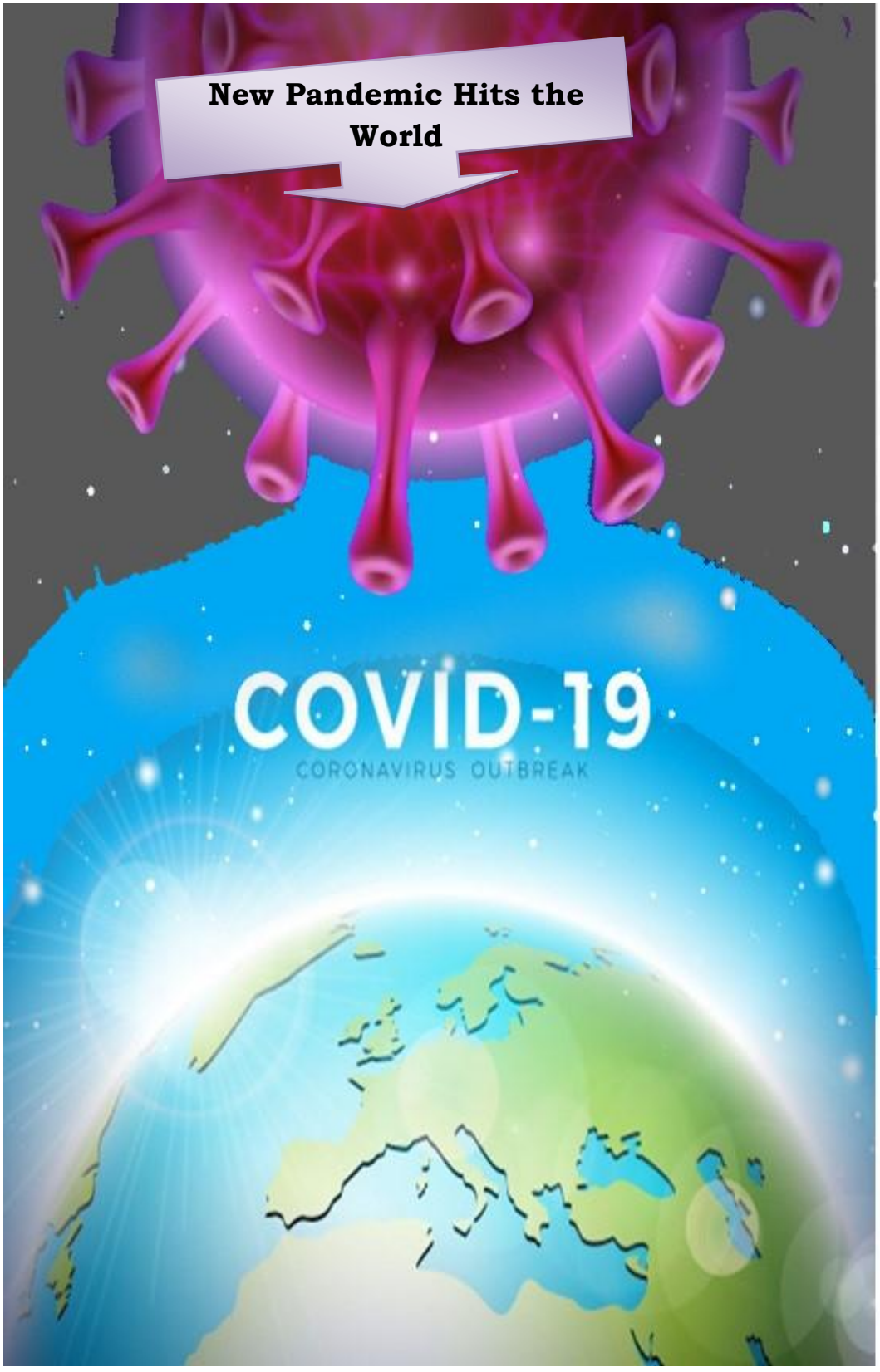
Issue No. - 12

January – June2020

NEWSLETTER



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INSIDE THIS ISSUE

NEWSLETTER RELEASE BY RESEARCH ADVISOR

Dear faculty members, researchers, students and other readers, it is our pleasure to release the 12th issue of this Research Newsletter. The theme of the present issue is "COVID-19 Coronavirus Outbreak". In this issue, we present information about a new WHO recognized worldwide disease Coronavirus Disease 2019 (COVID-19) emerged in past few months from its epicenter Wuhan, China.

