Ten years later, a second coronavirus, the Middle East respiratory syndrome coronavirus (MERS-CoV), was isolated from an individual suffering from severe respiratory disease and renal failure. As observed with SARS-CoV, MERS-CoV spread via travel and contact with infected individuals, resulting in transmission and mortality within and beyond mental basic and translational studies that customarily guide vaccine development and evaluation under non-pandemic circumstances. Accordingly, we discuss the challenges of rapid vaccine development during a pandemic response.

The SARS-CoV-2 Pandemic

SARS-CoV-2 is a positive-sense single-stranded RNA virus first isolated in Wu-



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Current Status of Vaccine Development

Cell Host & Microbe
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The Challenges of Vaccine Development against a New Virus during a Pandemic

Theodore C. Pierson[5,*]
... School of Medicine, St. Louis, MO 63110, USA
... University School of Medicine, St. Louis, MO 63110, USA
... University School of Medicine, St. Louis, MO 63110, USA
Washington University School of Medicine, St. Louis, MO 63110, USA
... Diseases, National Institutes of Health, Bethesda, MD 20892, USA
(T.C.P.)

...virus has resulted in a global ...d a clarion call for the im- ...eloping a vaccine

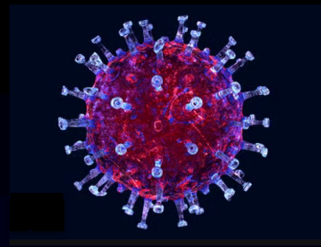
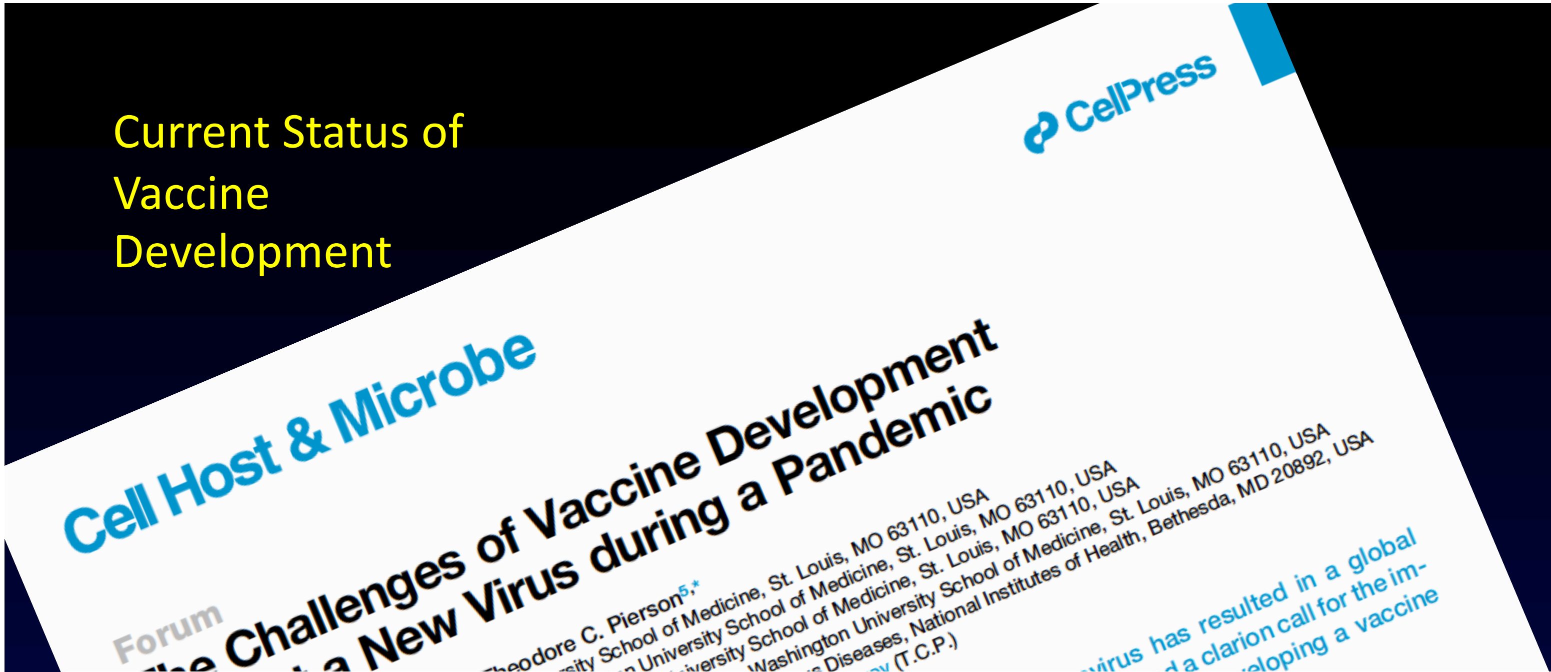


Table 1. Vaccine Candidates in Development against SARS-CoV-2

Vaccine Type	Platform	Protein Target	Stage	Clinical Trial Designation	Company or Institution	Vaccine Name	Status
mRNA	Lipid-encapsulated mRNA	S	Phase 1	NCT04283461 (45 subjects)	Moderna	mRNA-1273	Recruiting
DNA	DNA plasmid	S	Phase 1	NCT04336410 (40 subjects)	Inovio Pharmaceuticals	INO-4800	Recruiting
Human adenovirus (Ad5)	Viral-vectored	S	Phase 1	NCT04313127 (108 subjects)	CanSino Biologics	Ad5-nCoV	Active
Chimpanzee adenovirus	Viral-vectored	S	Phase 1/2	NCT04324606 (510 subjects)	University of Oxford	ChAdOx1 nCoV-19	Planned (4/20)
Spike protein	Bacterially produced soluble protein (oral)	S	Phase 1	NCT04334980 (84 subjects)	Symvivo Corporation	bacTRL-Spike	Planned (4/30)
BCG vaccine	Immune stimulatory	None	Phase 3	NCT04327206 (4170 subjects) NCT04328441 (1000 subjects)	Murdoch Childrens Research Institute University Medical Center, Netherlands	BCG vaccine	Recruiting

Information adapted from https://ClinicalTrials.gov.

Current Status of Vaccine Development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New Virus during a Pandemic
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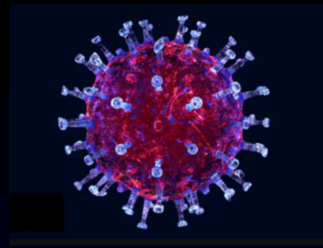

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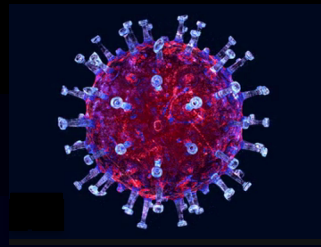
Information adapted from https://ClinicalTrials.gov.

- The BCG Vaccine for Tb Prevention



Cause: (Not a virus but a bacteria)
Mycobacterium tuberculosis (MTB)

- The BCG Vaccine for Tb Prevention

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Cell

Leading Edge

Perspective

Trained Immunity: a Tool for Reducing Susceptibility to and the Severity of SARS-CoV-2 Infection

Mihai G. Netea,[1,2,*] Evangelos J. Giamarellos-Bourboulis,[3] Jorge Domínguez-Andrés,[1] Nigel Curtis,[4] Reinout van Crevel,[1] Frank L. van de Veerdonk,[1] and Marc Bonten[5]

COMMENT

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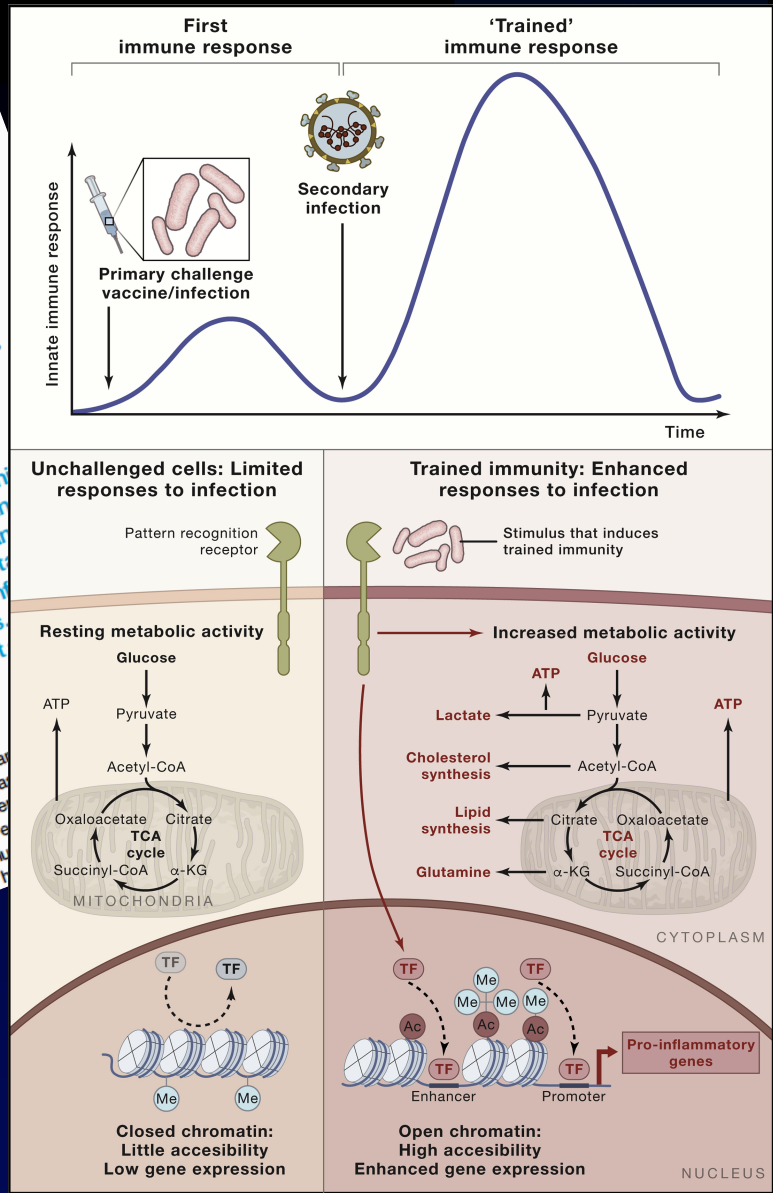
BCG-induced trained immunity: can it offer protection against COVID-19?

