LESSON 7

Acquired (specific) immunity. Immune system of human organism. Immune competent cells. Antigens. Immune response reactions. Antibodies. Serological tests.

specific immunity

- Specific immunity is formed in a person when the immune system comes into contact with a pathogen or antigen.
- A specific defense formed against an antigen cannot protect the body against other antigens..

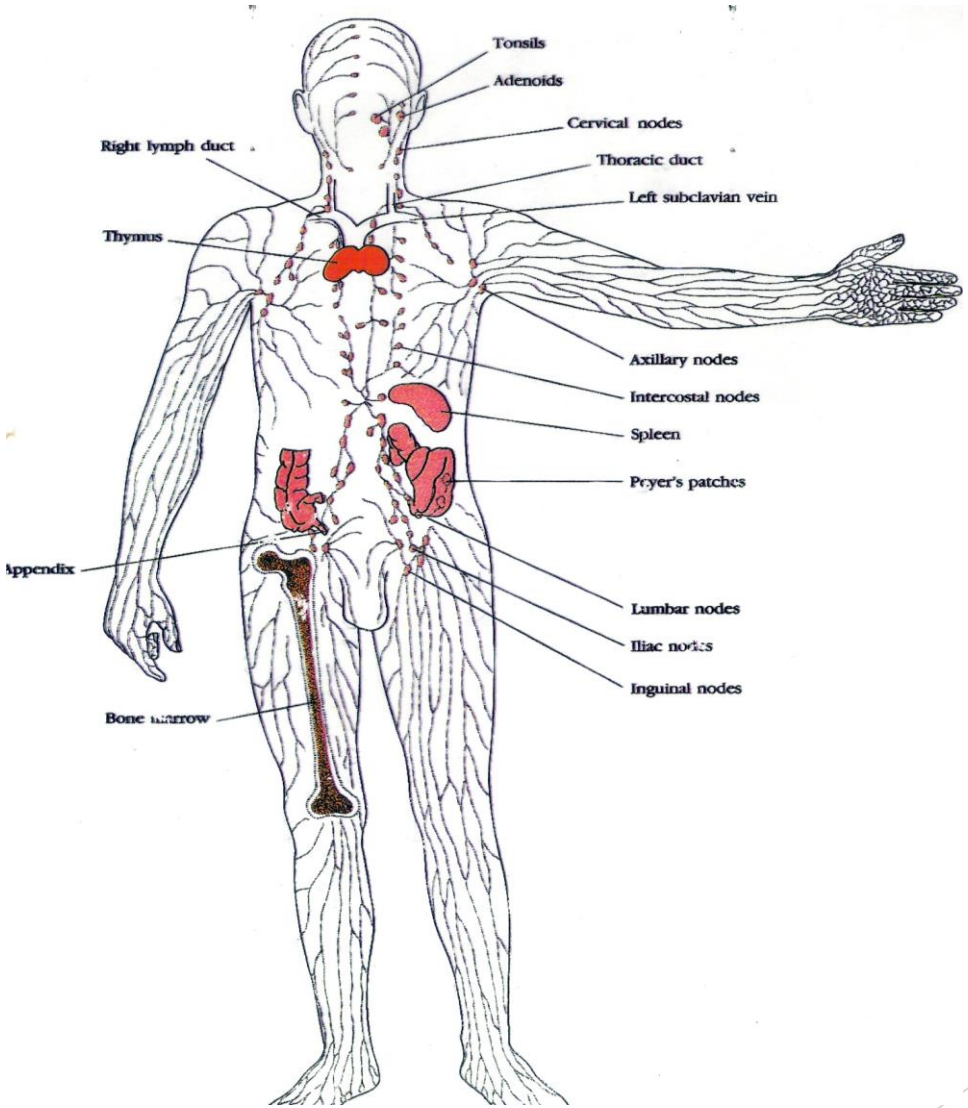
The immune system of body

To protect against foreign substances and maintain homeostasis in the body, there is a complex defense system called the immune system a collection of organs, lymphoid tissue, and individual cells.

The immune system of the ego is a specialized, anatomically isolated tissue scattered throughout the body in the form of various lymphoid formations and individual cells.

The most important function of the immune system is immunity: protecting the body from genetically alien substances of exogenous and endogenous origin. The properties of the immune system also include specificity, sensitivity, tolerance

