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Editorial

Viral diseases were largely untreatable 40 years ago. The first antivirals were developed in the 1960s, mostly to deal with herpes viruses, and were found using traditional trial-and-error drug discovery methods. This was a time-consuming, hit-or-miss procedure, performed in the absence of a good knowledge of how the virus propagated. It was not until the 1980s, when the full genetic sequences of viruses began to be unraveled, that researchers began to understand the virus life cycle in detail, and exactly what chemicals were needed to inhibit the specific reproductive steps. Now dozens of antiviral treatments are available, and medical research is rapidly exploiting new knowledge and technology to develop additional therapies. However there is still no or limited treatment available for many viral infections. Viral diseases such as human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV) have a major threat on human health in China and throughout the world. Furthermore, established viruses are now developing resistance to available therapies making this another important area for continued drug discovery.

Since the discovery of HIV and acquired immunodeficiency syndrome (AIDS) in 1981, this disease has become one of the most significant public health challenges globally. 2006 marks the 10th anniversary of the introduction of highly active antiretroviral therapy (HAART), a combination of three antiretrovirals (ARVs) from at least two drug classes that has led to significant reductions in HIV-related morbility and mortality. However, the HIV virus is capable of mutating rapidly to develop drug resistance, so it is imperative to develop more effective and safe drugs to overcome the growing resistance of the virus and identify new molecules that may block known viral targets or other new ones. Nevertheless, much has been learned in process of developing anti-HIV drugs, includes new insights into antiviral therapy and the underlying virology.

HBV is another virus that has a major impact on global public health. Despite the availability of an effective vaccine, there are still 400 million people worldwide who are chronically infected with hepatitis B virus. The major etiology of hepatocellular carcinoma (HCC) is chronic infection with HBV. Although fifth in cancer incidence worldwide, HCC/liver cancer is the third leading cause of cancer death. Due to lack of good cell and animal models, research on the mechanism of HBV replication has progressed very slowly. So far, therapy to HBV infection is limited to interferon and nucleos(t)ide analogs, but low response and drug resistance are often associated with these therapies. The current vaccines are effective, but they are expensive, and escape mutants may be a problem waiting to happen. Thus, without a doubt, more work needs to be done in all of the key areas of the management of HBV infection.

Hepatitis C virus (HCV) is a major cause of chronic

hepatitis, liver cirrhosis and hepatocellular carcinoma. A protective vaccine against HCV does not exist at present and therapeutic approaches are still limited. The only available treatment option is a long-acting pegylated-interferon-alpha, given in combination with nucleoside analog ribavirin, which is not very effective for about half of patients. However, for many years, a major obstacle in HCV research has been the lack of a cell culture system that can produce infectious viral particles. Significant breakthroughs in establishing an infectious HCV cell culture system (HCVcc) were achieved in 2005. HCV has evolved multiple strategies to survive and persist in hostile cellular environments; and the viral population is known to rapidly change during the course of a natural infection thereby escaping immune surveillance. Rapid mutations also help virus to survive by selecting for the variants which are resistant to antiviral drugs. A complete understanding of the HCV lifecycle is vital for developing a successful cure.

Antiviral therapy has made considerable advances over the past four decades. The methods used to produce antiviral drugs have seen many changes and are continually evolving, with a number of innovative techniques developed over time. Nevertheless, viruses have been shown to be adept at developing resistance to drugs, and the effective management of viral diseases may well rely on combination therapy. This can be achieved by either targeting a single virus function with multiple agents or using several agents to attack several targets in the life cycle. Substrate-based approaches provided early success in the preparation of the first generation of HIV proteinase inhibitors, but biostructural information, as it has become available, has played a key role in the discovery of newer classes of compounds. High-throughput screening has also been a particularly successful technique for identifying HIV RT inhibitors, generating a range of structurally diverse leads. However, many viral diseases still require new treatments which ensure that there will be many new challenges for antiviral drug therapy in the future.

In this special issue, we invited scientists from around the world to review several topics covering therapeutics for HIV, HBV and HCV infections, and related antiviral targets and assays with the purpose of highlighting the challenges for the development of new antiviral drugs.

Finally, I would like to thank all the contributors for their time and efforts to make this review issue possible.

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