



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 www.guidetopharmacology.org

which holds a list of the drugs being currently proposed or assessed for treatment (<https://www.guidetopharmacology.org/coronavirus.jsp>). 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 (<https://www.guidetoimmunopharmacology.org/immuno/index.jsp>). 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 www.Guidetomalariapharmacology.org, (Armstrong et al., 2020) of interest considering the evolving situation with chloroquine and hydroxychloroquine and therapy of COVID-19.

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

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.

Note: The Guide to Immunopharmacology has been funded by the Wellcome Trust (108420/Z/15/Z); the International Union of Basic and Clinical Pharmacology and the British Pharmacological Society (MED791). PEP has been funded by ASPET, The Japanese Pharmacology Society, The Chinese Pharmacology Society (CNPHARS) and the Hungarian Pharmacology Society. We are very grateful for this support, as databases are difficult to finance when set up.

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: <https://www.aspet.org/aspnet/news/news/2020/04/02/molecular-pharmacology-publishes-covid-19-perspective-article>
 - 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: <https://www.aspet.org/aspnet/news/covid-19-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-19. The control of COVID-19 in India is restricted to Phase-II to date. The **Indian** Council of Medical Research (ICMR) has formed 'Rapid Response Team for COVID-19' under leadership of Prof. Balram Bhargava 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.

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

References:

- Alexander SPH, Kelly E, Mathie A, Peters JA, Veale EL, Armstrong JF, Faccenda E, Harding SD, Pawson AJ, Sharman JL, Southan C, Buneman OP, Cidlowski JA, Christopoulos A, Davenport AP, Fabbro D, Spedding M, Striessnig J, Davies JA; CGTP Collaborators. THE CONCISE GUIDE TO PHARMACOLOGY 2019/20: Introduction and Other Protein Targets. *Br J Pharmacol*. 2019 Dec;176 Suppl 1:S1-S20. doi: 10.1111/bph.14747. PubMed PMID: 31710719; PubMed Central PMCID: PMC6844537.
- Armstrong JF, Faccenda E, Harding SD, Pawson AJ, Southan C, Sharman JL, Campo B, Cavanagh DR, Alexander SPH, Davenport AP, Spedding M, Davies JA; NC-IUPHAR. The IUPHAR/BPS Guide to PHARMACOLOGY in 2020: extending immunopharmacology content and introducing the IUPHAR/MMV Guide to MALARIA PHARMACOLOGY. *Nucleic Acids Res*. 2020 Jan 8;48(D1):D1006-D1021. doi: 10.1093/nar/gkz951. PubMed PMID: 31691834.
- Armstrong JF, Faccenda E, Harding SD, Pawson AJ, Southan C, Sharman JL, Campo B, Cavanagh DR, Alexander SPH, Davenport AP, Spedding M, Davies JA; NC-IUPHAR. The IUPHAR/BPS Guide to PHARMACOLOGY in 2020: extending immunopharmacology content and introducing the IUPHAR/MMV Guide to MALARIA PHARMACOLOGY. *Nucleic Acids Res*. 2020 Jan 8;48(D1):D1006-D1021. doi: 10.1093/nar/gkz951. PubMed PMID:31691834.
- Fung SY, Yuen KS, Ye ZW, Chan CP, Jin DY. A tug-of-war between severe acute respiratory syndrome coronavirus 2 and host antiviral defence: lessons from other pathogenic viruses. *Emerg Microbes Infect*. 2020 Mar 14;9(1):558-570. doi: 10.1080/22221751.2020.1736644. eCollection 2020. Review. PubMed PMID: 32172672.
- Harding SD, Faccenda E, Southan C, Maffia P, Davies JA. A new guide to immunopharmacology. *Nat Rev Immunol*. 2018 Dec;18(12):729. doi: 10.1038/s41577-018-0079-2. PubMed PMID: 30327546.
- Harding SD, Faccenda E, Southan C, Pawson AJ, Maffia P, Alexander SPH, Davenport AP, Fabbro D, Levi-Schaffer F, Spedding M, Davies JA. The IUPHAR Guide to Immunopharmacology: connecting immunology and pharmacology. *Immunology*. 2020 Feb 5. doi: 10.1111/imm.13175. [Epub ahead of print] Review. PubMed PMID: 32020584.
- Harding SD, Sharman JL, Faccenda E, Southan C, Pawson AJ, Ireland S, Gray AJG, Bruce L, Alexander SPH, Anderton S, Bryant C, Davenport AP, Doerig C, Fabbro D, Levi-Schaffer F, Spedding M, Davies JA; NC-IUPHAR. The IUPHAR/BPS Guide to PHARMACOLOGY in 2018: updates and expansion to encompass the new guide to IMMUNOPHARMACOLOGY. *Nucleic Acids Res*. 2018 Jan 4;46(D1):D1091-D1106. doi: 10.1093/nar/gkx1121. PubMed PMID: 29149325; PubMed Central PMCID: PMC5753190.
- Ishii M. Immunology proves a great success for treating systemic autoimmune diseases - a perspective on immunopharmacology: IUPHAR Review 23. *Br J Pharmacol*. 2017 Jul;174(13):1875-1880. doi: 10.1111/bph.13784. Epub 2017 Apr 24. Review. PubMed PMID: 28299772; PubMed Central PMCID: PMC5466525.
- Maffia P, Mantovani A, Spedding M. Scientists on the Spot: the Guide to Immunopharmacology as a new resource for the cardiovascular community. *Cardiovasc Res*. 2019 Jan 1;115(1):e5-e6. doi: 10.1093/cvr/cvy296. PubMed PMID: 30576437.
- Pinto B, Oliveira A, Singh Y, Jimenez L, Goncalves A, Ogava R, Creighton R, Peron J, Nakaya H. ACE2 Expression is Increased in the Lungs of Patients with Comorbidities Associated with Severe COVID-19 medRxiv 2020.03.21.20040261; doi: <https://doi.org/10.1101/2020.03.21.20040261>

Sharman JL, Harding SD, Southan C, Faccenda E, Pawson AJ, Davies JA; NC-IUPHAR. Accessing Expert-Curated Pharmacological Data in the IUPHAR/BPS Guide to PHARMACOLOGY. *Curr Protoc Bioinformatics*. 2018 Mar;61(1):1.34.1-1.34.46. doi: 10.1002/cpbi.46. PubMed PMID: 30040201.

Tiligada E, Ishii M, Riccardi C, Spedding M, Simon HU, Teixeira MM, Cuervo ML, Holgate ST, Levi-Schaffer F. The expanding role of immunopharmacology: IUPHAR Review 16. *Br J Pharmacol*. 2015 Sep;172(17):4217-27. doi: 10.1111/bph.13219. Epub 2015 Jul 21. Review. PubMed PMID: 26173913; PubMed Central PMCID: PMC4556463.