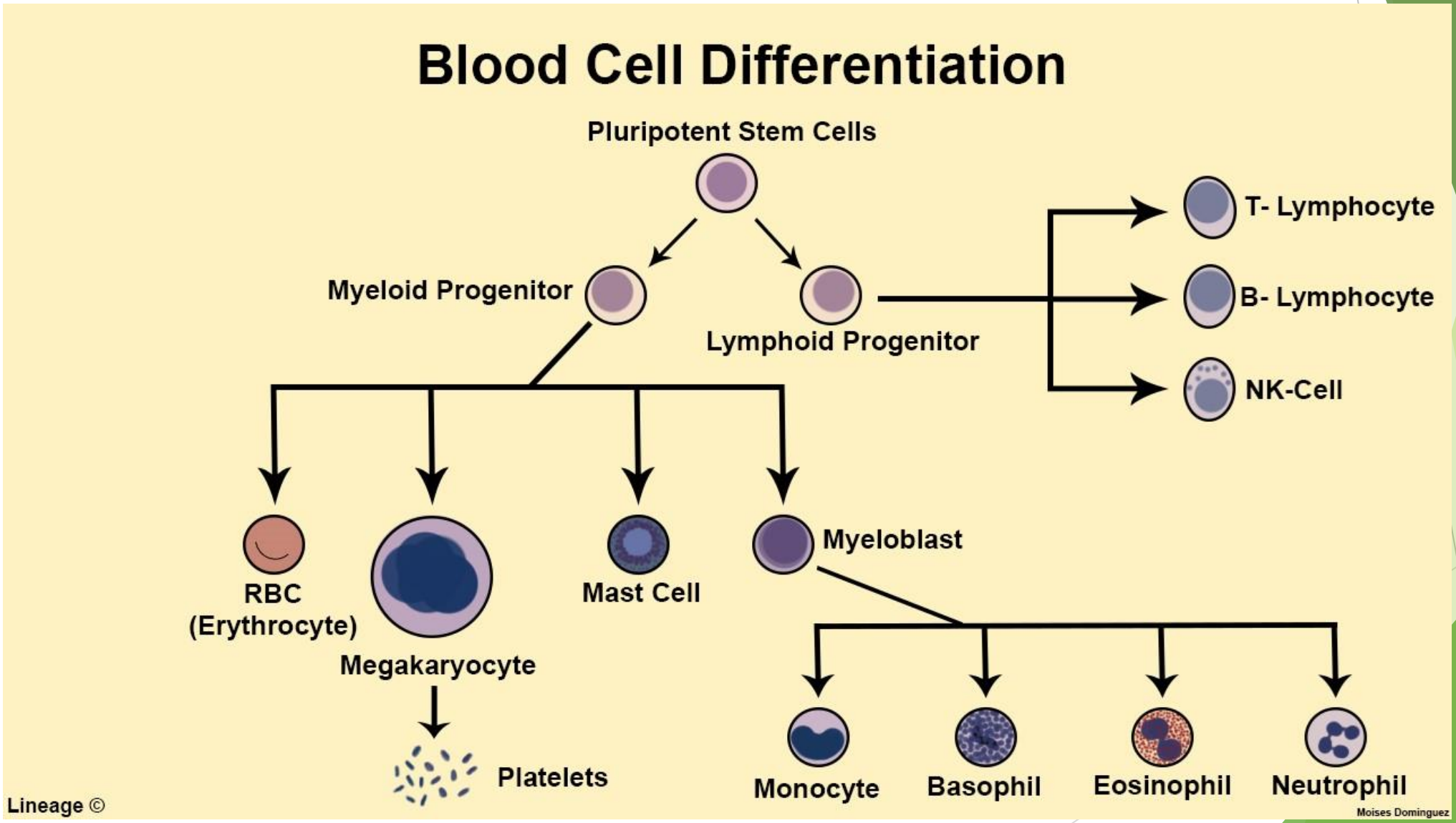
The immune system of body



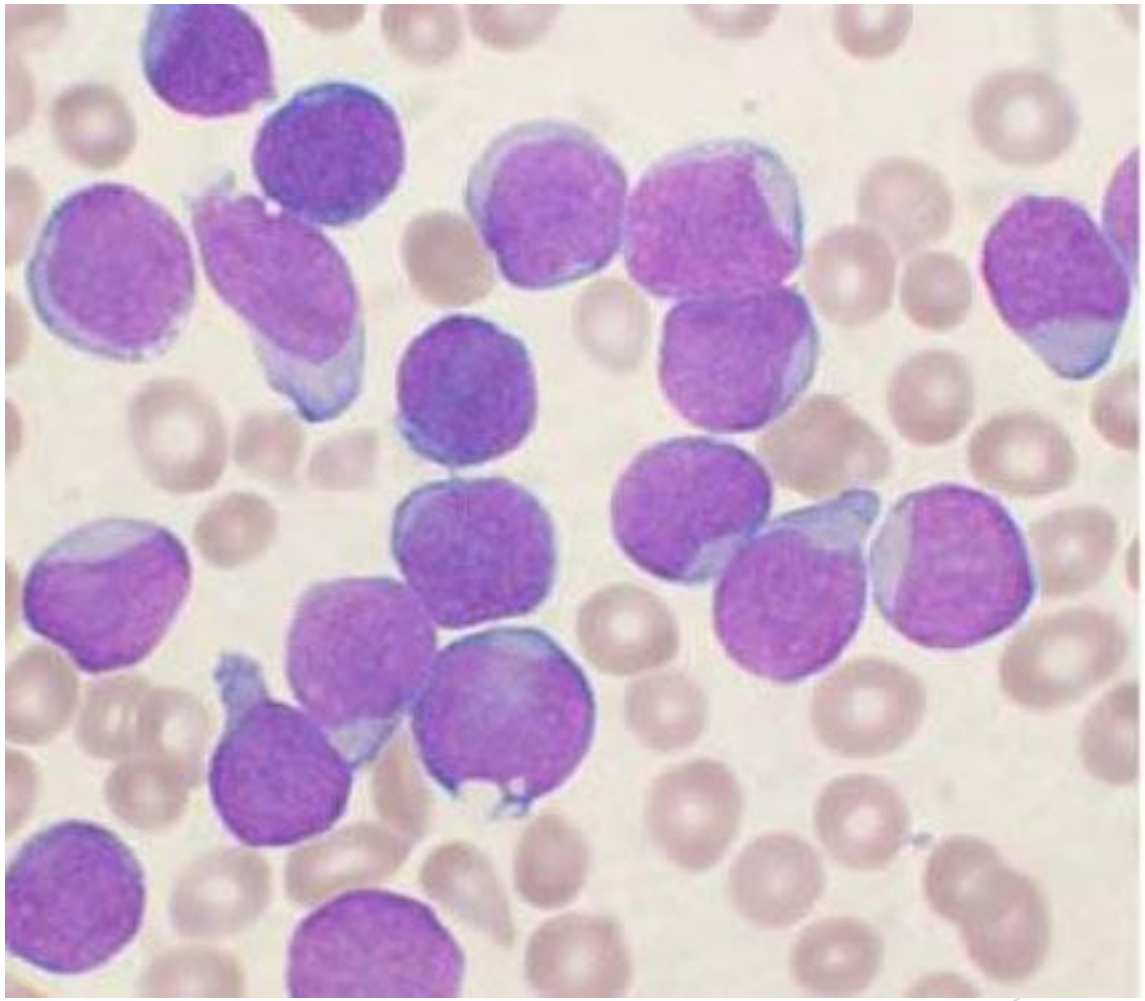
Organs of the immune system

- The central organs of the immune system are involved in the processes of antigen-independent differentiation and maturation of immune system cells.
- Bone marrow, thymus
- Peripheral organs of the immune system are involved in antigen-dependent differentiation of lymphocytes, antigen presentation, and immunogenesis of T- and B-lymphocytes.
- Spleen, lymph nodes, lymphoid follicles

Maturation of the cells of the immune system



Cells of the immune system - lymphocytes



Lymphocytes

Depending on the place of maturation in the body, these cells are divided into two heterogeneous populations.

- B - lymphocytes
- T - lymphocytes

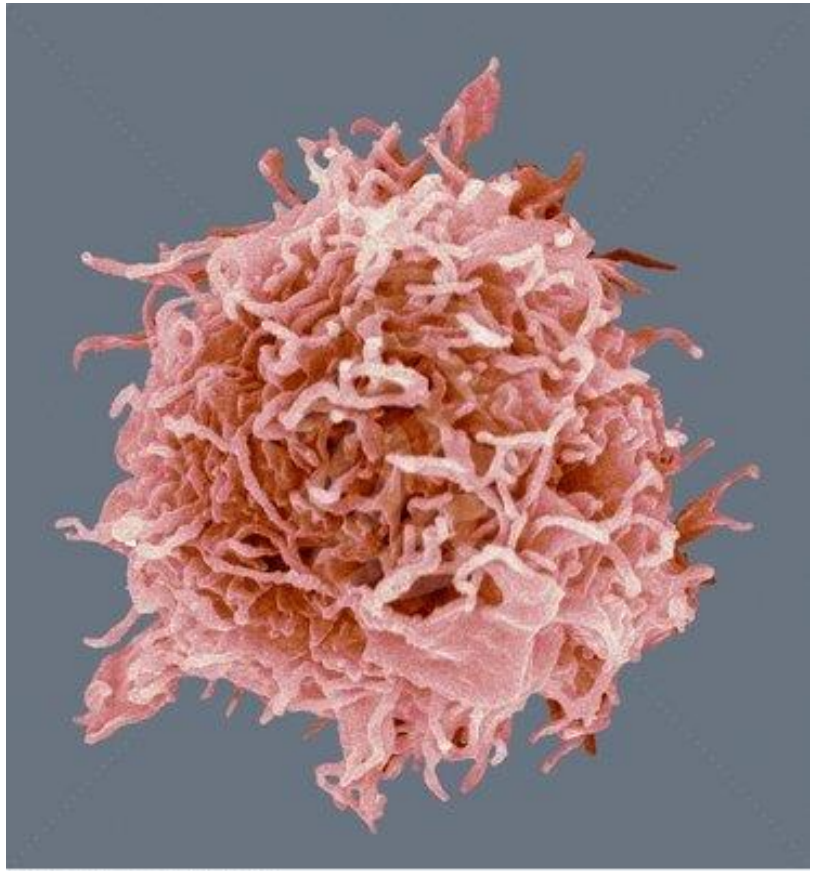
Cells without the hallmarks of T- and B-lymphocytes are called null cells.

