



# The National Academy of Sciences, India (NASI)

5, Lajpatrai Road, Prayagraj-211002, India

## Monthly Summary for the month of September 2020

1. NASI-HQ at Prayagraj and the Chapters collaborated/organised 'WEBINARS/Online Workshops', in joint collaboration with several institutions for the UG/PG students and researchers, with kind cooperation/support of its Fellows/Members and the Coordinators of the Programmes. Prof. G. Padmanaban, President, NASI and Prof. Manju Sharma, Past President, NASI, addressed the gathering of about 700 scientists/teachers/students in the WEBINAR organized by KBCNM University, Jalgaon on Geo-medical Health Hazards (details enclosed herewith - [Annex. 1](#)) on Sept. 17, 2020.
2. Hon'ble Prime Minister of India, declared the September month as '*Rashtriya Poshan Maah*'. The Academy immediately took necessary steps under its NASI-New Initiative Programmes (Chaired by Prof. Manju Sharma) to organize several activities to combat the menace of malnutrition, focusing on the poor health status of women, children and the rural population of the society. Professor Madhoolika Agrawal, Department of Botany, BHU and the Chairperson, NASI Varanasi Chapter organized the Poshan Maah on 18th September, 2020 ([Annex. 2 'a'](#)). A WEBINAR was organised jointly with INSA on Sept. 22, 2020 on Nutrition, coordinated/presided by Dr. Chandrima Shaha, President, INSA ([Annex. 2'b'](#)). Another webinar was also held at Mahendragarh on Sept. 24, 2020, coordinated by Prof. Paramjit Khurana ([Annex. 2'c'](#)). The detailed reports will be sent soon to the governmental & non-governmental agencies for their kind attention.
3. Several other WEBINARs were also held under the auspices of NASI Bhopal Chapter, Lucknow Chapter, Uttarakhand Chapter, Odisha Chapter and at Delhi; details are enclosed herewith as [Annex. 3](#) and [Annex. 4 \('a-d'\)](#). The main topics covered were - Plant Ecology; Health & diseases; Covid-19; Intellectual Property Rights; Abstracting & Indexing, and so on. About thousands of participants registered in each of these webinars.
4. Popular Science Web Lecture was also delivered for the +2 level school students; a brief report is enclosed herewith - [Annex. 5](#).
5. On the auspicious occasion of the '*Hindi Pakhwara*', several programmes were organized; and snippets written ([Annex. 6 & 7](#)).
6. An interesting scientific article on '...Prophylactic drug against COVID-19', published by NASI Fellow & others (Giri *et.al.*) was circulated among the scientists/teachers for dissemination of knowledge ([Annex. 8](#)).

**Several other NASI Chapters also organized online scientific activities.**



**SCHOOL OF ENVIRONMENTAL AND EARTH SCIENCES**  
KAVAYITRI BAHINABAI CHAUDHARI NORTH MAHARASHTRA UNIVERSITY JALGAON



Organized National Level Webinar on

**“GEOMEDICAL HEALTH HAZARDS AND ENVIRONMENTAL PROBLEMS IN TRIBAL AREAS: ISSUES, CHALLENGES AND OPPORTUNITIES”**

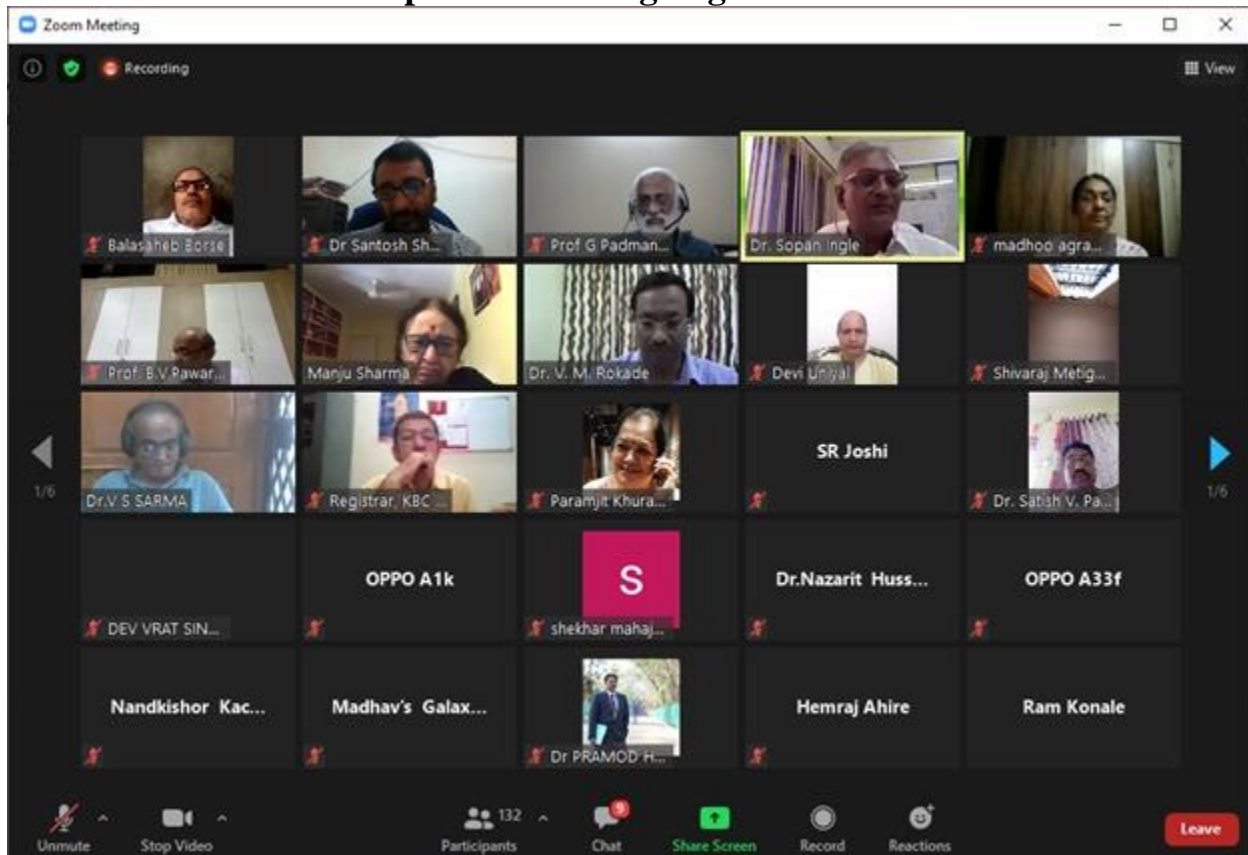
Date: 17<sup>th</sup> September, 2020 at 10:15 A.M. onward

Chief Patron	Patrons		Chief Guest	Guest of Honor
				
Prof. P. P. Patil Vice- Chancellor, Kavayitri Bahinabai Chaudhari North Maharashtra University, Jalgaon	Prof. P. P. Mahulikar Pro-Vice- Chancellor, Kavayitri Bahinabai Chaudhari North Maharashtra University, Jalgaon	Prof. B. V. Pawar Officiating Registrar, Kavayitri Bahinabai Chaudhari North Maharashtra University, Jalgaon	Prof. Manju Sharma, NASI-DST Distinguished Woman Scientist Chair, National Academy of Sciences India (NASI), Prayagraj	Prof. G. Padmanaban, President, National Academy of Sciences India (NASI), Prayagraj

Its free and open to all

Registration link: <https://forms.gle/AoitY8ms3mT1zNvc8>

**Snapshot of the ongoing WEBINAR**



Zoom Meeting

Recording

View

Balasaheb Borse

Dr. Santosh Sh...

Prof. G Padman...

Dr. Sopan Ingle

madhoo agra...

Prof. B.V.Pawar...

Manju Sharma

Dr. V. M. Rokade

Devi Uniyal

Shivaraj Metig...

Dr. V S SARMA

Registrar, KBC

Paramjit Khura...

SR Joshi

Dr. Satish V. Pa...

DEVI VRAT SIN...

OPPO A1k

shekhar mahaj...

Dr.Nazarit Huss...

OPPO A33f

Nandkishor Kac...

Madhav's Galax...

Dr. PRAMOD H...

Hemraj Ahire

Ram Konale

Unmute

Stop Video

Participants 132

Chat

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Reactions

Leave



# पोषण माह



## राष्ट्रीय विज्ञान अकादमी, भारत: वाराणसी अध्याय काशी हिन्दू विश्वविद्यालय, वाराणसी

In order to strengthen the noble vision of 'Prime Minister's Overarching Scheme for Holistic Nourishment' (POSHAN Abhiyan), especially for overcoming the health and nutritional challenges of the tribal women and also to make them aware regarding the need of healthy and balanced diet for boosting immunity and thereby combating many lifestyle diseases including COVID-19, the NASI-Varanasi Chapter organized the Poshan Maah on 18<sup>th</sup> September, 2020, by Professor Madhoolika Agrawal, Department of Botany, BHU and the Chairperson, NASI-Varanasi Chapter, along with Dr. PC Abhilash, Advisor, NASI-Varanasi Chapter (IESD, BHU), Mr. Durgesh Singh Yadav (Dept. of Botany, BHU), Mr. Pradeep Kumar Dubey (IESD, BHU), Mr. Ajeet Singh (IESD, BHU), and Mr. Sandeep Kumar (ReNew Power Ltd, Varanasi) for tribal women, children and adolescent girls in Dadra and Koori villages in Rajgarh block of Mirzapur district, and Bhawanipur, Jayapur and Paniyara villages in Arajiline block of Varanasi district.

The program benefitted more than 100 tribal women families, 85 children and 42 adolescent girls in the above villages. A 'poshan kit' consisted of nutrient supplements (calcium, iron, and B-complex for 1 month), Protein supplement, face mask, hand wash, towel, and a mega seed packet procured from Indian Institute of Vegetable Research (IIVR, Varanasi) having the seeds of 10 nutritious and delicious vegetables for making their own 'nutrigardens', were distributed to each tribal woman. Moreover, the 'poshan kit' also contained note books, pen, pencils, glucose biscuits and oral vitamin drops/tonics (calcium, iron, B-complex) for infants, children and adolescent girls. Prof. Madhoolika Agarwal explained the use of various supplements for a healthy and good quality life and she also detailed the importance of healthy practices like social distancing and personal hygiene, frequent hand washing and wearing of masks for preventing COVID-19. Importantly, she also explained them to develop a full nutrient garden (i.e. family/kitchen garden) using various vegetable seeds for a healthy and nutritious diet for their whole family. The NASI-Varanasi Chapter will continue this ambitious program for the next five months till February, 2021.



Poshan Maah conducted in Jayapur Village, Varanasi



Koori Village, Rajgarh, Mirzapur



## स्वास्थ्य पोषण के लिए एक दिवसीय जागरूकता अभियान सम्पन्न

सकलभित्त नून और जलसूत। राष्ट्रीय विज्ञान अकादमी के वाराणसी अध्याय द्वारा 18 दिसम्बर को भारत सरकार के विज्ञान सप्ताह माह राष्ट्रीय पोषण सप्ताह के अंतर्गत, उल्हास, मिर्जापुर के कृषि व दूरदर्शन में आदिवासी महिलाओं के स्वास्थ्य, पोषण व आजीवनिक समीक्षा एक दिवसीय जागरूकता एवं सामाजिक विचारण अभियान सम्पन्न हुआ।

कार्यक्रम का आयोजन राष्ट्रीय विज्ञान अकादमी के वाराणसी अध्याय की अध्यक्ष प्रो. मधुसूता अग्रवाल (राष्ट्रीय विज्ञान विभाग, काशी हिन्दू विश्वविद्यालय, वाराणसी) एवं सहकार्य डॉ. हीम शिव अभिलषण (समूहक अध्यक्ष, सर्वभारत एवं भारतीय विकास संघकार, काशी हिन्दू



विश्वविद्यालय, वाराणसी) द्वारा किया गया। करीब 100 महिलाओं को विभिन्न प्रकार की व्यक्तिगत एवं औपचारिक विशेष रूप से कुपोषण से प्रभावित बच्चों और गर्भवती महिलाओं को पोषण संबंधी सूख मॉनिटरिंग और दवाएं (जो की आयरन, कैल्शियम, प्रोटीन, विटामिन-डी और टी आरके के सूख हैं), विटने

कमन हेतु पोषण सप्लियों के वीर (जो की भारत सरकार समी अनुबंधन संस्था वाराणसी से लिए गए), संप्रोस कला में आयोजित आयोजक समूहों वीरें फल और गुंठ को खाने के लिए पैकेज का बालक/बेस कवर, ईडलका के लिए सलून और डीएलएडर, सलून को खाने खाने के लिए पेन, पोपल, सेटपुक

इत्यादि उपान किया गया। कार्यक्रम में परामर्श एवं धारणीय विकास संघकार, काशी हिन्दू विश्वविद्यालय, वाराणसी के प्रतिष्ठित डॉ. जय प्रदीप कुमर द्वारा, अजीत सिंह और दुर्गा मिश्र कला ने इस क्षेत्रक विज्ञान कार्यक्रम में सहयोग रूप से काम किया।

प्रो. मधुसूता अग्रवाल ने वही महिलाओं को कोरिण (एडवुड-19) परामर्श के बारे में कठना और वीरणी से बचने हेतु उन्हें 2 मीटर की खराबक दूरी रखने के लिए आग्रहक किया। यह कार्यक्रम राष्ट्रीय विज्ञान अकादमी के वाराणसी अध्याय द्वारा किया गया। कार्यक्रम में वाराणसी के जिलों के आदिवासी महिलाओं के स्वास्थ्य व स्वास्थ्य सम्बन्धन कार्यक्रम के नूतनता में सम्पन्न हुआ।



वाराणसी में आदिवासी महिलाओं में स्वास्थ्य पोषण माह।

### कुपोषित बच्चों और महिलाओं में दवा का वितरण

मिर्जापुर। राष्ट्रीय विज्ञान अकादमी वाराणसी की ओर से इतिहास को भारत सरकार के राष्ट्रीय पोषण सप्ताह के अंतर्गत, राजमण्ड विकास खंड के कृषि व दूरदर्शन में आदिवासी महिलाओं को जागरूक किया गया। अध्यक्ष प्रो. मधुसूता अग्रवाल (राष्ट्रीय विज्ञान विभाग, काशी हिन्दू विश्वविद्यालय, वाराणसी) एवं सहकार्य डॉ. हीम शिव अभिलषण (समूहक अध्यक्ष, सर्वभारत एवं भारतीय विकास संघकार, वाराणसी) की ओर से करीब 100 महिलाओं, कुपोषण बच्चों और गर्भवती महिलाओं को पोषण पूरक मॉनिटरिंग और दवाएं दी गईं। इसके अलावा विभिन्न स्थानों के लिए पोषण पत्रों के वीर (जो की भारतीय सलून अनुसंधान संस्थान, वाराणसी से लिए थे) मस्क/किस कवर, ईडलका, संप्रोसकल, वाराणसी से लिए थे, पोपल, सेटपुक इत्यादि उपान किया गया।



## Webinar on 'Nutrition in the times of pandemic'

jointly organized by NASI & INSA

**Date: September 22, 2020**

### Programme

- Opening Remarks (10:00 am) : **Dr. Shelley Praveen** (Convener)  
Head, Division of Biochemistry,  
Indian Agricultural Research Institute, New Delhi
- Brief remarks (10:05 am) : **Prof. (Mrs.) Manju Sharma** (Chair)  
Former Secretary to the Govt. of India  
Department of Biotechnology, New Delhi  
Distinguished Women Scientist Chair, NASI, Allahabad
- Brief remarks (10:10 am) : **Dr. Chandrima Shaha**  
President, Indian National Science Academy, New Delhi  
Professor of Eminence; & Former Director,  
National Institute of Immunology, New Delhi
- Key-note address (10:20 am): **Dr. Mahtab Bamji**  
INSA Emeritus, Scientist  
Dangoria Charitable Trust, Hyderabad  
Title: COVID 19, a new whammy to add to the country's resistant burden of malnutrition
- Lecture-1(10:45 am) : Meeting Nutritional Challenges of the EWS  
Speaker : **Prof. Paramjit Khurana**  
Head, Department of Plant Molecular Biology,  
University of Delhi South Campus, New Delhi;  
General Secretary (OS), NASI
- 11:10 am: 10 minutes break**
- Lecture- 2(11:20 am) : Role of plants in nutritional security of the underprivileged during COVID-19 pandemic  
Speaker : **Prof. Madhoolika Agrawal**  
Department of Botany, BHU, Varanasi
- Lecture- 3(11:45 am) : Plant-based nutrition during pandemic  
Speaker : **Prof. Akhilesh Tyagi**  
Past President, NASI; Formerly Director, NIPGR;  
Department of Plant Molecular Biology,  
University of Delhi South Campus, New Delhi

Lecture-4 (12:15 pm) : Holistic approach for a healthy well-being in times of COVID-19 epidemic in India

Speaker : **Dr. Namrata Singh**  
Dietitian, Department of Gastroenterology & Human Nutrition,  
All India Institute of Medical Sciences, New Delhi

Summary by the Chair

Vote of thanks : **Prof. Ajoy Ghatak**  
MN Saha Distinguished Chair Professor, NASI  
Formerly Professor at IIT, Delhi  
Chairman, NASI Delhi Chapter

**YouTube link for live streaming**

<https://www.youtube.com/c/INSASince1935>



# Central University of Haryana, Mahendragarh



In association with National Academy of Sciences,  
India (NASI)

Cordially invites you to

## National Webinar on

### Effective Poshan (Nutrition) during Pandemic Covid-19



Register here: <https://forms.gle/vJxuqTBJzo4t94z87>



Inaugural address  
Patron; Prof R C Kuhad,  
Honorable Vice Chancellor



Inaugural address  
Dr Manju Sharma,  
NASI-DST Distinguished Women Scientist Chair,  
Formerly Secretary, DBT, Govt of India



Introductory Remarks  
Prof Paramjeet Khurana,  
University of Delhi, Delhi  
General Secretary, NASI

### Speakers

### Sept 24, 2020

### Time 11 am onwards

Registration: Mr Naresh Kumar (9015590393); Certificate: Dr Tejpal Dhewa (7678622764), Dr Antresh Kumar, Dr Pramod Joshi



Dr Shubhra Chakraborty,  
Director, NIPGR, Delhi



Prof Neelam Sangwan,  
Convenor, CUH



Dr Manoj Tripathi,  
ICAR-CIAE, Bhopal



Prof. Sunita Mishra  
Dean & Head, BBAU, Lucknow

Organizing Team: Dr Gunjan Goel, Dr Pawan, Dr Usha, Dr Saurabh, Dr Maruthi, Dr Savita, Dr Inderjeet, Dr Namrata, Dr. Jitendra Saini



**Report on the  
International Webinar entitled ‘The Importance of Historical Ecology for Interpreting  
Processes of Evolution in Plants of Oceanic Islands’**

**Mansarovar Global University on September 11, 2020**

**Prof Arun Kumar Pandey, VC, Mansarovar Global University**

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The study of systematics and evolution are historical as they attempt to understand the long-term evolutionary processes of genetic differentiation and speciation that have occurred at the populational level. As the oceanic islands are relatively short-lived and undergo ontogenies with time, they are dynamic systems to study the macro- and micro-evolutionary processes. Hence, the webinar was organised to highlight the significance of different scientific disciplines such as anthropology, environmental science, landscape ecology, environmental history, etc. in explaining the changes in geomorphology and vegetation.

