Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Editorial overview: COVID-19 therapy: From lung disease to systemic disorder

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Two years after SARS-CoV-2 struck the city of Wuhan, China, it has infected billions of people worldwide and caused millions of deaths associated to the most severe manifestations of COVID-19. Since the beginning of the pandemic, research has focused on diagnostic, prophylactic and therapeutic interventions which have proven to be useful in mitigating the effects of COVID-19 around the world. Yet, efforts to understand the pathogenesis of COVID-19, the emergence of novel virus variants, the epidemiological behavior of the disease and the discovery of suitable models of infection remain crucial to improve the containment of the emergency. In this special issue of *Current Opinion in Pharmacology*, we collate review articles that provide insights into pharmaceutical strategies to control severe forms of SARS-CoV-2 looking beyond lung disease to approach COVID-19 as a multisystemic disorder.

With over 2 million SARS-CoV-2 whole-genome sequences obtained and shared worldwide, genomic surveillance has been pivotal to support public health decisions, particularly those regarding the implementation of sanitary countermeasures to avoid infections and the adequation of vaccination schemes to improve protection against specific variants. Importantly, sequencing has also allowed scientists to trace the SARS-CoV-2 variant distribution globally and to identify mutations in the viral genome near to real time. Although most mutations do not have a significant impact on the biology of SARS-CoV-2, there are some mutations that give rise to the defined variants of interest, which stand out in epidemiological terms (ex. When they begin to predominate amongst human populations) whereas changes in transmission rates, severity of the disease, difficulties in detecting the pathogen and alterations in susceptibility to vaccine-induced immunity and therapeutic agents against the virus correspond to the so called variants of concern [1]. Chiranjib Chakraborty et al. provide an overview of the impact of virus mutations with special emphasis on findings of mutations that confer resistance to small antiviral molecules.

The rapid and accurate identification of SARS-CoV-2 infection has become a matter of priority for monitoring and adopting effective public health measures in the context of COVID-19 waves. From the beginning of the pandemic different approaches have been exploited to develop reliable diagnostic, essential to follow the TETRIS (i.e., test, trace and isolate) program. This approach has shown to be beneficial in controlling transmission chains, preventing health care systems saturation, and reducing the economic impact of isolation measures. However, the

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Santiago Mirazo Ph.D. received the master's and doctoral degrees in biological sciences from the Universidad de la República, Uruguay. He was Assistant Professor, and he attained an Associate Professor position at the Facultad de Medicina, Universidad de la República. His research is focused on zoonotic viruses and the molecular mechanisms involved in pathogen emergence and cross-species events. Particularly, he is interested in the study of hepatitis E virus. Recently, he has been working in projects related to the immune response against SARS-CoV-2 and the detection and quantification of the virus in wastewater as a monitoring tool for COVID-19 in the community.

selection of the most convenient detection techniques for the diagnosis will depend on the goals pursued according to the testing strategy. Gonzalo Moratorio et al. provide a detailed and comprehensive review on the most widely available diagnostic tests. An algorithm for the implementation of SARS-CoV-2 antigen and RT-PCR test for an accurate diagnosis is presented.

Initially considered exclusively as a lung disease, the association of different non-respiratory symptoms in COVID-19 rapidly gained attention. These effects have been related to the broad tissue distribution of ACE-2, the canonic receptor for SARS-CoV-2. COVID-19 patients show pulmonary, cardiac, and thrombotic manifestations; thus, one might predict these to be the only sites of clinical care interest. However, it was suggested that other organs such as the intestine and the brain expressing ACE-2 may become infected and contribute to systemic damage. Severe forms of COVID-19 are associated with inflammatory changes in the brain and patients can also experiment neurological symptoms. One such example is the neuro-ophthalmic illness that has been linked to COVID-19. Priti Talwar & Arman Firoz reviewed the potential use of kaempferol as a natural therapeutic alternative to control common pathways in the setting of COVID-19 and macular degeneration.

It has been suggested that peripheral inflammation triggered by SARS-CoV-2 can still be relayed to brain cells, triggering inflammation into the central nervous system [2]. Neuroinflammation and its relationship to COVID-19 is illustrated by Edda Sciutto et al.; the appearance of neurological sequalae as well as the recently coined term NeuroCOVID, useful for the diagnosis, management and treatment of patients are summarized.

"All disease begins in the gut" suggested Hippocrates more than 2000 years ago. This may not be true for SARS-CoV-2 infection but what is true is that gastrointestinal (GI) symptoms are common during COVID-19. Moreover, pre-existing GI diseases may influence the disease [3]. Hassan Ashktorab et al. provide an overview of the impact of the digestive system on COVID-19 pathophysiology. GI symptoms and pre-existing GI diseases; comorbidities and the gut microbiota axis are also reviewed in terms of treatments and outcomes.

During the first two years of the pandemic almost a thousand clinical trials aimed to examine novel pharmaceutical interventions and drug repurposing to treat COVID-19 were carried out, most of which proved to be unsuccessful. Programmatic and large trails such as RECOVERY, SOLIDARITY and the US National Institutes of Health ACTT trials have been the exception. These trials randomized thousand patients during the first year of the pandemic [4]. However, with a struggling world and the difficult to access to resources to battle the pandemic, clinicians opted for small trials progress over global mega-trials. Andres Pizzorno et al. reviewed what we have learned from the therapeutic options during the first 18 months of the COVID-19 pandemic. A practical overview on the potential of combination therapies and the value of defining prognostic markers is also included.

In the middle of the crisis due to SARS-CoV-2, the economic backwardness of numerous nations in the world has been evidenced by the disparity in which the measures to contain the pandemic (vaccination, sequencing of viral genomes and clinical trials) have progressed. Latin America

exemplifies this situation. We summarized the demographic and economic features that might have impacted on the COVID-19 pandemic in Latin America and the Caribbean.

How would the current virus variants affect the pathobiological mechanisms of the infection? How would the microbiota affect COVID-19 outcomes? AAnd what can we expect in terms of cognitive and neurodegenerative disorders in the future as a consequence of the infection? The answers to these and other questions requires optimal models for the study of SARS-CoV-2 pathogenesis. Insights into the use of bioengineering for the development of organotypic tissue models to investigate SARS-CoV-2—host interactions; particularly their application to investigate pharmacological interventions to fight infection is provided by Volker M. Lauschke et al.

We deeply thank to all the leading experts who contributed to this special issue. Undebatably, the advances discussed open new avenues of investigation with therapeutical potential to successfully combat COVID-19 and to contain emerging virus in the future.

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