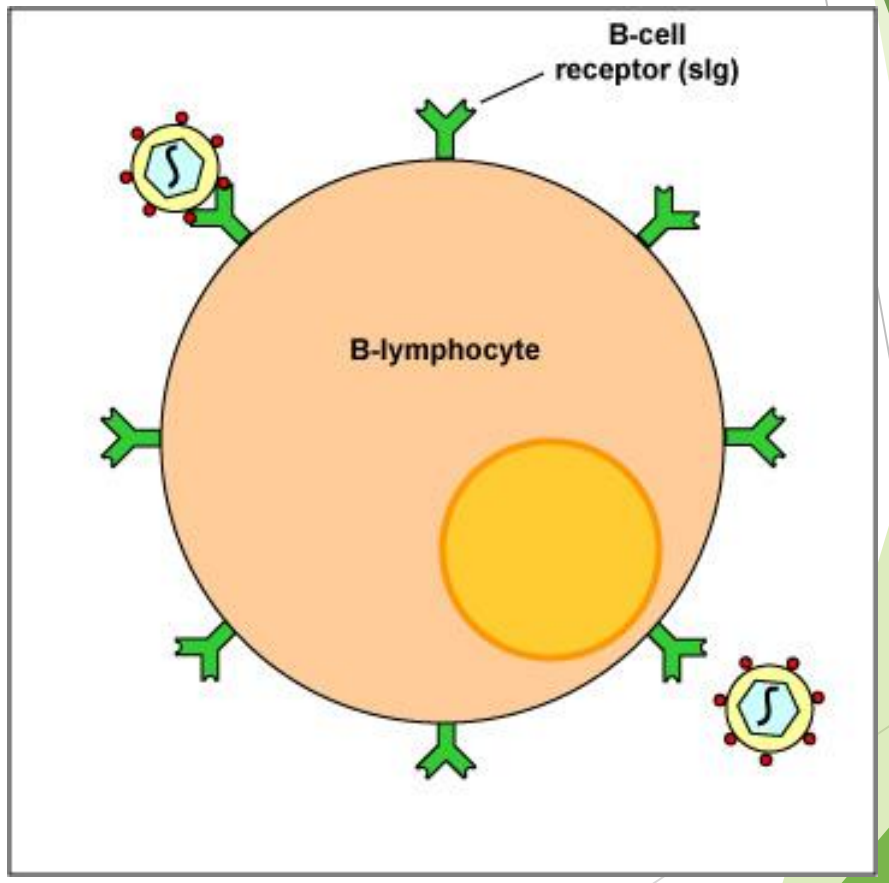
0 - lymphocytes

B-lymphocytes and plasmocytes

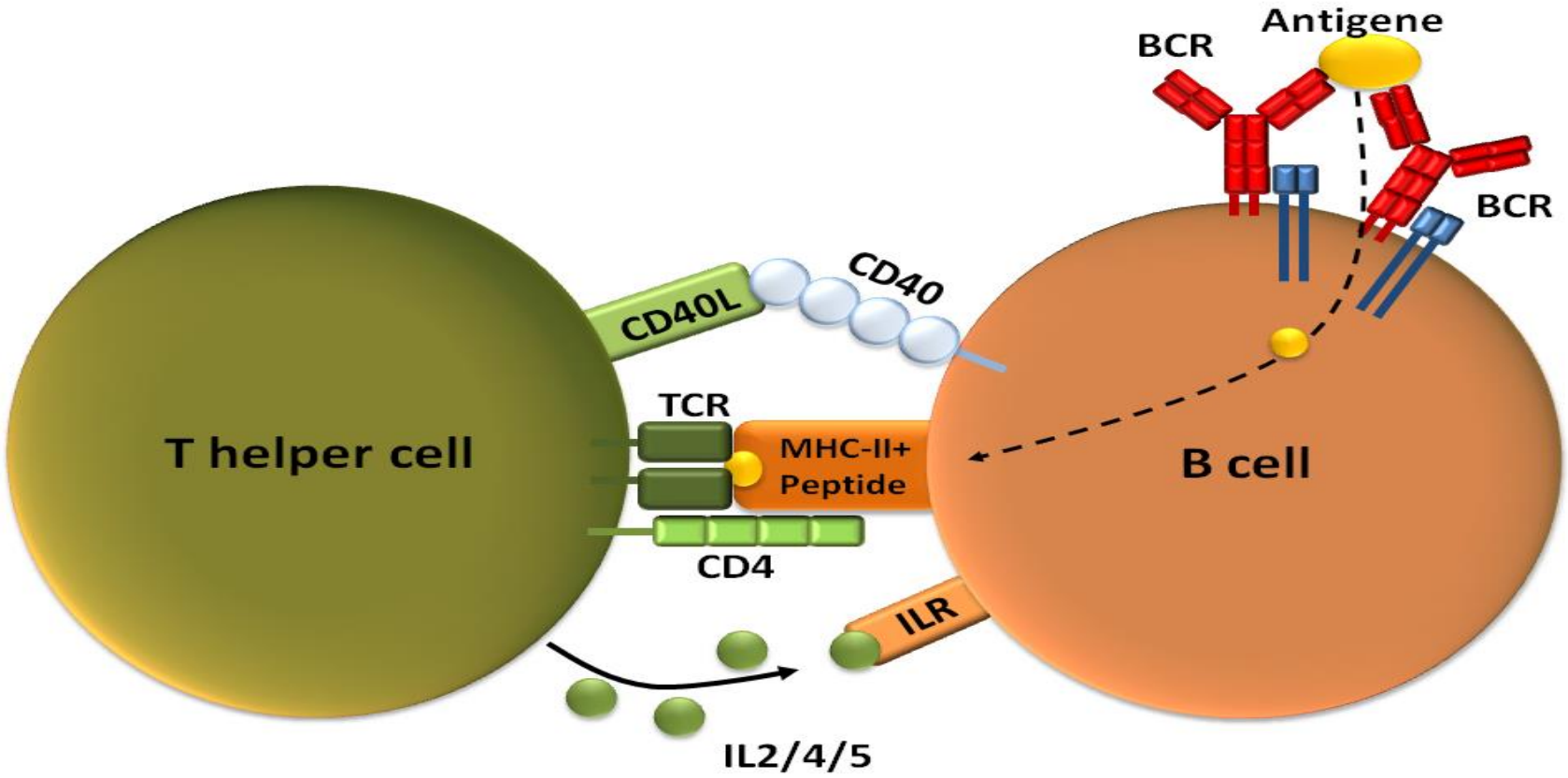
- The basis of the humoral adaptive immune response is the activation of B-lymphocytes and their differentiation into antibody-forming plasma cells.
- B-lymphocyte plays the role of an antigen-presenting and antibody-forming cell.
- Participate in the formation of immunological memory.
- Participate in the development of hypersensitivity reactions.

B-lymphocytes

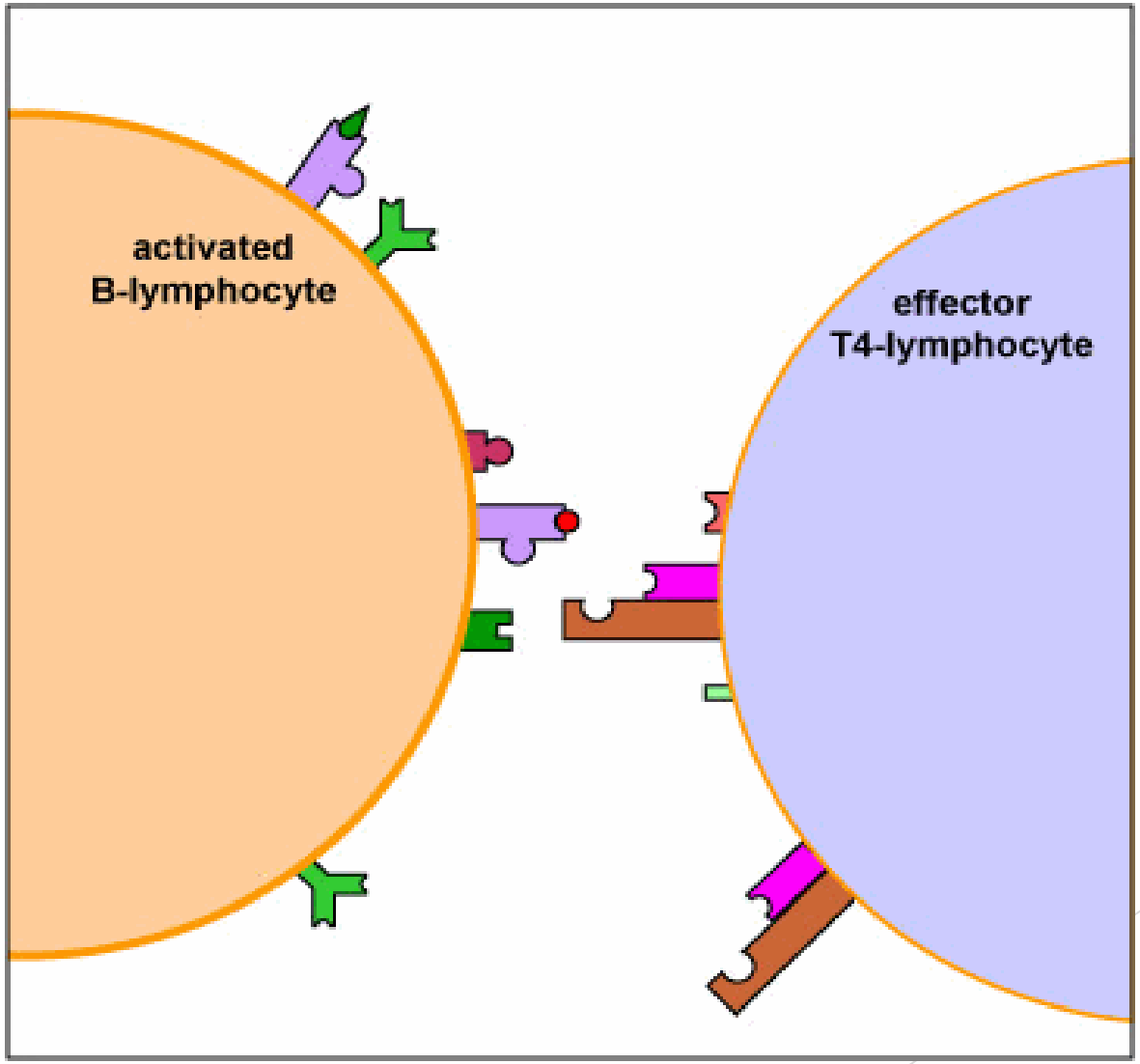




Transfer of antigen information from T-helper to B-lymphocyte



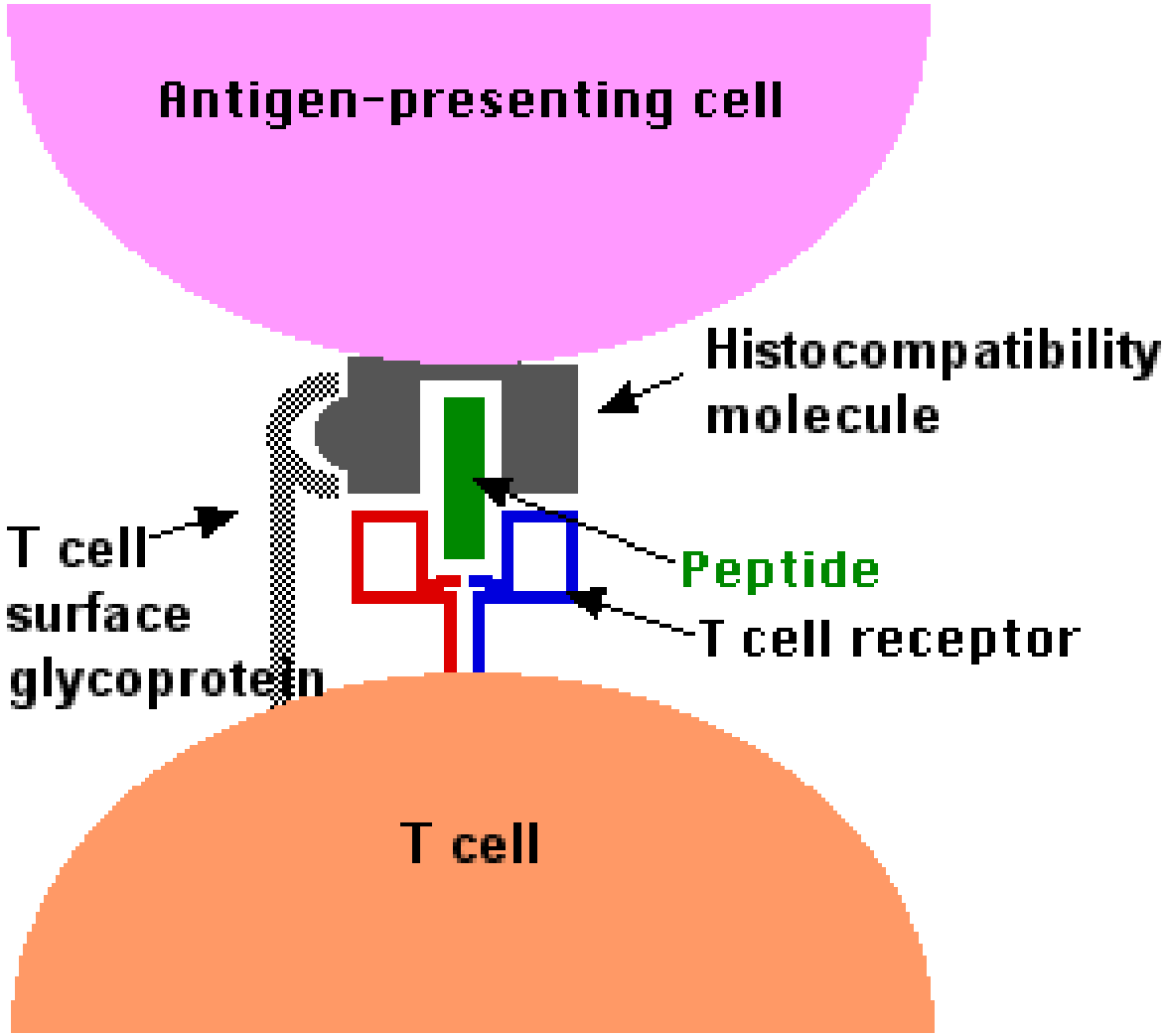
B-lymphocyte receives information about the antigen from the T-helper



