

➤ Third line of defense (Specific or true immunity)

Whenever our body first & second line defense is failed then third line of defense is stimulated in the following way.

- i. T- lymphocytes Cells mediated immunity
- ii. B- Lymphocytes Cells mediated immunity or Humoral immunity

Third line of defense is accomplished in five steps respectively.

- (i) **Recognition:** In this step an antigen is recognized as self or non- self-antigen. The antigen is recognized by using unique molecules on plasma membrane called Major Histocompatibility Complex (MHC).
- (ii) **Lymphocyte Selection:** The most common leukocytes of third line are lymphocytes that is T- lymphocytes and B- lymphocytes, specialized for different antigens. The binding of an antigen or foreign cell to a lymphocyte may select the lymphocyte and initiate proliferation or cloning because the lymphocyte to which the antigen effectively binds is "selected" and subsequently reproduces to make clones, or identical copies, of itself.
- (iii) **Lymphocyte activation:** When an antigen binds to a lymphocyte, the lymphocyte proliferates, producing numerous daughter cells, all identical copies of the parent cell. This process is called *clonal activation*, in most cases, however, a co stimulator is required before proliferation begins. Co stimulators may be chemicals or other cells.
- (iv) **Destruction of antigen:** When the antigen is recognized then it is displayed (epitope of antigen) by MHC on the basis of which lymphocytes are selected for destruction of antigen. If antigen is

displayed by MHC I then it will be destroyed by cytotoxic T- cells this response is mediated by macrophage through a secretion of chemicals known as inter Lukens (cells mediated immunity) but if antigen is displayed by MHC II, then B- lymphocytes will be selected by the mediation of T- helper cells by inter Lukens to destroy antigen using antibodies (Humoral immunity). The non-specific defense mechanism (phagocytes and NK cell) help to eliminate the invaders.

- (v) **Memorization:** B- & T-memory lymphocytes (long-lived) are produced and can quickly recognize and respond to future exposures to the antigen or foreign cell. It is quite important that memory cells would be produced only for those antigens or microbes which has stable DNA or RNA program as compare to those having changeable or mutable program.

➤ Specific defense mechanism

Specific defense mechanism is effective against specific antigen.

There are two types of specific defense mechanism

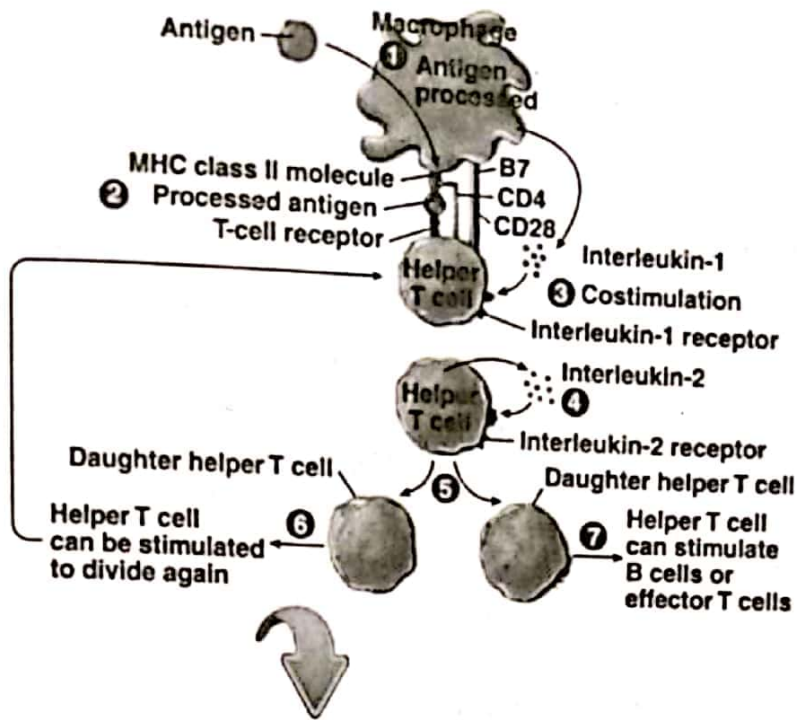
➤ Cell mediated immune response

Definition: An immunity in which response is given to antigen through lymphocytes including macrophages which mediate with T- cells may be helper or killer, is called cell mediated immunity.