Luke A. J. O'Neill[1] ✉ and Mihai G. Netea[1,2,3]

Bacillus Calmette–Guérin (BCG) vaccination has been reported to decrease susceptibility to respiratory tract infections, an effect proposed to be mediated by the general long-term boosting of innate immune mechanisms, also termed trained immunity. Here, we discuss the non-specific beneficial effects of BCG against viral infections and whether this vaccine may afford protection to COVID-19.

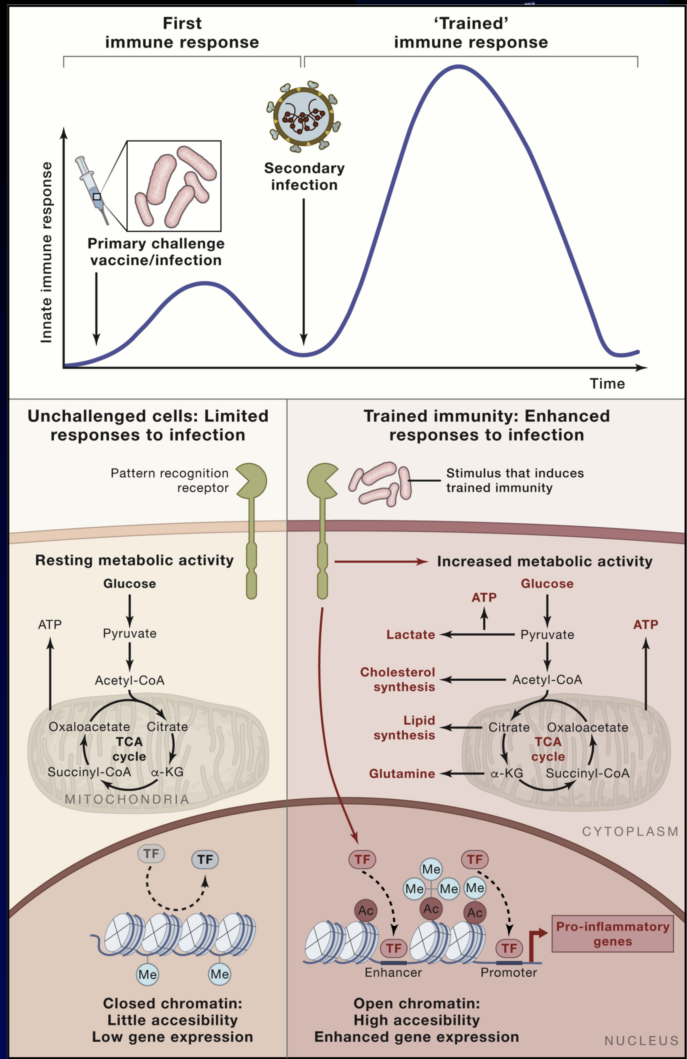
COVID-19 is a new form of respiratory tract infection that can be complicated by severe pneumonia and acute respiratory distress syndrome (ARDS). It is caused by a newly identified viral pathogen named on 11 February 2020 as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Most individuals infected with SARS-CoV-2 remain asymptomatic or develop a moderate disease that is mainly characterized by ... tract symptoms. However, a significant ... progress to severe pneumonia with ... and even death, particu-

introduction in Europe in the 1920s, epidemiological studies reported that BCG vaccination strongly reduced infant mortality, and this could not be explained by a reduction in tuberculosis alone (reviewed previously[2]). Later on, similar studies in other locations, including randomized controlled trials, showed an up to 50% reduction of mortality induced by BCG in young infants[3]. This reduction in childhood mortality by BCG appeared to be due to the protection against unrelated infectious agents and especially respiratory tract infections and neonatal sepsis. Although the authors did



Cause: (Not a virus but a bacteria) *Mycobacterium tuberculosis* (MTB)

- The BCG Vaccine for Tb Prevention



- The BCG Vaccine for Tb Prevention

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Supplementary Mat

Significantly Improved COVID-19 Outcomes in Countries with Higher BCG Vaccination Coverage: A Multivariable Analysis

Danielle Klinger, Ido Blass, Nadav Rappoport, Michal Linial

doi: https://doi.org/10.1101/2020.04.23.20077123

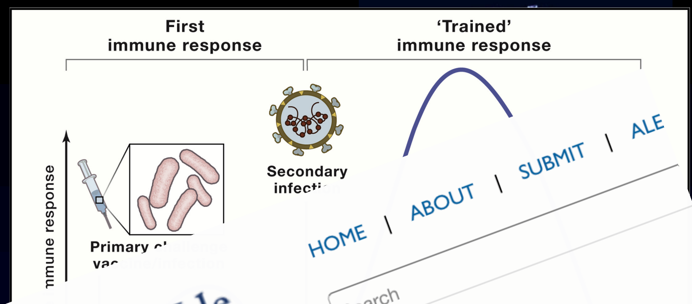
This article is a preprint and has not been peer-review reports new medical research that has yet to be evalu guide clinical practice.

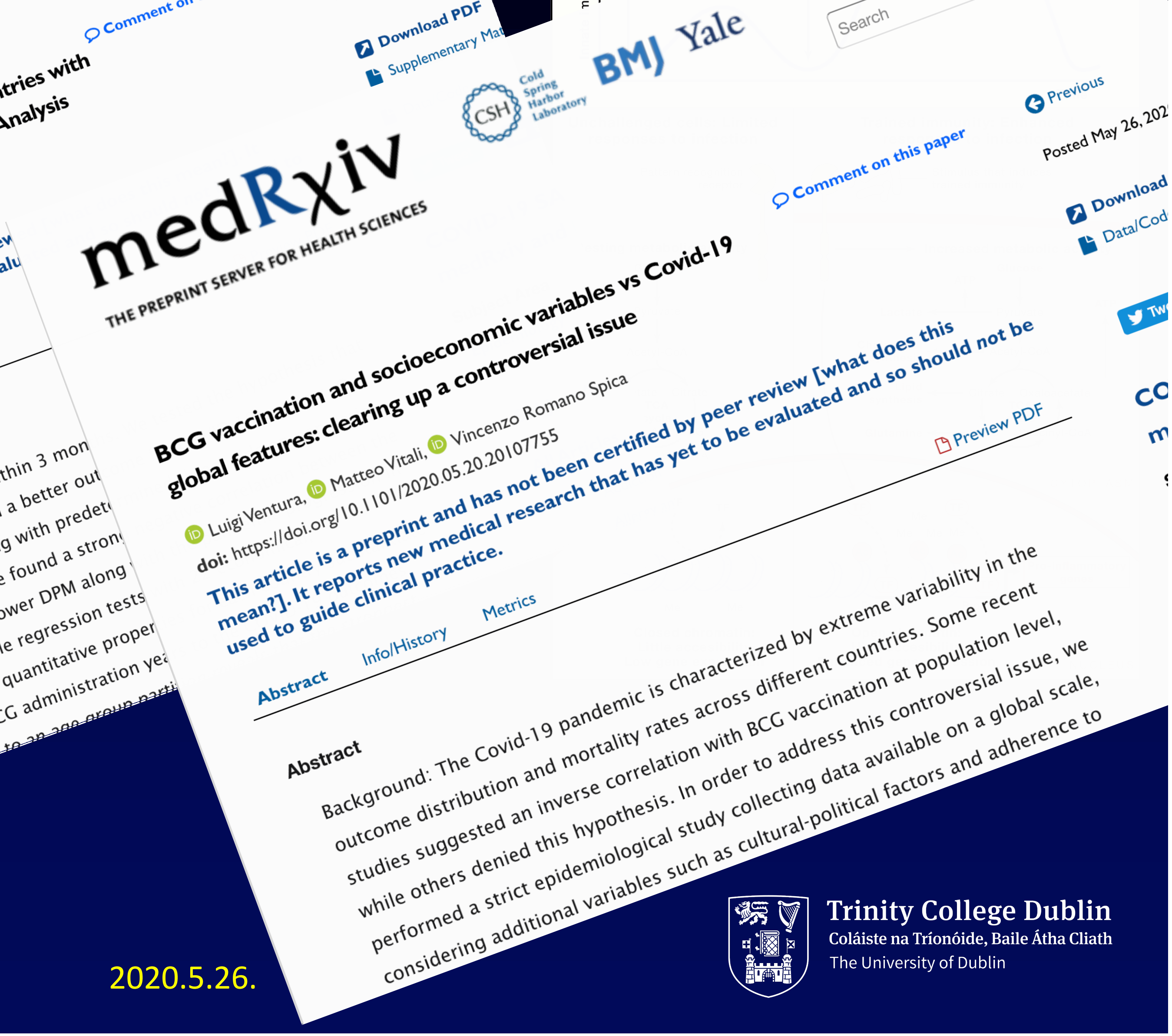
Abstract Info/History Metrics

Abstract

COVID-19 has spread to 210 countries within 3 mon the vaccination with BCG correlates with a better out analysis covers 55 countries, complying with predet size and deaths per million (DPM). We found a stron years of BCG administration and a lower DPM along regression tests time. The results from multivariable proper demographic, and health-related quantitative year the dominant contribution of BCG administration

2020.5.12.