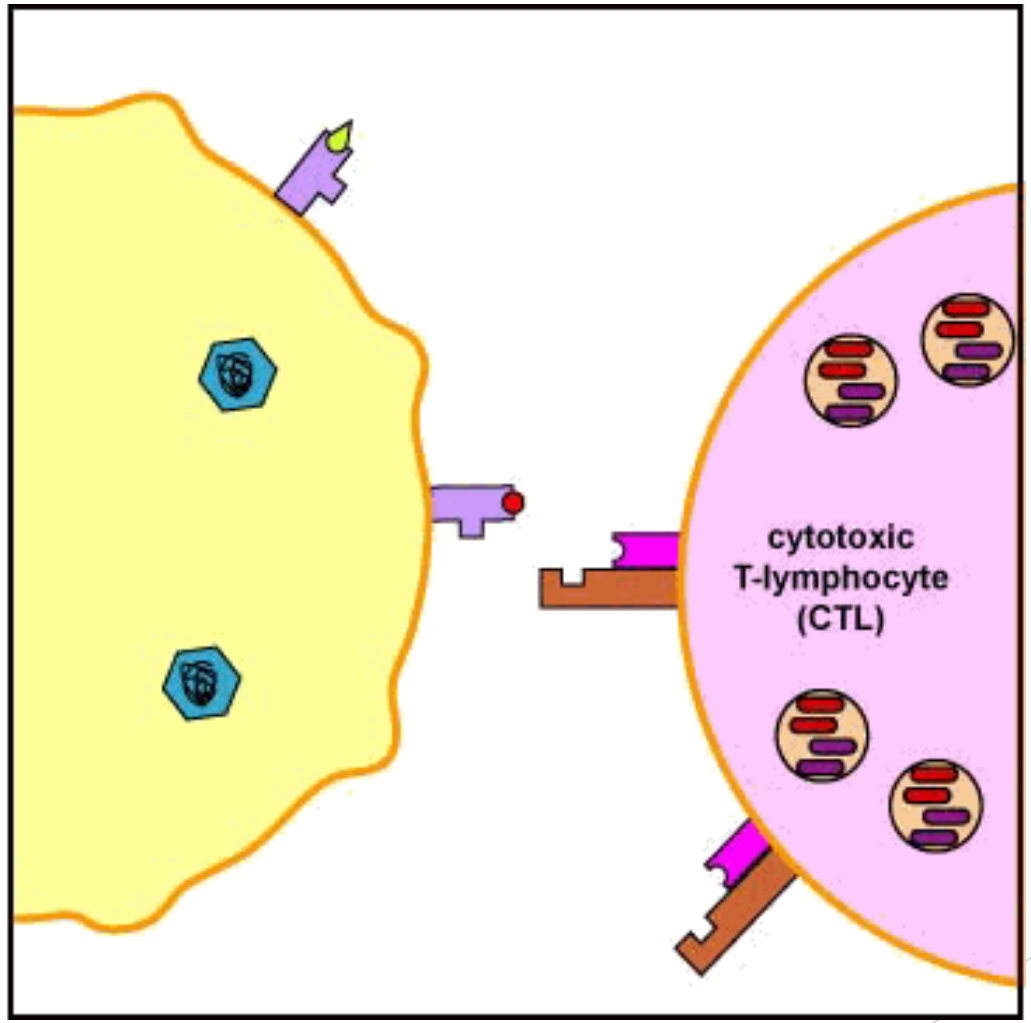
T-lymphocytes

- T-helpers (CD4)
- recognize antigen, transmit information from antigen-presenting cells to immunocompetent cells
- T-killers (CD8)
- lyse target cells carrying foreign or mutated autoantigens
- T-suppressors
- Regulate the intensity of the immune response, prevent the development of autoimmune reactions

Transmission of antigen information from macrophage to T-lymphocyte



Killer T cells kill target cells with antibody-independent cytotoxicity

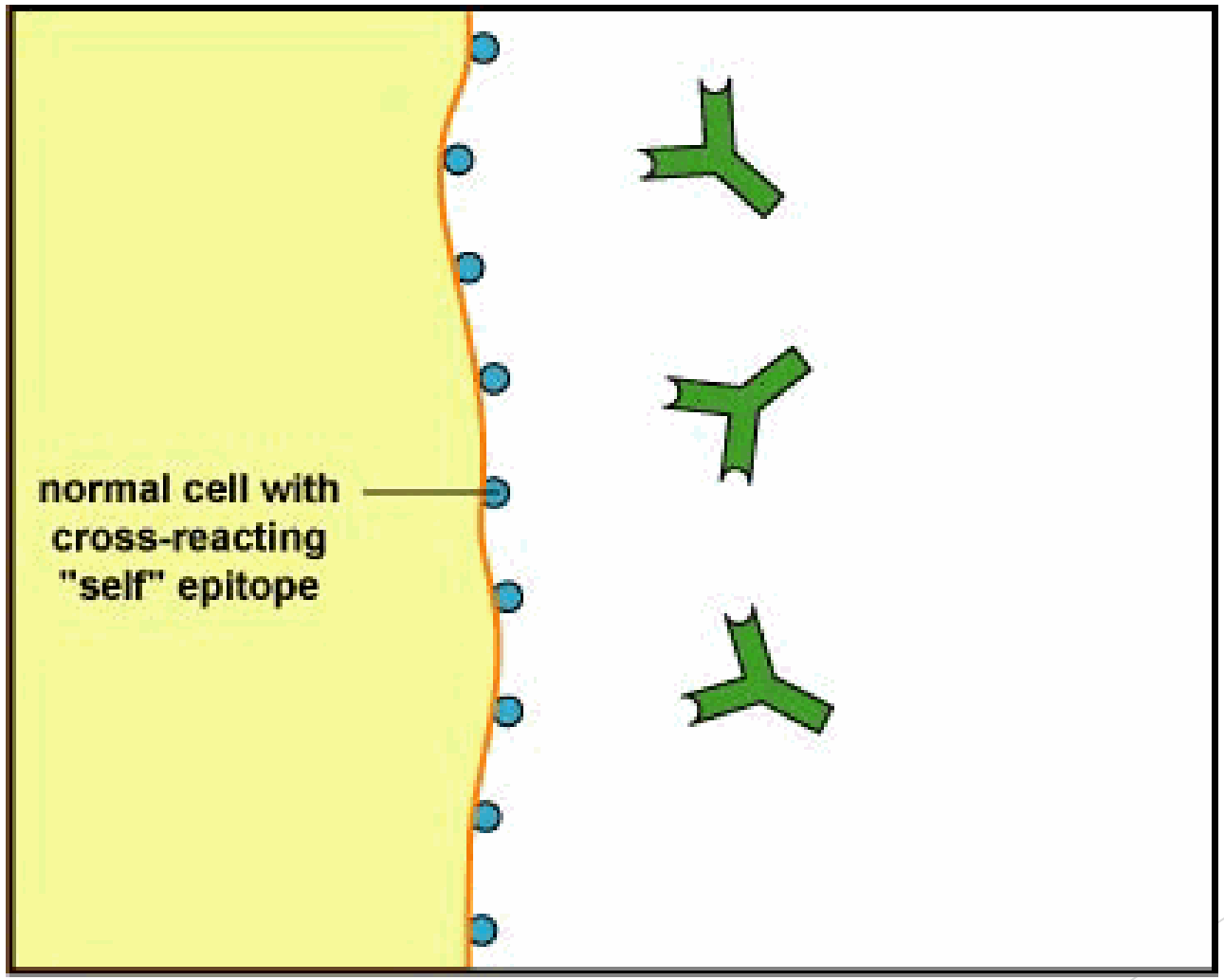


NK cells (English "natural killer" - natural killers)

- They specialize in the destruction of virus-infected, tumor cells, as well as cells with intracellular parasites.
- Destroy target cells by antibody-dependent and antibody-independent cytotoxicity

"attack" of the NK cell on the tumor cell

Action of the NK cell on the target cell



Antigens

- An antigen is a high-molecular compound that carries signs of a genetic foreignness, which, when it enters the body, can cause the development of immune reactions.
- Antigens are components and waste products of microbes, organisms of animals and plants. Antigens can be formed in one's own body with structural changes in molecules, they can be obtained artificially

Antigens

- Biopolymers of protein nature have the greatest antigenicity.
- In addition to proteins, the ability to sufficiently activate the immune system is also possessed by polysaccharides, LPS, glycoproteins, lipoproteins, and their copolymers.

