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## Challenges and Opportunities in the Development of Therapeutics for Viral Infectious Diseases in the $21^{st}$ Century

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Editorial

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Rapid emergence of drug-resistant viral mutants poses a significant challenge to effective treatment of viral infectious diseases and to the development of antiviral therapies. A better strategy is needed for developing a new class of antiviral drugs that minimize the emergence of drug-resistance and have a broad-spectrum antiviral efficacy.

Like antibiotics for treatment of bacterial diseases, most, if not all, of today's antiviral drugs are designed to target a specific virus-encoded gene or function. For examples, Zidovudine (AZT) is a nucleoside analog reverse transcriptase inhibitor that specifically inhibits the reverse transcriptase of retroviruses such as human immunodeficiency virus (HIV); Atazanavir (Reyataz) is a protease inhibitor that is also used to treat HIV infection; Osteltamivir (Tamiflu) is an inhibitor of the neuraminidase of influenza viruses. While these drugs are generally effective for treatment of particular diseases associated with the respective viruses when they are used initially, continual use of these drugs increases the selective pressure on the virus to acquire resistant mutations, often resulting in emergence of drug-resistant viruses [1,2,3], a phenomenon reminiscent of the emergence of antibioticsresistant bacteria. Moreover, mutation rates in RNA viruses are much higher, as virus-encoded polymerases are error-prone during genome replication, resulting in rapid accumulation of mutations and highfrequency generation of quasispecies.

Rapid emergence of drug-resistance can render a previously effective antiviral drug useless within a short period of time, which can result in enormous economic loss. The process of developing a new antiviral drug (from designing to laboratory testing to preclinical and clinical trials to manufacturing) is extremely lengthy and the associated cost is indeed enormous (ranging from multi-millions to multi-billions of dollars). What's more? When the drug is effective against only one virus, and if that virus rapidly develops drug-resistance, what will be the cost for developing a new drug against every newly-emerging, drug-resistant viral mutant?

The development of antiviral drugs that target host-encoded functions or pathways, on the other hand, would minimize the potential of developing drug-resistant mutations. As virus is an obligate intracellular parasite, it requires host functions for its infection, reproduction, and release (spread). As a result, drugs that target these essential host-encoded functions should be able to block virus infection, reproduction and spread. Furthermore, targeting host-encoded functions, as opposed to targeting virus-encoded function, can reduce selective pressure on the virus to acquire resistant mutations, making resistance less likely to emerge. Moreover, unlike virus-encoded function that is unique to a particular virus, many hostencoded functions or pathways are commonly used by multiple types of unrelated viruses, making these host-encoded functions excellent targets for broad-spectrum antiviral drugs.

The development of antiviral drugs that target host-encoded functions or pathways will provide potential solutions to these challenges. Future effort should be directed to accelerate the discovery of host targets for development of broad-spectrum antiviral drugs.

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