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Modes of action of anti HIV RT drugs: Challenges and strategies in chemotherapy

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Different combinations of on-going antiretroviral drugs for the treatment of Human Immunodeficiency Virus (HIV) infection have been found to successfully maintain long-term suppression of HIV-1 replication in blood plasma thereby dramatically reducing the viral load to below the limits of viral detection by using the most sensitive clinical assays (<50RNA copies/ ml) resulting in a significant reconstitution of host immune system. Though, none of these therapies is capable of completing eradicating the virus from the long-lived cellular reservoir such as monocyte-derived macrophages (MDM) that poses stumbling blockade to HIV therapy and cure. MDM are widely distributed in all tissues and organs, including central system nervous (CNS) where they represent the most frequent HIV-infected cells. The present FDA-approved 24 antiretroviral drugs used to treat HIV-1 infected individuals mostly target viral reverse transcriptase (HIV-1RT), protease, integrase, and entry processes (coreceptor or fusion blockade) in different combinations. These drugs exert mild to severe toxicity in the patients. It is therefore required to continue efforts to develop some new antiretrovirals targeting alternative steps in the virus lifecycle for further optimizing the therapeutic options, overcoming drug resistance, and contributing potentially to eliminate the of viruses from their cellular reservoirs. This presentation includes an updated account on these issues including the novel strategies being developed to address challenges in this context.

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