efficacy. In the case of CPG, Nierkens et al. (70) have shown that, where disruption of the tumor and where CPG administration occur concurrently, the CPG can be an effective anti-tumor agent, but where CPG is administered a day or so before (or after) tumor disruption, the CPG is not effective. In general, tumor disruption can be accomplished by cytotoxic drugs, radiation, or cryoablation. The issue of the route of administration also needs to be addressed in clinical trials that use drugs. In the case of CPG, Lou et al. (71) have shown that the route of administration can influence efficacy, where intratumor injection improves efficacy over intravenous injection.

5. Antibodies

Natalizumab is an antibody that blocks T cells and prevents the T cells from migrating from the bloodstream into the central nervous system. This antibody is used to treat multiple sclerosis. Ustekinubam is an antibody that binds to IL-12 (72). IL-12 is a Th1-type cytokine. This antibody is used for treating psoriasis. In view of the fact that psoriasis results, at least in part, from an increase in Th1-type immune response, it is logical that an antibody (such as ustekinubam) against a Th1-type cytokine (such as IL-12) should prove effective against this disease. Trastuzumab is an antibody that binds to HER-2. When trastuzumab binds to HER-2, located on the surface of cancer cells, the result is as follows. Natural killer cells (NK cells) can then attack the cancer cells, in a mechanism called antibody-dependent cell cytotoxicity (ADCC).

As described immediately below, anti-GITR is another antibody that modulates the immune system. This antibody is an agonistic antibody, that is, it transmits a signal to the cell. Thus, antibodies can be classified according to their physiological effect: (1) antibodies that block the activity of their target, such as natalizumab or ustekinubam; (2) antibodies having the immediate effect of provoking the transmission of a signal, such as anti-GITR antibody; and (3) antibodies that mediate ADCC, such as trastuzumab.

6. Treg inhibitors

The antibody anti-GITR antibody is a drug that inhibits T regulatory cells (Tregs). GITR stands for *Glucocorticoid-Induced TNF receptor-Related* protein. GITR is a membrane-bound protein that transmits signals to the cell. GITR is activated when GITR ligand (GITRL) binds to GITR, forming the GITRL/GITR complex. GITRL and GITR are each membrane-bound proteins. GITRL is expressed by parencymal tissue cells, while GITR is expressed by Tregs (73). Anti-GITR antibody is being tested with

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