Properties of antigens

- Foreignness is a must. The farther in the phylogenetic development the organisms are separated from each other, the more alien their antigens are in relation to each other.
- At the same time, antigenic determinants of even genetically unrelated animals or structurally different biopolymers can have a certain similarity. In this case, their antigens are able to specifically interact with the same immunity factors. Such antigens are called cross-reactive.
- The phenomenon when one microbe is masked by the antigens of another microbe or macroorganism for "protection" from immunity factors is called antigenic mimicry.

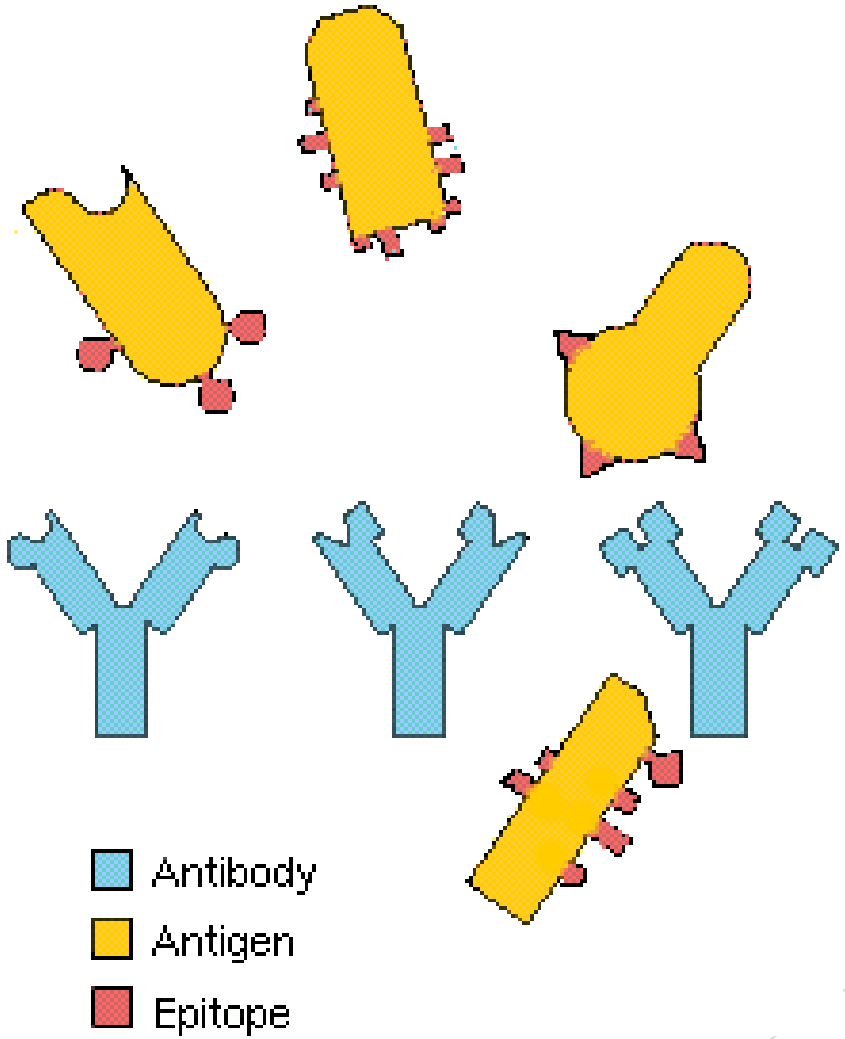
According to the degree of foreignness, they distinguish: xeno-, allo- and isoantigens.

- Xenogenic antigens (heterologous) - common to organisms belonging to different genera and species. Allogeneic antigens (group) - common to genetically unrelated organisms, but belonging to the same species. On the basis of alloantigens, the general population of organisms can be divided into separate groups. Allogeneic tissues are immunologically incompatible during transplantation - they are rejected or lysed by the recipient.
- Isogenic antigens (individual) - common only for genetically identical organisms, for example, for identical twins, inbred lines of animals. Examples of such antigens in the human population are histocompatibility antigens, and in bacteria, type antigens.

Properties of antigens

- Antigenicity characterizes the potential ability of an antigen molecule to activate components of the immune system and specifically interact with immunity factors (antibodies, a clone of effector lymphocytes).
- The components of the immune system do not interact with the entire antigen molecule at the same time, but only with its small area, which is called the "antigenic determinant" or "epitope". Antigens induce the synthesis of antibodies that can bind to them.
- In the structure of most antigens, many antigenic determinants are determined, which are recognized by antibodies and lymphocyte clones of different specificity (such antigens are multivalent).

Antigenic determinants (epitopes)



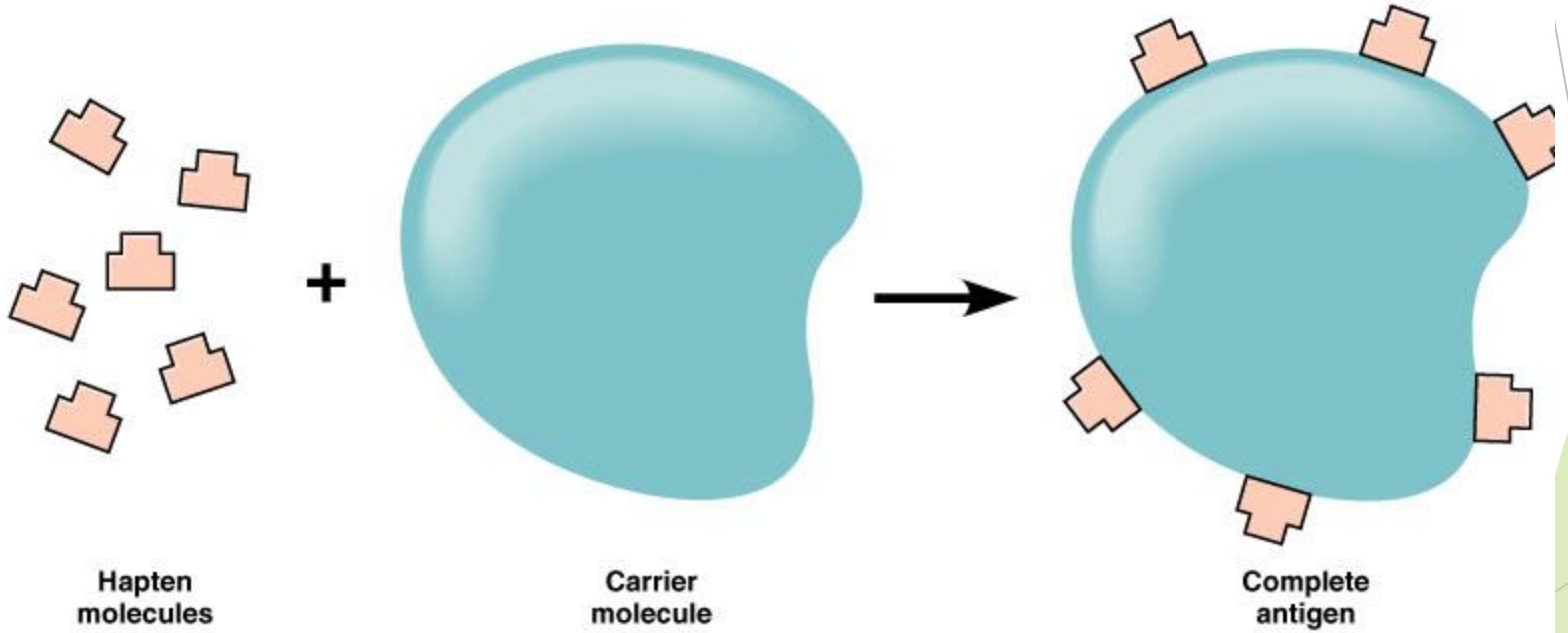
Properties of antigens

- Immunogenicity - the potential ability of an antigen to cause a specific protective reaction in relation to itself in the macroorganism.
- The degree of immunogenicity depends on a number of factors - the molecular characteristics of the antigen and the reactivity of the macroorganism
- There are some differences between the concepts of antigenicity and immunogenicity. For example, the causative agents of bacillary dysentery are highly antigenic, but the immunity formed after the disease is not sufficiently active, in other words, they have weak immunogenicity.

