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EDITORIAL

Editorial of virtual special issue: The development of antiviral drug discovery

Acta Pharmaceutica Sinica B is pleased to introduce a collection on The Development of Antiviral Drug Discovery, featuring articles published in the journal between January 2020 and January 2025.

The discovery of antiviral drugs is a complex and significant process that requires an in-depth understanding of the viral life cycle, as well as the identification and validation of potential drug targets. Historically, the development of antiviral drugs began in the 1950s. As comprehension of viral replication mechanisms deepened, a series of new antiviral agents were successfully developed. For instance, acyclovir was identified in the late 1970s as the safe and effective antiviral drug. Furthermore, the global spread of human immunodeficiency virus (HIV) in the early 1990s spurred research into antiretroviral drugs such as zidovudine. Over the past three decades, antiviral drugs have achieved numerous significant breakthroughs, particularly in combating chronic viral infections, profoundly changing the lifestyle of countless patients. Among the antiviral drugs approved in the past 30 years, the largest number is for HIV, followed by drugs for hepatitis C virus and hepatitis B virus (HBV). Additionally, drugs for treating influenza and cytomegalovirus have also been approved. Since the onset of the COVID-19 pandemic, there has been a consistent annual increase in the number of approved pharmaceuticals specifically targeting coronavirus. Despite the availability of over a hundred antiviral drugs currently on the market, there remains an insufficient arsenal to combat the diverse array of viruses that can infect humans. Therefore, it is imperative to continue the discovery of more reliable antiviral agents.

During the COVID-19 pandemic, researchers worldwide responded swiftly, accelerating the discovery and development of antiviral drugs. As of March 2024, seven oral drugs for COVID-19 have been launched in China, including azvudine, nirmatrelvir, molnupiravir, simnotrelvir, deuremidevir hydrobromide, leritrelvir and atilotrelvir. Additionally, various antibody therapeutics aimed at viral surface proteins and small molecules targeting viral replication mechanisms are under development. Driven by advancements in the fields of covalent inhibitors and targeted protein degradation technologies, new small molecule targeted drugs continue to emerge.

Basic scientific research is crucial for the development of antiviral drugs. It provides the theoretical foundation for the development of antiviral drugs and is also the driving force behind the development of innovative drugs. X-ray crystallography has provided a wealth of valuable evidence for the discovery of structure-based drug targets by elucidating the structure of viral proteins. From 2020, significant advancements have been made in the research and development of antiviral drugs, and the discovery of innovative drugs has made significant progress. This progress is highlighted by the discovery of new mechanisms (novel targets, allosteric sites, multiple targets) and new structural drugs (herbal medicines, natural products, macrolide antibiotics). Due to the pharmacokinetic and pharmacodynamic advantages of small-molecule drugs, research in this field is particularly abundant.

The future development of antiviral drugs is likely to place greater emphasis on the creation of broad-spectrum antiviral agents. These medications can target multiple viruses, thereby providing more extensive protection. Concurrently, as viruses continue to mutate, the research and development of antiviral drugs capable of addressing new variants has emerged as a significant area of focus. Moreover, strategies that target host factors for antiviral purposes represent an emerging field. This approach aims to inhibit viral replication by targeting host factors that are highly dependent on the virus. Such methods may offer a broader spectrum of antiviral activity and pose a lower risk of developing resistance. In addition, the application of some new technologies (artificial intelligence, machine learning, targeted protein degradation, covalent binding, targeted activator of cell kills) will also accelerate the discovery of antiviral drugs.

This Collection consists of 50 Original Articles published between January 2020 to January 2025. These articles cover a variety of virus (SARS-CoV-2, HIV, HBV, etc.) and a wide range of drug targets (such as the main protease, RNA-dependent RNA polymerase and papain-like protease of SARS-CoV-2). Among the articles, 25 out of 50 focus on SARS-CoV-2. Additionally, HIV

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has been extensively studied, with a total of 10 articles dedicated to this topic. These studies not only explore the discovery and modification of drug structures but also delve into the identification of drug targets. Moreover, driven by advancements in modeling techniques, hydrophobic tagging-based degraders are emerging as promising tools in antiviral research. Most of these articles are produced by universities and research institutions, with significant contributions also made by hospitals. In addition, pharmaceutical companies have also made contributions in this regard. The spread of the SARS-CoV-2 has significantly heightened researchers' enthusiasm for antiviral drug development, thereby facilitating advancements in the discovery of antiviral drugs.

Through this collection, we anticipate that this will serve as an opportunity to disseminate recent trends in antiviral drug discovery among a diverse array of scientists globally, as well as to encourage more researchers, particularly young scholars, to submit their original findings or insightful perspectives on antiviral drug discovery to *Acta Pharmaceutica Sinica B*.

List of Collection articles:

1. Zhou J, Xu W, Liu Z, Wang C, Xia S, Lan Q, et al. A highly potent and stable pan-coronavirus fusion inhibitor as a candidate prophylactic and therapeutic for COVID-19 and other coronavirus diseases. *Acta Pharm Sin B* 2022;**12**:1652−61. https://doi.org/10.1016/j.apsb.2021.07.026.
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