**The webinar was attended by over 650 participants. It was jointly organized by the Mansarovar Global University and the National Academy of Sciences, India (Bhopal Chapter).**

In the beginning of the session, Prof. Arun K. Pandey (Vice-Chancellor, Mansarovar Global University) welcomed and introduced the speaker Prof. Tod F. Stuessy, who is an eminent plant systematist and recipient of many prestigious awards like Engler Medal in Gold, recipient of the Stebbins Medal for Plant Taxonomy from the International Association for Plant Taxonomy, Asa Gray Award from the American Society of Plant Taxonomy, Merit and Centennial awards from the Botanical Society of America.

Prof. Tod F. Stuessy (Emeritus Professor, Ohio State University, USA) in his talk highlighted the importance of historical ecology in interpreting the biological processes occurring on oceanic islands. He explained how the climatic factors affect the biogeography of the islands and the impact of human activities on the island vegetation. With special reference to the Juan Fernández (Robinson Crusoe) Archipelago, he pointed out the transformations in the geomorphology of the island. He also discussed the impact of tsunami and human activities in the modification of the landscape on the northeastern side of Robinson Crusoe Island.

He talked about the various species of animals and plants that were introduced to the Archipelago, and how some of them became invasive and harmed the native vegetation of the island. He said that in order to know about the processes of evolution in oceanic islands, it is necessary to understand the natural and human-associated impacts on the ecosystem. He suggested that just by looking at the present spatial or ecological contexts, inferences about speciation should not be made.

He also spoke about the importance of history of genera *Robinsonia* and *Erigeron* in the Robinson Crusoe Island. Citing several examples, he explained that the evolutionary processes can be best studied in young islands that have been less impacted by natural and human factors. His lecture was followed by an interactive question and answer session.

During the interactions, the participants asked several questions related to speciation, conservation of endemic taxa, invasive species, and ecological processes. Prof. Stuessy clarified their doubts and suggested that for a meaningful interpretation of processes of evolution within the endemic flora of archipelagos, it is important to understand the historical ecology that has led to the present distributional and ecological patterns.

The major outcome of the webinar was the sensitization of the participants to the fact that interpretation of evolutionary processes in islands requires understanding the nature of landscape changes during the ontogeny which usually takes over several million of years. The webinar provided opportunity to the participants to discuss their queries on systematics and evolution of plants and provided them new ideas about the future research areas.

On behalf of the Mansarovar Global University and the National Academy of Sciences, India, Prof. Pandey thanked Prof. Stuessy for accepting the invitation and delivering wonderful lecture. Prof. Pandey also expressed his gratefulness to Dr Manju Sharma for her constant encouragement and support in organising different academic activities at Mansarovar Global University, Bhopal.





### The Importance of Historical Ecology Interpreting Processes of Evolution in Plants of Oceanic Islands

**Tod F. Stuessy**

Herbarium and Department of Evolution, Ecology, and Organismal  
Biology, The Ohio State University, Columbus, Ohio U.S.A.; and  
Department of Botany and Biodiversity Research, University of  
Vienna, Austria.

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**INTERNATIONAL WEBINAR**

ON

**THE IMPORTANCE OF HISTORICAL ECOLOGY FOR  
INTERPRETING PROCESSES OF EVOLUTION  
IN PLANTS OF OCEANIC ISLANDS**

SPEAKER	HOST
 <p><b>Prof. Tod F. Stuessy</b> Emeritus Professor Museum of Biological Diversity The Ohio State University Columbus, Ohio, USA</p>	 <p><b>Prof. Arun Pandey</b> Vice-Chancellor Mansarovar Global University Bhopal, Madhya Pradesh, INDIA</p>

\*E-CERTIFICATE WILL BE ISSUED TO ALL THE PARTICIPANTS

**REGISTER**  
<https://bit.ly/34rXz2f>

**DATE: 11 SEPT. 2020 FRIDAY**  
**TIME: 08:00 AM (USA) | 5:30 PM (INDIA)**




Mansarovar Global University  
<http://www.dny.ac/NGUYT>



Annex. 4 'a'



**INTELLECTUAL  
PROPERTY**

**WEBINAR SERIES ON**

**Intellectual Property Rights: Fundamentals  
and its importance in Present Context**

**8<sup>th</sup> to 11<sup>th</sup> Sep 2020 11:00 AM to 01:00 PM**

**INAUGURAL SESSION ( 8<sup>TH</sup> SEPT 2020 )**



**DR YASHWANT PANWAR**

Scientist 'F'  
and Director PFC, TIFAC



**DR RAJENDRA DOBHAL**

Director General, UGCST



**DR PRADEEP SRIVASTAVA**

Executive Director, TIFAC



**DR R. SAHA**

Advisor Global Institute  
of Intellectual Property &  
Senior Advisor, CII



**DR DP UNIYAL**

Joint Director, UGCST  
& Moderator, Webinar series

**Registration is  
Mandatory & Free**

**FOR REGISTRATION CLICK ON**

<https://forms.gle/NXkYTqeHSB4Es4Go8>

**Zoom link for attending meeting**

<https://zoom.us/j/91412940063?pwd=OXpBODJ6azJHOFIwMkIscStLZHVBUT09>

OR

**Meeting ID: 914 1294 0063  
Passcode: 778668**

E-Certificate is provided to  
only registered participants  
who have attended all four  
days session

**Contact us : 7906341484 / 7500582048  
pic.ugcost@gmail.com**

**9<sup>TH</sup> - 11<sup>TH</sup> SEP SESSIONS WILL START FROM 11:00 AM TO 01:00 PM**



**Streaming will also be done through facebook and youtube live**

# HEALTH AND DISEASE: CONTEMPORARY CONCERNS

11-21 SEPTEMBER 2020



IN COLLABORATION WITH



## SPEAKERS

**11 SEPTEMBER**  
**PROF. A. B. DEY**  
AIIMS, NEW DELHI

**12 SEPTEMBER**  
**PROF. PANKAJ SETH**  
NATIONAL BRAIN RESEARCH CENTRE, MANESAR

**13 SEPTEMBER**  
**DR. SUNIL RAGHAV**  
INSTITUTE OF LIFE SCIENCES, BHUBANESWAR

**14 SEPTEMBER**  
**PROF. THEODORE PRICE**  
CENTRE FOR ADVANCED PAIN STUDIES  
U OF TEXAS AT DALLAS, USA

**15 SEPTEMBER**  
**PROF. RENU WADHWA**  
NATIONAL INSTITUTE OF ADVANCED INDUSTRIAL SCIENCE &  
TECHNOLOGY  
TSUKUBA, JAPAN

**16 SEPTEMBER**  
**DR. MUNMUN CHATTOPADHYAY**  
TEXAS TECH UNIVERSITY  
EL PASO, USA

**17 SEPTEMBER**  
**DR. PUNIT PRASAD**  
INSTITUTE OF LIFE SCIENCES  
BHUBANESWAR

**18 SEPTEMBER**  
**PROF. N. K. MEHRA**  
AIIMS, NEW DELHI

**19 SEPTEMBER**  
**PROF. AJAY PARIDA**  
INSTITUTE OF LIFE SCIENCES  
BHUBANESWAR

**20 SEPTEMBER**  
**PROF. U. C. SRIVASTAVA**  
NATIONAL ACADEMY OF SCIENCES, INDIA  
ALLAHABAD

**21 SEPTEMBER**  
**PROF. MITUL MEHTA**  
KING'S COLLEGE, LONDON, UK

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ORGANISING CHAIR



**PROF. ISHAN PATRO**

**VICE-CHANCELLOR  
RAVENSHAW  
UNIVERSITY**



PARTNERS FOR VIRTUAL SERIES ON HEALTH AND DISEASE: CONTEMPORARY CONCERNS

RAVENSHAW UNIVERSITY, INSTITUTE OF LIFE SCIENCES, NASI, INDIAN ACADEMY OF NEUROSCIENCES



PROF. A. B. DEY  
DEPARTMENT OF  
GERIATRIC MEDICINE  
ALL INDIA INSTITUTE OF  
MEDICAL SCIENCES  
NEW DELHI

# HEALTHY AGEING

11 SEPTEMBER 2020  
(FRIDAY)  
4 P.M. IST

DAY 1: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=9A1HT6L04A8](https://www.youtube.com/watch?v=9A1HT6L04A8)



PARTNERS FOR VIRTUAL SERIES ON HEALTH AND DISEASE: CONTEMPORARY CONCERNS

RAVENSHAW UNIVERSITY, INSTITUTE OF LIFE SCIENCES, NASI, INDIAN ACADEMY OF NEUROSCIENCES

PROF. PANKAJ SETH  
NATIONAL BRAIN  
RESEARCH CENTRE  
MANESAR



HOW DO  
VIRUSES  
AFFECT THE  
HUMAN  
BRAIN?

12 SEP 2020  
(SATURDAY)  
4 P.M. IST

DAY 2: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=JFG7BG6CLRQ](https://www.youtube.com/watch?v=JFG7BG6CLRQ)



PARTNERS FOR VIRTUAL SERIES ON HEALTH AND DISEASE: CONTEMPORARY CONCERNS

RAVENSHAW UNIVERSITY, INSTITUTE OF LIFE SCIENCES, NASI, INDIAN ACADEMY OF NEUROSCIENCES



DR. SUNIL RAGHAV  
INSTITUTE OF  
LIFE SCIENCES  
BHUBANESWAR

DAY 3: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=YVG4WI0GQKY](https://www.youtube.com/watch?v=YVG4WI0GQKY)

GENETIC AND  
IMMUNOLOGICAL  
ASPECTS OF  
COVID19

13 SEPTEMBER 2020  
(SUNDAY)  
4 P.M. IST



PARTNERS FOR VIRTUAL SERIES ON HEALTH AND DISEASE: CONTEMPORARY CONCERNS

RAVENSHAW UNIVERSITY, INSTITUTE OF LIFE SCIENCES, NASI, INDIAN ACADEMY OF NEUROSCIENCES



PROF. THEODORE PRICE  
CENTRE FOR  
ADVANCED PAIN STUDIES  
UNIVERSITY OF TEXAS AT DALLAS,  
USA

IN CONVERSATION WITH  
DR. MUNMUN CHATTOPADHYAY



**TED'S JOURNEY ON  
SCIENCE OF  
CHRONIC PAIN  
FROM BENCH  
TO BEDSIDE**

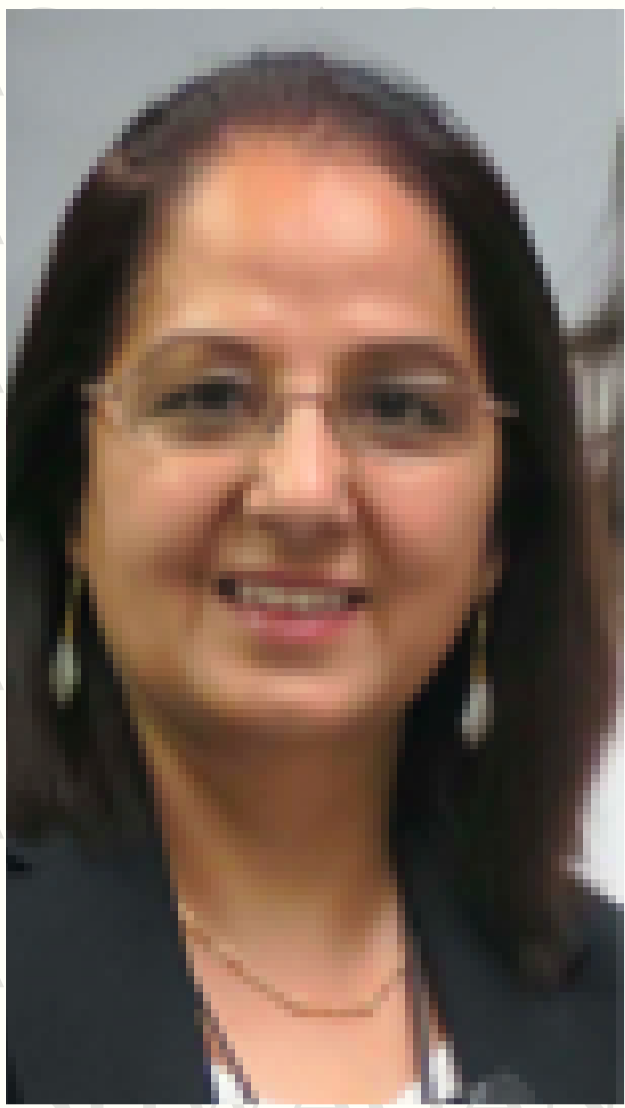
14 SEPTEMBER 2020  
(MONDAY)  
7 P.M. IST

DAY 4: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=MPJEPZPKYRO](https://www.youtube.com/watch?v=MPJEPZPKYRO)



PARTNERS FOR VIRTUAL SERIES ON HEALTH AND DISEASE: CONTEMPORARY CONCERNS

RAVENSHAW UNIVERSITY, INSTITUTE OF LIFE SCIENCES, NASI, INDIAN ACADEMY OF NEUROSCIENCES



**PROF. RENU WADHWA**  
**NATIONAL INSTITUTE OF**  
**ADVANCED INDUSTRIAL**  
**SCIENCE AND TECHNOLOGY**  
**TSUKUBA, JAPAN**

**ASHWAGANDHA**  
**FOR STRESS, HEALTH AND**  
**COVID19 MANAGEMENT**

**15 SEPTEMBER 2020**  
**(TUESDAY)**  
**4 P.M. IST**

**DAY 5: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=W8XWWP9TQ4G](https://www.youtube.com/watch?v=W8XWWP9TQ4G)**



**PARTNERS FOR VIRTUAL SERIES ON HEALTH AND DISEASE: CONTEMPORARY CONCERNS**

**RAVENSHAW UNIVERSITY, INSTITUTE OF LIFE SCIENCES, NASI, INDIAN ACADEMY OF NEUROSCIENCES**

**DR. MUNMUN  
CHATTOPADHYAY**  
PAUL L. FOSTER SCHOOL OF  
MEDICINE  
COE IN DIABETES AND  
METABOLISM  
HEALTH SCIENCES CENTRE  
TEXAS TECH UNIVERSITY, EL PASO,  
USA



CAN WE PUT A  
BREAK ON  
DIABETIC  
COMPLICATIONS?