Haptens

- Haptens or incomplete antigens are not able to induce an immune response in the body, as they have extremely low immunogenicity. However, they have not lost their antigenicity property, which allows them to specifically interact with ready-made immunity factors (antibodies, lymphocytes).
- Most often, haptens are low molecular weight compounds.
- Haptens elicit an immune response only after binding to a protein or other carrier polymer

Haptens



Properties of antigens

- Specificity refers to the ability of an antigen to induce an immune response to a well-defined epitope.
- The interaction of antibodies and antigens is highly specific, based on the ability of antibodies to bind to a strictly defined antigenic determinant.
- This property is due to the complementarity of the receptor apparatus of immunocompetent cells to a specific antigenic determinant. Therefore, the specificity of an antigen is largely determined by the properties of its constituent epitopes.
- The strength of the specific interaction of an antibody with an antigen (or the energy of their binding) is called affinity

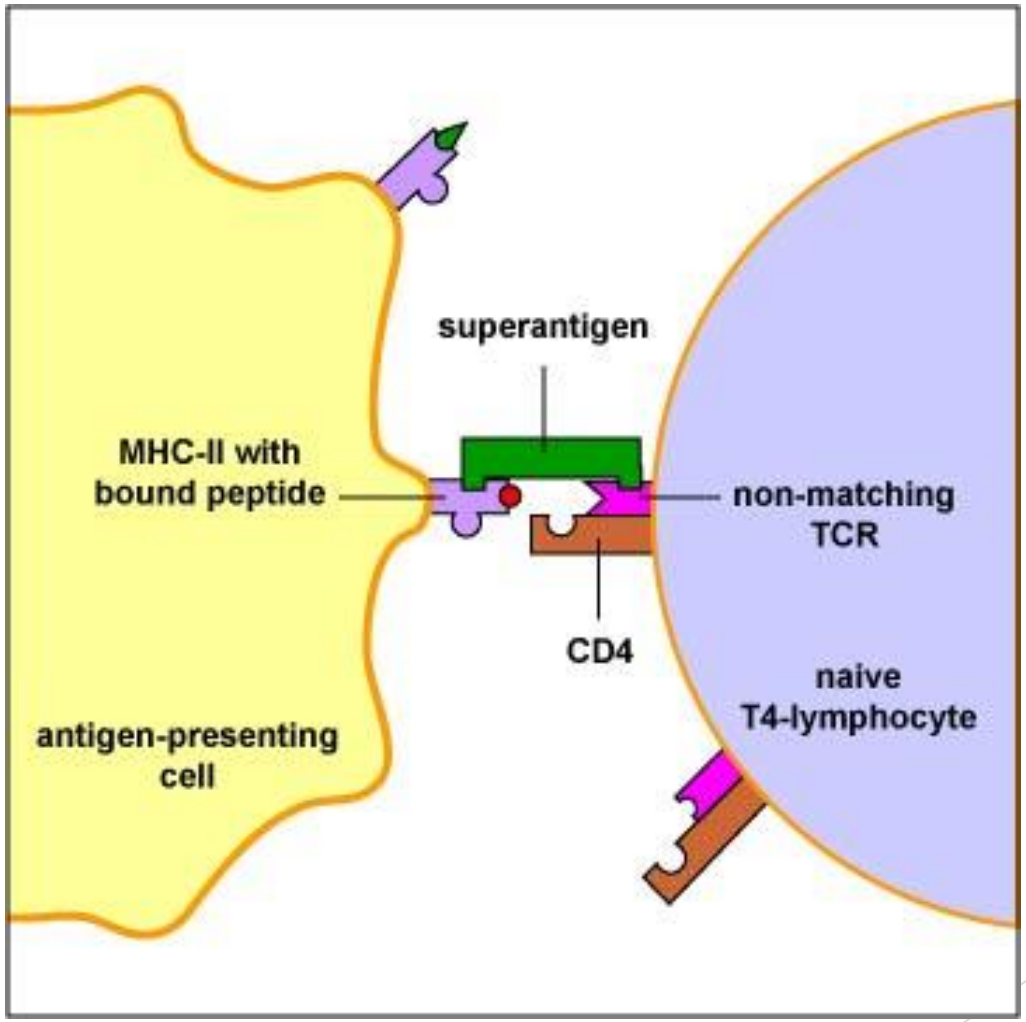
Immunogens, tolerogens, allergens

- Immunogens, when they enter the body, are able to induce a productive reaction of the immune system, which ends with the production of immunity factors (antibodies, antigen-reactive clones of lymphocytes).
- - T-dependent
- - T-independent
- A tolerogen is the exact opposite of an immunogen. Tolerogen is characterized by monomerism, low molecular weight, high epitope density and high dispersity (non-aggregation) of colloidal solutions.
- Allergen - forms a pathological reaction of the body in the form of immediate or delayed hypersensitivity.

Superantigens

- Superantigens - substances, mainly of microbial origin, which can non-specifically cause a polyclonal reaction. The superantigen molecule independently binds to the intercellular complex "class II histocompatibility antigen - T-cell receptor" and forms a false signal for recognition of a foreign substance.

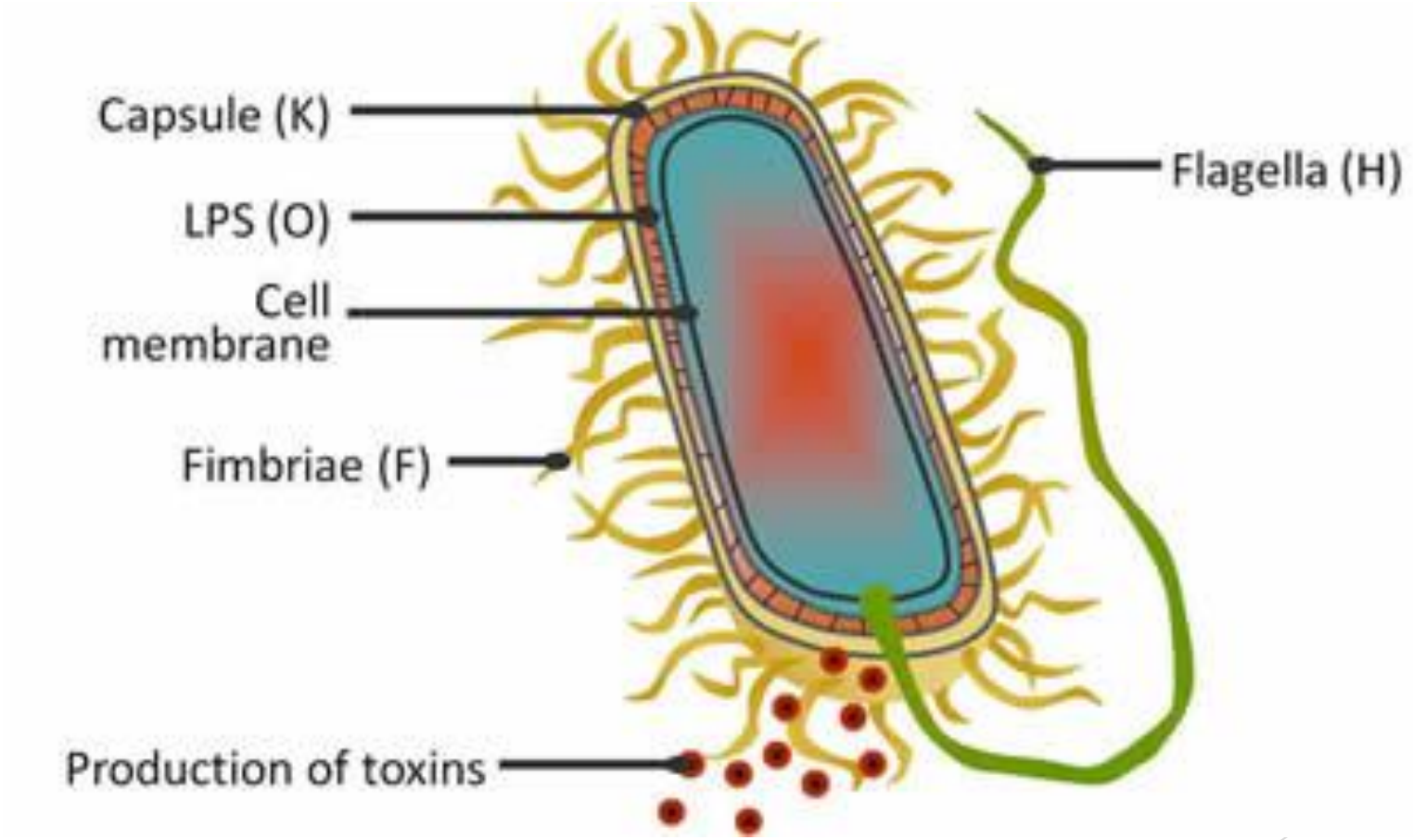
Superantigens



Antigens of microorganisms

- Bacterial antigens
- Flagella, or H-antigen,
- Somatic, or O-antigen,
- Capsular, or K-antigen,
- Virulence antigen, or Vi antigen,
- Exotoxins, enzymes
- Virus antigens
- virus-specific

Bacterial antigens



Antigens of the human body

- RBC antigens
- antigens of the ABO system
- Rh antigens
- Major histocompatibility complex, or MHC
- There are two main classes of MHC molecules.
- Class I MHCs are expressed on the surface of almost all cells, except for erythrocytes (there is no biosynthesis in nuclear-free cells) and villous trophoblast cells (“prevention” of fetal rejection).
- Class II MHCs are expressed on the cytoplasmic membrane of a special group of cells called antigen-presenting cells (APCs).