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BCG vaccination and socioeconomic variables vs Covid-19 global features: clearing up a controversial issue

Luigi Ventura, Matteo Vitali, Vincenzo Romano Spica

doi: https://doi.org/10.1101/2020.05.20.20107755

This article is a preprint and has not been certified by peer review [what does this mean?]. It reports new medical research that has yet to be evaluated and so should not be used to guide clinical practice.

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Abstract Info/History Metrics

Abstract

Background: The Covid-19 pandemic is characterized by extreme variability in the outcome distribution and mortality rates across different countries. Some recent studies suggested an inverse correlation with BCG vaccination at population level, while others denied this hypothesis. In order to address this controversial issue, we performed a strict epidemiological study collecting data available on a global scale, considering additional variables such as cultural-political factors and adherence to

2020.5.26.

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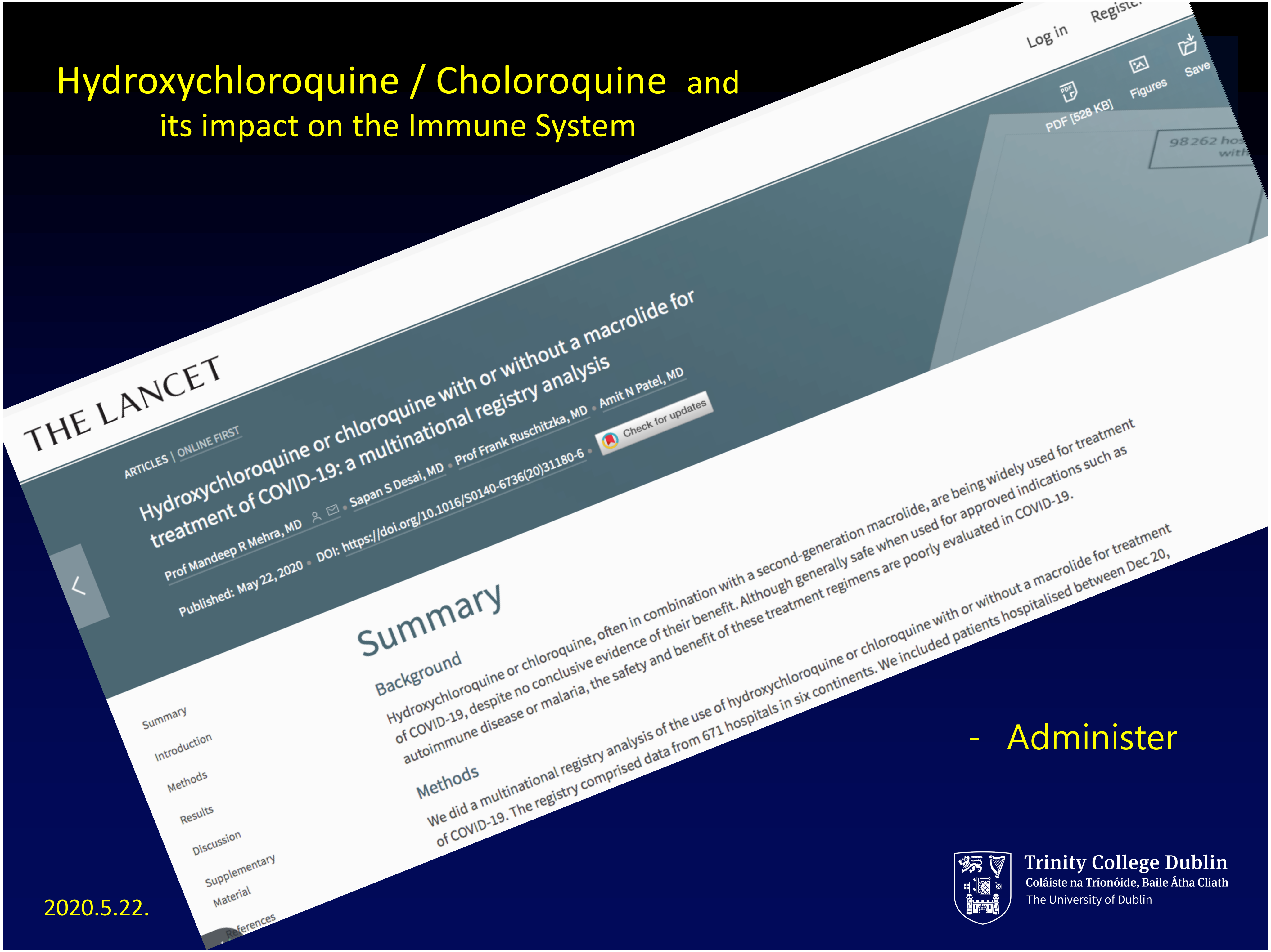
Hydroxychloroquine / Choloroquine and its impact on the Immune System



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Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis

Prof Mandeep R Mehra, MD • Sapan S Desai, MD • Prof Frank Ruschitzka, MD • Amit N Patel, MD

Published: May 22, 2020 • DOI: https://doi.org/10.1016/S0140-6736(20)31180-6 • Check for updates

Summary
Introduction
Methods
Results
Discussion
Supplementary Material
References

Summary

Background

Hydroxychloroquine or chloroquine, often in combination with a second-generation macrolide, are being widely used for treatment of COVID-19, despite no conclusive evidence of their benefit. Although generally safe when used for approved indications such as autoimmune disease or malaria, the safety and benefit of these treatment regimens are poorly evaluated in COVID-19.

Methods

We did a multinational registry analysis of the use of hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19. The registry comprised data from 671 hospitals in six continents. We included patients hospitalised between Dec 20,

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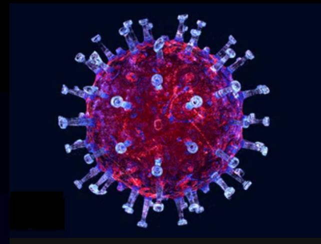
Vitamin D and Inflammation



Open access
BMJ Nutrition, Prevention & Health
Brief report

Vitamin D and SARS-CoV-2 virus/COVID-19 disease

Susan A Lanham-New,[1] Ann R Webb,[2] Kevin D Cashman,[3] Judy L Buttriss,[4] Joanne L Fallowfield,[5] Tash Masud,[6] Martin Hewison,[7] John C Mathers,[8] Mairead Kiely,[3] Ailsa A Welch,[9] Kate A Ward,[10] Pamela Magee,[11] Andrea L Darling,[1] Tom R Hill,[8] Carolyn Greig,[12] Colin P Smith,[13] Richard Murphy,[14] Sarah Leyland,[15] Roger Bouillon,[16] Sumantra Ray,[11,17,18] Martin Kohlmeier [18,19]

BMJNPH: first published as 10.1136/bmjnph-2020-0

BACKGROUND AND AIM

The spread of novel SARS-CoV-2 virus, and the disease COVID-19 that is caused by SARS-(and sl(of utm health and gc It is to the timely

vitamin D status may be exacerbated during this COVID-19 crisis (eg, due to indoor living and hence reduced sun exposure),

To cite: Lanham-New SA, Webb AR, Cashman KD, et al. Vitamin D and SARS-CoV-2 virus/COVID-19 disease. BMJ Nutrition, Prevention & Health 2020;0. doi:10.1136/bmjnph-2020-000089

For numbered affiliations see end of article.

Correspondence to
Professor Susan A Lanham-New, Nutritional Sciences, University

2020.5.13.

Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 113; No. 5; P81

Vitamin D and Inflammation: Potential Implications for Severity of Covid-19

E. Laird[1], J. Rhodes[2], R.A. Kenny[1]

1. The Irish Longitudinal Study on Ageing, School of Medicine, Trinity College Dublin, Ireland.
2. Institute of Translational Medicine, University of Liverpool.

Abstract

Background

Recent research has indicated that vitamin D may have immune supporting properties through modulation of both ...tive and innate immune system through cytokines and regulation of cell signalling pathways. We hypothesize ...status may influence the severity of responses to Covid-19 and that the prevalence of vitamin D ...l be closely aligned to Covid-19 mortality.

...(no language restriction) of vitamin D status (for older adul

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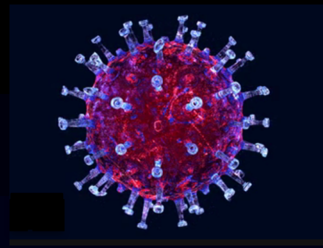
2020.5.