**16 SEPTEMBER 2020  
(WEDNESDAY)  
7 P.M. IST**

**DAY 6: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=NISF3ATJIQU](https://www.youtube.com/watch?v=NISF3ATJIQU)**



**PARTNERS FOR VIRTUAL SERIES ON HEALTH AND DISEASE: CONTEMPORARY CONCERNS**

**RAVENSHAW UNIVERSITY, INSTITUTE OF LIFE SCIENCES, NASI, INDIAN ACADEMY OF NEUROSCIENCES**



**DR. PUNIT PRASAD**  
**INSTITUTE OF**  
**LIFE SCIENCES**  
**BHUBANESWAR, INDIA**

**DAY 7: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=OM9PYIR43WA](https://www.youtube.com/watch?v=OM9PYIR43WA)**

**GUT**  
**MICROBIOME**  
**& COVID19**

**17 SEPTEMBER 2020**

**(THURSDAY)**

**4 P.M. IST**



**PARTNERS FOR VIRTUAL SERIES ON HEALTH AND DISEASE: CONTEMPORARY CONCERNS**  
**RAVENSHAW UNIVERSITY, INSTITUTE OF LIFE SCIENCES, NASI, INDIAN ACADEMY OF NEUROSCIENCES**

**PROF. N. K. MEHRA**

**FORMER DEAN AND**

**NATIONAL CHAIR**

**ALL INDIA INSTITUTE OF MEDICAL**

**SCIENCES**

**NEW DELHI**



**HOST  
IMMUNITY  
AND  
COVID19**

**18 SEP 2020**

**(FRIDAY)**

**4 P.M. IST**

**DAY 8: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=A6BWS9USKGQ](https://www.youtube.com/watch?v=A6BWS9USKGQ)**



**PARTNERS FOR VIRTUAL SERIES ON HEALTH AND DISEASE: CONTEMPORARY CONCERNS**

**RAVENSHAW UNIVERSITY, INSTITUTE OF LIFE SCIENCES, NASI, INDIAN ACADEMY OF NEUROSCIENCES**



**PROF. AJAY PARIDA**  
**DIRECTOR**  
**INSTITUTE OF LIFE**  
**SCIENCES**  
**BHUBANESWAR**

DAY 9: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=2WMTMI-9DYA](https://www.youtube.com/watch?v=2WMTMI-9DYA)

**SCIENTIFIC**  
**MANAGEMENT**  
**OF COVID19**  
**PANDEMIC**

**19 SEPTEMBER 2020**  
**(SATURDAY)**  
**4 P.M. IST**



**PARTNERS FOR VIRTUAL SERIES ON HEALTH AND DISEASE: CONTEMPORARY CONCERNS**  
**RAVENSHAW UNIVERSITY, INSTITUTE OF LIFE SCIENCES, NASI, INDIAN ACADEMY OF NEUROSCIENCES**



PROF. U. C. SRIVASTAVA  
NATIONAL ACADEMY  
OF SCIENCES (INDIA)  
ALLAHABAD

LIVING HEALTHY  
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HEALTHY  
LIVING

20 SEP 2020  
(SUNDAY)  
4 P.M. IST

DAY 10: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=VIWY97EByZM](https://www.youtube.com/watch?v=VIWY97EByZM)



PARTNERS FOR VIRTUAL SERIES ON HEALTH AND DISEASE: CONTEMPORARY CONCERNS  
RAVENSHAW UNIVERSITY, INSTITUTE OF LIFE SCIENCES, NASI, INDIAN ACADEMY OF NEUROSCIENCES

PROF. MITUL MEHTA  
INSTITUTE OF  
PSYCHIATRY,  
PSYCHOLOGY AND  
NEUROSCIENCE  
KING'S COLLEGE,  
LONDON, UK



DAY 11: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=UNQGWUYFLMQ](https://www.youtube.com/watch?v=UNQGWUYFLMQ)

THE EFFECTS OF EARLY  
INSTITUTIONAL  
DEPRIVATION ON  
BRAIN STRUCTURE AND  
FUNCTION IN EARLY  
ADULTHOOD

21 SEPTEMBER 2020

(MONDAY)

3.30 P.M. IST



PARTNERS FOR VIRTUAL SERIES ON HEALTH AND DISEASE: CONTEMPORARY CONCERNS

RAVENSHAW UNIVERSITY, INSTITUTE OF LIFE SCIENCES, NASI, INDIAN ACADEMY OF NEUROSCIENCES





# MODERATORS

PROF. LUNA SAMANTA



DR. DIPTI RAUT



DR. RAKESH KUMAR

# ORGANISER

CENTRE FOR EXCELLENCE IN ENVIRONMENT AND PUBLIC HEALTH  
RAVENSHAW UNIVERSITY



DAY 1: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=9A1HT6L04A8](https://www.youtube.com/watch?v=9A1HT6L04A8)

DAY 2: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=JFG7BG6CLRQ](https://www.youtube.com/watch?v=JFG7BG6CLRQ)

DAY 3: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=YVG4WI0GQKY](https://www.youtube.com/watch?v=YVG4WI0GQKY)

DAY 4: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=MPJEPZPKYRO](https://www.youtube.com/watch?v=MPJEPZPKYRO)

DAY 5: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=W8XWWP9TQ4G](https://www.youtube.com/watch?v=W8XWWP9TQ4G)

DAY 6: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=NISF3ATJIQU](https://www.youtube.com/watch?v=NISF3ATJIQU)

DAY 7: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=OM9PYIR43WA](https://www.youtube.com/watch?v=OM9PYIR43WA)

DAY 8: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=A6BWS9USKGQ](https://www.youtube.com/watch?v=A6BWS9USKGQ)

DAY 9: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=2WMTMI-9DYA](https://www.youtube.com/watch?v=2WMTMI-9DYA)

DAY 10: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=VIWY97EBYZM](https://www.youtube.com/watch?v=VIWY97EBYZM)

DAY 11: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=UNQGWUYFLMQ](https://www.youtube.com/watch?v=UNQGWUYFLMQ)



[HTTPS://WWW.FACEBOOK.COM/MYRAVENSHAW/VIDEOS/346270313214476/](https://www.facebook.com/myravenshaw/videos/346270313214476/)



PARTNERS FOR VIRTUAL SERIES ON HEALTH AND DISEASE: CONTEMPORARY CONCERNS

RAVENSHAW UNIVERSITY, INSTITUTE OF LIFE SCIENCES, NASI, INDIAN ACADEMY OF NEUROSCIENCES

Rudra deo Tripathi

1:46 PM (1  
hour ago)

to Tushar, acsrivastava\_dr, C, Rakesh, rakesh, aksinha8, amita, amiyapbhaduri, Asha, ashok, bndhawan, Bhola, BP, cipisharma, khetrapal, ddpatra, ddpatra\_cimap, LuckDevikaNag, Dr, Director, director, dr\_nigam17, dr\_nigam19, drbrahm, Kalpana, drpkmurthy, drspradhan, UK, ukmisra, Gp, gangcbmr, Ganesh, jighosh, jk\_ghosh, kambojvp, Ved, VED, U, lavania, madhu\_dikshit, madhudikshit, Mukul, mukul, Mohan, mpverma50, nitya, Dr, Prahlad, SETH, pcsrivastava31, Prabodh, Director, CEO, PURSHOTTAM, qamar\_15, Ram, rajaroy\_cdri, PV, Rashmi, rastogiak, Anil, rcs\_bits, rcsobti, vc, msodha, rkapoor, rprastogi, Ram, Shailja, shailjacdri, shajra, saumen.hajra, shally, Shally, Kamla, Man, MAN, SK, SUNIL, skjainbotanist, Soniya, Soniya, sri\_scs, s.banerjee, Director, director, suprabhatray, Anju, Umesh, chaturvediuc, D, Dalip, Suman, Sanjay, Sanjay, sanyal, CDRI,, Samir, Samir, saman\_habib, anuradha\_dube, alok.kalra, vkkhanna1, Vinay, CDRI,, Lucknow, rspleducation, Pradeep, drs, sema, CDRI,, Niraj, me, Pramod, Pramod, Veena, Dr, Suchitra, Suchitra, Saroj, SK, dhawanalok, Rudra, Raj, Science, myedrsaxena, paramjitkhurana, Satya

Dear NASI Fellows & Members,

We are pleased to inform you that National Academy of Science, India (NASI) Lucknow Chapter and Regional Science City are jointly organizing a webinar entitled “**COVID-19: IMMUNITY IS THE BEST VACCINE**” by Prof. Surya Kant, Head, Respiratory Medicine of King George Medical University, Lucknow on September 4, 2020 (Friday) at 4.00 p.m. online (<https://meet.google.com/nop-wmau-txd>). Registration form is also available online (<https://forms.gle/nhLYv8uATscUkqnu6>).

Please find attached herewith the invitation letter and detailed Programme. The invitation letter also contains the above web links.

On behalf of Prof. Pramod Tandon, Chairman, NASI Lucknow Chapter we are pleased to invite you all to join the program online **on 04 September 2020 (Friday) at 4.00 pm.**

Thanking you for your co-operation.

Stay safe and blessed.

Best kind regards,

R.D. Tripathi

Advisor, NASI Lucknow Chapter

Nidhi Chandhoke

to NASI, me, mittaljp2003@yahoo.co.in, mittaljp@barc.gov.in, ced.proc.a.nasi@gmail.com, amitghosh24@yahoo.com, Amit, govil@tifr.res.in, Pavitra, pavitra.nasi@rediffmail.com, drvridhi.nasi@gmail.com, Shilpa, Suvira

Dear Neeraj ji,  
Dear Esteemed Editor-in-Chiefs,  
Dear Academy colleagues,  
Hope you all are doing well!

Please find enclosed details of online webinar organised by Springer Nature in collaboration with 'Delcon, DBT e-library Consortium members institutions'. The topic of the webinar is **Abstracting & Indexing – how to get indexed and how to increase the research impact**. Ms. Sonal Shukla, Head of Abstracting & Indexing at Springer Nature will deliver the session.

The invitation is attached. Below are the details.

Registration details are provided below. Once registered, email will be automatically received in your inbox to accept the same.

**Topic** - Abstracting & Indexing – how to get indexed and how to increase the research impact

**Date and Time** - 9th Sep 2020, 4.15 PM - 6.15 PM IST

**Speaker** - Ms. Sonal Shukla, Head - Abstracting and Indexing, Springer Nature, New York

**Link to Register** - <https://attendee.gotowebinar.com/register/7517860586539207950>



**SPRINGER NATURE**

**SPRINGER NATURE**

in collaboration with

**DeLCON**  
DBT e-LIBRARY CONSORTIUM

is organizing a three-webinar series on the theme

**ALL ABOUT SCIENTIFIC PUBLISHING - TRENDS,  
NUANCES, TOOLS, ETHICS ETC!**

Springer Nature global publishing team will take up all the sessions.

**Register for the second webinar scheduled on 9<sup>th</sup> Sep 2020**

Webinar II

**Topic:** **Abstracting & Indexing – how to get indexed and how to increase the research impact**

**Date:** 9<sup>th</sup> Sep 2020, Wednesday | **Time:** 4.15 – 6.15 PM IST

**Link to Register:** <https://attendee.gotowebinar.com/register/7517860586539207950>

**राष्ट्रीय विज्ञान अकादमी, भारत द्वारा  
शिक्षक दिवस के तत्वाधान में आनलाइन व्याख्यान का आयोजन**

राष्ट्रीय विज्ञान अकादमी, भारत द्वारा शिक्षक दिवस के तत्वाधान में आज दिनांक 5 सितम्बर, 2020 को राजकीय बालिका विद्यालय, सिविल लाइन्स, प्रयागराज में एक व्याख्यान का आयोजन किया गया।

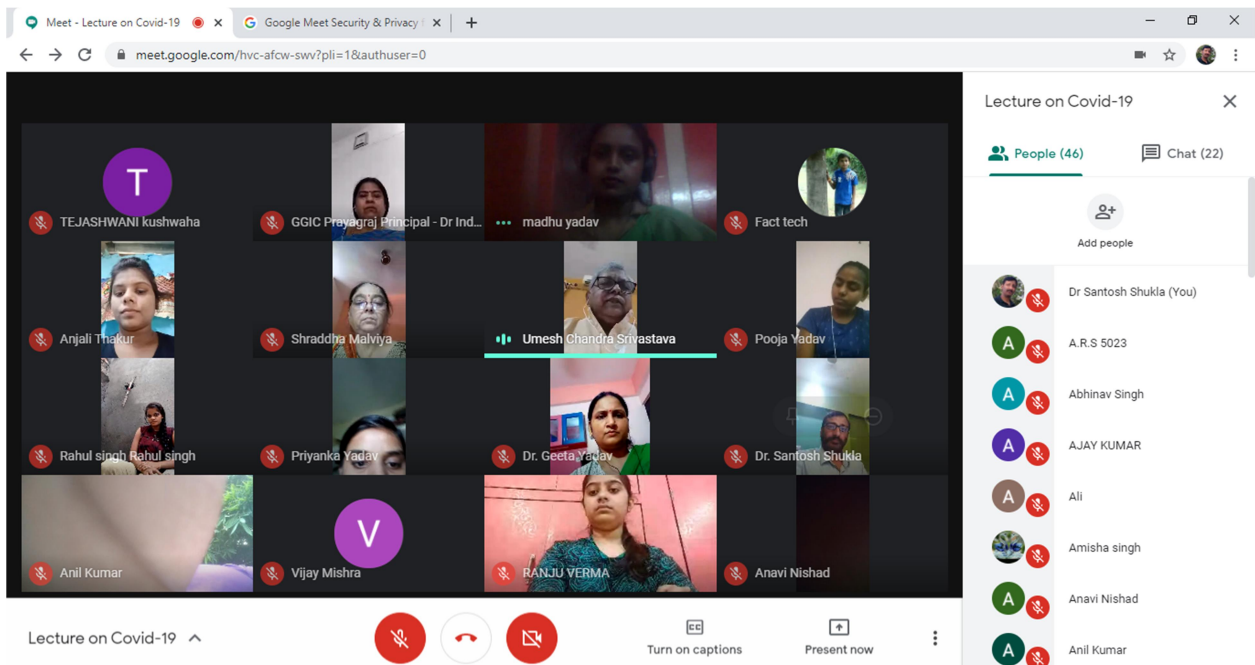
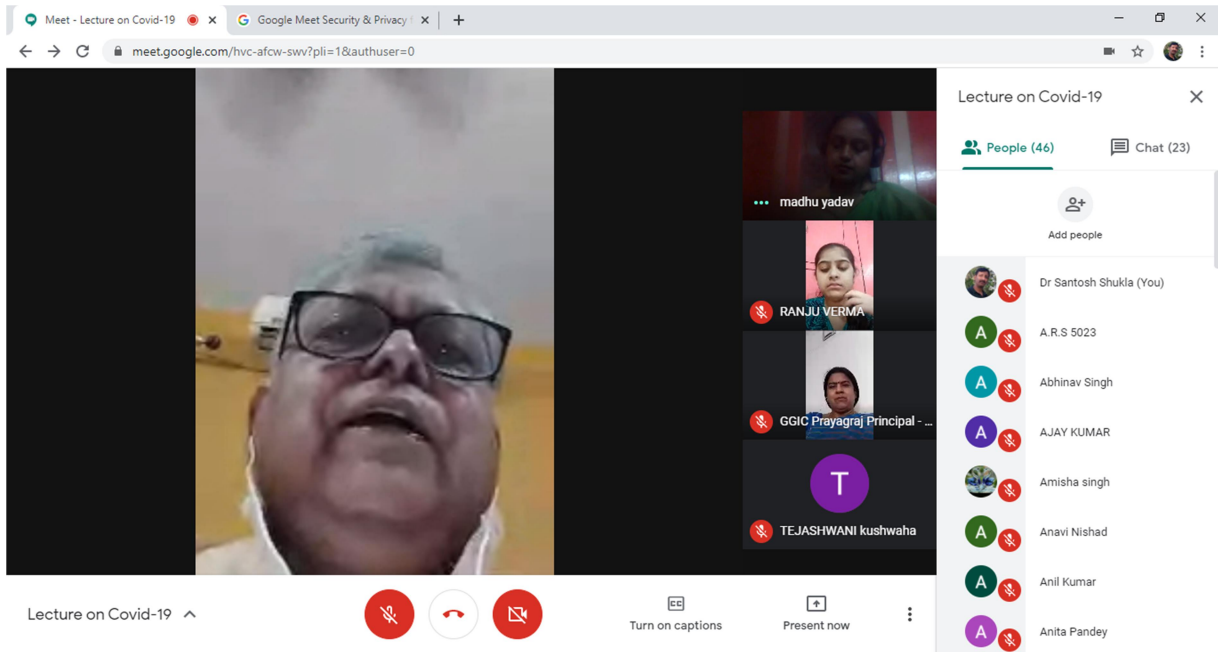
कार्यक्रम के मुख्य वक्ता इलाहाबाद विश्वविद्यालय के जीव विज्ञान विभाग के भूतपूर्व प्रोफेसर व नासी के कोषाध्यक्ष प्रो.यू.सी. श्रीवास्तव थे। कार्यक्रम में अतिथियों का स्वागत विद्यालय की प्रधानाचार्या डा.इन्दू सिंह ने किया।

प्रो.यू.सी.श्रीवास्तव ने कोरोना महामारी विषय में जानकारी देते हुए बताया कि यह बيمारी कोविड नामक वायरस के कारण होती है। यह अतिसूक्ष्म वाइरस संक्रमित व्यक्ति द्वारा कपडो,धातु,वायु,जल तथा अन्य जीवित अथवा मृत चीजों के माध्यम से हम सभी में फैलता है।

प्रो. श्रीवास्तव ने कोरोना से बचने के लिए शरीर की रोग प्रतिरोधक क्षमता बढ़ाने वाले खाद्य पदार्थ को अपने दैनिक भोजन में शामिल करने की सलाह दी। उन्होंने कहा कि फल, सब्जियों के अतिरिक्त मसालों का सही अथवा अल्प मात्रा में उपयोग हमारी प्रतिरक्षा प्रणाली को मजबूत करता है। किन्तु इनका अधिक मात्रा में उपयोग हमारे शरीर को अत्यधिक हानि भी पहुँचाता है। लहसुन, काला जीरा, हींग,हल्दी, अश्वगंधा,सौफ,ग्रीन टी आदि के लाभदायक गुणों को बताते हुए प्रो. श्रीवास्तव ने इनको अधिक

मात्रा में उपयोग करने से शरीर में होने वाले हानिकारक प्रभावों के बारे में भी बताया।

कार्यक्रम का संचालन डा.मधु यादव ने किया। कार्यक्रम में डा. गीता यादव, श्रीमती श्रद्धा मालविया, श्रीमती अनीता पाण्डेय तथा विद्यालय के अन्य शिक्षक के साथ 60 से अधिक छात्राओं ने भाग लिया।