Histocompatibility antigens

- Histocompatibility antigens are found on the cytoplasmic membranes of almost all cells of the macroorganism. Most of them belong to the system of the main histocompatibility complex, or MHC (abbr. from the English Main Hystocompatibility Complex).

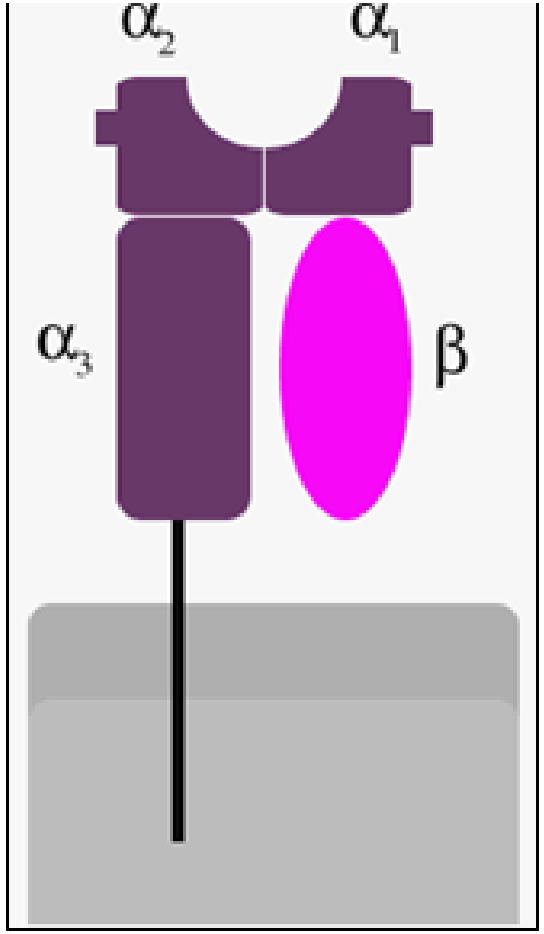
MHC

- In humans, MHC was associated with leukocytes, so it was designated as HLA (abbr. from the English Human Leukocyte Antigen). HLA biosynthesis is determined by genes localized simultaneously in several loci of the short arm of the 6th chromosome.
- HLA-A, HLA-B, and HLA-C genes encode MHC class I proteins Some HLA-D loci encode MHC class II proteins (DP, DQ DR)
- Between the loci of classes I and II is located III locus.
- The MNS III class includes some components
- complement (C2, C4), heat shock proteins, factors
- tumor necrosis, etc.

MHC

- Each person is strictly unique in terms of a set of histocompatibility antigens, with the exception of identical twins, who are absolutely similar in terms of a set of genes.
- Histocompatibility antigens play a key role in the specific recognition of "friend or foe" and the induction of the acquired immune response. They determine the compatibility of organs and tissues during transplantation within the same species, genetic restriction (restriction) of the immune response, and other effects.
- MHC class I induces a predominantly cellular immune response, and MHC class II induces humoral.

. MHC I glycoproteins are expressed on the surface of almost all nucleated cells.



HLA class I determine the biological identity ("biological passport") and are markers of "their own" for immunocompetent cells.

- Infection of a cell with a virus or mutation changes the structure of HLA class I.
- The MHC class I molecule containing foreign or modified peptides has an atypical structure for this organism and is a signal for the activation of T-killers (CD8+-lymphocytes).
- Thus, cells that differ in class I are destroyed as foreign

MHC class II

MHC II class is expressed on the surface of a limited number of cells: dendritic, B-lymphocytes, T-helpers, activated macrophages, mast, epithelial and endothelial cells.

Involvement of MHC class II in the induction of the acquired immune response

- It happens like this:
- Fragments of the antigen molecule are expressed on the cytoplasmic membrane of antigen-presenting cells as a complex MHC II molecule + antigen
- MHC class II with the peptide included in it is perceived and analyzed by T-helpers (CD4+-lymphocytes).
- If a decision is made about the foreignness of the peptide included in the MHC class II, the T-helper begins the synthesis of the corresponding immunocytokines, and the mechanism of a specific immune response is activated.

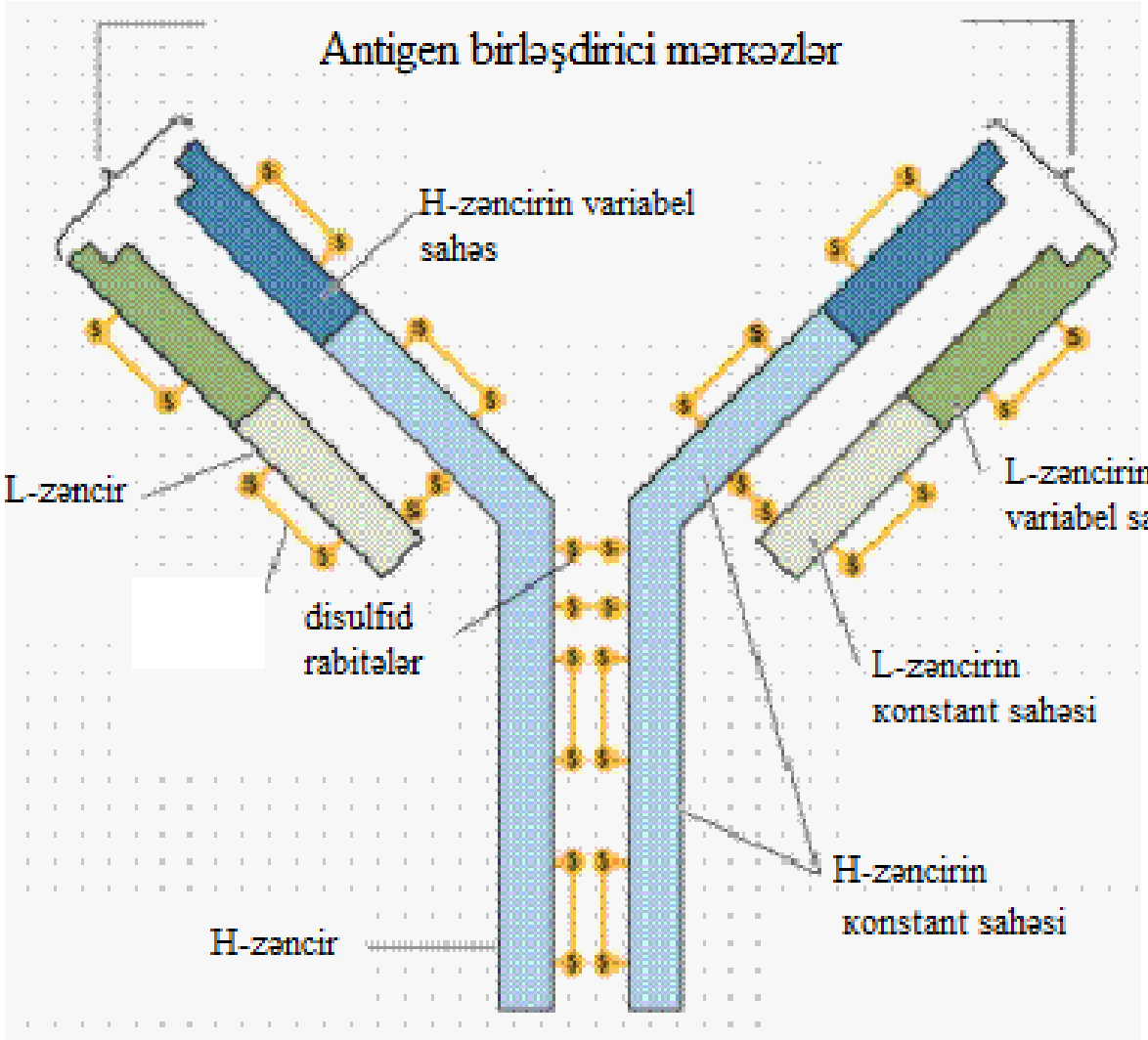
Immunoglobulins, antibodies

- The synthesis of antibodies occurs as a result of the cooperation of three cells - macrophages, Th- and B-lymphocytes.
- After processing, antigen fragments are exposed on the surface of macrophages in combination with class II MHC proteins. These molecules bind to specific receptors on Th cells.
- T-lymphocytes synthesize cytokines - IL2 (T-cell growth factor), IL4 (B-lymphocyte growth factor) and IL5 (B-lymphocyte differentiation factor). These cytokines activate antigen-specific B-lymphocytes.
- Activated B-lymphocytes multiply, differentiate and turn into plasma cells that synthesize immunoglobulins (antibodies).

