



Antiviral Medication Development Requires Coming Up with Novel Ways to Combat both Existing and New Viruses

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COMMENTARY

As the first HIV treatment, Azidothymidine (AZT) served as a catalyst for many scientists and pharmaceutical firms to develop antiviral drug development. Since 1987, about 25 HIV medicines targeting viral proteins have been approved, with the exception of the co-receptor antagonist maraviroc. Antiretroviral combination therapy has turned the life of those who with HIV from a death sentence to a manageable chronic condition.

Nonetheless, HIV infected people have an increased mortality risk and must take their medicine for the rest of their lives. The current goal is to establish an HIV cure by utilizing several ways to eventually eradicate the latent HIV from its refuge locations methods involving gene silencing or genome editing. Off-target and immunogenic effects can be avoided, and effective delivery can be obtained, and siRNA mediated gene silencing is progressing from research to medical technology, due to promising results from clinical studies in, for example, the cancer area. For a few viral infections, siRNA treatment is already in clinical trials.

Similarly, the discovery of CRISPR/Cas9 may not only reshape molecular biology practices in research laboratories, but may also lead to the development of some revolutionary therapies to cure HIV or other chronic infections caused by, for example, Hepatitis B (HBV), Hepatitis C (HCV), or Epstein-Barr virus. Regulatory difficulties related to CRISPR/Cas9 clinical application are actively being addressed.

Specifically for viruses, some challenges remain, such as selecting the optimum viral target, effective distribution through viral or non-viral vectors, and resistance development. The approach to an HBV cure is being researched. More than 240 million people are infected with this virus on a regular basis. Fifty years after its discovery, HBV is still the leading cause of hepatocellular carcinoma, the third most lethal cancer in the world.

In most treated individuals, anti-HBV nucleus tide medicines achieve viral suppression and remission of liver disease, lowering (but not eliminating) the incidence of hepatocellular cancer. Unfortunately, these antivirals are unable to eliminate HBV Covalently Closed Circular (CCC) DNA from infected cells, necessitating life-long treatment to avoid virus comeback. As a result, the research aims to find a treatment for HBV by either lowering and removing the intrahepatic pool of cccDNA or suppressing its transcriptional activity. Direct antivirals and immunotherapeutic

methods are two approaches under investigation.

HBV entry blockers; medications that destroy or mute the cccDNA; siRNA or antisense oligonucleotides to target viral transcripts; nucleocapsid assembly modulators; and techniques to reduce HBsAg release in blood comprise the first class. Toll like receptor 7 agonists are among the most studied drugs in clinical trials for immunotherapy against chronic HBV infection.

The expression of co-inhibitory receptors and immunosuppressive cytokines contributes to the absence of T cell response in chronic HBV. In animal models and *ex vivo* human research, novel anticancer approaches based on checkpoint inhibitors to reestablish antitumor immunity have generated encouraging results for HBV. The effects of therapeutic vaccinations have been dismal, although novel vaccine formulations are being tested in clinical trials. To eventually cure HBV, we will most likely need to combine antiviral medicines that block many phases in the HBV lifecycle with immunomodulatory methods that restore the antiviral immune response.

Antiviral medications are now available to address illnesses caused by herpesviruses, HIV, hepatitis B or C virus or influenza virus. On the other hand, there are still a number of medically significant viruses for which there is no effective treatment. Surprisingly, this list contains prevalent or possibly pandemic viruses as well as dangerous infections (such as Ebola, yellow fever or Zika virus) that can resurface at any time if a vaccine is not available or is employed improperly. Because sophisticated research technologies, such as crystallography and *in silico* design of small molecule ligands; recombinant protein engineering; gene silencing and genome editing, are now widely available, we have the tools to develop effective therapies against old bugs and be creative when confronted with new ones.