This pandemic has spread to most parts of our country and hence, this situation has forced the Government to impose never before new rule of nationwide lockdown. This has had huge impact on overall economy, livelihood and healthcare. With new challenges like COVID-19, our team of doctors is ready to handle every situation. I wish these COVID-19 warriors all the best for managing and handling this sudden pandemic. I hope this newsletter will bring new insights into this disease so that appropriate measures and worthy information may be generated for new innovations and research in the healthcare field.

Dr. Usha Shah
Research Advisor, SVDU

FROM THE DESK OF RESEARCH DIRECTOR

It is a moment of owning great responsibility and duty as a part of medical education & research institution through research, development and clinical healthcare work to serve the mankind in these testing times of new pandemic COVID-19. This newsletter attempts to bring to your kind notice, the latest developments and research in understanding the risk factors, symptoms, updated research activities all around the world.

We hereby present the important research article links to enhance current scientific knowledge on SARS-CoV2 genome and protein structure. This will help our staff and researchers to develop new project proposals for increasing the fundamental knowledge about the COVID-19, the scope of development of new therapeutics and discovery of new vaccine candidates.

I hope this will aim to promote research on the same subject in all the constituent institutes of Sumandeep Vidyapeeth with active participation of all the researchers and faculty members. We believe that the students, faculty and clinicians should jointly collaborate for designing and submission of research proposals leading to development of products and innovations leading to IPR generation as well as societal benefit. We welcome your kind suggestions to make this communication more meaningful.

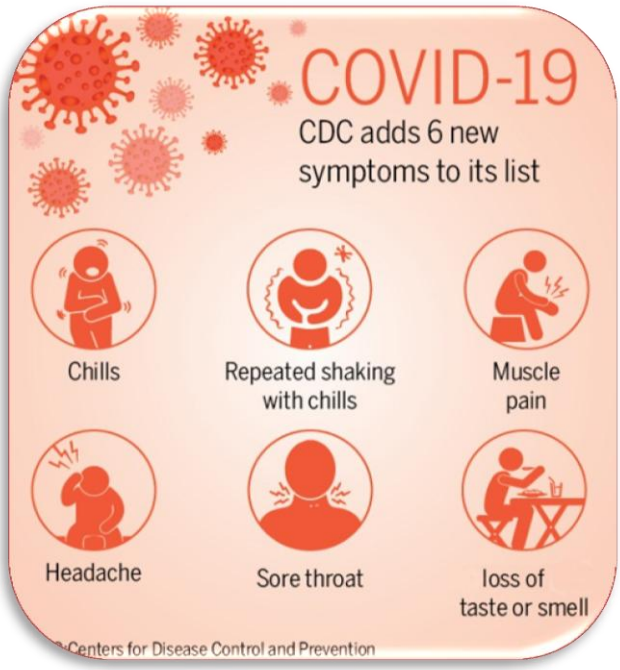
Dr. Avinash K. Seth
Director Research

INTRODUCTION

In early 2020, after a December 2019 outbreak in Wuhan, China, the World Health Organization identified the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV-2 as a new type of coronavirus, which was named on February 11, 2020 by the International Committee for the classification of viruses.