# राष्ट्रीय विज्ञान अकादमी, भारत

- (i) हिंदी पखवाड़े का शुभारंभ – सोमवार 14/09/2020 को सायं 4:00 बजे हिंदी पखवाड़े का शुभारंभ होगा। इस अवसर पर मुख्य अतिथि डा० पृथ्वी नाथ पाण्डेय जी द्वारा व्याख्यान दिया जायेगा।
- (ii) प्रतियोगितायें–
- बुद्धवार 16/09/2020 को सायं 4 से 5 के मध्य व्यक्तिगत अनुभव पर आधारित कहानी लेखन प्रतियोगिता
  - शुक्रवार 18/09/2020 को सायं 4 से 5 के मध्य शब्दावली प्रतियोगिता
  - सोमवार 21/09/2020 को सायं 4 से 5 के मध्य वाद–विवाद प्रतियोगिता (वाद–विवाद का विषय दिनांक 17/09/2020 की दोपहर में डीएसटी द्वारा पता चलेगा)
  - मंगलवार 22/09/2020 को सायं 5 से 6 के मध्य हिंदी टंकण प्रतियोगिता
  - बुद्धवार 23/09/2020 को सायं 4 से 5 के मध्य “प्राकृतिक आपदा” विषय पर हिंदी निबन्ध लेखन प्रतियोगिता
  - गुरुवार 24/09/2020 को सायं 4 से 5 के मध्य “कोविड 19” विषय पर अभिभाषण प्रतियोगिता
  - शुक्रवार 25/09/2020 को सायं 3:30 से 4:30 के मध्य 10 पंक्तियों का कविता पाठ प्रतियोगिता एवं डॉ० संतोष कु० शुक्ला, सहायक कार्यकारी सचिव द्वारा “प्राचीन भारतीय जीवन पद्धति – पुर्नजागरण” विषय पर व्याख्यान (कार्यशाला)।
- (iii) हिन्दी पुस्तकों की प्रदर्शनी – 28/09/2020 को प्रातः 10.00 बजे से सायं 4.00 तक।
- (iv) हिन्दी पखवाड़ा का समापन समारोह सोमवार 28/09/2020 को अपराह्न 4:00 बजे से।

# राष्ट्रीय विज्ञान अकादमी, भारत (नासी)

5, लाजपतराय रोड़, प्रयागराज

अध्यक्ष, राजभाषा कार्यान्वयन समिति, नासी द्वारा समर्पित कविताएं

सोचा चलो कुछ नया करें  
 कुछ फुर्सत मिली है वर्षों बाद  
 लगा, तिनकों को जोड़ने  
 क्यों न एक घर ही बना लूं  
 पर बुनियाद का क्या,  
 वो तो खोखली पड़ी है  
 अच्छा फिर क्यों न इसे  
 प्यार से सींच दूं जड़ तक  
 पर पहले की गर्मजोशी कहां!!  
 पर बिना इन जज्बातों के, जब  
 दीवार खड़ी कर दी, तो पता चला  
 मानवता ही कैद हो गई, और हम तो  
 बाहर रह गये, फिर लगा हम तो  
 कुछ नया कर गये इस बार।

\*\*\*\*\*

न मौलवी, न पादरी, न पुजारी,  
 खुद जिंदगी से बड़ा कोई नहीं  
 जो जीना सिखा दे।  
 जिन्दगी की जद्दोजहद ही है  
 हमें जीने का ढंग सिखाती,  
 वर्ना किताबों की लकीरों को  
 पढ़ किसने है सफलता पाई,  
 जिंदगी जीते हैं वही, जिन्होंने  
 तूफां से लड़ने की पुरजोर कोशिशें की,  
 और लहरों से विपरीत है  
 कशती अपनी चलाई

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माँ, अपने आप में सम्पूर्ण बोध  
पूर्ण काव्य, ममता का कोष,  
हमारे अस्तित्व का आधार है।  
दूर रहते हुए ममत्व की  
गगरी से छलकता हुआ प्यार है।

हम समझे या न समझे  
वो समझती हमारी पुकार है,  
हमें पुचकारती कभी फटकारती  
हमें है सुसंस्कृत बनाती, वही तो  
हमारी जिन्दगी की अलंकार है.

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रफ्तार इतनी तेज थी कि  
मंजिल कब पीछे छूट गयी  
पता ही नहीं चल सका,  
जब पीछे मुड़ कर देखा  
धुंध में अपनों के निशां  
बदले से लगे वो इंसान,  
लगा फिर तेज चलने से  
नहीं बनती अपनी पहचान  
कितनों को साथ जोड़ा है किसी ने  
कहते हैं वही उसकी कामयाबी की दास्ताँ।

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कैसे कहूँ कि इस रात की  
सुबह हो गयी,  
अभी खुमारी तो गयी नहीं  
बीते अहसासों की,  
और उम्मीदों की किरणों का  
स्पर्श पलकों की ओस पर  
टकराना भी तो बाकी है.

लेकिन लगता है जैसे कि  
सुबह हो गयी, क्योंकि  
समय ने करवटे हैं ले ली,  
ताजी हवाओं के झोके हैं  
टकरा रहे, और  
आशाओं की चहचहाट ने  
नींद से है जगा दिया

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निशब्द भी एक प्रवाह है  
सशक्त अभिव्यक्ति का,  
बस निर्मल सोच की  
अंतस में स्थापना हो,

कोई मलिन न कर जाये  
तेरी आत्मा, मन के प्रहरी  
को सजग रख, ध्यान में  
उसका ही बस हो स्वरूप  
स्फुरित होंगे फिर शब्द, तेरी  
प्रकृति के अनुरूप  
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इस दुनिया से कोई कुछ लेकर जाता नहीं,  
रूपया पैसा तो हाथों का मैल है,  
ऐसा कह गये सब लोग पुराने।  
तुम्हारे द्वारा की गयी नेकी और भलाई  
ही तय करती तेरे पास-फेल का खेल है।

तो दोस्त ऐसे बना जो स्व से कम  
स्वजनों से ज्यादा जुड़े,  
जिन्हें दरियादिली से प्यार हो  
दौलत जिनके लिए बेकार हो, और  
मिटा सकने की खुद को हो हिम्मत  
जिसमें दुनियां के लिए, ऐसे ख्यालातों  
पे उन्हें अहंकार हों।  
\*\*\*\*\*

कभी तो लगता है कि हम  
उसके बहुत करीब हैं, पर  
दूसरे ही पल वो हमें अपने से  
दूर होने का एहसास  
करा देता है,

फिर हमें लगता है कि इबादत  
में कमी रह गयी है हमारे, वर्ना  
उसकी झोली में सौगातों की कमी कहाँ!!

पर क्यों बार बार वो लेता है हमारे  
इम्तहां, क्या अपने बंदों पर खुद  
खुदा को है भरोसा नहीं?

फिर ऐसी खुदाई का हम क्या करें  
जहाँ बंदगी की अदायगी नहीं  
कोई पहुँचा दे हमारी ये दरखास्त  
कि दूरी अब नहीं होती हमें बरदास्त.  
\*\*\*\*\*

उपासना के तरीके है कई,  
भक्ति में डूबने से लेकर  
शक्ति की आराधना तक,  
लीन होना ध्यान में उसके  
या समाहित करना वजूद को  
या फिर प्रेम का अतिरेक हो,  
पर, इन सबसे अलग है एक  
और तरीका, कि उसे मजबूर कर  
देना, कि वो खुद तुममें समा जाये।

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प्रार्थना है पर विश्वास नहीं  
नजदीकियां है पर अहसास नहीं  
नगमें है पर सुर का समास नहीं  
जीवन है पर जीने का उल्लास नहीं।

पर फिर भी जीते जा रहे हैं  
इस उम्मीद पर, कि  
हमारी प्रार्थना होगी कुबूल।

भेजा उसी ने विश्वास से,  
दूरियां मिटती है प्रयास से,  
सुर सजते हैं रियाज से, और  
जीना कहते हैं हम उसे जो  
दूसरों की जिंदगी से ले गम को बटोर,  
हंस सके अट्टहास से।

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संग बंधना संबंधों की अभिव्यक्ति है  
तो हृदयगत स्पंदन भावनाओं की,  
जिस्मानी तौर पर दोनो की स्वीकृति  
पूर्णता को देती है भावाभिव्यक्ति

फिर भी नैसर्गिक प्यार को समझाना  
भौतिकता से पृथक वो बोध है, जो  
निराकार को बना सकता है साकार,  
सपनों की अनुभूति से भी ऊपर है  
इक दुनिया, जहाँ नहीं है कोई अहंकार

इसी की खोज करती है जब बेचैन,  
भाव बंध नहीं पाते है किनारों में  
मन उतर जाता है आत्मा की  
गहराइयों में,  
और तलाश की छटपटाहट करती है  
मजबूर मुझे लिखने को नया कुछ ऐसा  
कि तोड़ बंधनों को उभर कर व्यक्त  
हो उठती है —भावाभिव्यक्ति

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गुरु शिष्य की परंपरा है भारत  
की पहचान, इस पवित्र बंधन का  
देश के विकास में है सदियों से महति योगदान।

माता पिता से भी ज्यादा होता था  
इस देश में गुरुओं का सम्मान, दोनों  
पक्ष निभाते थे संबंधों की मर्यादा, देते थे राष्ट्र विकास में अपने योगदान।

रविन्द्रनाथ हों या प्रफुल्लचन्द्र, साहा,  
विवेकानन्द हों या हों सी०वी० रमन, फिर  
जब याद आते है हमें गुरुओं में राधाकृष्णन, हम भूल नहीं पाते हैं  
शिष्यों में राजेन्द्र प्रसाद सा विलक्षण।

पर कहाँ चले गये इस महान परंपरा  
के धरोहर, संयुक्त परिवार की भांति  
धीरे धीरे सूखता गया क्यों ये पवित्र  
संबंधों का जीवनदायी सरोवर।

क्यों न कुछ मंथन करें आज कि  
किसकी नजर लग गयी इस वृहत्  
परंपरा के अद्भुत विस्तार पर, क्यों  
खत्म हो रही संस्कृति की पहचान हमारी, क्या नहीं बनती जवाबदेही  
कोई समाज के ठेकेदारों पर?????

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समस्याओं का समाधान निहित होता है  
उनके श्रोत, संचरण एवं सम्मान में,  
कभी कभी लघु समस्या वृहद का  
रूप धारण कर लेती है, तो कभी  
व्यापक बन जाती है लौकिक।

कभी तो हमारा नजरिया गलत होता है  
तो कभी अंदाजे नजरिया, कभी  
हम होते ही नहीं हैं समस्या में तो  
कभी समस्या ही नहीं होती हमारी।

पर हर समस्या का उसके वजूद से  
है रिश्ता अनोखा, तो कभी वजूद  
ही लगता है समस्या सरीखा।

पर हर समस्या की जड़ में छुपे  
होते हैं कई राज, तो कभी समस्या  
बना देती है किसी को हमराज।

तो समस्या ये है कि समस्या क्या है  
तो पते की बात है कि जो न समझ  
सके, वो तुम्हारी समस्या हैं, और जो  
समझ के भी नासमझ है, वो है भारी समस्या।

पर समाधान सिर्फ हैं, 'उसके' पास,  
जो न समझे इस बात को,  
मुश्किले हालात बन जाती हैं  
हमारी समस्या।

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दोस्त होते हैं जरूरी जिंदगी के लिए  
गर्मों को बाटने का शगल आता है उन्हें  
तो खुशियों का मजा आता है साथ उनके,  
और दुखी कर जाता है सबब बिछड़ने का,  
हंसी दोस्ती के लिए।

ऐ दोस्त आ जरा थोड़ी देर साथ बैठ लें  
भुला कर सारे गिले शिकवे पुराने,  
बहुत सी खुशगवार यादें हैं दोस्त  
जिन्हें जिंदगी की जश्न में हैं शामिल करना,  
जो तेरे बिना लगता नहीं अब मुमकिन मुझे।

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कई बार लगता है मैं किसी दायरे  
के अंदर खड़ा हूँ, तो कभी दायरा  
खुद मुझे अपने में समा लेता है।

पर मुश्किल होता है पता लगाना  
कि दायरे ने विस्तार कर लिया है  
मुझे निगल, या मैंने खुद सीमाओं  
का कर दिया है अन्जाना उल्लंघन

एक अजीब अनुभूति का भान  
होता है दायरे से बाहर निकल,  
जब अनन्त इच्छाओं के भंवर से  
मन स्वच्छंद होने को होता है विकल

रक्ताभ किरणों को बेध, इन्द्र धनुष सी  
छटा, पूरे वजूद पर हावी हो जाती है,  
मन दूर नभ में जंगल में चौकड़ी भरते  
हिरन के समान वेग से उफनता है, और  
फिर मैं अपने आप को एक नये दायरे खड़ा पाता हूँ

एक दायरे से दूसरे दायरे का सफर ही  
तो कहीं जिन्दगी का नाम नहीं, जहाँ  
विस्तार बदलते हैं, पर अहसास नहीं,  
सिर्फ अंत ही खत्म करता है दायरों को  
तो क्यों न हम अंत में विलीन हो जाएं  
और अनंत का हिस्सा बन  
दायरों को निगल जाएं

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बया के घोसले और जीने के बहाने,  
एक समान होते हैं जिंदगी के ताने बाने,  
तिनके तिनके कर जुड़ते हैं,  
फिर हैं आपस में उलझतें जाते,

समाने का रास्ता होता है सिर्फ एक  
निकलना होता है फिर मुश्किल,  
पर सुकून मिलता है घोसले में,  
विश्राम के क्षण भी मिलते हैं वही।

पर कुछ ही दिनों में सीख जाते हैं  
उड़ना, और छोड़ जाते हैं घोसले  
खाली रह जाते हैं फिर यादों को  
समेटे, जिंदगी की दास्ताँ बयां करते,  
किसी यादगार स्वरूप बया के घोसले।

पर इस बीच सैकड़ों उडान भरती है बया,  
जिंदगी को सर्जोती, और बीत जाता है  
समय का सफर उसका, रह जाती है  
खाली घोसले की अद्भुत कारीगरी,  
फिर शुरू होती है उमंगो की नई उडान,  
नये नीड, और अलग पहचान

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न धन्यवाद  
14/9/2020  
Executive Secretary  
The National Academy of Sciences, India  
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REVIEW

Open Access



# Mutagenic, Genotoxic and Immunomodulatory effects of Hydroxychloroquine and Chloroquine: a review to evaluate its potential to use as a prophylactic drug against COVID-19

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## Abstract

Hydroxychloroquine (HCQ) and Chloroquine (CQ) are two anti-malarial drugs that are now being extensively used by front-line healthcare workers and other common people as a prophylactic drug against the Corona Virus Disease – 19 (COVID-19) in India and as well as in many parts of the world. While only a few in vitro studies have pointed to some efficacy of these drugs as a prophylactic against COVID-19, to date, there are no clinical studies that have established any clinical efficacy of these drugs as a prophylactic. These drugs are commonly used for the treatment of Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus (SLE) because of its immunomodulatory effects. Previously, we have evaluated the genetic toxicology of different drugs and chemicals including antimalarial drug CQ both in vitro and in vivo. Thus, we recognize the need to critically review the mutagenic, genotoxic, and immunomodulatory effects of these drugs, to find out whether it is safe to use as a prophylactic drug against COVID-19. Existing literature suggests that CQ can induce mutagenic and genotoxic effects in multiple test systems and both the drugs have immunomodulatory effects. There was no data available to evaluate the mutagenicity and genotoxicity for HCQ. However, during metabolism about 60% of both the drugs remain unchanged and about 40% of the drugs are metabolized into two metabolites, desethylchloroquine and bisdesethylchloroquine by the action of the cytochrome P450 (CYP) enzymes in the liver. Both HCQ and CQ are immunomodulatory drugs and have the potential to suppress normal immune system activation. In this review, we have elucidated the mechanism of immunomodulation by both HCQ and CQ and highlighted the mutagenic and genotoxic effects from the available literature. This article is written with the sole objective that the reader will be able to recognize the adverse effects of these drugs when consumed by healthy individuals as a prophylactic. Current literature indicates that healthy individuals should refrain from the use of these drugs until further investigation.

**Keywords:** Hydroxychloroquine, Chloroquine, Mutagenicity, Genotoxicity, Immunomodulation, prophylactic use, COVID-19

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## Background

The novel Severe Acute Respiratory Syndrome Corona Virus 2 (COVID-19) pandemic has now become a nightmare throughout the world. This pandemic has caused serious health crisis not only among the poor nations but also across the world's advanced countries. Researches all across the globe are trying to find an effective drug that would show promising results to prevent or to treat and control the COVID-19. Recently, scientists have pointed out that the novel COVID-19 was transmissible in aerosol [1]. Thus, it puts the healthcare workers at risk who works in close proximity with COVID-19 patients. This demanded the need for a prophylactic drug against COVID-19 amongst healthcare workers.

Hydroxychloroquine (HCQ) and Chloroquine (CQ) are two antimalarial drugs that remain the universally accepted drugs for the treatment of Rheumatoid arthritis and Systemic Lupus Erythematosus [2–5]. These two drugs have shown some results in inhibiting the novel COVID-19 in vitro [6, 7]. A recent study demonstrated that certain cell types when treated with HCQ or CQ and then exposed to the novel COVID-19 strain, presented antiviral activity and that HCQ was more potent than CQ [8]. On the other hand, another in vitro study found out that CQ was potent than HCQ at all four different multiplicities of infection to act as antiviral when exposed to COVID-19 post-incubation with these drugs [7]. Additionally, CQ was able to act as anti-viral both pre and post-infection against the COVID-19 in vitro [6]. These findings may have led to the proposal and optimistic use of HCQ and CQ as prophylactics.

