Retrovirology



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Inhibitors of human immunodeficiency virus type I Daria I Hazuda*

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The virally encoded enzyme integrase plays a critical role in HIV-1 replication and has long been considered a promising target for the development agents to treat HIV-1 infection. However, it is only recently that the efficacy of integrase inhibitors has been demonstrated in experimental animal model systems of retroviral infection and in HIV-1 infected subjects. MK-0518 is the most advanced of the clinical candidates in this new class. MK-0518 has demonstrated robust efficacy in short term monotherapy studies and in phase 2 combinations studies in treatment naïve subjects and in patients with multi-class resistance. Although the first integrase inhibitors are still in clinical development, insights from the study of integrase function and inhibitor mechanism of action as well as observations from clinical and animal studies suggest important implications for the development of this new antiretroviral class and the effect of these agents on HIV-1 infection.