

IUPHAR and COVID-19

IUPHAR is responding to the current crisis by coordinating pharmacological resources worldwide, particularly the responses of the pharmacological community, and posting key documents, on this site and on the site of the IUPHAR/BPS <u>www.guidetopharmacology.org</u>

which holds a list of the drugs being currently proposed or assessed for treatment (<u>https://www.guidetopharmacology.org/coronavirus.jsp</u>). This effort, thanks to our long-term collaboration with the British Pharmacological Society, is being continually updated by the Guide's curators in Pr Jamie Davies' group at the University of Edinburgh, supported by (at least) weekly meetings of NC-IUPHAR (chaired by Steve Alexander, backed up by the many IUPHAR expert subcommittees). An article on drug testing against SARS-CoV-2 is available in preprint for comments on Authorea "A rational roadmap for SARS-CoV-2/COVID-19 pharmacotherapeutic research and development" at: https://doi.org/10.22541/au.158679935.58510327.

In this first webpage announcement we list the most advanced progress of some of the world's pharmacological societies, but this will be continuously updated, as we have more news from societies, and key recommendations, with the ultimate aim of global coverage.

A key issue for us is the alliance we announced last year, with the International Union of Pharmacological Societies (IUIS), and the reinforcement of IUPHAR's immunology group, Immuphar, led by Francesca Levi-Schaffer (Tiligada et al., 2015, Ishii, 2017). This alliance, coupled with a 0.5M£ three-year grant from the Wellcome trust, allowed us to create the Guide to Immunopharmacology (<u>https://www.guidetoimmunopharmacology.org/immuno/index.jsp</u>). This Guide lists up-to-date information on the science underlying each immune target, coupled to the immunological cell type involved. It is important to note that these freely-available databases are constantly evolving, so can never be perfect, and always benefit from constructive criticism and input from users – please help!

The best way to use these databases are outlined in Harding et al. (2018,2020).

Coronaviruses have major immunological effects after targeting ACE2 (Pinto et al, 2020), or their other targets. The cytokine storm, and massive lung fibrosis following SARS in very seriously affected patients, is mediated by the classical immunological mediators recently described by Fung et al., (2020). The immunological profile of patients in recovery is a critical factor to be defined.

In addition to this the clinical division of IUPHAR, led by Caroline Samer, who is also IUPHAR's representative to WHO, is working on clinical trials, and data assessment, co-organizing a review with the Chinese Pharmacology Society, CNPHARS (see www.iuphar.org), on the clinical data coming from the first country to be confronted by this worldwide health challenge.

IUPHAR, in conjunction with the Medicines for Malaria Venture, MMV, funded by the Gates Foundation, has also produced the <u>www.Guidetomalariapharmacology.org</u>, (Armstrong et al., 2020) of interest considering the evolving situation with chloroquine and hydroxychloroquine and therapy of COVID-19.

Clinical studies also described ,Immunopaedia case are in (https://www.immunopaedia.org.za/), the IUIS immunology education platform, which is now **IUPHAR** Pharmacology linked the Education Project (PEP) to (www.pharmacologyeducation.org/pharmacology/immunopharmacology); so education in both pharmacology and immunology is now linked.

Several Pharmacology Societies have benefitted from David Lewis' hands on educational courses. With national lock downs, the closure of Universities and the shift to online teaching in response to the Covid pandemic, there is a global need from pharmacology educators for simulations and other electronic learning resources that can be used in undergraduate education as alternatives to face-2-face practicals. Dave Lewis (University of Leeds, UK) is leading a global search for simulations, computer models/programmes, or any other e-learning resources which he will collate and share. If you have any resources or know of any, please get in touch with him (d.i.lewis@leeds.ac.uk). Also get in touch if you would like to be sent details of the discovered resources. Please share this call with your colleagues and across your networks.

Furthermore, the IUPHAR Early Career Investigators Committee, led by Carl White, unites 14 young investigators nominated by pharmacology societies around the world, who are eager to help.

