In the thymus, the recognition of self-peptides on thymic epithelial cells, thymic macrophages, and DCs plays an important role in shaping T-cell repertoire. As immature cortical thymocytes begin to express surface TCR for antigen, thymocytes with TCRs capable of interacting with self-peptides in the context of self-MHC antigens with low affinity are activated and survive (positive selection). Thymocytes with TCRs that are incapable of binding to self-MHC antigens or bind with high affinity die of attrition (no selection) or by apoptosis (negative selection). Thymocytes that are positively selected undergo maturation into CD4 or CD8 single positive T cells, and then migrate to the thymus medulla where they interact with self-peptide–self-MHC molecules, where they can again undergo selection. The purpose of negative and positive thymocyte selection is to eliminate potential pathogenic autoreactive T cells, and at the same time, select a repertoire of mature T cells capable of recognizing foreign antigens.

Mature TCRαβ thymocytes that are positively selected are functional MHC class II–restricted CD4+ T cells (Fig. 349-2), or they are CD8+ T cells destined to become CD8+ MHC class I–restricted cytotoxic T cells. *MHC class I* or *class II restriction* means that T cells recognize antigen peptide fragments only when they are presented in the antigen-recognition site of a class I or class II MHC molecule, respectively. After thymocyte maturation and selection, CD4 and CD8 thymocytes leave the thymus and migrate to the peripheral immune system. The thymus can continue to be a contributor to the peripheral immune system well into adult life, both normally and when the peripheral T-cell pool is damaged, such as occurs in AIDS and cancer chemotherapy.

MOLECULAR BASIS OF T-CELL RECOGNITION OF ANTIGEN The TCR for antigen is a complex of molecules consisting of an antigen-binding heterodimer of either αβ or γδ chains noncovalently linked with five CD3 subunits (γ, δ, ε, ζ, and η) **(Fig. 349-7)**. The CD3 ζ chains are either disulfide-linked homodimers (CD3-ζ_2) or disulfide-linked heterodimers composed of one ζ chain and one η chain. TCR-αβ or TCR-γδ molecules must be associated with CD3 molecules to be inserted into the T-cell surface membrane, TCR-α being paired with