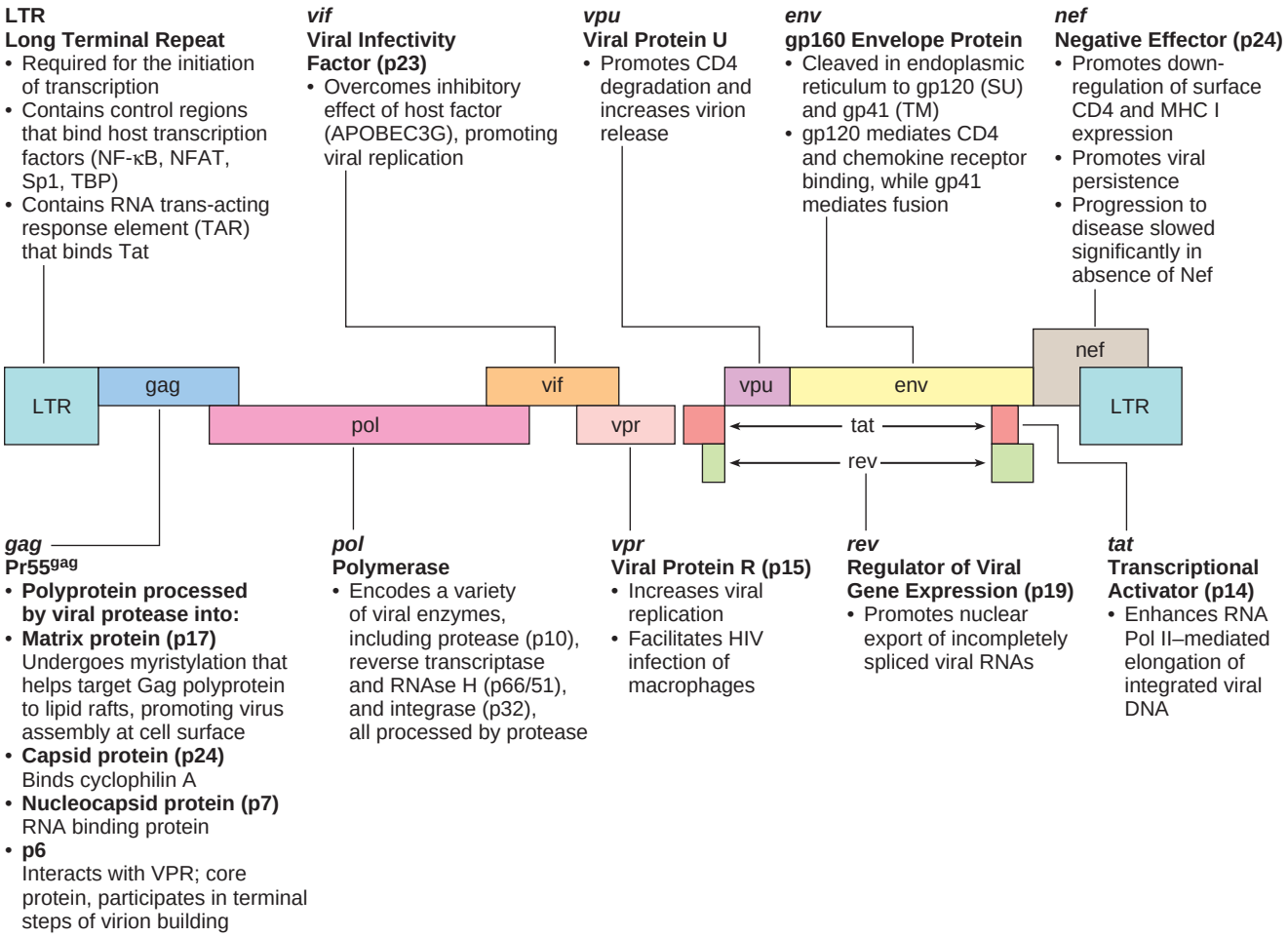

Figure 6-39 The HIV genome. Several viral genes and the functions of the encoded proteins are illustrated. The genes outlined in red are unique to HIV; others are shared by all retroviruses.

as well as impairment in the function of surviving helper T cells. As discussed later, macrophages and dendritic cells are also targets of HIV infection. HIV enters the body through mucosal tissues and blood and first infects T cells as well as dendritic cells and macrophages. The infection becomes established in lymphoid tissues, where the virus may remain latent for long periods. Active viral replication is associated with more infection of cells and progression to AIDS. We first describe the mechanisms involved in viral entry into T cells and macrophages and the replicative cycle of the virus within cells. This is followed by a more detailed review of the interaction between HIV and its cellular targets.

Life Cycle of HIV

The life cycle of HIV consists of infection of cells, integration of the provirus into the host cell genome, activation of viral replication, and production and release of infectious virus (Fig. 6-40). The molecules and mechanisms of each of these steps are understood in considerable detail.

Infection of Cells by HIV

HIV infects cells by using the CD4 molecule as receptor and various chemokine receptors as coreceptors (Fig. 6-40). The requirement for CD4 binding explains the selective tropism of the virus for CD4+ T cells and other CD4+ cells, particularly monocytes/macrophages and dendritic cells. Binding to CD4 is not sufficient for infection, however. HIV gp120 must also bind to other cell surface molecules (coreceptors) for entry into the cell. Chemokine receptors, particularly CCR5 and CXCR4, serve this role. HIV isolates can be distinguished by their use of these receptors: R5 strains use CCR5, X4 strains use CXCR4, and some strains (R5X4) are dual-tropic. R5 strains preferentially infect cells of the monocyte/macrophage lineage and are thus referred to as M-tropic, whereas X4 strains are T-tropic, preferentially infecting T cells. In approximately 90% of cases, the R5 (M-tropic) type of HIV is the dominant virus found in the blood of acutely infected individuals and early in the course of infection. Over the course of infection, however, T-tropic viruses gradually accumulate; these are especially virulent because T-tropic viruses are capable of infecting many T cells and even thymic T-cell precursors and cause greater T-cell depletion and impairment.

Molecular details of the deadly handshake between HIV glycoproteins and their cell surface receptors have been elucidated and are important to understand because they may provide the basis of anti-HIV therapy. The HIV envelope contains two glycoproteins, surface gp120 noncovalently attached to a transmembrane protein, gp41. **The initial step in infection is the binding of the gp120 envelope glycoprotein to CD4 molecules, which leads to**