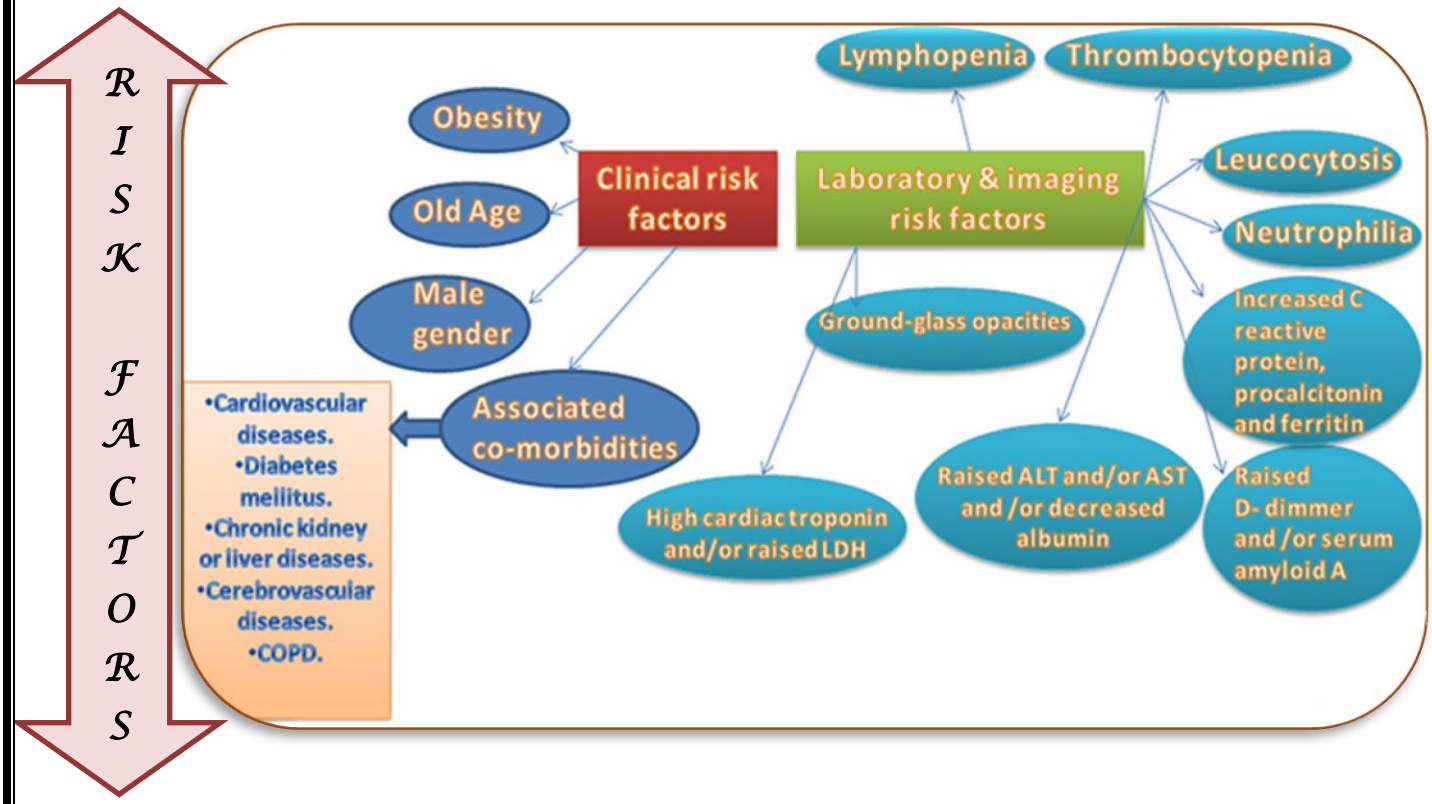
The outbreak quickly spread around the world.