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Some examples of how the world's pharmacology societies are organizing in the crisis:

- 1. The French Society for Pharmacology and Therapeutics (SFPT, President Silvy) has benefitted by its well organised clinical and pharmacovigilance group, to organize an expert question and answer site for the general public (https://sfpt-fr.org/covid19). Pharmacovid is supported by a network of the major clinical pharmacologists and epidemiologists in France which meet, virtually, round a dedicated platform everyday, to field and reply to questions, via dedicated experts, with links to regulatory bodies. Furthermore, the site has an ongoing metanalysis analysis of the results every 6 hours for the drugs being analysed all round the world (http://www.metaevidence.org/COVID19.aspx) for professionals. Thus, SFPT has set up a major well-coordinated initiative, with the capacity to react rapidly in this rapidly evolving situation. Their site is the preferred Francophile site. The following YouTube video has also been developed for reference: https://www.youtube.com/user/SFPTFrance/.
- 2. ASPET has responded to the COVID-19 pandemic in the following ways:
 - Published a COVID-19 perspective article in *Molecular Pharmacology* which was made freely accessible immediately. To access this page: <u>https://www.aspet.org/aspet/news/news/2020/04/02/molecular-pharmacology-publishes-covid-19-perspective-article</u>
 - Been working to identify and fast-track COVID-19-related manuscripts and ensure accepted manuscripts are freely accessible immediately.
 - Created an information page about ASPET's journals for authors, reviewers, readers in light of COVID-19.
 - Prepared a COVID-19 resource page that is freely available to members and the public. To access this page: <u>https://www.aspet.org/aspet/news/covid-19-</u> resources-and-information

- Initiated our new ASPETConnect community to provide a forum for discussion and to pro-actively communicate with our members.
- Offered flexibility and no-cost extensions for ASPET-funded summer undergraduate research programs that have been impacted by COVID-19.
- 3. BPS's response to the COVID-19 pandemic can accessed here: https://www.bps.ac.uk/covid-19. Also a message from their president, Professor Sir Munir Pirmohamed, can be found here https://www.bps.ac.uk/publishing/blog/april-2020/message-from-our-president-on-covid-19. All published articles relevant for COVID-19 in the BJP and the BJCP have been, or will be, made free to access immediately. (PR&P is entirely open access.) The Society's journals accept manuscripts that have already been posted as a preprint, and all authors submitting to the BJP or the BJCP may post their manuscript as a preprint in Authorea as part of the submission process. Explore BPS Journals: https://www.bps.ac.uk/publishing. In addition the British Journal of Pharmacology will be publishing a special Themed **Issue** on the Pharmacology of COVID-19: https://bpspubs.onlinelibrary.wiley.com/hub/journal/14765381/covid19.html.

4. The German Society for Experimental and Clinical Pharmacology and Toxicology has established a team of experts to respond to urgent questions and has published the statements of SIF.

The lead in the public discussion is taken by virologists by Christian Drosten, Charité. He is a corona specialist and was the first world-wide to establish the first SARS-CoV-2 PCR test. Now a mutual initiative of all 38 German medical faculties has been launched by Angela Merkel having a first budget of 150 Mio €. It is expected that more money will come in the form of an investment program. So it's less pharmacology but a mutual framework of many medical disciplines.

- 5. The Swiss Society of Pharmacology and Toxicology response to the COVID-19 pandemic can be seen here: https://sciencesnaturelles.ch/organisations/sscpt/covid 19.
- 6. The Indian Pharmacological Society is intimately involved in the response to COVID-The control of COVID-19 in India is restricted to Phase-II to date. 19. The Indian Council of Medical Research (ICMR) has formed 'Rapid Response Team for COVID-19' under leadership of Prof. Balram Bharghava Director General-ICMR (reporting directly to N Modi) and is the major agency to undertake all type of research and epidemiology studies apart from supplying testing kits and national level monitoring. ICMR-NIN is part of local coordination with Dinesh Kumar (past President) is a member of this team. All clinical trial and related studies of COVID-19 will be monitored from central team of ICMR. This includes selecting the protocol design, ethical approvals and rationale of selecting sites etc. Recommendations are on the IUPHAR web site. Natural products will be assessed depending on a strict rationale in comparison or association with marketed and new drugs. In this respect, Prof Bhargava was the patron of the IUPHAR/IPS World congress on Natural Products, held at Hyderabad last December, with strong recommendations in preparation. Dr. Nilima A. Kshirsagar, is National Chair of Clinical Pharmacology, and member IUPHAR exec. Dr Shiv Prakash, President IPS is involved with clinical trials. Thus IPS is at a pivotal position in the response to COVID-19.
- 7. The Spanish Society of Clinical Pharmacology is contributing to the COVID19 crisis from by actively collaborating in the preparation and transmission of information on the treatment and therapeutics of COVID19. We have collaborated in the preparation of protocols that the Spanish Ministry of Health has made available on its website for

health professionals on the clinical management of COVID19 in intensive care units and hospital care. We collaborated in the preparation of information on the possible medicines available and their conditions of use for the management of respiratory infection by SARS-CoV-2 prepared by the Spanish Agency for Medicines and Health Products (AEMPS in Spanish) for health professionals.