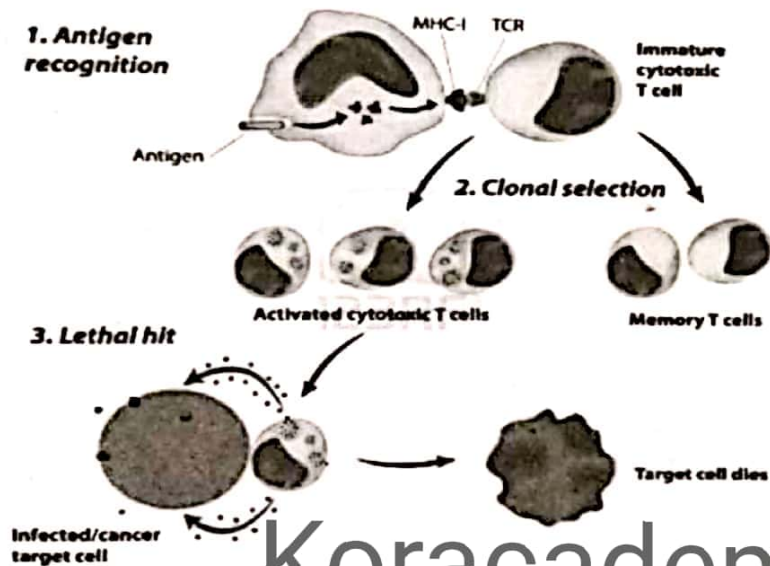
Mechanism

- (i) **Recognition of antigen:** When antigen is attached then recognized as self or non-self-antigen. Macrophage will engulf antigen, digest it and its epitope is translated and displayed through MHC.
- (ii) **Selection of lymphocytes:** If antigen is displayed by MHC I then T- Killer (CD8) cells are selected & activated by means of interleukin which is secreted by infected cells or macrophages for destruction of antigen.
- (iii) **Activation of lymphocytes:** The infected cells secrete specific type of interleukin which activates T-Killer Cells.
- (iv) **Destruction of antigen:** When antigen is intracellular and second line of defense had failed then antibody cannot work to control antigen inside the cell because antibodies are destroying extra cellular pathogens however antibodies can limit its spread before entering into cell or if life cycle involves extra cellular phase. In such cases the antigen is destroyed by T-Killer or cytotoxic cells (CD-8, Cluster differentiation). T-lymphocytes do not produce antibody molecules. Rather, they leave the lymphatic tissues and enter the circulation. They circulate through the blood vessels and gather at the infection site. Here they interact directly with organisms such as fungi, protozoa, cancer cells, and transplant cells. They also interact with virus-infected cells and bacteria-infected cells (such as lung cells infected with tuberculosis) & secreting perforin which perforate the infected cell & then secreting granzymes which is entered the infected cell and initiating apoptosis.
- (v) **Memorization:** In this process through complex molecular mechanism the ectopic protein sequence is saved to germinal lines of T- Killer cells (CD-8) which respond very quickly if the same antigen infect the body next time, will be destroyed without any selection. T-memory Cells are stimulated by T-helper cells directly to destroy antigen.

However when pathogens are inside the macrophage and macrophages can't destroy it, then they are destroyed by delayed type of hypersensitivity.