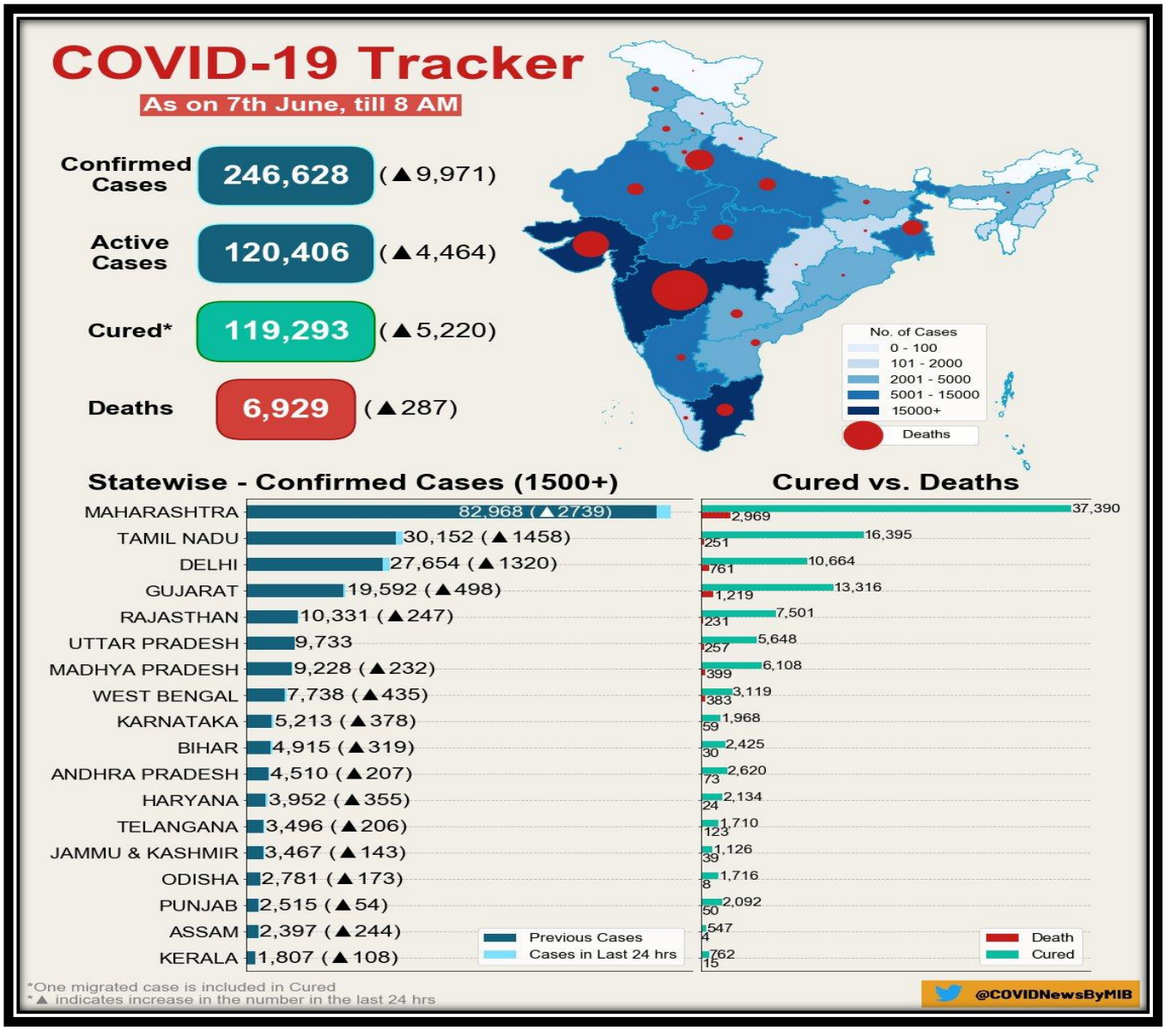
- COVID-19 is caused by infection with SARS-CoV-2 virus strains.
- SARS-CoV-2 is one of seven types of coronavirus, including the ones that cause severe diseases like Middle East respiratory syndrome (MERS) and sudden acute respiratory syndrome (SARS).
- The virus is transmitted through direct contact with respiratory droplets of an infected person (generated through coughing and sneezing)



SYMPTOMS OF COVID-19

- *Fever*
- *Coughing*
- *Trouble/ Shortness of breath*
- *Body aches*
- *Chills*
- *Sore throat*
- *Loss of smell or taste*
- *Nausea*


RISK FACTORS
Lymphopenia
Thrombocytopenia
Obesity
Clinical risk factors
Laboratory & imaging risk factors
Leucocytosis
Old Age
Neutrophilia
Male gender
Ground-glass opacities
Increased C reactive protein, procalcitonin and ferritin
•Cardiovascular diseases.
•Diabetes mellitus.
•Chronic kidney or liver diseases.
•Cerebrovascular diseases.
•COPD.
Associated co-morbidities
High cardiac troponin and/or raised LDH
Raised ALT and/or AST and/or decreased albumin
Raised D-dimmer and/or serum amyloid A