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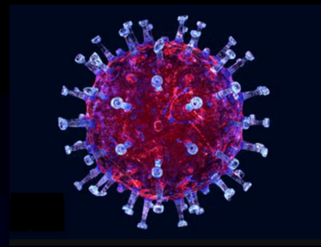
The Proteomics & Metabolomics of Covid-19 Patients

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Proteomic and Metabolomic Characterization of COVID-19 Patient Sera

Bo Shen, Xiao Yi, Yaoting Sun, Xiaojie Bi, Juping Du, Chao Zhang, Sheng Quan, Fangfei Zhang, Rui Sun, Liujia Qian, Weigang Ge, Wei Liu, Shuang Liang, Hao Chen, Ying Zhang, Jun Li, Jiaqin Xu, Zebao He, Baofu Chen, Jing Wang, Haixi Yan, Yufen Zheng, Donglian Wang, Jiansheng Zhu, Ziqing Kong, Zhouyang Kang, Xiao Liang, Xuan Ding, Guan Ruan, Nan Xiang, Xue Cai, Huanhuan Gao, Lu Li, Sainan Li, Qi Xiao, Tian Lu, Yi Judy Zhu, Huafen Liu, Haixiao Chen, Tiannan Guo

doi: https://doi.org/10.1101/2020.04.07.20054585

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Abstract Info/History Metrics

Abstract

Severe COVID-19 patients account for most of the mortality of this disease. Early detection and effective treatment of severe patients remain major challenges. Here, we ...d proteomic and metabolomic profiling of sera from 46 COVID-19 and 53 ... We then trained a machine learning model using proteomic and ... from a training cohort of 18 non-severe and 13 severe ... severe patients with an accuracy of 93.5%, and ...nts, seven of which were correctly

- 21 Covid-19 Severe Cases
- 25 Covid-19 Minor Cases
- 25 non-Covid-19 patients
- 28 Healthy Controls

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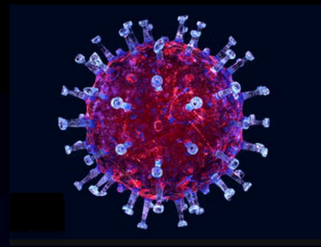
The Proteomics & Metabolomics of Covid-19 Patients



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- Biomarker Identification
- Elucidation of the Pathways

- **Early Diagnosis of severe Covid-19 cases**

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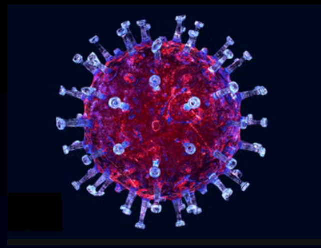
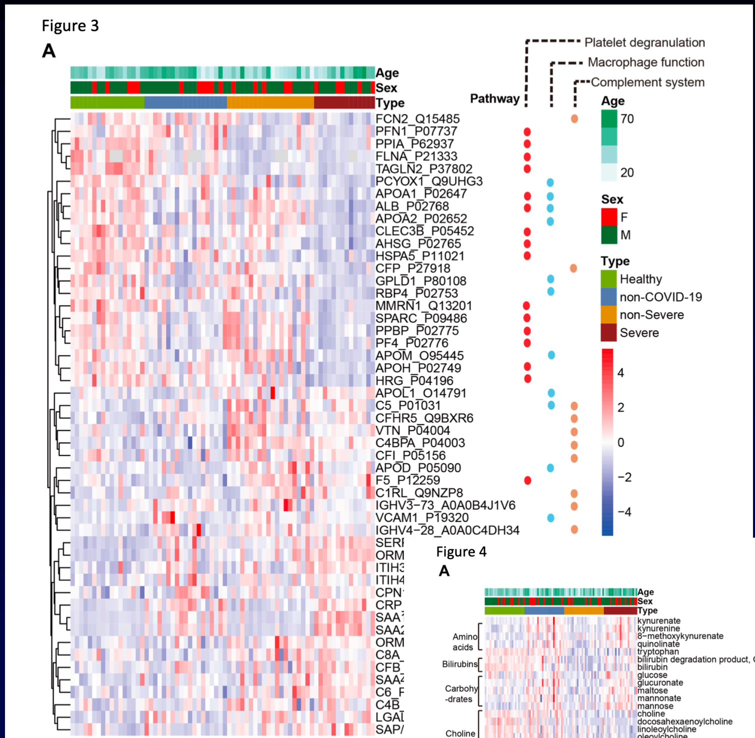
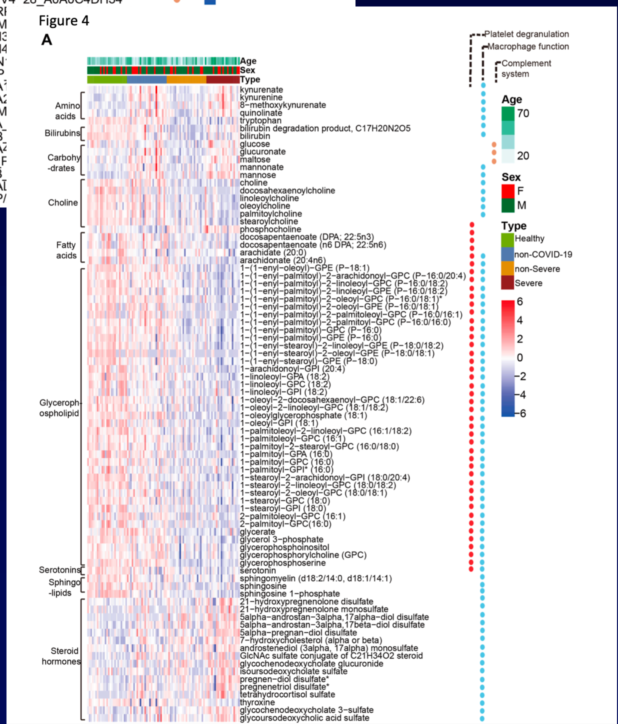
The Proteomics & Metabolomics of Covid-19 Patients







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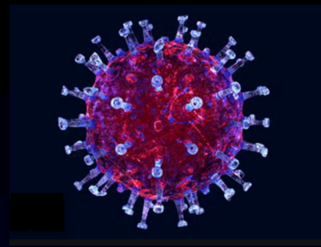

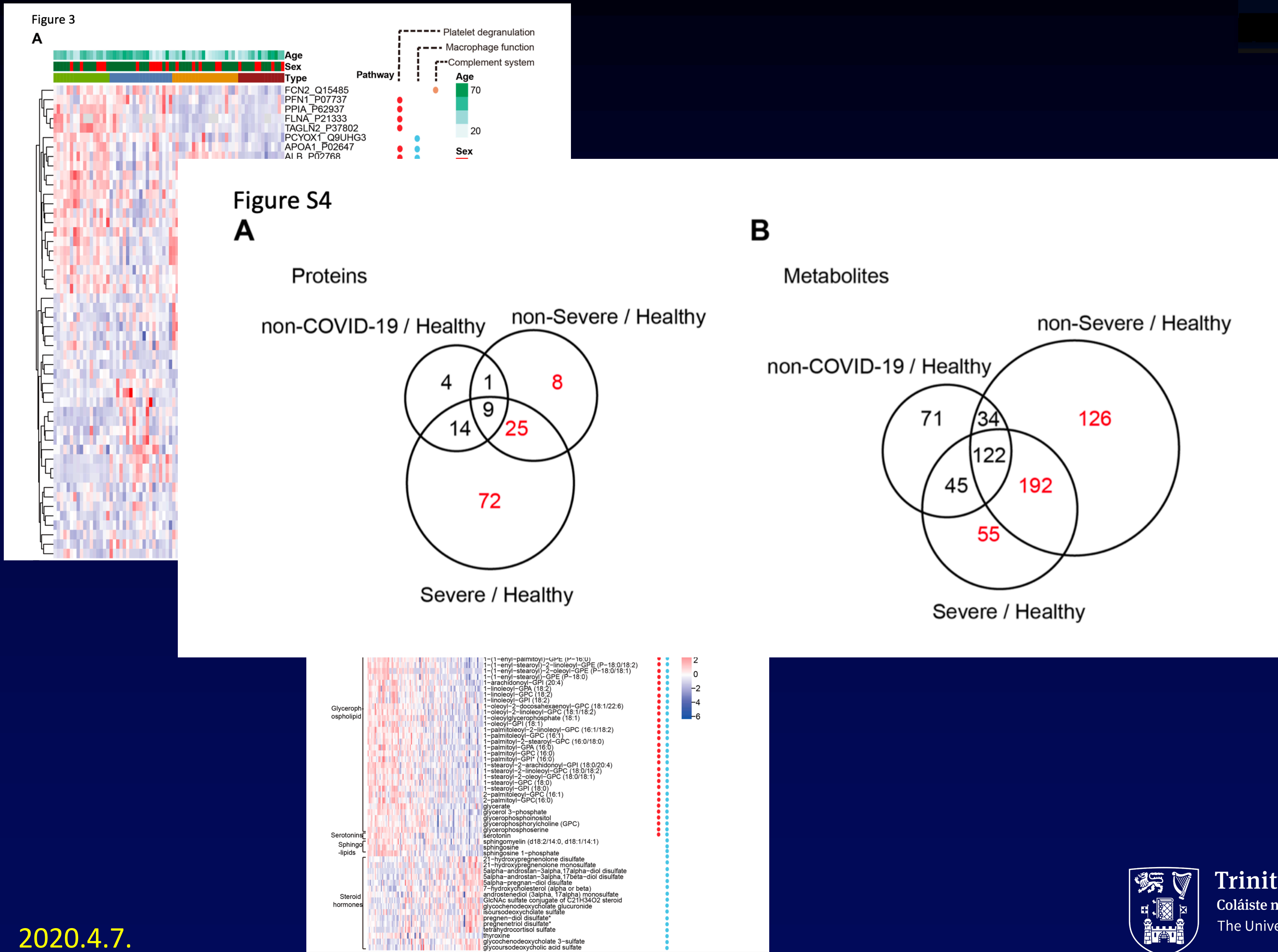

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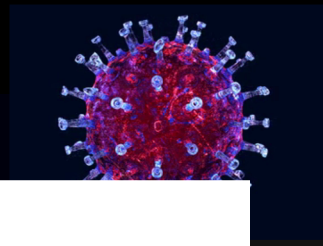