Yet historically, we have seen that in vitro studies don't always translate in vivo or human subjects. For instance, despite the strong evidence of CQ as a prophylactic against influenza A and B in vitro, CQ was not effective to prevent either influenza A or B in the human subjects [9]. Rather, dizziness, nausea, and diarrhea were more common in the CQ group compared to the control (placebo) group. Another study showed that Ebola virus replication was successfully inhibited in vitro by CQ, however, it failed in guinea pig models in vivo [10]. Yet another study showed CQ enhanced Chikungunya virus replication in vivo when in fact CQ had been shown to have an effective inhibitory effect in vitro [11]. Thus, to date, with the lack of any controlled clinical trials, the clinical effectiveness of these drugs as prophylactics against COVID-19 in vivo remains unanswered.

Like any other drugs, these drugs also comes with certain risks. So, we mustn't overlook the toxicological risks while making a rational decision of using these drugs as prophylactics. Previously, we have extensively reviewed and evaluated the genetic toxicology of antimalarial, analgesics, antipyretic drugs including CQ [12–14]. CQ and HCQ are both water-soluble drugs that are absorbed

rapidly in the gut and have a long elimination half-life in the plasma of 900 and 1300 h respectively [15]. Multiple authors, including us, have reported in vitro and in vivo evidence of CQ-induced genotoxicity in the mammalian system. These drugs also possess immunomodulatory roles that have the potential to suppress the activation of the immune system in healthy individuals [16–18]. Considering the current situation, there is an urgent need for clinical studies to evaluate the clinical efficacy of HCQ and CQ as a prophylactic drug against COVID-19. We have not included the long-term side effects of these drugs since it is unlikely that prophylactic use of these drugs would be for a long time. Here in this review, we mainly aim to critically review and discuss the mutagenic, genotoxic, and immunomodulatory aspects of HCQ and CQ using the available literature.

## Review

### Mutagenic and genotoxic effect

Table 1 summarizes the mutagenic, genotoxic and carcinogenic effects of CQ in multiple test systems. It is interesting to note that there is almost no report on the mutagenic and genotoxic effects of HCQ both in vitro and in vivo. However, both HCQ and CQ have a very similar, flat aromatic core structure with a basic side chain. The only difference is the presence of an additional hydroxyl (–OH) group in HCQ. During metabolism, about 60% of both the drugs remain unchanged and about 40% of both the drugs are metabolized into two common metabolites desethylchloroquine and bisdesethylchloroquine by the action of the cytochrome P450 (CYP) enzymes in the liver [46]. Despite CQ being recognized as more toxic than HCQ, the tissue and plasma distribution of these two drugs were reported to be nearly identical when administered in equivalent dosage in humans [46]. Figure 1 shows the comparison of structures and metabolism of HCQ and CQ as described by Schrezenmeier and Dorner [47]. HCQ produces two first-stage metabolites instead of one. One being Desthylhydroxychloroquine and the other Desthylchloroquine. Desthylchloroquine is also the first-stage metabolite product of Chloroquine. Both the first-stage metabolites are further metabolized to a common product, Bisdesthylchloroquine [47].

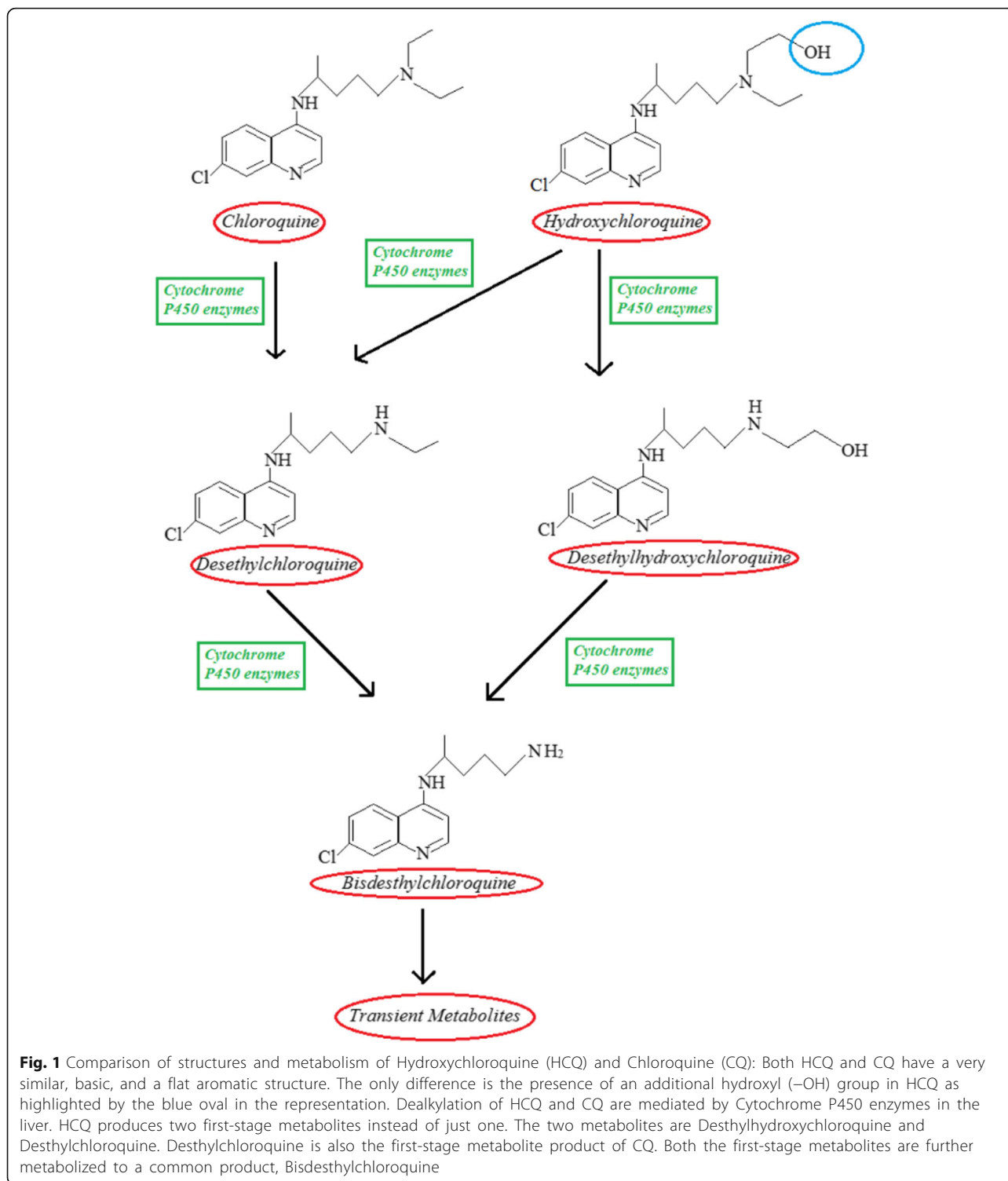
While many authors have reported CQ to induce mutagenic effects in bacterial systems [20–22, 24, 27–30, 32], few authors had found weak or no mutagenic associations in certain bacterial strains [14, 23, 25, 28, 31–33]. Positive mutagenic effects (either weak positive or positive) reported by several authors showed that CQ is capable of inducing mutation in the Salmonella strains TA97, TA97a, TA153 and TA1538, which are used to detect the frame-shift mutations. During the mutagenicity assay, most studies did not find any significant differences in the revertant numbers either with or without metabolic activation



**Table 1** Mutagenic, genotoxic and carcinogenic effects of chloroquine in multiple test systems

Test system	Dose Used	Endpoints	Effects	References
<b>Bacterial strains</b>				
<i>Escherichia coli</i>	1 X 10 <sup>-3</sup> M	DR	+	[19]
<i>Salmonella typhimurium</i> TA1537	100 and 250 µg/ml	MU	+	[20]
<i>Escherichia coli</i> B/r	50 µg/ml	MU	+	[21]
<i>Salmonella typhimurium</i> TA1537	10–10,000 µg/plate	MU	+	[22]
( <i>Salmonella typhimurium</i> TA1537, TA1538, TA98 and TA100)	5–5000 µg/plate	MU	–	[23]
<i>Escherichia coli</i>	300–500 µg/ml	DR	+	[24]
<i>Salmonella typhimurium</i> TA1537 and TA97a	312–500 µg/plate	MU	–	[25]
<i>Drosophila melanogaster</i>	3–10 mM	SRL	+	[26]
<i>Salmonella typhimurium</i> TA100, TA1537, TA1538	5–10 µg/plate	MU	+	[27]
<i>Salmonella typhimurium</i> TA97 <i>Escherichia coli</i> EE97 and EE102	25–200 µg/ml	MU	+	[28]
<i>Salmonella typhimurium</i> , TA102 <i>E. coli</i> strains WP2, WP2hcr, WP6 and WP67	25–200 µg/ml	MU	–	[28]
<i>Salmonella typhimurium</i> TA97 <i>Escherichia coli</i> DG1669	25–500 µg/plate	MU	+	[29]
<i>Salmonella typhimurium</i> TA1537, TA1538, TA98 and TA100	100–600 µg/ml	MU	+	[30]
<i>Salmonella typhimurium</i> TA1977, TA1978	100–600 µg/ml	MU	–	[30]
<i>Salmonella typhimurium</i> TA97a and TA100, TA104	0.1–10,000 µg/plate	MU	±	[14]
<i>Salmonella typhimurium</i> TA98	192.5–6160 µg/plate	MU	±	[31]
<i>Salmonella typhimurium</i> TA98, TA100, TA97, TA1537	0–10,000 µg/plate; 250 µg/plate; 200 µg/ml	MU	+	[32]
<i>Salmonella typhimurium</i> TA1535, TA1977, TA102, TA104	10,000 µg/plate; 600 µg/plate 5000 µg/plate	MU	–	[32]
<i>Salmonella typhimurium</i> TA100	10–5000 µg/plate	MU	±	[33]
<b>In vitro studies on mammalian systems</b>				
Rat liver cells	0.2 mM	DR	+	[34]
Human lymphocytes	15–100 µg/ml	CA	+	[35]
Chinese hamster ovary (CHO) cells	5–100 µM	MN SCE	+	[36]
Chinese hamster lung fibroblast (V79) & Rat hepatocyte cells (H4)	0.001–10 µg/ml	SCE	+	[27]
Chinese hamster lung fibroblast V79 cells	1–340 µM	MN	+	[37]
Rat liver cells	Full text not available	DD	+	[38]
Rat liver cells	0–1000 µM	DD	+	[39]
<b>In vivo studies in multiple test systems</b>				
Rheumatoid patients	250 mg/day for 6 years	CA	+	[40]
Patients with aplastic anemia	Data not available. Patients took CQ for several months	CO <sup>a</sup>	+	[41]
Mouse bone marrow cells	12.5–100 mg/kg in single i.p. dose	CA SCE	+	[14]
Wistar rats	20 mg/kg orally thrice a week continued up to 400 days.	CO <sup>b</sup>	+	[42]
Mouse bone marrow cells	10–30 mg/kg in single i.p. dose and one sub acute i.p.dose 10 mg daily for 3 days.	MN CA	+	[43]
Egyptian Toad <i>Bufo</i>	Toads weighing 50 g gavaged 0.5 mg and after 6 h 0.1 mg and then 0.1 mg daily for 3 days	CO	+	[44]
Male Wistar rats	10 mg/kg i.p. for once a day for 7, 14 and 21 days	DD	+	[45]

+: Positive effect, ±: Weakly positive effect, -: Negative (non mutagenic) effect,  
 MU: Mutagenicity assay, CA: Chromosomal aberrations, SCE: Sister-Chromatid Exchange,  
 SRL: Sex linked recessive lethals. DD: DNA Damage, DR: Inhibition of DNA Repair,  
 MN: Micronuclei formation, CO: Carcinogenicity (Lymphosarcomas),  
 CO<sup>a</sup>: Carcinogenicity (Myeloblastic leukaemia), CO<sup>b</sup>: Co-Carcinogenic effects



system (S9). This indicates that CQ is a direct-acting mutagen. In addition to *Salmonella* strains, CQ showed mutagenic effects in *Escherichia coli* EE97, EE102, DG1669 strains, and WP2, WP2hcr, WP6 and WP67 strains [21, 28–30]. CQ also can interact with DNA and

produce an intercalated complex that may induced frameshift mutation by shifting the reading frame [48, 49]. This also indicates it's DNA damage and inhibition of DNA repair potentials reported by several authors [19, 34, 38, 39, 45]. CQ is further reported to induce sex-linked recessive

lethal mutation in *Drosophila melanogaster* [26]. These results indicate the mutagenic potentials of CQ in bacterial systems.

In a broad genotoxic review on several antimalarial drugs, cumulative pieces of evidence pointed out that CQ is also a genotoxic drug [50]. Our study on CQ has demonstrated genotoxic effect as measured by chromosomal aberrations (CA), sister chromatid exchange (SCE), and micronuclei (MN) formations in vivo in mice [14]. These results are in agreement with several other authors who have reported CQ to be a genotoxic drug in both in vitro and in vivo systems [35–37, 40, 43]. CQ has also been reported to induce oxidative stress in animal models [51]. For instance, when CQ administered intraperitoneally in rats, it induced DNA breaks in the kidney within 1 to 2 weeks and in the liver within 2 to 3 weeks [45]. Chromosomal Aberrations (CA) have also been long considered to be a predictor for cancer. Rossner et al., [52] reported a strong association between increased frequencies of CA in cells and an increased risk for cancer using a cohort of 11,834 subjects. CA along with other genotoxic effects like SCE and MN as reported here, suggests that long-term use of CQ can induce significant chromosomal damages which may lead to an increased risk of cancer in humans.

CQ is not considered carcinogenic due to inadequate evidence pointing to carcinogenicity in humans. Yet, a well-controlled study by El-Mofty et al., [44] in Egyptian toad showed that separately CQ and primaquine can induce tumor formation in 14 and 19% of the toads respectively. They further showed that CQ and primaquine when used together the incidence of tumor rose to 23.5% [44]. This type of co-tumorigenic effect of CQ was also observed in another study by Reyes et al., [42] where CQ promoted the carcinogenic effect of a drug called ethylnitrosourea on ependymal cells of rodents in vivo. The only report of CQ induced Aplasia and leukemia was observed in a patient treated with long term CQ therapy [41]. Brambilla and Martelli, [53] showed that *N*-nitroso compounds, which are capable of inducing genotoxic effects and tumor formation in animal models, can be formed in the gastric environment when CQ is used with nitrite drugs. So, the genotoxic-carcinogenic effect may be induced when nitrite drugs are taken along with amine drugs like CQ and HCQ. Results presented in the Table 1 indicate that CQ is mutagenic and genotoxic drug in both bacterial systems, and in vitro and in vivo on mammalian systems.

#### **Immunomodulatory effects**

Table 2 summarizes the available reports on the immunomodulatory aspects of HCQ and CQ in multiple test systems. Both HCQ and CQ has been reported to inhibit the activation of the immune system in many ways.

Lysosomotropic drugs (like HCQ and CQ) can accumulate inside lysosomes and being basic they can increase the pH inside the lysosomes and prevent its normal functions [63, 64]. These drugs can also cause lysosomal membrane destabilization and thus the release of lysosomal contents and enzymes inside the cells [63]. Lysosomes have an essential role in the exogenous (lysosomal) pathways of antigen presentation and therefore proper lysosome functions are essential for MHC class II antigen processing and presentation. The intervention of HCQ and CQ in the exogenous pathway of antigen presentation has been presented in Fig. 2 [64].

Autophagy is an implied concept in immunity development. Besides the degradation and recycling of endogenous substrates, the process of autophagy is a key mechanism used by cells to tackle intracellular pathogens [65]. HCQ and CQ both can potentially inhibit the normal autophagy processes. Autophagosomes require fusion with the lysosomes to start the process of degradation. The increased pH of lysosomes, due to HCQ and CQ intervention, inhibits the maturation of the autolysosome. The inhibition of autophagy has been further linked to the induction of apoptosis of memory T-cells, which is the basis of the mechanism of immunomodulation by these drugs in several autoimmune diseases [59, 66]. Mechanism of the inhibition of autophagy by HCQ and CQ which triggers apoptosis has been presented in Fig. 3 [59]. HCQ can further block endosomal activation of NADPH oxidase (NOX2) that normally generates the reactive oxygen species and involved in the proinflammatory response of the immune system [60]. With a decreased activity of NADPH oxidase, cells can phagocyte pathogens but can't degrade them inside the phagocytic vesicle.

HCQ can also function as an immunosuppressant by blocking steps in the T-cell activation pathway. HCQ has been shown to inhibit transcription factor NFAT (Nuclear Factor of Activated T-cells) upon T-cell activation in vivo and block expression of co-stimulatory ligand CD154 i.e. CD 40L, which initiates T-cell dependent B-cell proliferation and antibody formation [17]. The probable mechanism of the interference in the T-cell activation by HCQ has been presented in Fig. 4 [17, 18]. HCQ intervention can further down-regulate the CD69 marker in healthy controls by inhibiting calcium mobilization and dephosphorylation of NFAT [18]. CD69 functions as a costimulatory molecule for T-cell activation and proliferation. The same study showed that B-cell antigen receptor calcium signaling was also reduced by HCQ intervention [18].

