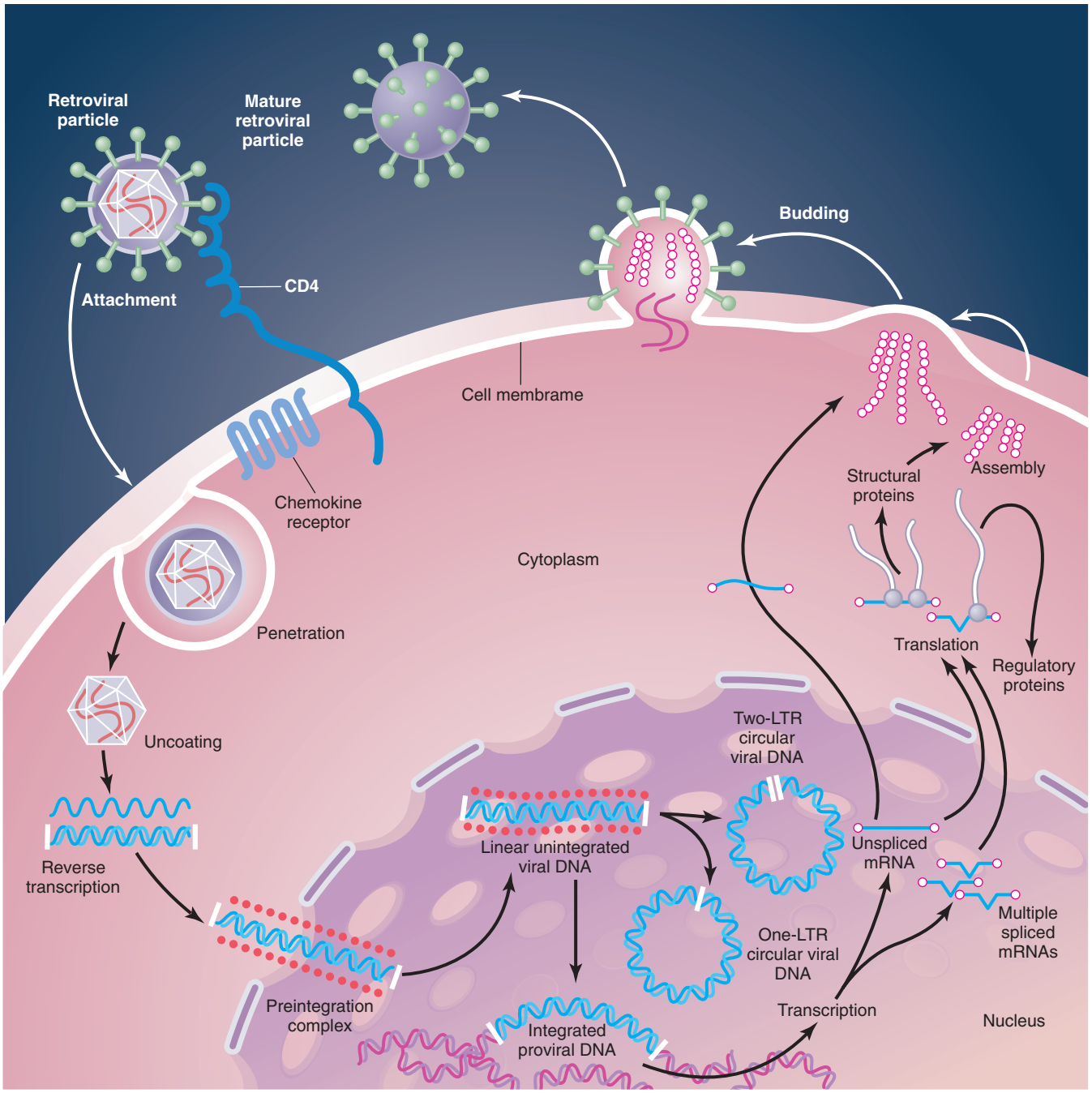

FIGURE 101-2 HIV viral replication. Key steps in the pathway targeted by antiretroviral therapy include membrane binding and fusion, reverse transcription, integration of proviral DNA, and protein synthesis. LTR, Long terminal repeat; mRNA, messenger RNA. (Modified from Furtado MR, Callaway DS, Phair JP, et al: Persistence of HIV-1 transcription in patients receiving potent antiretroviral therapy, N Engl J Med 340:1614–1622, 1999.)

binding to another cellular coreceptor (the most important of these are the chemokine receptors CCR5 and CXCR4). This second binding event promotes a major conformational change that causes approximation of the viral and cellular membranes; fusion of these membranes is mediated by insertion of the newly exposed fusion domain of the envelope gp41 into the host cell membrane.

As a result of these processes, the HIV nucleoprotein complex enters the cytoplasm, where the RNA viral genome undergoes reverse transcription by the virally encoded reverse transcriptase. The resulting double-stranded viral DNA enters the nucleus, where proper localization of the viral preintegration complex is mediated by host proteins, and integration of the DNA provirus into the host chromosome is catalyzed by the retroviral integrase. Latently infected resting memory CD4 lymphocytes serve as reservoirs of persistent infection for the life of the infected patient even with effective ART (see later discussion). However, the bulk of viral replication takes place in activated T cells, which are both more susceptible to HIV infection and more capable of supporting productive HIV replication.

When a CD4 lymphocyte is activated, expression of HIV messenger RNA (mRNA) is enhanced. Core proteins, viral enzymes, and envelope proteins are encoded by the *gag*, *pol*, and *env* genes of HIV, respectively. Recent data indicate that more than 100 host