Figure 3

A

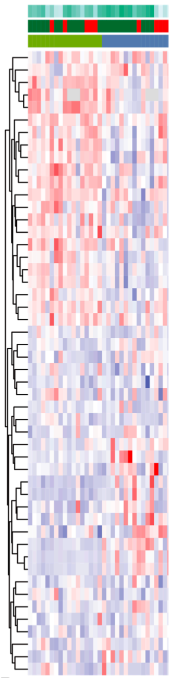
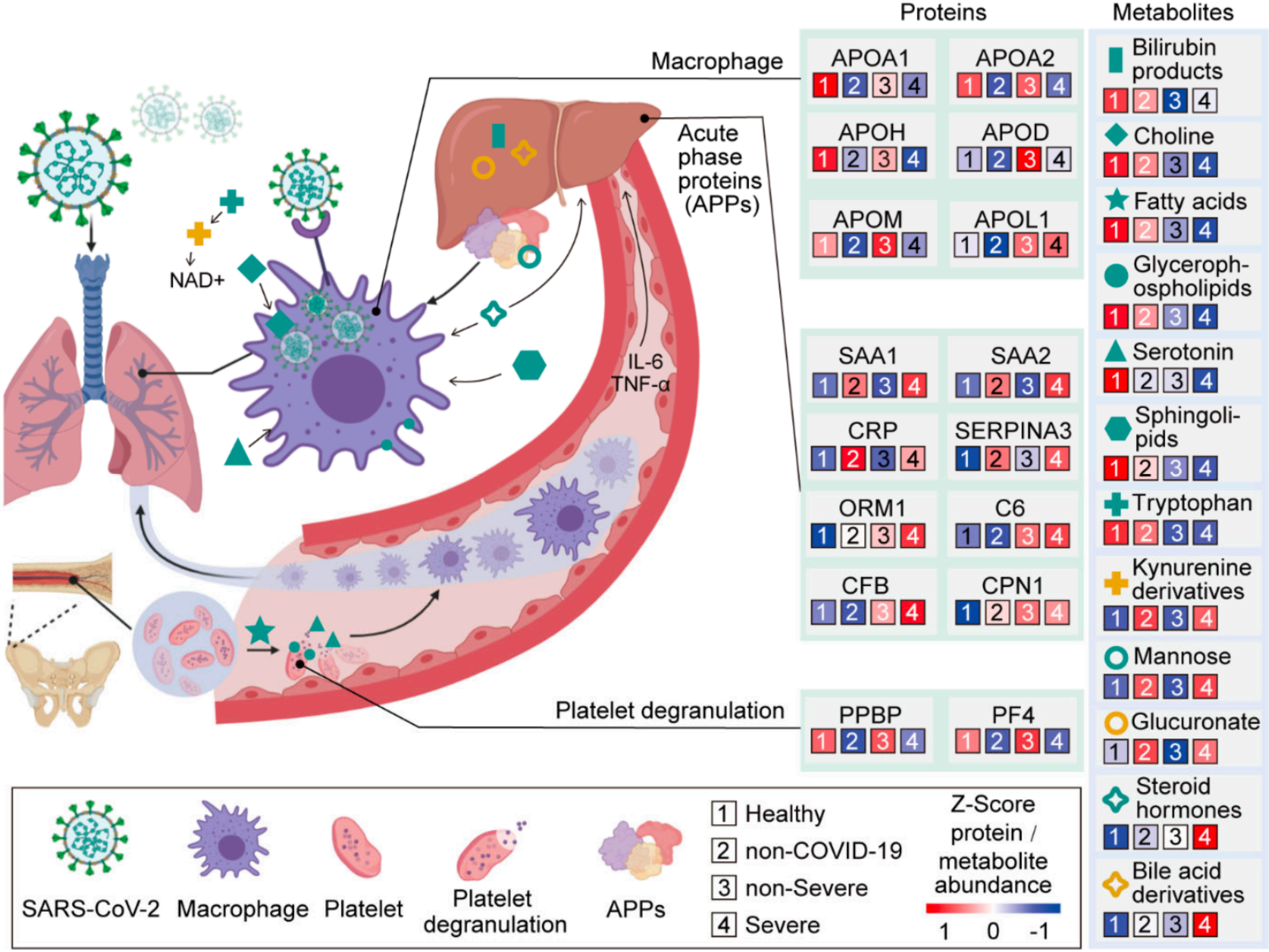


Figure 5



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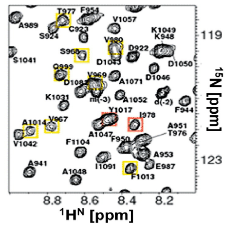
Mok group expertise: Technology and/or Instrumentation

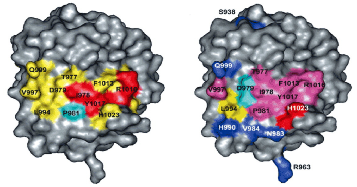
The NMR Facility at TCD

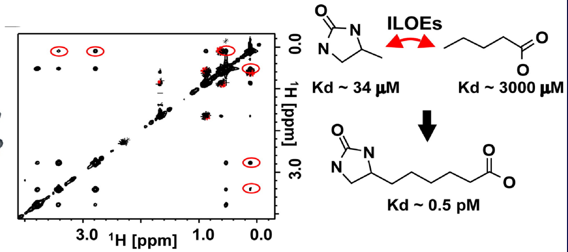
What is NMR?

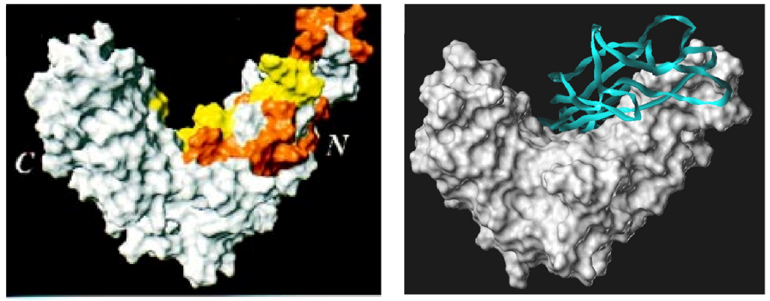
- High-resolution, atomic-level methodology for the determination of chemical and biochemical structures of molecules.
- Proteins, nucleic acids, sugars, lipids, drugs

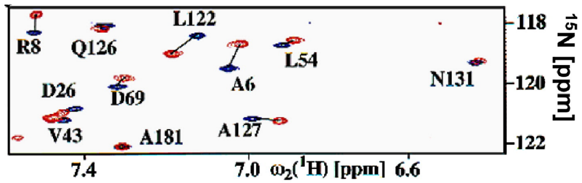
The principle of NMR is identical to:









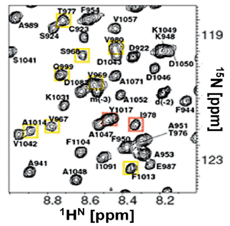


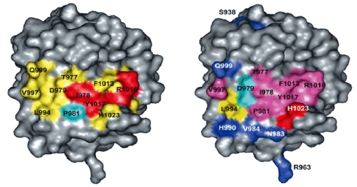
Mok group expertise: Technology and/or Instrumentation

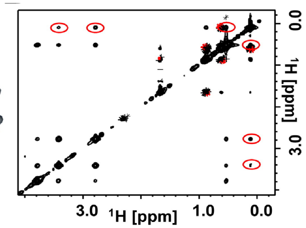
The NMR Facility at TCD

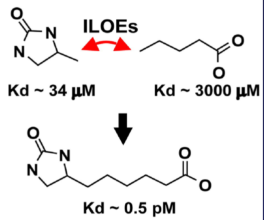
High-resolution NMR capacity realises:

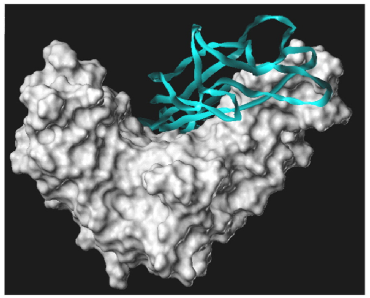
- **Novel drug development** ("SAR-by-NMR")
- **The validation of molecular identity (biosimilars / protein aggregation)**
- **Metabolomics of cells, serum, urine – Large-scale biobank profiling**
- **Atomic-level 3D biomolecular structure**
- **Structure elucidation of nano-scale / inorganic materials**

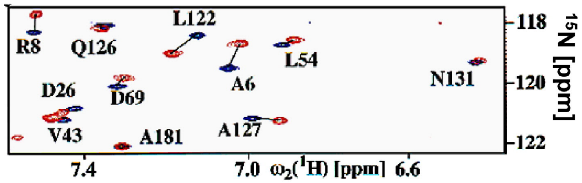












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- With the cold probe, capabilities of **detecting metabolites and *in vivo* sample concentrations of sub-μmolar range**.

