Cellular Immunity Response Process

Humoral antibodies are effective against pathogens that are circulating freely in the body, where the antibodies can make contact with them. But intracellular antigens, such as a virus, certain bacteria, and some parasites, are not exposed to these circulating antibodies since they enter host cells. T cells likely evolved to combat the problem posed by these intracellular pathogens. They are also the way in which the immune system recognizes other cells that are abnormal—especially cancer cells. Like B cells, each T cell is specific for only a certain antigen. However, T cells will recognize only antigen fragments bound to MHC.

M cells: are located over Peyer's patches, which are secondary lymphoid organs located on the intestinal wall. M cells take up antigens from the intestinal tract and allow their transfer to the lymphocytes and antigen-presenting cells of the immune system found throughout the intestinal tract, just under the epithelial-cell layer but especially in the Peyer's patches. It isalso here that antibodies, mostly IgA essential for mucosal immunity, are formed and migrate to the mucosal lining.

Antigen-Presenting Cells (APCs)

Antigen-presenting cells (APCs) associated with cellular immunity include B cells, dendritic cells, and activated macrophages. All APCs have MHCs on their surfaces that presents potential antigenic fragments to T cells. T cells interacting with the antigenic epitope and MHC will lead to T cell activation. APCs produce IL-12, which activates TH1 cells.

Classes of T Cells

There are classes of T cells that have different functions, rather like the classes of immunoglobulins. As mentioned previously, T helper cells (TH cells) cooperate with B cells in the production of antibodies, mainly through cytokine signaling. For their role in cellular immunity, T cells interact more directly with antigens.

T cells are also classified by certain glycoproteins on their cell surface called clusters of differentiation, or CD. These are membrane molecules that are especially important for adhesion to receptors. The CDs of greatest interest are CD4 and CD8; T cells that carry these molecules are named CD4+ and CD8+ cells, respectively. (For the importance of these molecules in HIV infection, T helper cells are classified as CD4+, which bind to MHC class II molecules on B cells and

other APCs. CTL cells are classified as CD8+, which bind to MHC class I molecules. T cells that have not encountered a pathogen are called naïve. After contact with a pathogen, the T cell is activated and can form effector and memory cells. T Helper Cells (CD4+ T Cells) T helper cells can recognize an antigen presented on the surface of a macrophage and activate it, making the macrophage more effective in both phagocytosis and in antigen presentation.

Dendritic cells are especially important in the activation of T helper cells and in developing their effector functions.

T Regulatory Cells

T regulatory (Treg) cells make up about 5–10% of the T cell population.They are a subset of the T helper cells and are distinguished by carrying an additional CD25 molecule. Their primary function is to combat autoimmune reactions by suppressing T cells that escape deletion in the thymus without the necessary ―education‖ to avoid reacting against the body's self.are also useful in protecting the resident microbiota that live in our intestines and aid digestion. Similarly, in pregnancy they may play a role in protecting the fetus from rejection as nonself. Recently, researchers have discovered evidence of Treg involvement in establishing the skin microbiome.

Cytotoxic T Lymphocytes (CD8+ T Cells)

A class of T cells called precursor T cytotoxic cells (CTLp) can differentiate into an effector cell called a cytotoxic T lymphocyte. Cytotoxic T lymphocytes, or CTLs, are not capable of attacking any target cell as they emerge from the thymus as CTLp cells. However, they quickly attain this capability. This differentiation requires sequential—and complex—activation of the CTLp by an antigen processed by an antigen-presenting cell and interaction with a T helper cell and costimulatory signals. The resulting CTL is an effector cell that has the ability to recognize and kill target cells that are considered no self.

Primarily, these target cells are self-cells that have been altered by infection with a pathogen, especially viruses. On the infected cell's surface, they carry fragments of endogenous antigens that are generally synthesized within the cell and are mostly of viral or parasitic origin. Other important target cells are tumor cells and transplanted foreign tissue. Rather than reacting with antigenic fragments presented

by an APC in complex with MHC class IImolecules, the CTL recognizes endogenous antigens on the target cell's surface that are in combination with an MHC class I molecule. MHC class I molecules are found on nucleated cells; therefore, a CTL can attack almost any cell of the host that has been altered.In its attack, a CTL attaches to the target cell and releases a pore-forming protein, perforin. Pore formation contributes to the subsequent death of the cell and is similar to the action of the complement membrane attack complex. Granzymes, proteases that induce apoptosis, are then able to enter through the pore.

Apoptosis (a-pah-TO-sis; from the Greek for falling away like leaves) is also called programmed cell death. This is a necessary process in multicellular organisms.

