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Editorial overview: Special issue on antiviral strategies in 
Current Opinion in Virology

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Richard K. Plempner is the Director of the Center for Translational Antiviral Research and Distinguished University Professor at Georgia State University. His research focuses on the biology of respiratory RNA viruses with particular emphasis on developing direct-acting small-molecule therapeutics targeting the entry and replication machineries of viral pathogens of the paramyxovirus, orthomyxovirus, and coronavirus families. He has made numerous contributions to developing novel drug screening technology, isolating druggable targets, and identifying and characterizing novel antiviral candidates directed against respiratory syncytial virus, parainfluenzaviruses, and influenza viruses. His laboratory was instrumental in the development of EIDD-2801/molnupiravir against influenza and the subsequent repurposing of the drug for the treatment of SARS-coV-2 infection.

The COVID-19 pandemic has resulted in approximately 200 million cases and an estimated 4 million deaths worldwide to date. The impact on global health, economies, and politics is unprecedented for a single viral pathogen. Since the first reports of the emergence of a novel betacoronavirus appeared in 2019 and a global pandemic was declared in early 2020, SARS-CoV-2 has created a watershed moment also for the research community in terms of unparalleled need for effective therapeutics and vaccines, the goal of dramatically shortened timelines to advance drug candidates to the clinic, and in meeting public expectations. Exciting new technologies have been developed and innovative collaborative initiatives launched, but also lessons of pitfalls in drug discovery relearned.

This year’s annual issue of Antiviral Strategies in Current Opinion in Virology focusses exclusively on the SARS-CoV-2 challenge. Opinions on what constitutes the most effective response strategy to the still raging pandemic vary widely and it may take years until the individual impact of different approaches can be fully appreciated. At the current phase from widespread SARS-CoV-2 community transmission to increased vaccination coverage, reopening of large geographical areas, and the emergence of a number of viral variants of concern, this issue has collected the insight of subject experts in an attempt to provide an early retrospective.

Opinion articles herein address three broad areas of COVID-19 response research: i) foundational studies of SARS-CoV-2 biology; ii) drug discovery, development, and repurposing research; and iii) the development of novel vaccine technologies.

- Specifically, contributing authors Lowen [1] and de Swart [2] and their co-authors discuss animal models developed for studying SARS-CoV-2 pathogenesis and transmission, respectively, which are instrumental for preclinical stage drug and vaccine development. Cox et al. [3] examine the importance of protein structural information to the identification of druggable targets and structure-guided drug optimization, whereas Gotte [4] evaluate the impact of in vitro biochemical assays on drug development by example of the mechanistic characterization of remdesivir. Lee and co-authors (insert LINK) summarize current SARS-CoV-2 entry assay technology and illuminate the importance of standardized assay conditions for reproducible results.
- In two articles directed at drug discovery strategies, Jonsson [5] and Sourimant [6] and colleagues assess the effectiveness of the many open drug discovery and drug repurposing screens that were launched in 2020 in response to the mounting pandemic. Focusing on specific
druggable targets for direct-acting antivirals, Painter [7] and Deval [8] and co-authors recapitulate the development of EIDD-2801/molnupiravir and SARS-CoV-2 protease inhibitors, respectively. Ngo and Gewirtz [9] provide a broader view on the effect of the host microbiome on COVID-19 progression, whereas Glazier and colleagues (insert LINK) discuss the predictive power of in silico modeling to appreciate the dynamic interplay between virus and host.

- On COVID-19 prophylaxis, Kurup and Schnell [10] examine vaccine technologies considered to prevent SARS-CoV-2 infection. This overview is complemented by a discussion of the specific strengths and challenges of mRNA nanoparticle vaccines by Iggyarto et al. [11]. Summarizing the unprecedented expansion of diagnostic capacity during the pandemic, Greninger [12] discusses the impact of newly established infrastructure on surveillance and our ability to gauge therapeutic success.

COVID-19 was certainly not the last pandemic viral threat to human health. Assessing the effectiveness of response research strategies will be important to improve pandemic preparedness. Ideally, the compendium of opinion articles forming this special issue will contribute to identifying approaches that have meaningfully contributed towards this goal.

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