COVID-19 Tracker
As on 7th June, till 8 AM
Confirmed Cases 246,628 (▲9,971)
Active Cases 120,406 (▲4,464)
Cured* 119,293 (▲5,220)
Deaths 6,929 (▲287)
No. of Cases
0 - 100
101 - 2000
2001 - 5000
5001 - 15000
15000+
Deaths
Statewise - Confirmed Cases (1500+)
MAHARASHTRA 82,968 (▲2739)
TAMIL NADU 30,152 (▲1458)
DELHI 27,654 (▲1320)
GUJARAT 19,592 (▲498)
RAJASTHAN 10,331 (▲247)
UTTAR PRADESH 9,733
MADHYA PRADESH 9,228 (▲232)
WEST BENGAL 7,738 (▲435)
KARNATAKA 5,213 (▲378)
BIHAR 4,915 (▲319)
ANDHRA PRADESH 4,510 (▲207)
HARYANA 3,952 (▲355)
TELANGANA 3,496 (▲206)
JAMMU & KASHMIR 3,467 (▲143)
ODISHA 2,781 (▲173)
PUNJAB 2,515 (▲54)
ASSAM 2,397 (▲244)
KERALA 1,807 (▲108)
Previous Cases
Cases in Last 24 hrs
Cured vs. Deaths
2,969
37,390
251
16,395
761
10,664
1,219
13,316
231
7,501
257
5,648
399
6,108
383
3,119
59
1,968
30
2,425
73
2,620
24
2,134
123
1,710
39
1,126
8
1,716
50
2,092
4
547
15
762
Death
Cured
*One migrated case is included in Cured
*▲ indicates increase in the number in the last 24 hrs
@COVIDNewsByMIB

Lockdown Scenario: Its Impact on Livelihood

FIRST GENOME SEQUENCE REPORTS FROM INDIA

Indian J Med Res 151, February & March 2020, pp 200-209
DOI: 10.4103/ijmr.IJMR_663_20

Quick Response Code:

Full-genome sequences of the first two SARS-CoV-2 viruses from India

Pragya D. Yadav[1,*], Varsha A. Potdar[2,*], Manohar Lal Choudhary[2], Dimpal A. Nyayanit[1], Megha Agrawal[4], Santosh M. Jadhav[4], Triparna D. Majumdar[1], Anita Shete-Aich[1], Atanu Basu[3], Priya Abraham[2] & Sarah S. Cherian[4]

[1]*Maximum Containment Laboratory,* [2]*Influenza Group,* [3]*Electron Microscopy &* [4]*Bioinformatics & Data Management Group,* [5]*ICMR-National Institute of Virology, Pune, Maharashtra, India*

***Background & objectives*:** Since December 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has globally affected 195 countries. In India, suspected cases were screened for SARS-CoV-2 as per the advisory of the Ministry of Health and Family Welfare. The objective of this study was to characterize SARS-CoV-2 sequences from three identified positive cases as on February 29, 2020.

***Methods*:** Throat swab/nasal swab specimens for a total of 881 suspected cases were screened by *E* gene and confirmed by *RdRp* (1), *RdRp* (2) and *N* gene real-time reverse transcription-polymerase chain reactions and next-generation sequencing. Phylogenetic analysis, molecular characterization and prediction of B- and T-cell epitopes for Indian SARS-CoV-2 sequences were undertaken.

***Results*:** Three cases with a travel history from Wuhan, China, were confirmed positive for SARS-CoV-2. Almost complete (29,851 nucleotides) genomes of case 1, case 3 and a fragmented genome for case 2 were obtained. The sequences of Indian SARS-CoV-2 though not identical showed high (~99.98%) identity with Wuhan seafood market pneumonia virus (accession number: NC 045512). Phylogenetic analysis showed that the Indian sequences belonged to different clusters. Predicted linear B-cell epitopes were found to be concentrated in the S1 domain of spike protein, and a conformational epitope was identified in the receptor-binding domain. The predicted T-cell epitopes showed broad human leucocyte antigen allele coverage of A and B supertypes predominant in the Indian population.

