Recent advances in the Drug discovery of anti- HIV/AIDS agents

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HIV and AIDS remain a persistent problem for the United States. In 2015, 39,513 people were diagnosed with HIV. Since the beginning of the epidemic, nearly 675,000 people with AIDS in the United States have died, and even today, nearly 13,000 people with AIDS in the United States die each year. While great progress has been made in preventing and treating HIV, but challenges remain. These challenges include the current drug resistance and toxicity and unresponsiveness of the treatment to suppress HIV replication in all patients. These challenges incite searching for novel anti-HIV drugs and a new strategy to control the multiple-target viral replication. Likely, the HIV replication cycle offers multiple receptor sites for chemotherapeutic intervention, including the proteases, integrase, reverse transcriptase, cellular ATPase DDX3, viral envelope glycoprotein (gp120), transmembrane glycoprotein (gp41), and viral co-receptors (CXCR4 and CCR5) as a valid anti-HIV targets. Therefore, the use of chemotherapy to suppress replication of HIV has tremendously improved the treatment of AIDS in the last decades. Dual chemotherapy such as cabotegravir and rilpivirine or dolutegravir plus lamivudine which have opened the door to a new treatment paradigm in HIV therapeutics. Furthermore, cell or gene therapy by allogeneic stem cell transplantation have had a resurgence of interest to control the HIV virus which may point towards a future drug-free therapy for HIV-1 infection. The application of the computer-aided drug design (CADD) has become one of the core technologies in the current discovery of the anti-HIV inhibitors. Accordingly, the cost of drug development was reduced by up to 50% and the ADMET properties of the potential anti-HIV inhibitors become feasible. Structural-based drug design plays a significant role in the current success of discovery of highly selective inhibitors of protease (PR), reverse transcriptase (RT) and/or integrase (IN) of the pol gene of HIV-1. In recent years, computer-based approaches are widely and effectively applied in virtual screening and de novo design of protein–protein interaction inhibitors (PPI) for the discovery of highly active antiretroviral therapy (HAART) against HIV/AIDS. Furthermore, the application of simulation to drug design incorporated with experimental techniques has developed considerable numbers of novel fusion inhibitors, reverse transcriptase inhibitors (RTI), integrase inhibitors (II), and protease inhibitors (PI). Furthermore, the Nanosystems (liposomes, nanoparticles, niosomes, polymeric micelles, and dendrimers) used for HIV therapeutics offer some unique advantage like enhancement of bioavailability, water solubility, stability, and targeting ability of ARV drugs. Currently, the main attention is paid on vaccines are made from deactivated versions of HIV so that HIV can fight with HIV or any other vaccines approaches. The rapid emergence of drug-resistant HIV-1 mutants and serious adverse effects have highlighted the need for further discovery of new drugs and new targets. The problem of drug resistance development due to mutations in HIV-1 proteins targeted by antiviral drugs could be overcome by the development of specific DEAD-box RNA helicase/ATPase DDX3 inhibitors as effective anti-HIV agents..

Speaker Biography

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