We disseminated information about COVID19 through Twitter on the treatment protocols that the Ministry of Health has prepared, on some information notes that the AEMPS has generated on controversial therapeutic issues such as the use of non-steroidal anti-inflammatory drugs or angiotensin-converting enzyme inhibitors or angiotensin II antagonists in patients with COVID19. Via Twitter, we have cautioned regarding the use of drugs and treatments for which, in general, very little evidence is available and therefore has recalled the need to generate better evidence through its use in well-designed clinical trials and studies that allow the generation of quality information.

The Spanish Society of Clinical Pharmacology is also collaborating in the design and development of clinical trials or other kind of studies or carrying out some studies. Different members of our society, as a priority in the context of the SCReN Platform (Spanish Clinical Research Network - Platform of Clinical Research Units and Clinical Trials), are either collaborating in clinical trials, cohort studies or other kind of pharmacoepidemiological designs to evaluate efficacy and / or safety of different treatments for COVID19. A significant proportion of these studies are multicenter (ConPlas-19, PamCovid, Tocovid, etc.), and multinational, and some of them are carried out under the auspices of the WHO (Solidarity clinical trial) with the support of the Instituto de Salud Carlos III (ISCIII) and the AEMPS collaboration. Our society has also promoted an observational collaborative study aimed at assessing the effectivity of tocilizumab in patients with COVID19 pneumonia.

- 8. The Canadian Society of Pharmacology and Therapeutics has cancelled its annual conference because of the Covid-19 pandemic. In its place we will be holding a virtual conference that will include ten-minute oral platform and three-minute thesis style presentation competitions for trainees, CSPT award recipient research presentations and our annual general meeting. The virtual conference will be held on June 10th, 11th and 12th from 1 PM to 3:30 PM EDT. We have also cancelled our planned summit on high-cost high-value drugs for children, which was to be held in conjunction with our annual conference. The summit will be postponed to Fall 2020. To help inform the Canadian Pharmacology Community the CSPT is also working on a series of position statements related to COVID-19 Pharmacology, which will be posted on our society website in the near future https://pharmacologycanada.org/. Also CSPT is working with the Public Health Agency of Canada to create a COVID-19 Pharmacotherapy Task Force.
- 9. Hong Kong, interacting with the Pharmacological Society, has been successful in controlling the pandemic partly because of the previous experience with SARS in 2003, which was a very rapid learning experience. Ever since then, the medical service has maintained a high level of alert which is partly related to the constant threat of avian flu as well as regular flu. Any patient admitted with fever was tested for flu and other virus before being put on a ward for the last few years. It has been routine for years to ask patients with fever if they visited wet markets in China or even in Hong Kong. We have always taught the medical students to wear masks and take other precautions in clinical areas because of the danger identified by SARS. Hong Kong closed the boarders with China quite early. Most of the recent cases have come into Hong Kong from overseas. Hong Kong has a very effective isolation,

quarantine and contact tracing system. The number of isolation beds in the public hospitals was almost overwhelmed because of the extreme precautions right from the start. The combination of interferon beta-1b, lopinavir–ritonavir,and ribavirin treated early has been very effective (Hung et al. 2020, Lancet, https://doi.org/10.1016/S0140-6736(20)31042-4).

10. The Israeli Association of Clinical Pharmacology activities in response to the COVID-19 pandemic has been to establish a network of hospitalist clinical pharmacologists, sharing experiences, local decisions and research. Clinical Pharmacologists countrywide lead local hospital decisions on evolving treatment guidelines and pharmacovigilance. We issued guidance for use of the various medications suggested for COVID-19 treatment and responded to various notions on popular media such as NSAIDS and COVID, ACE and ARBs and COVID in collaboration with the Pharmaceutical Society of Israel. Joint statements were published for medical staff and for the public.

We designed and are leading national multicenter clinical trials of COVID-19 therapeutics and pharmacovigilance efforts in collaboration with the government health ministry.

We will continue to add the progress made by the world's pharmacology societies **here** as content is received.

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