Patients on antimalarial drugs like HCQ and CQ have lower levels of IL-6, soluble CD8, and IL-2 receptors which is beneficial for those suffering from autoimmune diseases like SLE and RA [55]. Studies have shown that CQ, at doses that are expected in the serum of treated

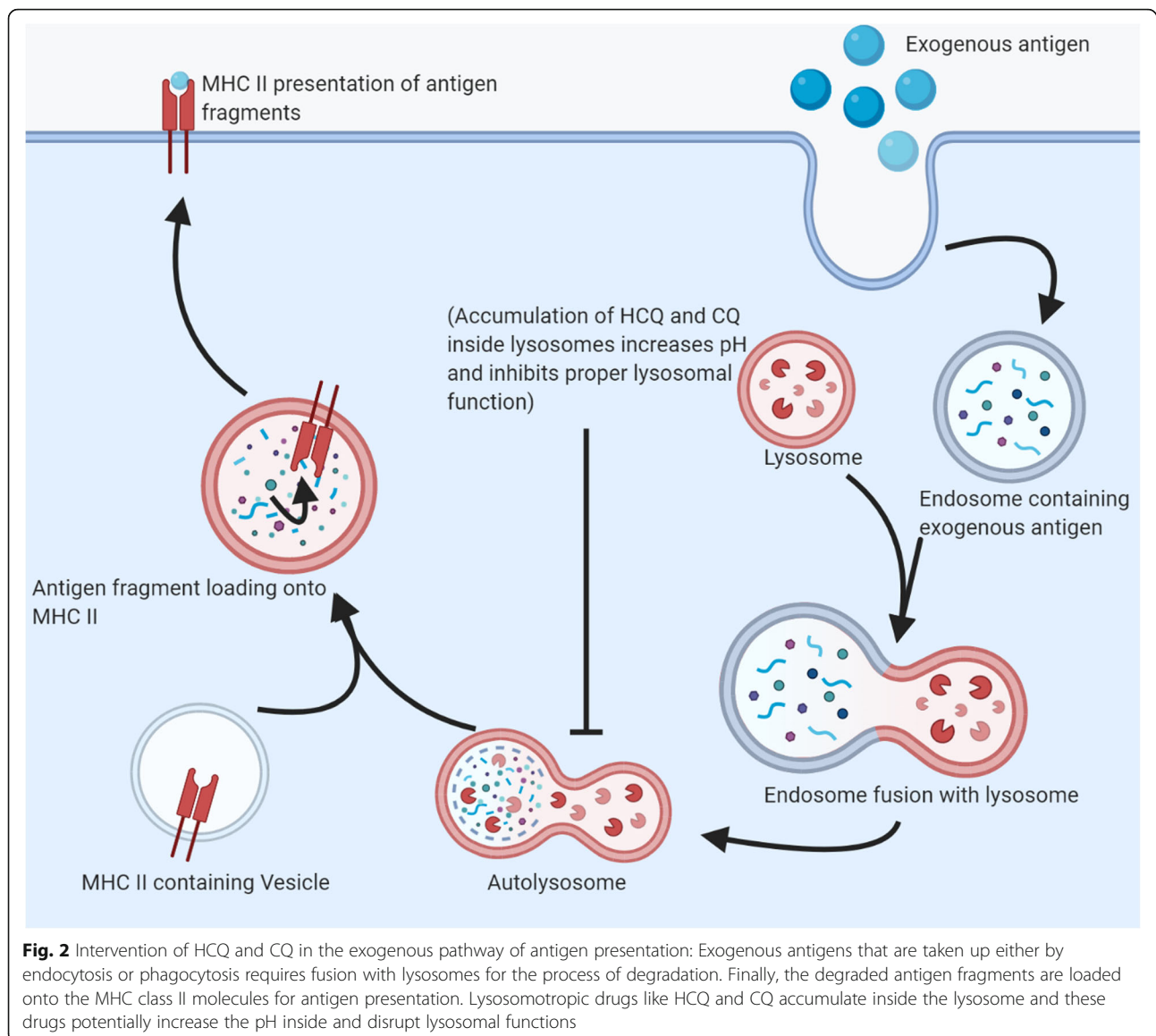
**Table 2** Immunomodulatory effects of hydroxychloroquine (HCQ) and chloroquine (CQ) in multiple test systems

Test systems	Drugs	Dose Range	Endpoints	Effects	References
Human lymphocytes in vitro (PBMC)	CQ	0–25 µg/ml	Inhibition of generation of immunoglobulin-secreting cells and IL-1 secretion	+	[54]
Systemic Lupus Erythematosus Patients	HCQ	400 mg/day for 12 weeks	Decreased levels of cytokines (IL-6), soluble CD8 and soluble IL-2 receptors	+	[55]
T-cell line	HCQ	0–100 µM	Inhibits calcium signals in T cells	+	[18]
PBMC from healthy donors	CQ	0–10 µM	Inhibition of RNA- mediated TLR7 activation; inhibition of IFN-α	+	[56]
PBMC and monocytic U-937 and THP-1 cells in vitro	CQ	0–100 µM	Inhibition of cytokine (TNF-α, IL-1β and IL-6) production.	+	[57]
Macrophage-like RAW264 cells in vitro	CQ	0–100 µM	Inhibition of Toll-like Receptor (TLR) signalling pathways	+	[58]
Systemic Lupus Erythematosus Patients, Human embryonic kidney cells	CQ	5–10 µg/ml	Inhibits activation of endosomal TLRs	+	[4]
Systemic Lupus Erythematosus Patients	HCQ	200–400 mg/day	Impaired IFN-α and TNF-α production	+	[5]
Human lymphocytes in vitro (PBMC)	HCQ	0–20 nmol/L	Inhibition of autophagy, and induction of apoptosis of memory T-cells	+	[59]
MonoMac1 (MM1) cells, human monocytes	HCQ	0–100 µM	Inhibits pro-inflammatory signaling pathways, prevents the induction of endosomal NADPH oxidase	+	[60]
Systemic Lupus Erythematosus Patients and on Jurkat Cell	HCQ	Patients blood samples and in Jurkat cell 600–6000 ng/ml	Inhibition of NFAT signaling in activated T cells and CD154 expression in CD4 <sup>+</sup> T cells	+	[17]
A549Pt and A549cisR non-small-cell lung cancer cell lines	CQ	25–100 µM	Lysosomal membrane destabilization and autophagy	+	[16]
PBMC from healthy volunteer	HCQ	Data not available	BlocksTLR9 ligation in class-switched memory B cells, suppress mTORC1 signaling.	+	[61]
Rosetta BL21 pLysS cells	HCQ and CQ	1–4 µM	Blockade of c-GAS-DNA interaction	+	[62]

+: positive effects, CQ: Chloroquine, HCQ: Hydroxychloroquine, IL: Interleukin,

TLR: Toll-like receptor, PBMC: Peripheral blood mononuclear cells,

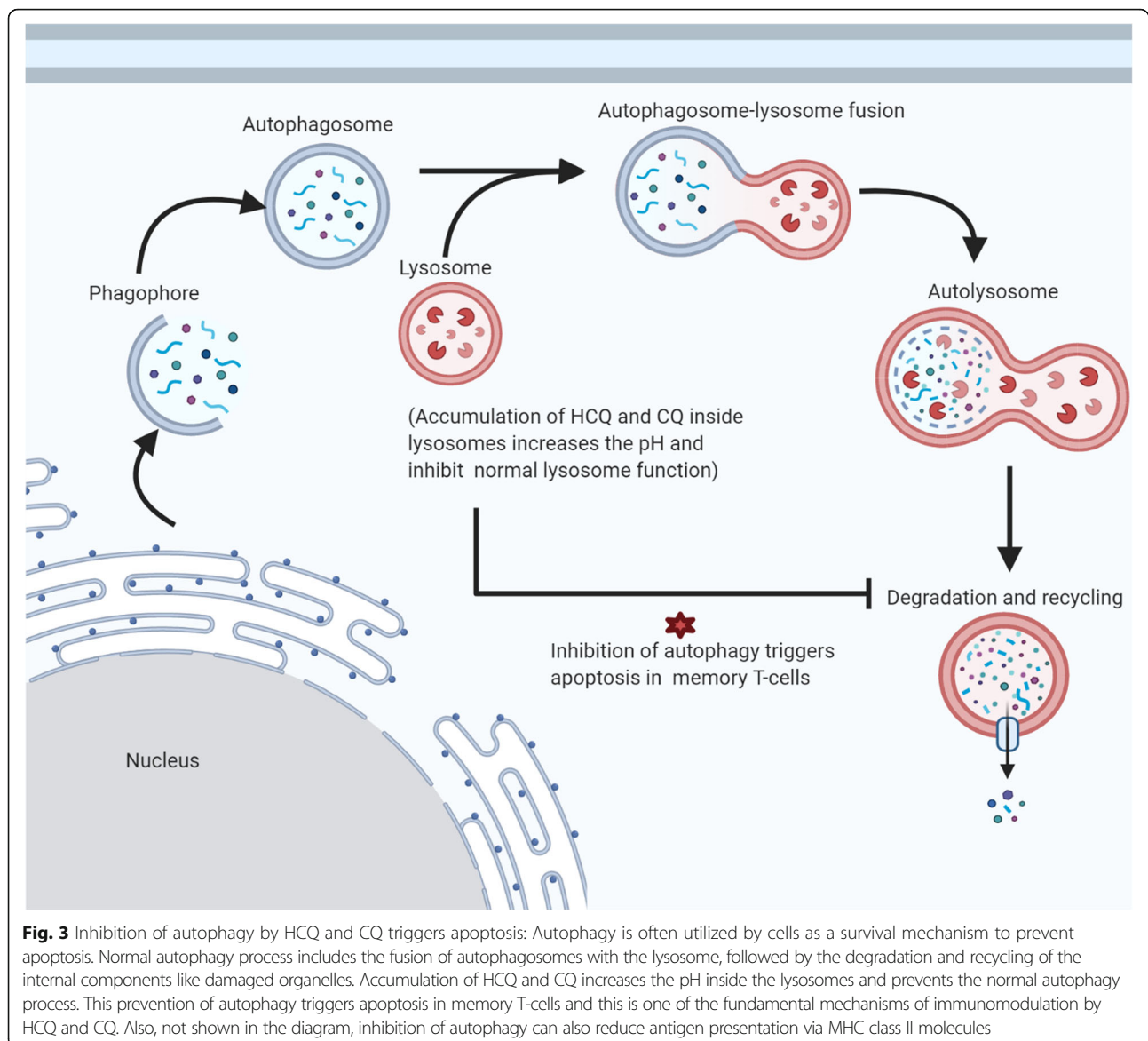
TNF: Tumor necrosis factor; cGAS: Cyclic GMP-AMP synthase



patients, was able to interfere with mitogenic-response of monocytes and this diminished mitogenic response was determined to be irreversible [54]. Furthermore, CQ inhibited the generation of Immunoglobulin-secreting cells by preventing the capacity of monocytes to secrete factors like IL-1 [54]. Normal secretion of TNF- $\alpha$ , IL-1b, and IL-6 by monocytes or macrophages was also inhibited by CQ [57].

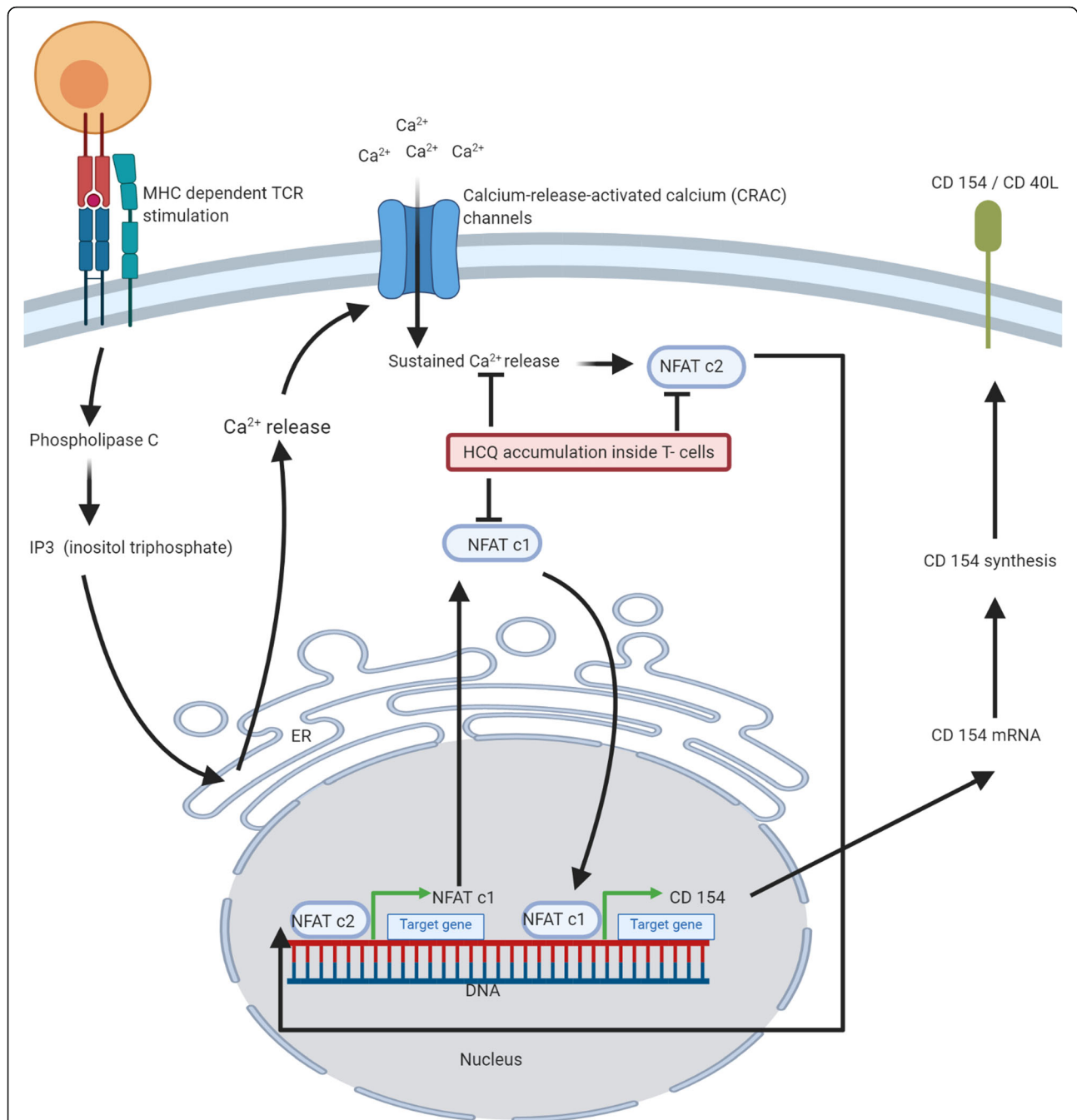
HCQ and CQ can potentially inhibit Toll-like receptor (TLR) signaling of TLR7 and TLR9 in Antigen Presenting Cells (APCs) including dendritic cells, macrophages and B-cells. Normally, upon activation of by nucleic acids, endolysosomal TLR7 and TLR9 are cleaved which in turn activates MyD88 and triggers an innate immune response in the downstream cascade. This proteolytic cleavage is inhibited by the changes in the endosomal

pH as a result of HCQ and CQ interference [58]. The mechanism of the inhibition of endosomal TLR 7 and TLR9 by HCQ and CQ has been presented in Fig. 5 [58]. HCQ and CQ have further been shown to directly bind to nucleic acid, inhibiting TLR-nucleic acid interaction and preventing TLR9 activation [4], and CQ has been shown to inhibit RNA-mediated TLR7 activation [56]. HCQ treatment in vivo caused a significant reduction of the production of INF- $\alpha$  and TNF- $\alpha$  by the plasmacytoid Dendritic cells by suppressing the activation of TLR7 and TLR9 [5]. Innate TLR signaling leads to the production of cytokines such as IL-6, TNF- $\alpha$ , and IL-1 that eventually triggers the adaptive immune response. At clinical concentration, HCQ can efficiently block TLR9 ligation and have an inhibitory effect on class-switched memory B-cells [61].

