

antibodies, such as trastuzumab (36,37) also known as Herceptin[®], and which is used to treat breast cancer, kill cancer cells by way of the mechanism of ADCC. Another anti-cancer antibody, cetuximab, also known as Erbitux[®], binds to a membrane-bound protein on the surface tumor cells, epidermal growth factor receptor, causing ADCC (38).

Anti-cancer therapy might be compared to anti-cancer therapy by way of a vaccine.

Anti-cancer therapy with a vaccine has more requirements. First, the vaccine needs to stimulate immune response, that is, to provoke the immune system to generate CD8⁺ T cells (as well as CD4⁺ T cells) that are specific for the tumor antigen. This means that the vaccine needs to be taken up by dendritic cells, that the dendritic cells need to be stimulated to mature, that the dendritic cells process the vaccine and present it to T cells, and that the T cells become optimally activated. Vaccine-induced antibodies can also be a component of anti-cancer therapy using a vaccine.

Second, for ADCC to work, the antigen of the tumor cell can be attached to (or associated with) the tumor cell, either by being a membrane-bound protein, or by way of presentation via MHC class I.

In contrast, cytotoxic lymphocyte response (CTL response) requires that the tumor cell is actively presenting the tumor antigen on the tumor cell's MHC class I. For CTL response to work, it is not sufficient that the antigen merely take the form of a classical, transmembrane, membrane-bound protein.

In any consideration of immune response against tumors, it should be kept in mind that the response of the immune system against a cancer can differ, depending on the stage of the cancer (39).

c. Regulatory T cells

Anti-cancer drugs also include drugs that block normally occurring mechanisms that set upper limits to immune response. Upper limits to immune response are imposed by a class of T cells called T regulatory cells (Tregs) (Fig. 26.2). If Tregs did not exist, it is likely that every human being would suffer from various autoimmune disorders. Tregs guard against autoimmunity, but in the context of a cancer patient, what is desirable is to inhibit Tregs (40). Cancer patients may have increased levels of Tregs and, in

³⁶ Varchetta S, Gibelli N, Oliviero B, et al. Elements related to heterogeneity of antibody-dependent cell cytotoxicity in patients under trastuzumab therapy for primary operable breast cancer overexpressing Her2. *Cancer Res.* 2007;67:11991–11999.

³⁷ Arnould L, Gelly M, Penault-Llorca F, et al. Trastuzumab-based treatment of HER2-positive breast cancer: an antibody-dependent cellular cytotoxicity mechanism? *Br J Cancer.* 2006;94:259–267.

³⁸ Vincenzi B, Zoccoli A, Pantano F, Venditti O, Galluzzo S. Cetuximab: from bench to bedside. *Curr Cancer Drug Targets.* 2010;10:80–95.

³⁹ Badoual C, Hans S, Fridman WH, Brasnu D, Erdman S, Tartour E. Revisiting the prognostic value of regulatory T cells in patients with cancer. *J Clin Oncol.* 2009;27:e5–e6.

⁴⁰ Siddiqui SA, Frigola X, Bonne-Annee S, et al. Tumor-infiltrating Foxp3-CD4 + CD25 + T cells predict poor survival in renal cell carcinoma. *Clin Cancer Res.* 2007;13:2075–2081.