Viral Infection & Drug Development

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There are many viruses around us and we are interacting with these viruses. Some viruses don't affect us, but some cause serious illness. This presentation contains brief introduction about what virus is and some pathogenic viruses such as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and Hepatitis B virus (HBV). About drug development story, anti-HBV drug development will be presented, which is the main story of this presentation. HBV is a double-stranded DNA virus and a member of the hepadnaviridae family of viruses. Chronic HBV infection is a major global cause of hepatocellular carcinoma (HCC); chronic carriers have a >100-fold increased relative risk of developing HCC. HBV can be treated with nucleos(t)ide analogs (NAs) that inhibit the HBV polymerase, such as tenofovir (TDF) and entecavir (ETV); both are potent and have a high genetic barrier to drug resistance. However, they are unable to cure HBV because of the remarkable stability of the viral cccDNA intermediate, which is not directly targeted by NAs. Thus, new therapies are needed for chronic HBV-infected patients. In our study, ciclopirox, which is capsid assembly inhibitor, reduced HBV particle secretion synergistically with TDF and ETV. Since this synergistic effect may reflect the fact that multiple steps in the HBV life cycle (*i.e.*, HBV polymerase and HBV capsid assembly) are targeted by the combination treatment, it supports the notion that targeting multiple HBV life cycle steps improves HBV treatment efficacy and this can block *de novo* synthesis of cccDNA. In conclusion, we suggest that targeting multiple steps of the HBV life cycle is a good strategy for the complete treatment of HBV.