***Interpretation & conclusions*:** The two SARS-CoV-2 sequences obtained from India represent two different introductions into the country. The genetic heterogeneity is as noted globally. The identified B- and T-cell epitopes may be considered suitable for future experiments towards the design of vaccines and diagnostics. Continuous monitoring and analysis of the sequences of new cases from India and the other affected countries would be vital to understand the genetic evolution and rates of substitution of the SARS-CoV-2.

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Article | Published: 30 March 2020

Structure of the SARS-CoV-2 spike receptor-binding domain bound to the ACE2 receptor

Jun Lan, Jiwan Ge, Jinfang Yu, Sisi Shan, Huan Zhou, Shilong Fan, Qi Zhang, Xuanling Shi, Qisheng Wang, Linqi Zhang ✉ & Xinquan Wang ✉

Nature **581**, 215–220(2020) | Cite this article

Abstract

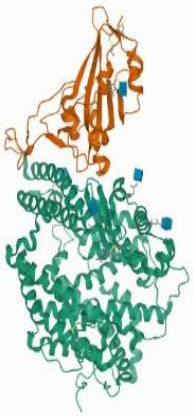
A new and highly pathogenic coronavirus (severe acute respiratory syndrome coronavirus-2, SARS-CoV-2) caused an outbreak in Wuhan city, Hubei province, China, starting from December 2019 that quickly spread nationwide and to other countries around the world[1,2,3]. Here, to better understand the initial step of infection at an atomic level, we determined the crystal structure of the receptor-binding domain (RBD) of the spike protein of SARS-CoV-2 bound to the cell receptor ACE2. The overall ACE2-binding mode of the SARS-CoV-2 RBD is nearly identical to that of the SARS-CoV RBD, which also uses ACE2 as the cell receptor[4]. Structural analysis identified residues in the SARS-CoV-2 RBD that are essential for ACE2 binding, the majority of which either are highly conserved or share similar side chain properties with those in the SARS-CoV RBD. Such similarity in structure and sequence strongly indicate convergent evolution between the SARS-CoV-2 and SARS-CoV RBDs for improved binding to ACE2, although SARS-CoV-2 does not cluster within SARS and SARS-related coronaviruses[1,2,3,5]. The epitopes of two SARS-CoV antibodies that target the RBD are also analysed for binding to the SARS-CoV-2 RBD, providing insight[illegible] future identification of cross-reactive antibodies.

Novel Studies decipher Crystal structure

RCSB PDB Deposit Search Visualize Analyze Download Learn More Documentat[illegible] MyPDB

Structure Summary | 3D View | Annotations | Experiment | Sequence | Genome | Versions

Biological Assembly 1



3D View: Structure | Electron Density | Ligand Interaction

Global Symmetry: Asymmetric - C1
Global Stoichiometry: Hetero 2-mer - A1B1

[illegible]play Files | Download Files

6M0J

Crystal structure of SARS-CoV-2 spike receptor-binding domain bound with ACE2

DOI: 10.2210/pdb6M0J/pdb

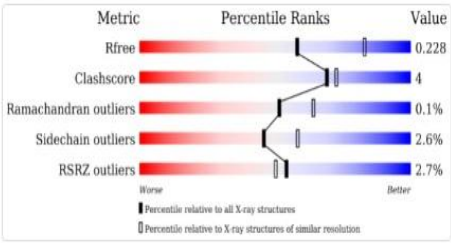
Classification: VIRAL PROTEIN/HYDROLASE
Organism(s): Homo sapiens, Severe acute respiratory syndrome coronavirus 2
Expression System: Trichoplusia ni
Mutation(s): No