Nonspecific Cells and Extracellular Killing by the Adaptive Immune System

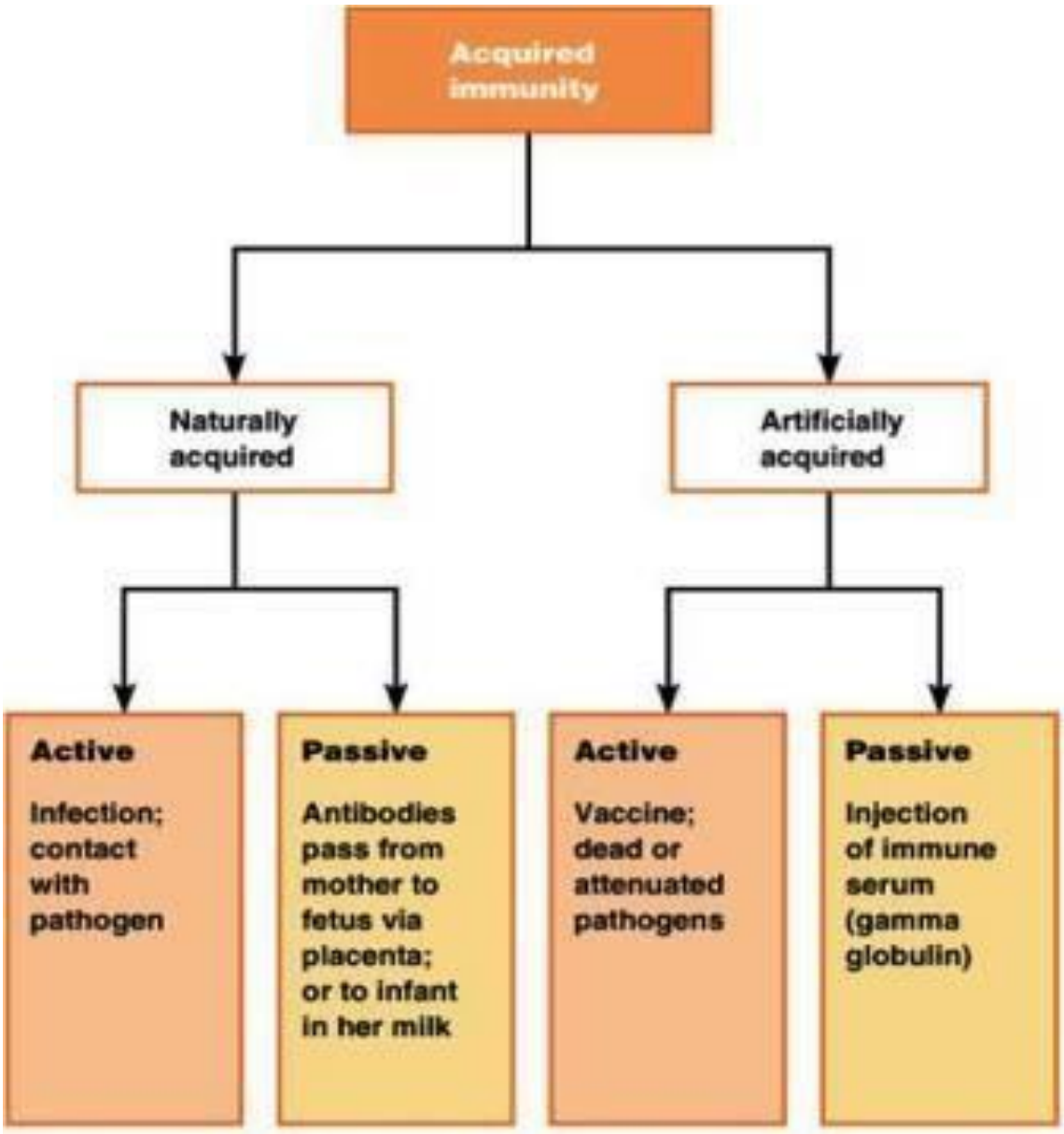
CTLs are not the only cells that can lead to the destruction of a target cell. Natural killer (NK) cells can also destroy certain virus-infected cells and tumor cells and can attack parasites, which are normally much larger than bacteria.to kill targeted cells. In this way, an organism such as a fungus, protozoan, or helminth that is too large to be phagocytized can be attacked by immune system cells. This is referred to as antibody-dependent cell-mediated cytotoxicity (ADCC). The target cell is first coated with antibodies. A variety of cells of the immune system bind to the Fc regions of these antibodies and, thus, to the target cell. The attacking cells secrete substances that then lyse the target cell. The functions of NK cells and the other principal cells involved in cellular immunity are briefly summarized in Table 17.2.

TABLE 17.2 Principal Cells That Function in Cell-Mediated Immunity

Cell	Function
T Helper (T_H1) Cell	Activates cells related to cell-mediated immunity: macrophages, Tc cells, and natural killer cells
T Helper (T_H2) Cell	Stimulates production of eosinophils, IgM, and IgE
Cytotoxic T Lymphocyte (CTL)	Destroys target cells on contact; generated from T cytotoxic (Tc) cell
T Regulatory (T_{reg}) cell	Regulates immune response and helps maintain tolerance
Activated Macrophage	Enhanced phagocytic activity; attacks cancer cells
Natural Killer (NK) Cell	Attacks and destroys target cells; participates in antibody-dependent cell-mediated cytotoxicity

Types of Adaptive Immunity

Immunity is acquired actively when a person is exposed to microorganisms or foreign substances and the immune system responds. Immunity is acquired passively when antibodies are transferred from one person to another. Passive immunity in the recipient lasts only as long as the antibodies are present— in most cases, a few weeks. Both actively acquired immunity and passively acquired immunity can be obtained by natural or artificial means.


Acquired immunity
Naturally acquired
Artificially acquired
Active
Infection; contact with pathogen
Passive
Antibodies pass from mother to fetus via placenta; or to infant in her milk
Active
Vaccine; dead or attenuated pathogens
Passive
Injection of immune serum (gamma globulin)