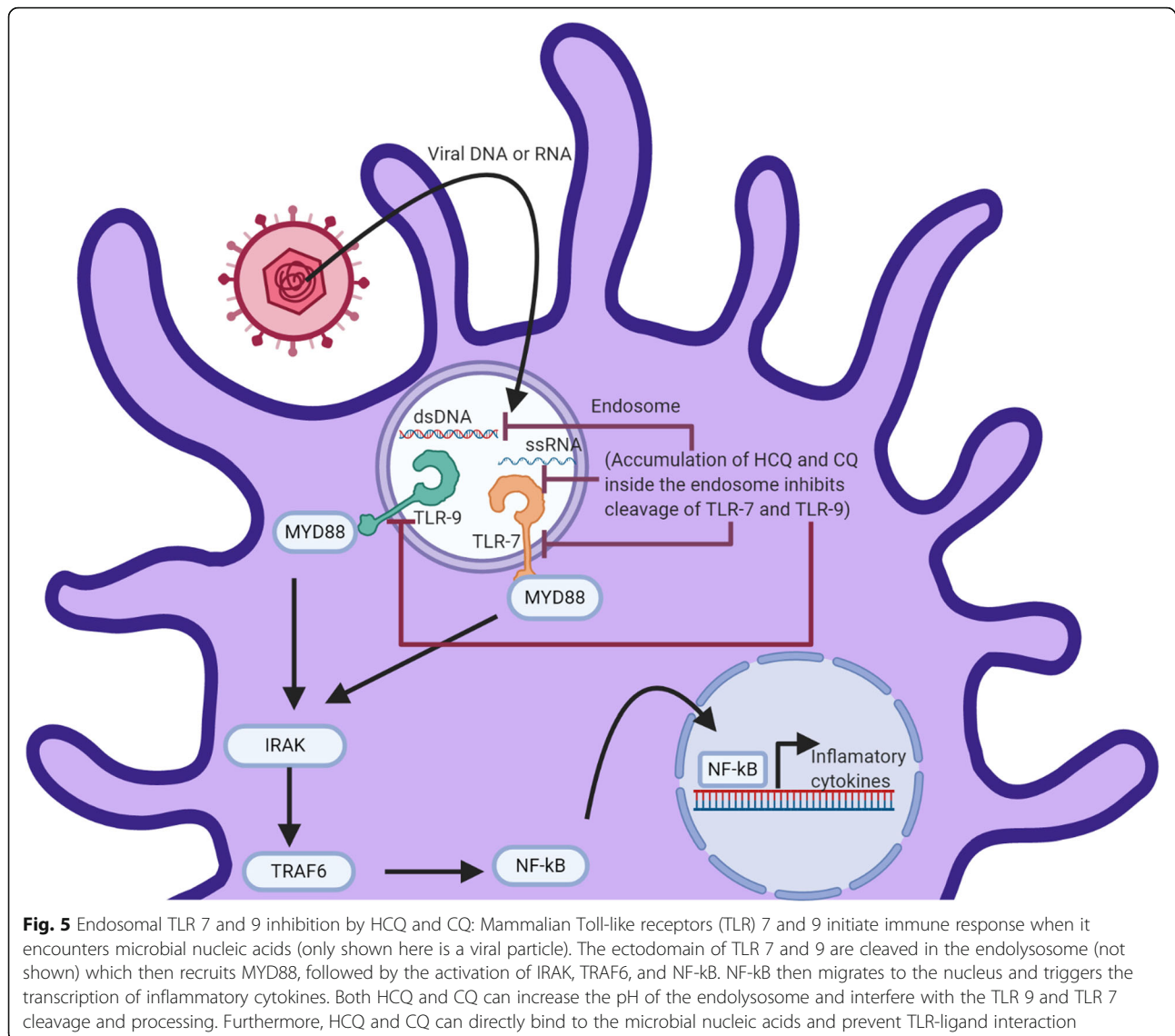


The cGAS-STING is another pathway that is involved in the type I interferon response of innate immunity. Cyclic GMP-AMP synthase (cGAS) is a nucleotidyltransferase that is activated to cGAMP (2',5' -cyclic GMP-AMP dinucleotide) when dsDNA, usually from a viral or bacterial origin, binds to it. cGMAP then activates an endoplasmic reticulum membrane-associated protein known as the STING (stimulator of interferon genes). Activation of STING leads to the activation of the transcription factor IRF3 and NF- $\kappa$ B, which then can migrate to the nucleus to activate the Type I IFNs and cytokines [67]. Evidence suggests one-way HCQ and CQ can achieve the immunomodulatory effect is because of its ability to suppress the activation of this pathway by inhibiting ligand binding [62]. The mechanism of the inhibition of cGAS-STING Pathway by HCQ and CQ has been presented in Fig. 6 [62].

Given all the above mechanisms, it is now clear that these drugs can effectively modulate cellular signaling. Sometimes, this can be helpful but only when used by patients infected with COVID-19. For instance, COVID-19 patients have usually higher levels of inflammatory cytokines which ultimately result in collateral damage to the host tissues. The use of HCQ and CQ has been reported to reduce the overproduction of IL-1 $\beta$ , IL-6, and Granulocyte-colony stimulating factor (GM-CSF). The reduction in endosomal acidification as a result of HCQ and CQ accumulation is believed to halt or reduce the disruption of viral particles and thus the release of infectious nucleic acid. The ACE2 receptors of the lungs are required for SARS-CoV2 entry into the host cells. Glycosylation of ACE2 receptors is required for the translocation of ACE2 receptors to the cell membrane. HCQ has



**Fig. 4** HCQ interference in the T-cell activation pathway and transcription of CD 154: When T-cell receptor (TCR) is stimulated by antigen via MHC, a series of events leads to the activation of the Phospholipase C, which then generates Inositol triphosphate (IP3). IP3 induces the release of calcium from the endoplasmic reticulum (ER). Calcium acts as a secondary messenger to activate Calcium-release-activated Calcium channel (CRAC) for a steady influx of extracellular calcium. Intracellular calcium binds to calmodulin and activates the phosphatase calcineurin (not shown in the diagram). Calcineurin dephosphorylates and activates transcription factor NFATc2. NFATc2 migrates the nucleus and triggers the transcription of NFATc1. NFATc1 mRNA is exported outside the nucleus where de novo synthesis of transcription factor NFATc1 occurs. NFATc1 then migrates back into the nucleus to triggers the transcription of CD 154. HCQ can potentially interfere with intracellular calcium signaling and prevent dephosphorylation and activation of the transcription factor NFAT. This is one of the mechanisms by which HCQ interfere in T-cell activation and CD 154 transcription



also been shown to reduce this glycosylation step [68]. These studies have together motivated healthcare workers to use these drugs as a prophylactic, post-exposure prophylactic, and as a curative drug. Unfortunately, these results were only successful *in vitro*. As we will discuss later, large clinical trials have found no evidence of the benefit of using these drugs.

#### Genetic variation leading to a difference in the metabolism of HCQ and CQ

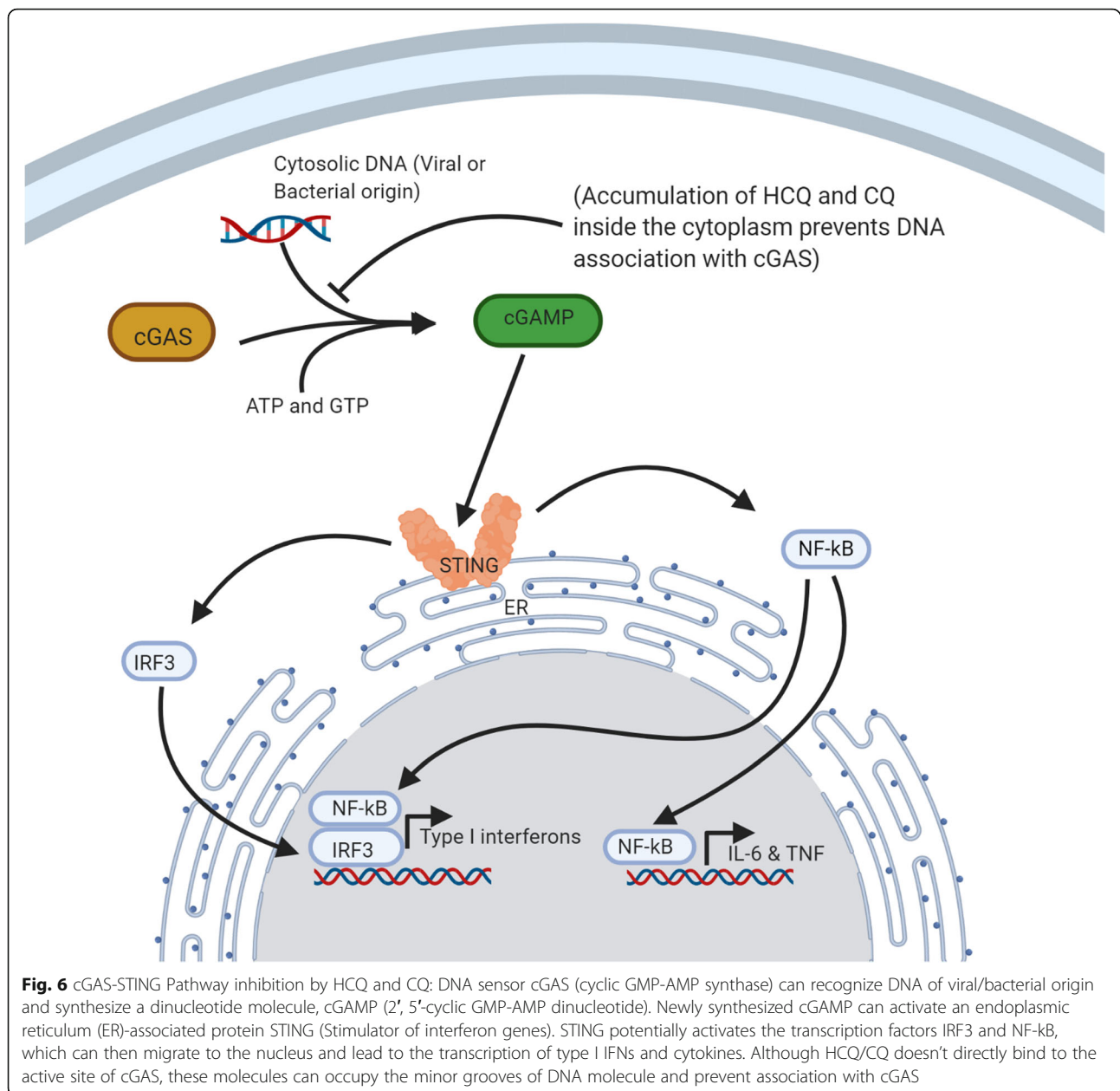
It is important to remember the metabolism of these drugs *in vivo*. Both HCQ and CQ are metabolized in the liver by an enzyme known as cytochrome P450 (CYP) and the gene expression of this enzyme varies between different individuals as a result of the difference in nucleotide polymorphisms [69]. Furthermore, these polymorphisms have been associated with the formation of

unstable enzymes and thus a decreased in its activity [70]. Some ethnicities have a complete absence of certain functional CYP enzymes like the CYP 2D6, which is one of the important CYP enzymes that is actively involved in the metabolism of these drugs [69]. An Individual's P450 polymorphisms should be taken into account when considering to prescribe HCQ since there is a clear association between different polymorphisms in CYP 2D6 and the blood concentration of HCQ in SLE patients [69]. These polymorphisms have also been linked to the toxic accumulation of these drugs in the blood of the patients treated with HCQ and CQ [71].

#### Latest clinical findings

To date, there is still no evidence that points to any benefit of using these drugs against the COVID-19 as a prophylactic. Moreover, the potentials of these drugs as





**Fig. 6** cGAS-STING Pathway inhibition by HCQ and CQ: DNA sensor cGAS (cyclic GMP-AMP synthase) can recognize DNA of viral/bacterial origin and synthesize a dinucleotide molecule, cGAMP (2', 5'-cyclic GMP-AMP dinucleotide). Newly synthesized cGAMP can activate an endoplasmic reticulum (ER)-associated protein STING (Stimulator of interferon genes). STING potentially activates the transcription factors IRF3 and NF- $\kappa$ B, which can then migrate to the nucleus and lead to the transcription of type I IFNs and cytokines. Although HCQ/CQ doesn't directly bind to the active site of cGAS, these molecules can occupy the minor grooves of DNA molecule and prevent association with cGAS

a post-exposure prophylactic or curative drug has also been called into question. Recently, the Food and Drug Administration (FDA) of the United States (US) has revoked their Emergency Use Authorization (EUA) for emergency use of these drugs [72], and the World Health Organization (WHO) [73], along with National Institute of Health (NIH) [74] in the US had also stopped conducting further clinical studies because of sufficient evidence that these drugs provided no benefit.

Initially, a few in vitro evidence and small studies suggested that these medications might be helpful, however, large scale studies have found no such significance. The first clinical evidence of a positive result stems from a

small study in China where 100 subjects treated with CQ were found to have a superior benefit over the control group suffering from COVID-19 pneumonia [75]. Another small study in France with only 26 subjects, who received HCQ, showed a significant reduction in the viral load compared to the control group [76]. The time to clinical recovery was also shown to be reduced in those under HCQ treatment in a small randomized trial of just 62 COVID-19 patients [77]. Clearly, the small sample size was a major drawback in these studies. However, larger clinical randomized controlled trial has now been conducted and results have provided us with a different outcome. For instance, a recent study in Brazil

with 504 confirmed COVID-19 patients, HCQ treatment had no significant benefit over no treatment group [78]. Furthermore, Chloroquine at high doses (600 mg, twice daily) for 10 consecutive days was associated with higher lethality and is now not recommended for critically ill patients [79]. A large randomized clinical study investigating the post-exposure prophylactic role of HCQ found that a higher dose of HCQ did not prevent infection when treatment was initiated within 4 days after exposure [80]. Another study showed us that in 368 COVID-19 patients those taking HCQ only or HCQ plus Azithromycin had a death rate of 27.8 and 22.1% respectively when compared to 11.4% in the no-treatment group [81].

## Conclusions

Most pathogenic microorganisms that infect humans are tackled satisfactorily by the innate and adaptive immune system of our body. Healthy humans have an extraordinary capability to fight off infections caused by pathogenic microorganisms. The activation of innate immunity initiates the first line of defense until the more specific adaptive immunity develops. Existing literature suggests that HCQ and CQ can potentially interfere with both innate and adaptive immune responses in multiple ways. Here in this review, we have highlighted the known pathways where HCQ and CQ can intervene to achieve its immunomodulatory effects and also provided systematic diagrams for a better understanding of the affected pathways.

Furthermore, CQ has been recognized to induce genomic instability by inducing mutagenic, genotoxic, and DNA damages both in vivo and in vitro systems. Most authors, including us, found weak to moderately strong mutagenic effects in different *Salmonella* strains routinely used for mutagenicity screening of drugs and chemicals. Moreover, almost all authors who worked on genotoxicity assays have reported positive genotoxic effects of CQ in multiple test systems. This indicates that CQ is a mutagenic and genotoxic drug. However, with a lack of sufficient studies on the genetic toxicology of HCQ both in vitro and in vivo, the mutagenic and genotoxic effects of HCQ remains inconclusive.

Current evidence cumulatively demonstrates that both HCQ and CQ are not effective against the COVID-19 infection either as post-exposure prophylaxis or as a curative drug. No studies on the prophylactic role of these drugs have been evaluated to date. The world is going through tremendous turmoil because of the COVID-19 pandemic. Thus, we do recognize the importance of optimism and the implementation of any advancement in science during this emergency. Thus, the use of these drugs post-infection might be useful, but this discussion is beyond the scope of this review. Here, we are mainly concerned with the use of these drugs by

healthy individuals as a prophylactic without any evidence. So, without any clinical or in vivo evidence, current literature suggests that healthy individuals should refrain from the use of these drugs as prophylactics until further investigation.

## Abbreviations

CQ: Chloroquine; HCQ: Hydroxychloroquine; COVID-19: novel Severe Acute Respiratory Syndrome Corona Virus 2; RA: Rheumatoid Arthritis; SLE: Systemic Lupus Erythematosus; CYP: cytochrome P450; S9: Metabolic activation system; +: Positive effect; ±: Weakly positive effect; -: Negative (non mutagenic) effect; MU: Mutagenicity assay; CA: Chromosomal aberrations; SCE: Sister-Chromatid Exchange; SRL: Sex linked recessive lethals; DD: DNA Damage; DR: Inhibition of DNA Repair; MN: Micronuclei formation; CO: Carcinogenicity; IL: Interleukin; TLR: Toll-like receptor; PBMC: Peripheral blood mononuclear cells; TNF: Tumor necrosis factor; NFAT: Nuclear Factor of Activated T-cells; cGAS: Cyclic GMP-AMP synthase; STING: Stimulator of interferon genes; ACE2: Angiotensin-converting enzyme 2; GM-CSF: Granulocyte-colony stimulating factor

## Acknowledgments

The authors are grateful to the Indian National Science Academy to provide the INSA-Senior Scientist position to AKG. Authors are also grateful to the U.S. Federal Government for providing financial support to AG for Graduate Studies in Kansas City University of Medicine and Biosciences and to the Council of Scientific and Industrial Research, New Delhi for providing CSIR-NET (JRF) to AD. Our deep gratitude also to Dr. Pritha Bhattacharjee, Department of Environmental Sciences, University of Calcutta for allowing her student Ms. Ankita Das to work in this review and also for her valuable suggestions. All the Figures in this review have been created with [BioRender.com](https://www.biorender.com)

## Authors' contributions

AG: Planning and designing of the review, literature search, interpretation of results and manuscript writing. All the figures in this manuscript have been prepared by AG. AD: Literature search, preparation of tables and references. AKS: Interpretation of results and manuscript editing. AKG: Concept, planning and designing of the review, literature search, interpretation of results, manuscript editing and supervision of the work. The author(s) read and approved the final manuscript.

## Funding

There is no funding for this work.

## Availability of data and materials

Not applicable.

## Ethics approval and consent to participate

Not applicable.

## Consent for publication

Not applicable.

## Competing interests

The authors declares that he have no competing interests.