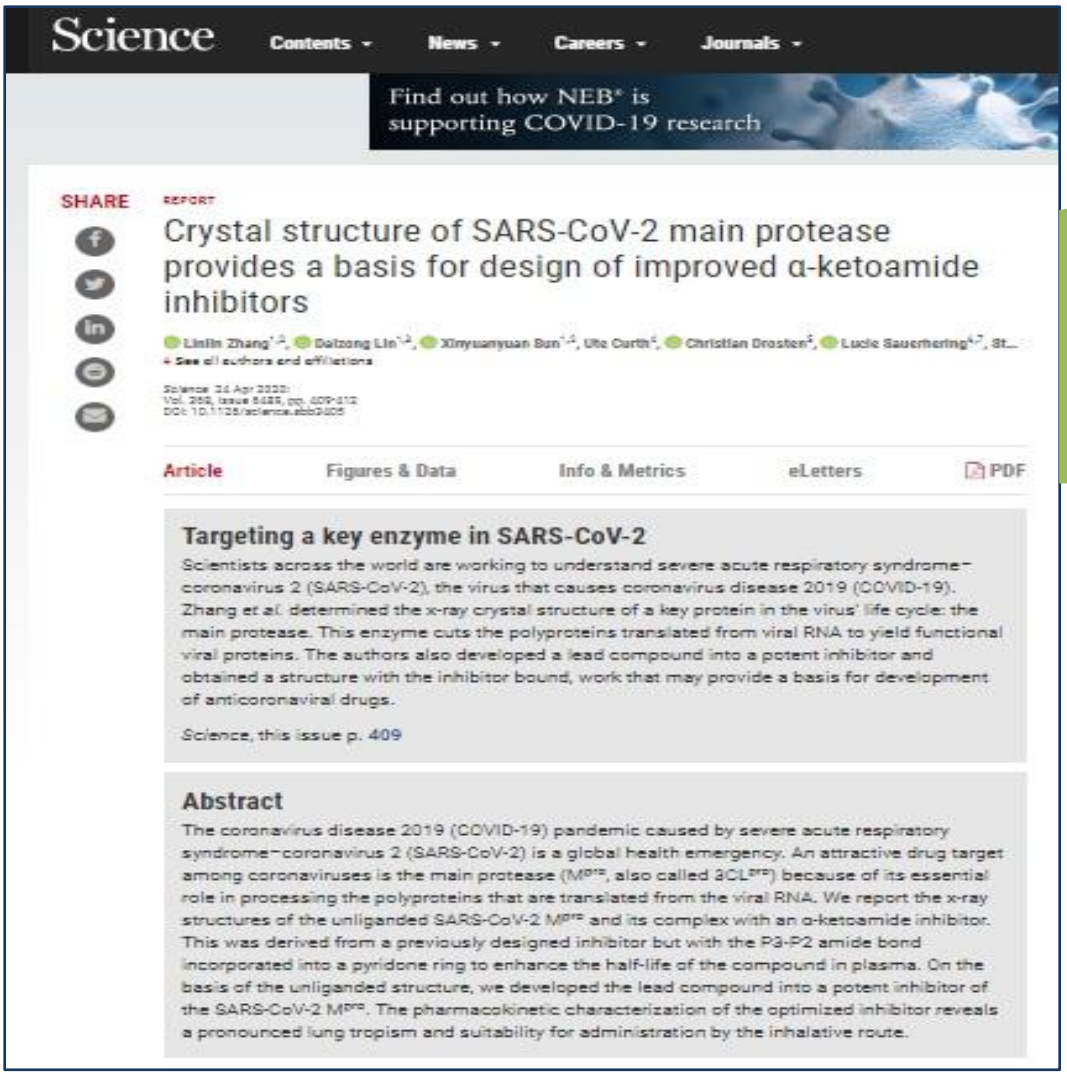
Deposited: 2020-02-21 **Released:** 2020-03-18
Deposition Author(s): Wang, X., Lan, J., Ge, J., Yu, J., Shan, S.