Mok group expertise: Technology and/or Instrumentation

The NMR Facility at TCD

High-resolution NMR capacity realises:

- **Novel drug development** ("SAR-by-NMR")
- **The validation of molecular identity (biosimilars / protein aggregation)**
- **Metabolomics of cells, serum, urine – Large-scale biobank profiling**
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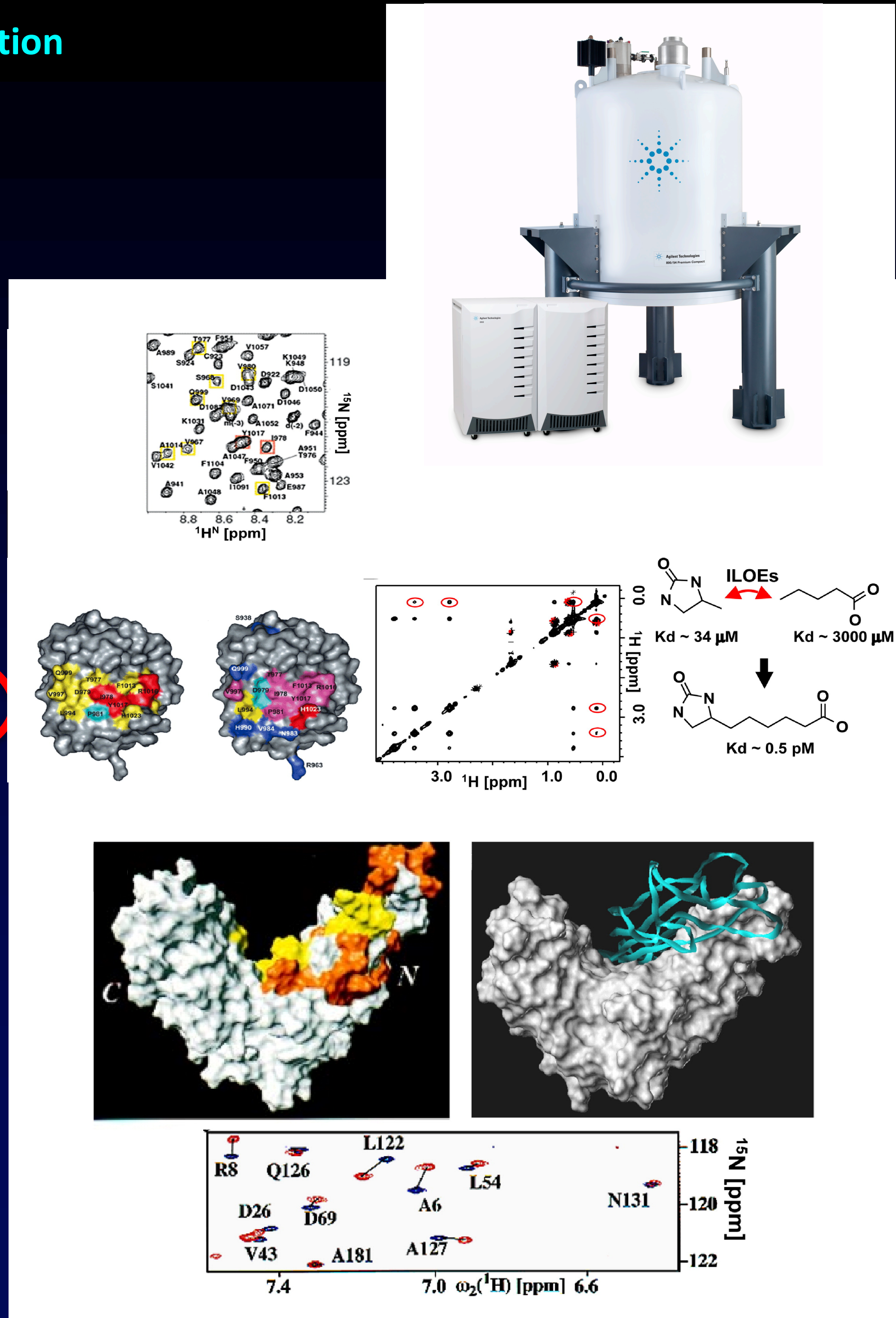

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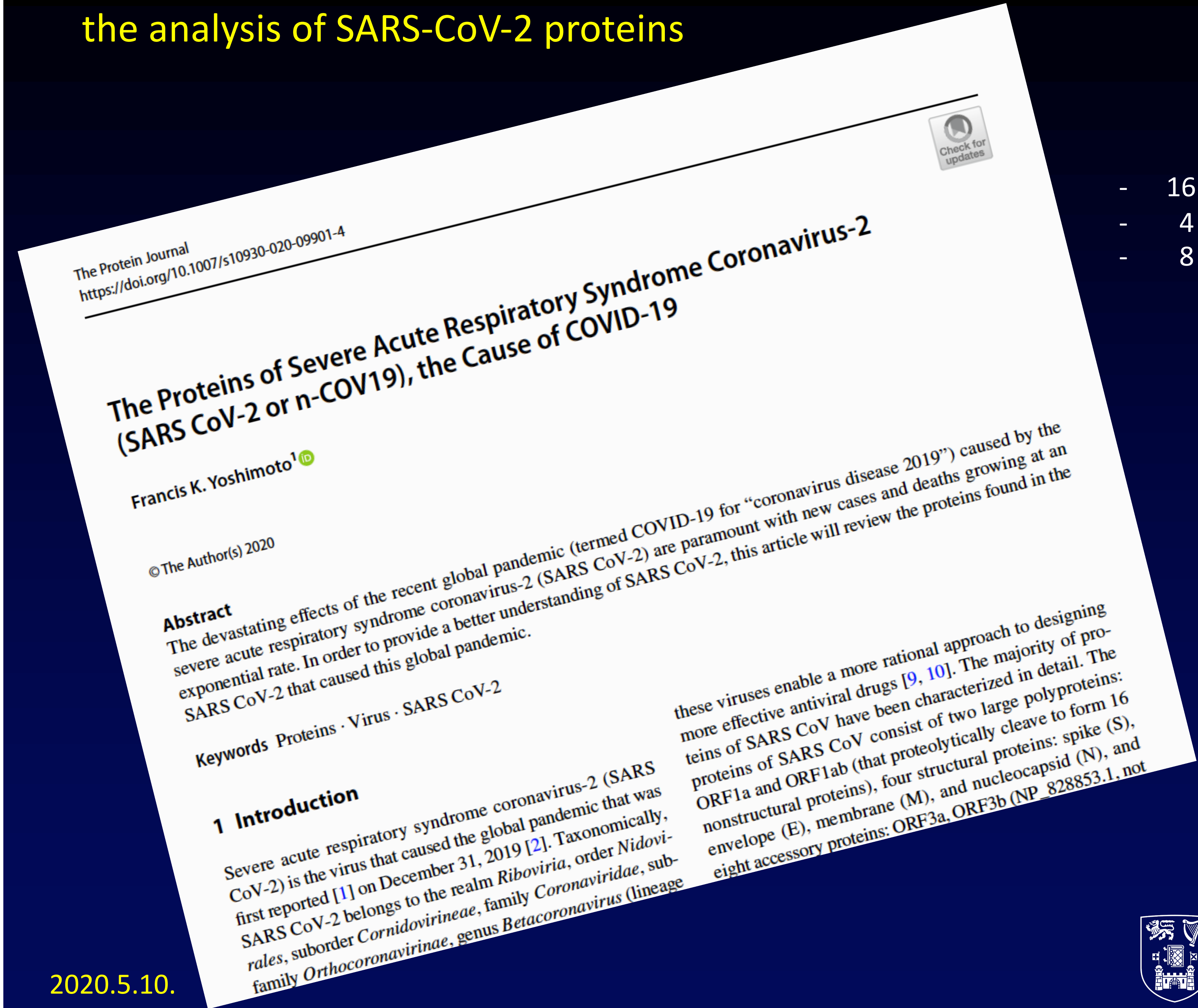

The Protein Journal
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Keywords Proteins · Virus · SARS CoV-2

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Severe acute respiratory syndrome coronavirus-2 (SARS CoV-2) is the virus that caused the global pandemic that was first reported [1] on December 31, 2019 [2]. Taxonomically, SARS CoV-2 belongs to the realm *Riboviria*, order *Nidovirales*, suborder *Cornidovirineae*, family *Coronaviridae*, subfamily *Orthocoronavirinae*, genus *Betacoronavirus* (lineage

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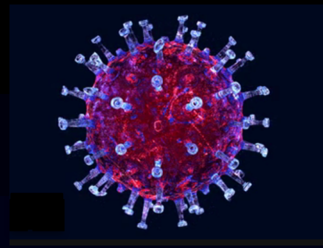