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Received: 28 July 2020 Accepted: 20 August 2020

Published online: 02 September 2020

## References

- van Doremalen N, Bushmaker T, Morris DH, Holbrook MG, Gamble A, Williamson BN, et al. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. *N Engl J Med*. 2020;382(16):1564–7.
- Siddiqui AK, Huberfeld SI, Weidenheim KM, Einberg KR, Efferen LS. Hydroxychloroquine-induced toxic myopathy causing respiratory failure. *Chest*. 2007;131(2):588–90.
- Joyce E, Fabre A, Mahon N. Hydroxychloroquine cardiotoxicity presenting as a rapidly evolving biventricular cardiomyopathy: key diagnostic features and literature review. *Eur Heart J Acute Cardiovasc Care*. 2013;2(1):77–83.
- Kuznik A, Bencina M, Svajger U, Jeras M, Rozman B, Jerala R. Mechanism of endosomal TLR inhibition by antimalarial drugs and imidazoquinolines. *J Immunol*. 2011;186(8):4794–804.
- Sacre K, Criswell LA, McCune JM. Hydroxychloroquine is associated with impaired interferon-alpha and tumor necrosis factor-alpha production by plasmacytoid dendritic cells in systemic lupus erythematosus. *Arthritis Res Ther*. 2012;14(3):155–65.
- Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, Shi Z, Hu Z, Zhong W, Xiao G. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res*. 2020;30(3):269–71.
- Liu J, Cao R, Xu M, Wang X, Zhang H, Hu H, Li Y, Hu Z, Zhong W, Wang M. Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection in vitro. *Cell Discov*. 2020;6(1):1–4.
- Yao X, Ye F, Zhang M, Cui C, Huang B, Niu P, Liu X, Zhao L, Dong E, Song C, Zhan S. In vitro antiviral activity and projection of optimized dosing design of hydroxychloroquine for the treatment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). *Clin Infect Dis*. 2020. <https://doi.org/10.1093/cid/ciaa237>.
- Paton NI, Lee L, Xu Y, Ooi EE, Cheung YB, Archuleta S, Wong G, Smith AW. Chloroquine for influenza prevention: a randomised, double-blind, placebo controlled trial. *Lancet Infect Dis*. 2011;11(9):677–83.
- Dowall SD, Bosworth A, Watson R, Bewley K, Taylor I, Rayner E, Hunter L, Pearson GL, Easterbrook J, Pitman R. Chloroquine inhibited Ebola virus replication in vitro but failed to protect against infection and disease in the in vivo Guinea pig model. *J Gen Virol*. 2015;96(12):3484–92.
- Roques P, Thiberville SD, Dupuis-Maguiraga L, Lum FM, Labadie K, Martinon F, Gras G, Lebon P, Ng LF, De Lamballerie X, Le Grand R. Paradoxical effect of chloroquine treatment in enhancing chikungunya virus infection. *Viruses*. 2018;10(5):268.
- Giri AK. Genetic toxicology of paracetamol and aspirin - a review. *Mutat Res*. 1993;296:199–210.
- Giri AK, Adhikari N, Khan KA. Comparative genotoxicity of six salicylic acid derivatives in bone marrow cells of mice. *Mutat Res*. 1996;370:1–9.
- Chatterjee T, Mukhopadhyay A, Khan K. A. Giri AK. Comparative mutagenic and genotoxic effects of three antimalarial drugs, chloroquine, primaquine and amodiaquine. *Mutagenesis*. 1998;13:619–24.
- Pereira BB. Challenges and cares to promote rational use of chloroquine and hydroxychloroquine in the management of corona virus disease 2019 (COVID-19) pandemic: a timely review. *J Toxicol Environ Health*. 2020. <https://doi.org/10.1080/10937404.2020.1752340>.
- Circu M, Cardelli J, Barr M, O'Byrne K, Mills G, El-Osta H. Modulating lysosomal function through lysosome membrane permeabilization or autophagy suppression restores sensitivity to cisplatin in refractory non-small-cell lung cancer cells. *PLoS One*. 2017; 13(5), <https://doi.org/10.1371/journal.pone.0184922>.
- Wu SF, Chang CB, Hsu JM, Lu MC, Lai NS, Li C, Tung CH. Hydroxychloroquine inhibits CD154 expression in CD4+ T lymphocytes of systemic lupus erythematosus through NFAT, but not STAT5, signaling. *Arthritis Res Ther*. 2017;19(1):183–96.
- Goldman FD, Gilman AL, Hollenback C, Kato RM, Premack BA, Rawlings DJ. Hydroxychloroquine inhibits calcium signals in T cells: a new mechanism to explain its immunomodulatory properties. *Blood*. 2000; 95(11):3460–3466.
- Yielding KL, Yielding L, Gaudin D. Inhibition by chloroquine of UV repair in E. coli B. *Proc Soc Exp Biol Med*. 1970;133(3):999–1001.
- Schupbach ME. Mutagenicity evaluation of the two antimalarial agents Chloroquine and mefloquine, using a bacterial fluctuation test. *Mutat Res*. 1979;68(1):41–9.
- Sideropoulos AS, Specht SM, Jones MT. Feasibility of testing DNA repair inhibitors for mutagenicity by a simple method. *Mutat Res*. 1980;74(2):95–105.
- Cortinas de Nava C, Espinosa J, Garcia L, Zapata AM, Martinez, E. Mutagenicity of antiamebic and anthelmintic drugs in the Salmonella typhimurium microsomal test system. *Mutat Res*. 1983; 117: 79–91.
- Kadotani S, Arisawa M, Maruyama HB. Mutagenicity examination of several non-steroidal anti-inflammatory drugs in bacterial systems. *Mutat Res*. 1984; 138:133–6.
- Sideropoulos AS, Specht SM, Katarincic J, Paszul PJ. The role of chloroquine supplementation in liquid holding recovery and ultraviolet lethality of Escherichia coli strains. *Curr Microbiol*. 1985;12(5):251–5.
- O'Donovan MR. The comparative responses of Salmonella typhimurium TA1537 and TA97A to a range of reference mutagens and novel compounds. *Mutagenesis*. 1990;5:267–74.
- Xamena N, Creus A, Velazquez A, Marcos R. Testing of chloroquine and quinacrine for mutagenicity in Drosophila melanogaster. *Mutat Res*. 1985; 158:177–80.
- Shubber EK, Jacobson-Kram D, Williams JR. Comparison of the Ames assay and the induction of sister chromatid exchanges: results with ten pharmaceuticals and five selected agents. *Cell Biol Toxicol*. 1986;2(3):379–99.
- Obaseki-Ebor EE, Obasi EE. Aspects of chloroquine mutagenicity. *Mutat Res*. 1986;175(2):51–9.
- Thomas SM, Silburn KA, MacPhee DG. Frameshift mutagenesis by chloroquine in Escherichia coli and Salmonella typhimurium. *Mutat Res*. 1987;192(4):233–7.
- Espinosa-Aguirre JJ, Santos JR, Cortinas de Nava C. influence of the Uvr repair system on the mutagenicity of antiparasitic drugs. *Mutat Res*. 1989; 222(3):161–6.
- Riccio ES, Lee PS, Winegar RA, Krogstad DJ, De D, Mirsalis JC. Genetic toxicology testing of the antimalarial drugs Chloroquine and a new analog, AQ-13. *Environ Mol Mutagen*. 2001;38(1):69–79.
- U.S. National Library of Medicine-Toxnet, Toxicology Data Network. <http://www.toxnet.nlm.nih.gov>.
- Kumar R and Banjare L. Study of the evaluation of mutagenic effects of antimalarial drug chloroquine in Ames Salmonella assay. *J drug delivery and therapeutics (JDDT)*. 2013; 3(6), 70–5.
- Michael RO, Williams GM. Chloroquine inhibition of repair of DNA damage induced in mammalian cells by methyl methanesulfonate. *Mutat Res*. 1974; 25(3):391–6.
- Shalunashvili MA, Sigidin IA. Cytogenetic effects of chloroquine in human lymphocyte cultures. *Biull Eksp Biol Med*. 1976;82(7):879–81.
- Raj AS, Heddle JA. Simultaneous detection of chromosomal aberrations and sister-chromatid exchanges: experience with DNA intercalating agents. *Mutat Res*. 1980;78(3):253–60.
- Snyder RD, Arnone MR. Putative identification of functional interactions between DNA intercalating agents and topoisomerase II using the V79 in vitro micronucleus assay. *Mutat Res*. 2002;503:21–35.
- Mohamed MM. Anti-malarial chloroquine stimulate p53-apoptotic pathway in rat hepatocytes. *J Egypt Soc Parasitol*. 2005;35(1):19–32.
- Farombi EO. Genotoxicity of chloroquine in rat liver cells: protective role of free radical scavengers. *Cell Biol Toxicol*. 2006;22(3):159–67.
- Neill WA, Panayi GS, Duthie JJ, Prescott RJ. Action of chloroquine phosphate in rheumatoid arthritis. II. Chromosome damaging effect. *Ann Rheum Dis*. 1973;32(6):547–50.
- Nagaratnam N, Chetiyawardana AD, Sudarshini R. Aplasia and leukaemia following chloroquine therapy. *Postgrad Med J*. 1978;54:108–12.
- Reyes S, Rembao D, Sotelo J. The antimalarials quinacrine and chloroquine potentiate the transplacental carcinogenic effect of ethylnitrosourea on ependymal cells. *Brain Tumor Pathol*. 2001;18(2):83–7.
- Roy LD, Mazumdar M, Giri S. Effects of low dose radiation and vitamin C treatment on Chloroquine-induced genotoxicity in mice. *Environ Mol Mutagen*. 2008;49(6):488–95.
- El-Mofty MM, Khudoley VV, Sakr SA, Abdel-Gawad HS. The carcinogenicity of some antimalarial drugs using the Egyptian toad bufo regularis as a biological test animal. *Nutr Cancer*. 1992;18(2):191–8.
- Giovannella F, Ferreira GK, Pra SDD, Carvalho-Silva M, Gomes LM, Scaini G, Goncalves RC, Michels M, Galant LS, Longaretti LM, Dajori AL. Effects of primaquine and chloroquine on oxidative stress parameters in rats. *An Acad Bras Cienc*. 2015;87(2):1487–96.
- Mcchesney EW. Animal toxicity and pharmacokinetics of hydroxychloroquine sulfate. *The Am J Medicine*. 1983;18:11–8.

47. Schrezenmeier E, Dorner T. Mechanisms of action of hydroxychloroquine and chloroquine: implications for rheumatology. *Nat Rev Rheumatol*. 2020; 16:155–66.
48. Cohen SN, Yielding KL. Spectrophotometer studies of the interaction of chloroquine with deoxyribonucleic acid. *J Biol Chem*. 1965;240:3123–31.
49. Waring M. Variation of the supercoils in closed circular DNA by binding of antibiotics and drugs evidence for molecular models involving interaction. *J Mol Biol*. 1970;54:247–79.
50. Brambilla G, Martioli F, Robbiano L, Martelli A. Carcinogenicity of antibacterial, antiviral, antimalarial and antifungal drugs. *Mutagenesis*. 2012; 7:387–413.
51. Magwere T, Naik YS, Hasler JA. Effects of chloroquine treatment on antioxidant enzymes in rat liver and kidney. *Free Rad Bio & Medicine*. 1997; 22:321–7.
52. Rossner P, Boffetta P, Ceppi M, Bonassi S, Smerhovsky Z, Landa K, Juzova D, Sram RJ. Chromosomal aberrations in lymphocytes of healthy subjects and risk of cancer. *Environ Health Perspect*. 2005;113:517–20.
53. Brambilla G, Martelli A. Genotoxic and carcinogenic risk to human of drug-nitrite interaction product. *Mutat Res*. 2007;635:17–52.
54. Salmeron G, Lipsky PE. Immunosuppressive potential of antimalarials. *Am J Med*. 1983;75(1):19–24.
55. Wallace DJ, Linker-Israeli M, Metzger AL, Stecher VJ. The relevance of antimalarial therapy with regard to thrombosis, hypercholesterolemia and cytokines in SLE. *Lupus*. 1993;2(1):13–5.
56. Vollmer J, Tluk S, Schmitz C, Hamm S, Jurk M, Forsbach A, Akira S, Kelly KM, Reeves WH, Bauer S, Krieg AM. Immune stimulation mediated by autoantigen binding sites within small nuclear RNAs involves toll-like receptors 7 and 8. *J Exp Med*. 2005;202(11):1575–85.
57. Jang CH, Choi JH, Byun MS, Jue DM. Chloroquine inhibits production of TNF- $\alpha$ , IL- $\beta$  and IL-6 from lipopolysaccharide-stimulated human monocytes/macrophages by different modes. *Rheumatology*. 2006;45(6): 703–10.
58. Ewald SE, Lee BL, Lau L, Wickliffe KE, Shi GP, Chapman HA, Barton GM. The ectodomain of toll-like receptor 9 is cleaved to generate a functional receptor. *Nature*. 2008;45:658–62.
59. van Loosdregt J, Spreafico R, Rossetti M, Prakken BJ, Lotz M, Albani S. Hydroxychloroquine preferentially induces apoptosis of CD45RO+ effector T cells by inhibiting autophagy: a possible mechanism for therapeutic modulation of T cells. *J Allergy Clin Immunol*. 2013;131(5):1443–6.
60. Müller-Calleja N, Manukan D, Canisius A, Strand D, Lackner KJ. Hydroxychloroquine inhibits proinflammatory signalling pathways by targeting endosomal NADPH oxidase. *Ann Rheum Dis*. 2017;76(5):891–7.
61. Torigoe M, Sakata K, Ishii A, Iwata S, Nakayamada S, Tanaka Y. Hydroxychloroquine efficiently suppresses inflammatory responses of human class-switched memory B cells via toll-like receptor 9 inhibition. *Clin Immunol*. 2018;195:1–7.
62. An J, Woodward JJ, Sasaki T, Minie M, Elkon KB. Cutting edge: antimalarial drugs inhibit IFN- $\beta$  production through blockade of cyclic GMP-AMP synthase–DNA interaction. *J Immunol*. 2015;194:4089–93.
63. Circu M, Cardelli J, Barr M, O'Byrne K, Mills G, El-Osta H. Modulating lysosomal function through lysosome membrane permeabilization or autophagy suppression restores sensitivity to cisplatin in refractory non-small-cell lung cancer cells. *PLoS One*. 2017; 12(9): <https://doi.org/10.1371/journal.pone.0184922>.
64. Fox RI. Mechanism of action of Hydroxychloroquine as an Antirheumatic drug. *Semin Arthritis Rheum*. 1993;23:82–91.
65. Levine B, Mizushima N, Virgin HW. Autophagy in immunity and inflammation. *Nature*. 2011;469:323–35.
66. Boya P, Lez-Polo R-AG, Casares N, Perfettini J-L, Dessen P, Larochette N, Me'tivier D, Meley D, Souquere S, Yoshimori T, Pierron G, Codogno P, Kroemer G. Inhibition of macroautophagy triggers apoptosis. *Mol Cell Biol*. 2005;25:1025–40.
67. Motwani M, Scott P, Fitzgerald KA. DNA sensing by the cGAS–STING pathway in health and disease. *Nat Rev Genet*. 2019;20:657–74.
68. Pahan P, Pahan K. Smooth or risky revisit of an old malaria drug for COVID-19? *J Neuroimmune Pharmacology*. 2020. <https://doi.org/10.1007/s11481-020-09923-w>.
69. Neafsey P, Ginsberg G, Hattis D, Sonawane B. Genetic polymorphism in cytochrome P450 2D6 (CYP2D6): population distribution of CYP2D6 activity. *J Toxicol Environ Health B Crit Rev* 2009; 12: 334–361.
70. Lee JY, Vinayagamoorthy N, Han K, Kwok SKJH, Park KS, Jung SH, Park SW, Chung Y-J, Park SH. Association of polymorphisms of cytochrome P450 2D6 with blood hydroxychloroquine levels in patients with systemic lupus erythematosus. *Arthritis Rheumatol*. 2016;68(1):184–90.
71. Sortica VA, Lindenau JD, Cunha MG, Ohnishi, MDO, Ventura AM R, Ribeiros-Santos a Kc, Santos SEb, Guimaraes L Sp. and Hutz M H. the effect of SNPs in CYP450 in chloroquine/ primaquine plasmodium vivax malaria treatment. *Pharmacogenomics*. 2016;17:1903–11.
72. U.S. Food & Drug Administration. Letter revoking EUA for chloroquine phosphate and hydroxychloroquine sulfate. 2020. <https://www.fda.gov/media/138945/download>.
73. World Health Organization. Q&A: Hydroxychloroquine and COVID-19. 2020. <https://www.who.int/news-room/q-a-detail/q-a-hydroxychloroquine-and-covid-19>.
74. National Institutes of Health. NIH halts clinical trial of Hydroxychloroquine. Study shows treatment does no harm, but provides no benefit. 2020. <https://www.nih.gov/news-events/news-releases/nih-halts-clinical-trial-hydroxychloroquine>.
75. Gao J, Zhenxue T, Yang X. Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. *BioScience Trends*. 2020;14:72–3.
76. Gautret P, Lagier J-C, Parola P, Hoang VT, Meddeb L, Mailhe M, Doudier B, Courjon J, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Intl J Antimicrobial Agents*. 2020;56:105949. <https://doi.org/10.1016/j.ijantimicag.2020.105949>.
77. Chen Z, Hul J, Zhang Z, Jiang S, Han S, Yan D, Zhuang R, Hu Ben, Zhang Z. Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial. 2020; *MedRxiv*, <https://doi.org/10.1101/2020.03.22.20040758>.
78. Cavalcanti AB, Zampieri FG, Rosa RG, Azevedo LCP, Veiga VC, Avezum A, Damiani LP, Marcadenti A, et al. Hydroxychloroquine with or without azithromycin in mild-to-moderate Covid-19. *New England J Medicine*. 2020. <https://doi.org/10.1056/NEJMoa2019014>.
79. Borba MGS, Almeida FF, Sampaio VS, Alexandre MAA, Melo GC, Brito M, Mourao MPG, et al. Effect of High vs Low Doses of Chloroquine Diphosphate as Adjunctive Therapy for Patients Hospitalized With Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection A Randomized Clinical Trial. *JAMA*. 2020;3(4.23): e208857. doi:<https://doi.org/10.1001/jamanetworkopen.2020.8857>.
80. Boulware DR, Pullen MF, Bangdiwala AS, Pastick KA, Lofgren SM, Okafor EC, Skipper CP, et al. A randomized trial of Hydroxychloroquine as Postexposure prophylaxis for Covid-19. *N Engl J Med*. 2020;383:517–25.
81. Magagnoli J, Narendran S, Pereira F, Cummings T, Hardin JW, Sutton SS, Ambati J. Outcomes of hydroxychloroquine usage in United States veterans hospitalized with Covid-19. *Med*. 2020. <https://doi.org/10.1016/j.medj.2020.06.001>.

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