Experimental Data Snapshot

Method: X-RAY DIFFRACTION
Resolution: 2.45 Å
R-Value Free: 0.227
R-Value Work: 0.192
R-Value Observed: 0.194

wwPDB Validation | 3D Report | Full Report





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REPORT

Crystal structure of SARS-CoV-2 main protease provides a basis for design of improved α-ketoamide inhibitors

Linlin Zhang[1,2], Daizong Lin[1,2], Xinyuanyuan Sun[1,2], Ute Curth[3], Christian Drosten[3], Lucie Sauerhering[4,7], St...
+ See all authors and affiliations

Science 24 Apr 2020:
Vol. 368, Issue 6489, pp. 409-412
DOI: 10.1126/science.abb3405

Article Figures & Data Info & Metrics eLetters PDF

Targeting a key enzyme in SARS-CoV-2

Scientists across the world are working to understand severe acute respiratory syndrome–coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19). Zhang *et al.* determined the x-ray crystal structure of a key protein in the virus' life cycle: the main protease. This enzyme cuts the polyproteins translated from viral RNA to yield functional viral proteins. The authors also developed a lead compound into a potent inhibitor and obtained a structure with the inhibitor bound, work that may provide a basis for development of anticoronaviral drugs.

Science, this issue p. 409

Abstract

The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome–coronavirus 2 (SARS-CoV-2) is a global health emergency. An attractive drug target among coronaviruses is the main protease (M^{pro}, also called $3CL^{pro}$) because of its essential role in processing the polyproteins that are translated from the viral RNA. We report the x-ray structures of the unliganded SARS-CoV-2 M^{pro} and its complex with an α-ketoamide inhibitor. This was derived from a previously designed inhibitor but with the P3-P2 amide bond incorporated into a pyridone ring to enhance the half-life of the compound in plasma. On the basis of the unliganded structure, we developed the lead compound into a potent inhibitor of the SARS-CoV-2 M^{pro}. The pharmacokinetic characterization of the optimized inhibitor reveals a pronounced lung tropism and suitability for administration by the inhalative route.

New insights into Structure of SARS-Cov-2

New evidence of existence of thrombotic complications – A breakthrough in treatment

> Thromb Res. 2020 Jul;191:145-147. doi: 10.1016/j.thromres.2020.04.013. Epub 2020 Apr 10.

Incidence of thrombotic complications in critically ill ICU patients with COVID-19

F A Klok [1], M J H A Kruip [2], N J M van der Meer [3], M S Arbous [4], D A M P J Gommers [5], K M Kant [6], F H J Kaptein [7], J van Paassen [4], M A M Stals [7], M V Huisman [7], H Endeman [5]

Affiliations + expand

PMID: 32291094 PMCID: PMC7146714 DOI: 10.1016/j.thromres.2020.04.013

Free PMC article

Abstract

Introduction: COVID-19 may predispose to both venous and arterial thromboembolism due to excessive inflammation, hypoxia, immobilisation and diffuse intravascular coagulation. Reports on the incidence of thrombotic complications are however not available.

Methods: We evaluated the incidence of the composite outcome of symptomatic acute pulmonary embolism (PE), deep-vein thrombosis, ischemic stroke, myocardial infarction or systemic arterial embolism in all COVID-19 patients admitted to the ICU of 2 Dutch university hospitals and 1 Dutch teaching hospital.

Results: We studied 184 ICU patients with proven COVID-19 pneumonia of whom 23 died (13%), 22 were discharged alive (12%) and 139 (76%) were still on the ICU on April 5th 2020. All patients received at least standard doses thromboprophylaxis. The cumulative incidence of the composite outcome was 31% (95%CI 20-41), of which CTPA and/or ultrasonography confirmed VTE in 27% (95%CI 17-37%) and arterial thrombotic events in 3.7% (95%CI 0-8.2%). PE was the most frequent thrombotic complication (n = 25, 81%). Age (adjusted hazard ratio (aHR) 1.05/per year, 95%CI 1.004-1.01) and coagulopathy, defined as spontaneous prolongation of the prothrombin time > 3 s or activated partial thromboplastin time > 5 s (aHR 4.1, 95%CI 1.9-9.1), were independent predictors of thrombotic complications.

PREVENTION IS BETTER B'COZ THERE'S NO CURE

ACKNOWLEDGEMENTS

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Ms. Mitali (Research Assistant)

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