- 16 Non-structural proteins
- 4 Structural proteins
- 8 Accessory proteins

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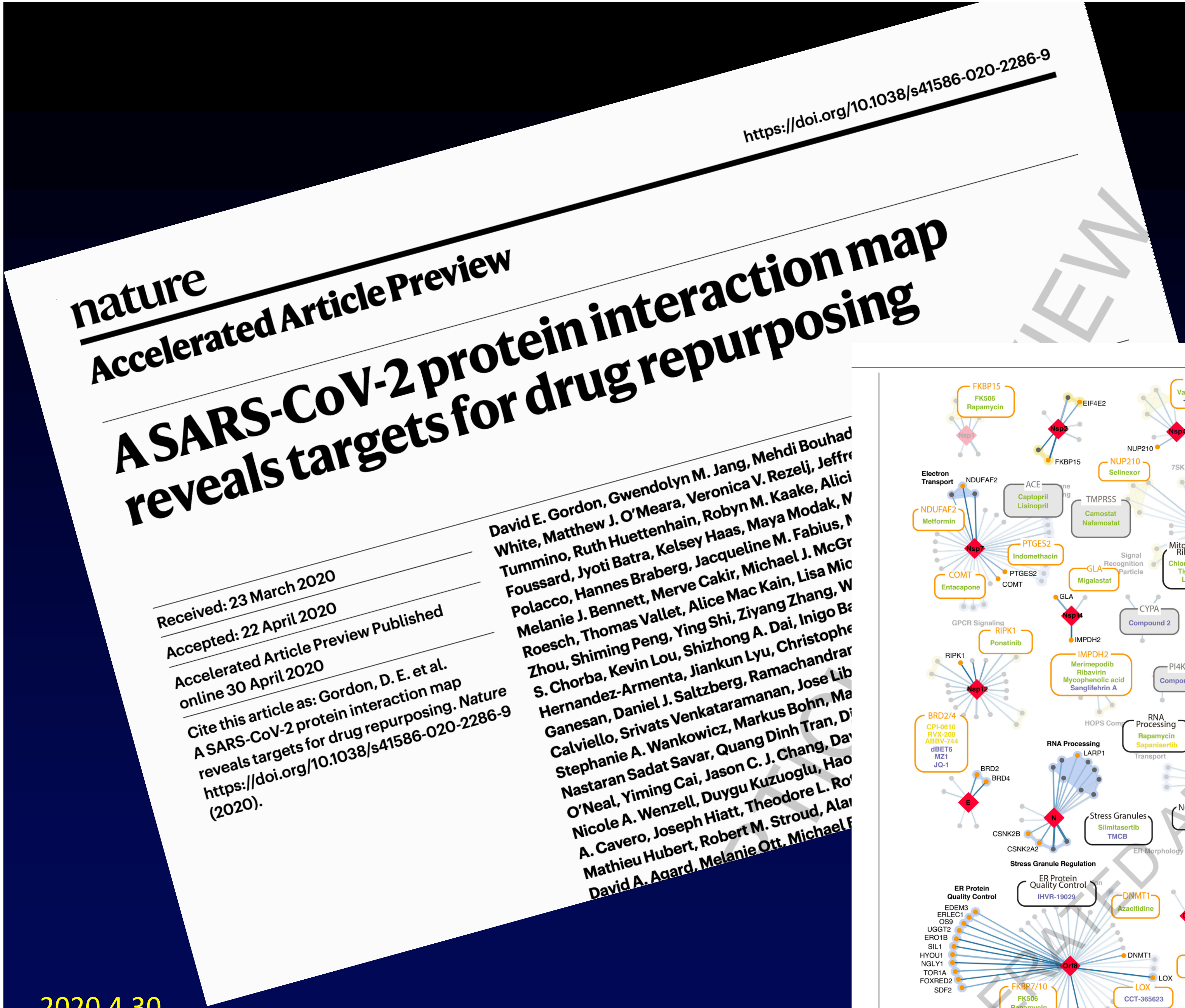

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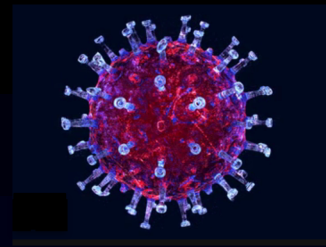

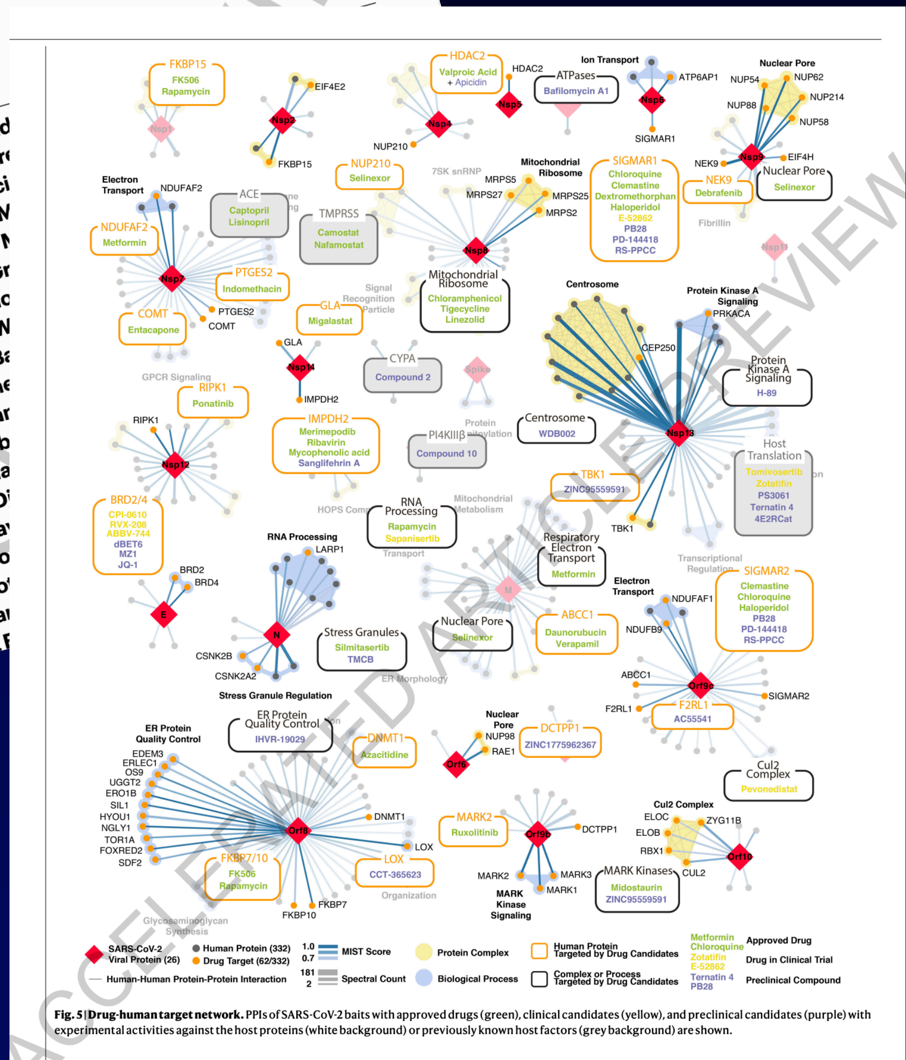

Fig. 5 | Drug-human target network. PPIs of SARS-CoV-2 baits with approved drugs (green), clinical candidates (yellow), and preclinical candidates (purple) with experimental activities against the host proteins (white background) or previously known host factors (grey background) are shown.

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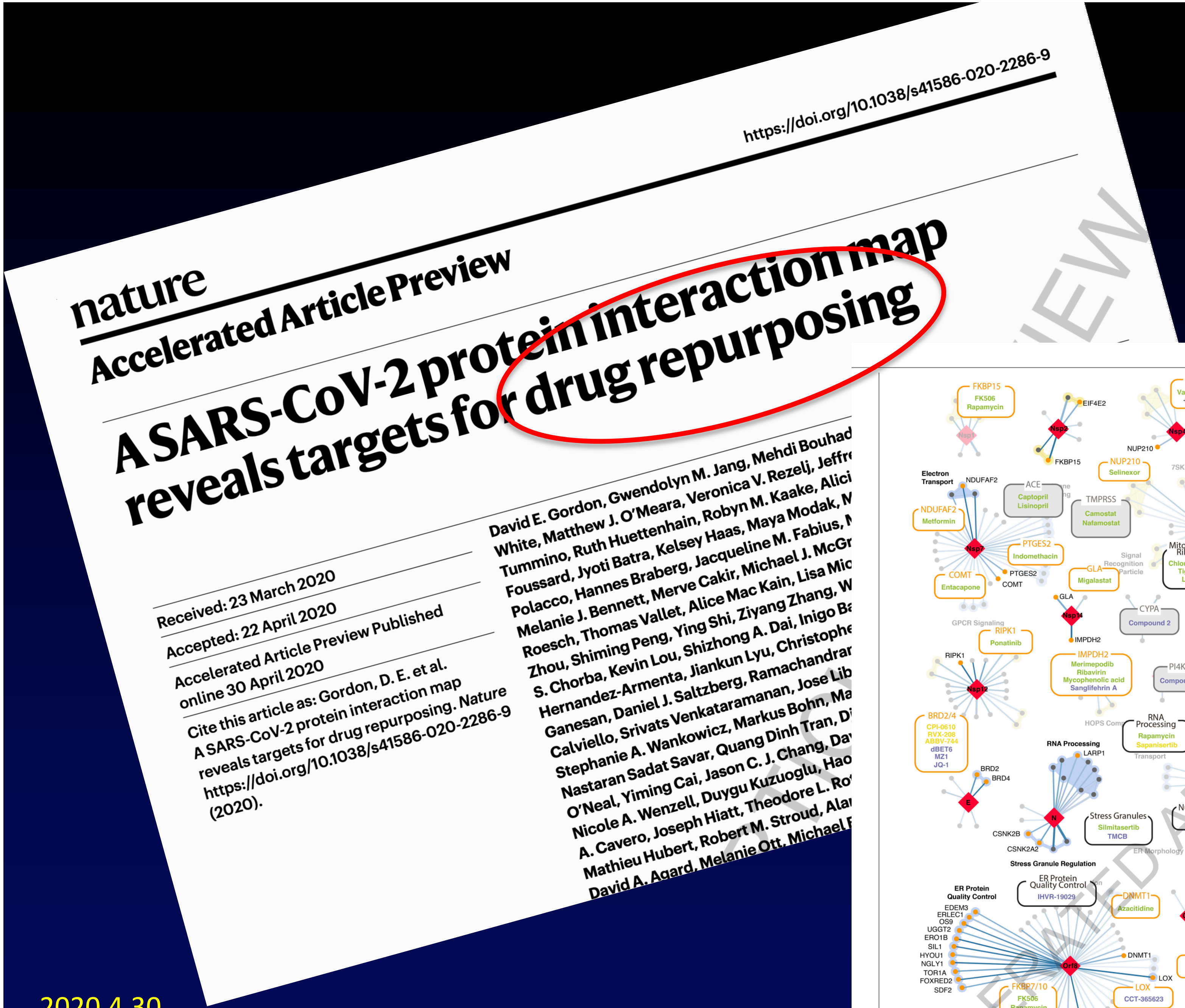

