



FIGURE 27.3 Signaling via PD-1, PD-L1, and CTLA-4 during communication between a DC, T cell, and cancer cell. The goal of the DC is to stimulate the T cell to mount immune response against the cancer cell. The goal of the cancer cell is to inhibit the T cell.

d. Immune Response Against Cancer Summarized by a Picture of Three Different Cells

Figure 27.3 summarizes the immune response against cancer. The figure shows a DC, a T cell, and a cancer cell. DCs and T cells collaborate and orchestrate the immune response against cancer cells. The T cell recognizes the cancer cell, by way of tumor antigens that are expressed by MHC of the cancer cell. On the other hand, the cancer cell engages in immune evasion, and dampens this immune response, by expressing PD-L1, which directly dampens the activity of T cells. **Figure 27.3** illustrates CTLA-4, PD-1, and PD-L1, which are membrane-bound proteins, and which are each a target of a recombinant antibody that has proven success in treating cancer.

In the figure, the rows of vertical lines indicate noncovalent binding interactions between ligands and receptors. A row of vertical lines is conventionally used to represent hydrogen bonds (⁵⁷). The long segmented rectangles represent oligopeptides that are held and positioned on the outside surface of DCs.

The term, “immune synapse,” refers to the point of contact between the T cell and DC, and to the signals that are transmitted when peptides are bound to MHC are presented to the T cell. Membrane-bound proteins of the DC, such as B7-1 and B7-2, are involved in the immune synapse. At a later point in the timeframe of the immune synapse’s existence, B7-1 or B7-2 transmits an inhibiting signal to CTLA-4 of the T cell, which limits and dampens the activation of the T cell, thereby preventing pathological consequences, such as autoimmune disease.

After the DC and T cell have parted ways, the T cell infiltrates tumors, where it attempts to kill cancer cells. The T cell recognizes tumor cells by way of tumor antigens that are presented by the cancer cell on the tumor cell’s own MHC. However, the cancer cell fights back, and transmits inhibiting signals to the T cell, by way of the cancer cell’s PD-L1.

Figure 27.3 discloses targets of antibodies that are used to treat various cancers. Anti-CTLA-4 antibodies reverse the inhibition that results from immune tolerance, and antibodies that target PD-1 or PD-L1 prevent cancer cells from engaging in their tactic of immune evasion.

⁵⁷Nelson DL, Cox MM. Lehninger principles of biochemistry. 5th ed. New York: W.H. Freeman and Co.; 2008. pp. 44–6, 49–50.