

interferon-gamma (29), can enhance the tumor cell's behavior in expressing certain tumor antigens, that is, expression by major histocompatibility complex (MHC) class I by the tumor cell. Interferon-gamma, which is a Th1-type cytokine, is produced by immune cells, or it can be administered as a drug, for the treatment of cancer or infections.

The following concerns $CD4^+$ T cells, also known as helper T cells. $CD4^+$ T cells contribute to immune response against tumors in a number of ways. According to Chaput et al. (30), several mechanisms are possible. $CD4^+$ T cells contribute directly to $CD8^+$ T-cell function by increasing their survival, by improving division and effector function, and by modifying the trafficking of $CD8^+$ T cells into tumor sites.

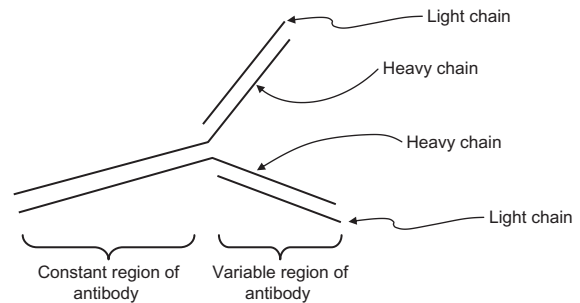
Colorectal cancers are commonly infiltrated by immune cells. The most frequent among these are T cells and B cells, though natural killer cells (NK cells), DCs, macrophages, and neutrophils also infiltrate tumors. According to Morris et al (31), increased number of tumor-infiltrating lymphocytes are correlated with increased survival of the patient.

b. NK Cells and ADCC

NK cells can kill cancer cells by way of antibody-dependent cell cytotoxicity (ADCC). Although NK cells are classified as part of the innate immune response pathway it is the case that ADCC depends on the presence of antibodies, either antibodies that are naturally acquired by way of adaptive immune response,

or administered antibodies. When the antibody is present, it serves as a bridge between the NK cell and the tumor. Manegold et al. (32) provide a diagram showing the expression of antibodies by a B cell, the binding of these antibodies to a tumor cell resulting in a "decorated tumor cell," and the subsequent attack by NK cells against the antibody-decorated tumor cell.

As disclosed in Chapter 1, antibodies contain four polypeptide chains, two heavy chains and two light chains (see in-text diagram). The four chains are covalently attached to each other by way of disulfide bonds (bonds not shown). When fully assembled, the antibody contains a constant region and a variable region. The constant region contains regions that can bind tightly to Fc receptors, for example, Fc receptors on the surface of NK cells. The variable region, which recognizes a specific antigen, binds tightly to the antigen. In drawings of antibodies, the antibody takes the form of tweezers, where the Fc receptor-binding region is the handle of the tweezers, and the variable region is the tweezer prongs.



²⁹Weidanz JA, Nguyen T, Woodburn T, et al. Levels of specific peptide-HLA class I complex predicts tumor cell susceptibility to CTL killing. *J Immunol.* 2006;177:5088–97.

³⁰Chaput N, Darrasse-Jèze G, Bergot AS, et al. Regulatory T cells prevent CD8 T cell maturation by inhibiting CD4 Th cells at tumor sites. *J. Immunol.* 2007;179:4969–78.

³¹Morris M, Platell C, Iacopetta B. Tumor-infiltrating lymphocytes and perforation in colon cancer predict positive response to 5-fluorouracil chemotherapy. *Clin. Cancer Res.* 2008;14:1413–7.

³²Manegold C, Gravenor D, Woytowicz D, et al. Randomized phase II trial of a toll-like receptor 9 agonist oligodeoxynucleotide, PF-3512676, in combination with first-line taxane plus platinum chemotherapy for advanced-stage non-small-cell lung cancer. *J. Clin. Oncol.* 2008;26:3979–86.