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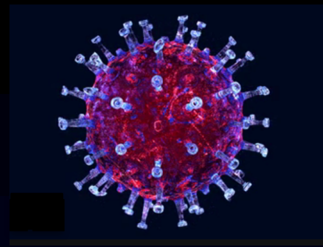

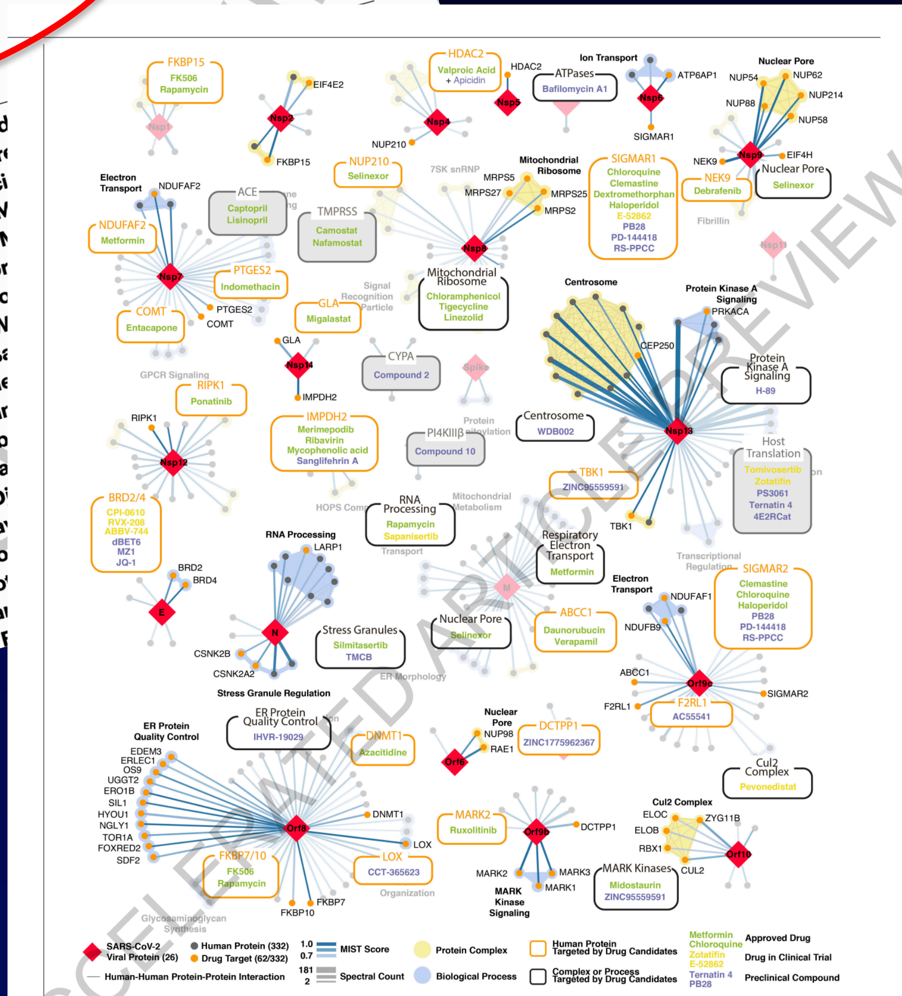

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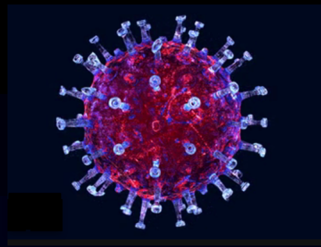

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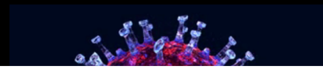

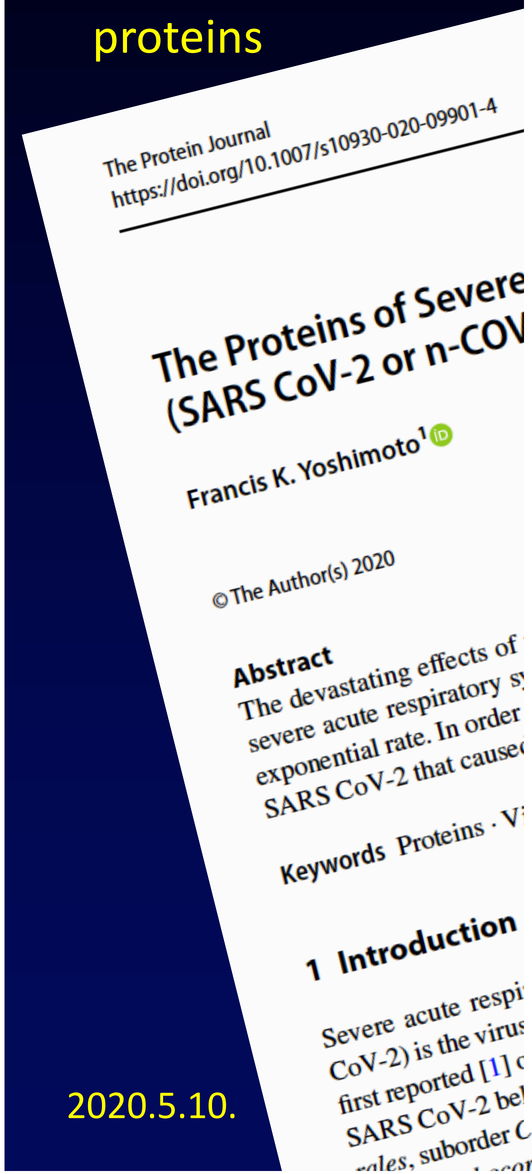
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2	N protein-(CSNK2A2)	Silmitasertib (cancer),[c] TMCB[a]
3	NSP5-(HDAC2)	Apicidin,[a] Valproic acid (CNS disease, cancer)[c]
4	NSP6-(ATP6AP1)	Bafilomycin A1[a]
5	NSP6-(SIGMAR1)	E-52862,[b] PD-144418,[a] RS-PPCC,[a] PB28,[a] Haloperidol (CNS disease)[c]
6	NSP6-(SLC6A15)	Loratadine (antihistamine)[3]
7	ORF9C-(TMEM97)	PB28,[a] haloperidol (CNS disease)[c]
8	M protein-(ATP6V1A)	Bafilomycin A1[a]
9	NSP7-(COMT)	Entacapone (Parkinson's disease)[c]
10	NSP7-(PTGES2)	Indomethacin (inflammation/pain)[c]
11	NSP7-(NDUFs)	Metformin (diabetes)[c]
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13	NSP12-(RIPK1)	Ponatinib (cancer)[c]
14	NSP13-(PRKACA)	H-89[a]
15	NSP14-(IMPDH2)	Merimepodib[b]
16	NSP14-(GLA)	Migalastat (Fabry disease)[c]
17	NSP14-(IMPDH2)	Mycophenolic acid (organ rejection),[3] ribavirin (virus)[c]
18	ORF8-(DNMT1)	Azacitidine[c]
19	ORF8-(LOX)	CCT 365623[a]
20	ORF9b-(MARK2/3)	Midostaurin,[3] Ruxolitinib[c]
21	ORF9b-(DCTPP1)	ZINC1775962367,[a] ZINC4326719,[a] ZINC4511851[a]
22	ORF9b/NSP13-(MARK3/TBK1)	ZINC95559591[a]
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34	ORF10-(VCP)	CB5083[b]
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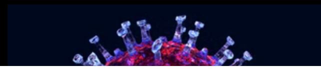

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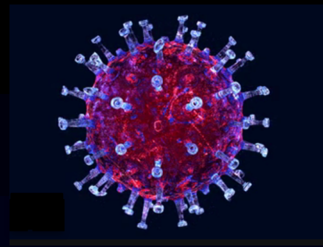

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