Cytotoxic T cell Activation and Action



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Cells mediated immunity

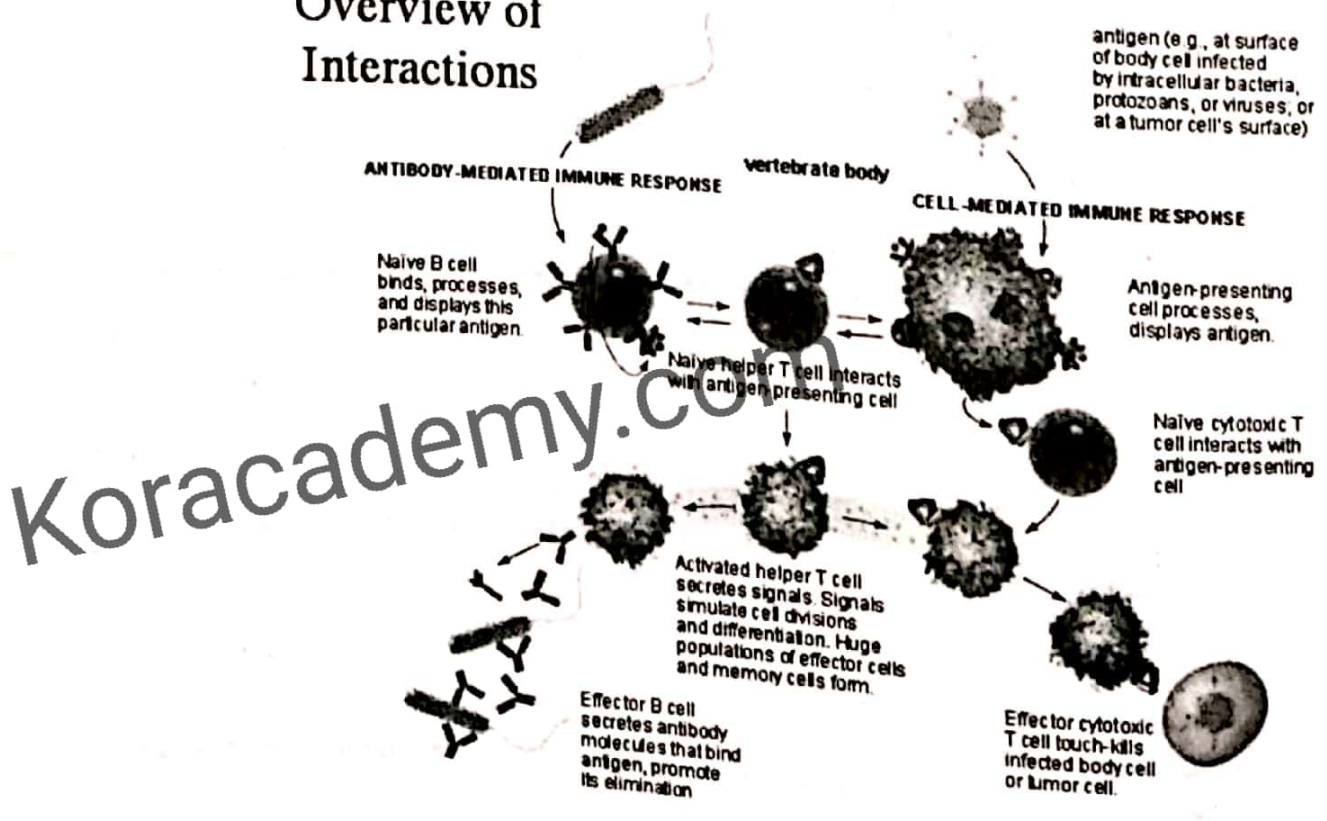
> The antibody mediated immunity (Humoral immunity)

Definition: Type of immunity which is related to antigen-antibody association is called antibody mediated immunity or humoral immunity.

- Mechanism**
- (i) **Recognition of antigen:** When antigen is attached then recognized as self or non-self-antigen. Macrophage will engulf antigen, digest it and its epitope is translated and displayed through MHC.
 - (ii) **Selection of lymphocytes:** If antigen is displayed by MHC I then T-helper (CD-4) cells are selected & activated by means of interleukin which is secreted by infected cells or macrophages for destruction of antigen. When CD-4 cells attached to MHC II, it then select & stimulate B- plasma cells to secrete specific antibodies and to handle antigen.
 - (iii) **Activation of lymphocytes:** The T-helper cells secrete interleukin which activates B- plasma cells to secrete antibodies.

- (iv) **Antigen destruction:** On exposure to antigenic determinants in lymphatic organs, B-lymphocytes are activated and differentiated to form plasma cells or macrophage mediate it by means of T-helper cells through interleukins. Plasma cells are specialized, differentiated cells that synthesize and secrete antibodies specific for an antigen along with production of B-memory cells. These cells can be activated later to differentiate to B-plasma cells for rapid antibody production. This antibody production will occur on future reentry of the antigen to the body and is the basis of long-term immunity. Antibody is secretory material due to which term "Humora" is used for it. Antigen-Antibody complex (Immune complex) is formed by the reaction of epitope & paratope, its study is known as serology. Immune complex is processed in following different ways.
 - Agglutination:** Antibodies bind to antigens, thus forming an antigen-antibody complex. This complex attracts macrophages, which will phagocytize any foreign substance that has that specific antigen-antibody complex. The formation of these complexes also known as clumping.
 - Neutralization:** In the immunological sense refers to the ability of antibodies to block the site(s) on bacteria or viruses that they use to enter their target cell. One example of this within biology is a neutralizing antibody.
 - Precipitation:** Soluble antigens are precipitated and destroyed by the phagocytes.
 - Opsonization:** In this method, antibodies are coated on microbial surface after which antigen locks in. This makes it more susceptible or capable to phagocytosis.
 - Complement Activation:** Once the lock and key mechanism perfectly fits into the place, it leads to cell lysis.
- (v) **Memorization:** In this process through complex molecular mechanism the ectopic protein sequence is saved to germinal lines of B-plasma cells which respond very quickly if the same antigen infect the body next time then B-memory cells are activated by T-helper cells, antibodies are secreted without selection & antigen is immobilized.

Overview of Interactions



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