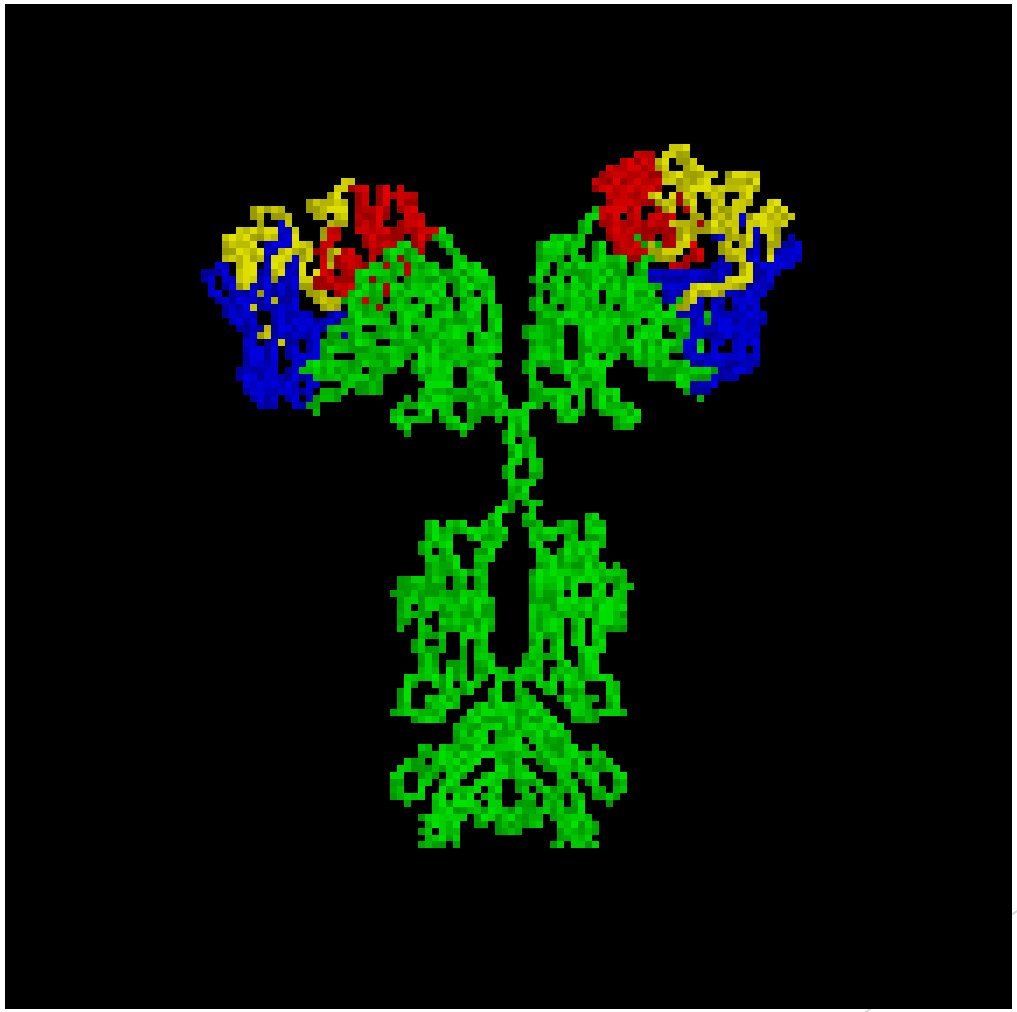
Immunoglobulins

- Antibodies belong to the ??-globulin fraction of blood serum proteins.
- The Ig molecule consists of 2 pairs of polypeptide chains: two H- (from English heavy - heavy) and two L- (from English light - light) chains connected in pairs by disulfide bonds (-S-S-).
- The molecular weight of heavy chains is 50-70 kDa,
- the molecular weight of the lungs is 20-25 kDa
- The composition of light and heavy chains has permanent or C-domains, and V-domains with a variable structure.

The structure of the immunoglobulin molecule



Model of an immunoglobulin molecule



The structure of the immunoglobulin molecule

- The light chain contains one V- and C-domain each, and the heavy chain contains one V- and 3-4 C-domains. It is noteworthy that not the entire variable domain is variable in its amino acid composition, but only a small part of it is the hypervariable region, which accounts for about 25%.
- The light and heavy chain variable domains together form a region that specifically binds to an antigen. This is the antigen-binding center of the Ig molecule, or paratope, which is located in the Fab-fragment (from the English "antigen-binding fragment") of the Ig molecule.
- Antigen-antibody binding occurs due to weak interactions (van der Waals forces, hydrogen bonds, electrostatic interactions) within the antigen-binding center.

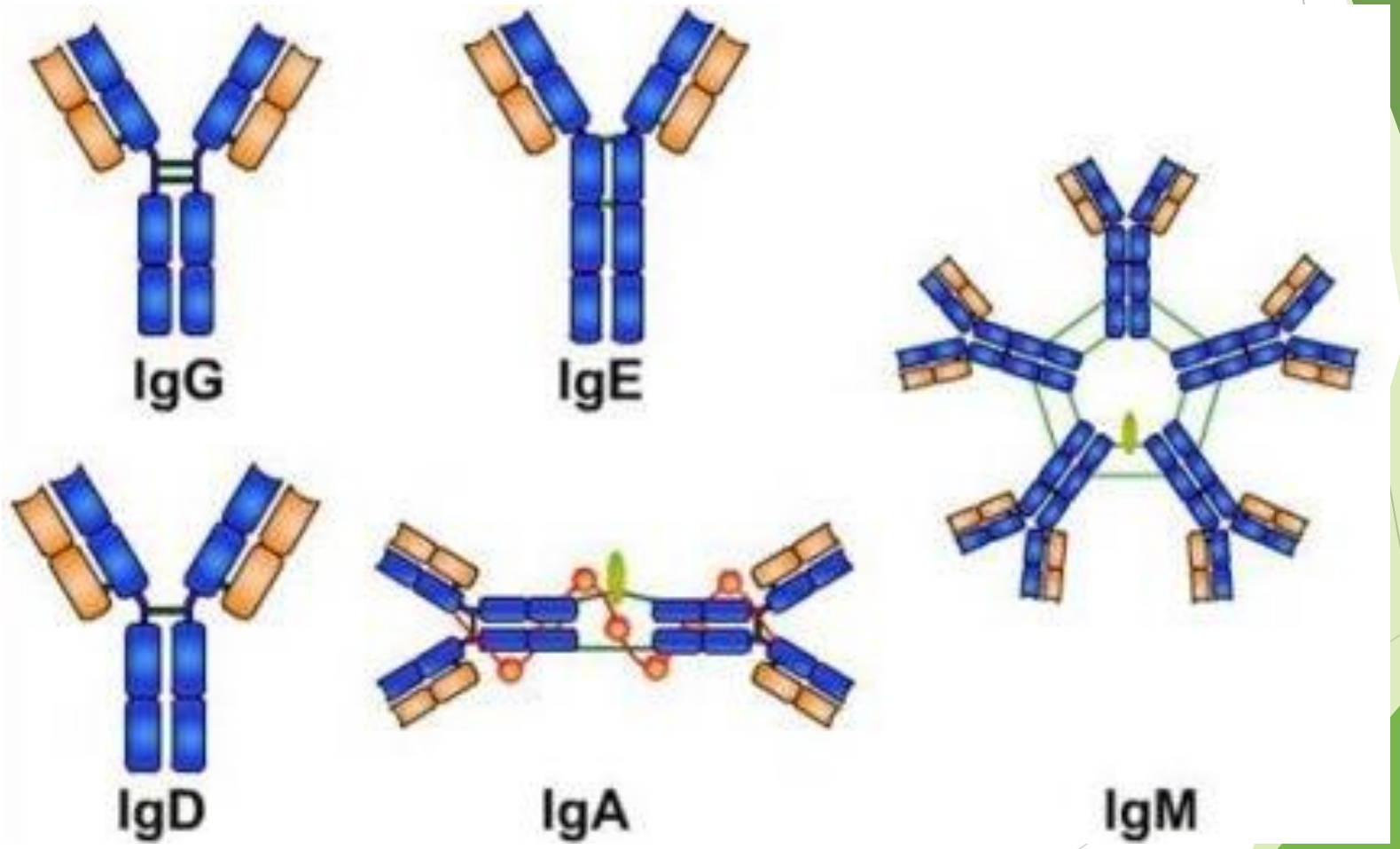
The structure of the immunoglobulin molecule

- A fragment of immunoglobulins, consisting of the C-domains of the heavy and light chains, was called the Fc fragment (from the English “crystallizing fragment”), as it is able to form crystals. It is responsible for binding to host cell membrane receptors (Fc receptors) and some microbial superantigens.
- Obtaining individual fragments of the Ig molecule is possible after their treatment with proteolytic enzymes.

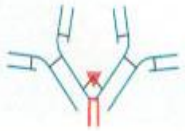
Immunoglobulin class

- Depending on the features of the molecular structure of the heavy chain, 5 classes, or Ig isotypes, are distinguished.
- Molecules containing an α-type heavy chain are referred to as isotype A (abbreviated as IgA); IgD has a δ chain, IgE has an ε chain, IgG has a γ chain, and IgM has a μ chain. According to the structural features of heavy chain subtypes, Ig subclasses are also distinguished.
- Some immunoglobulins may have 4 subtypes: eg, IgG1, IgG2, IgG3, IgG4; IgA, IgM və IgD - have 2 subtypes

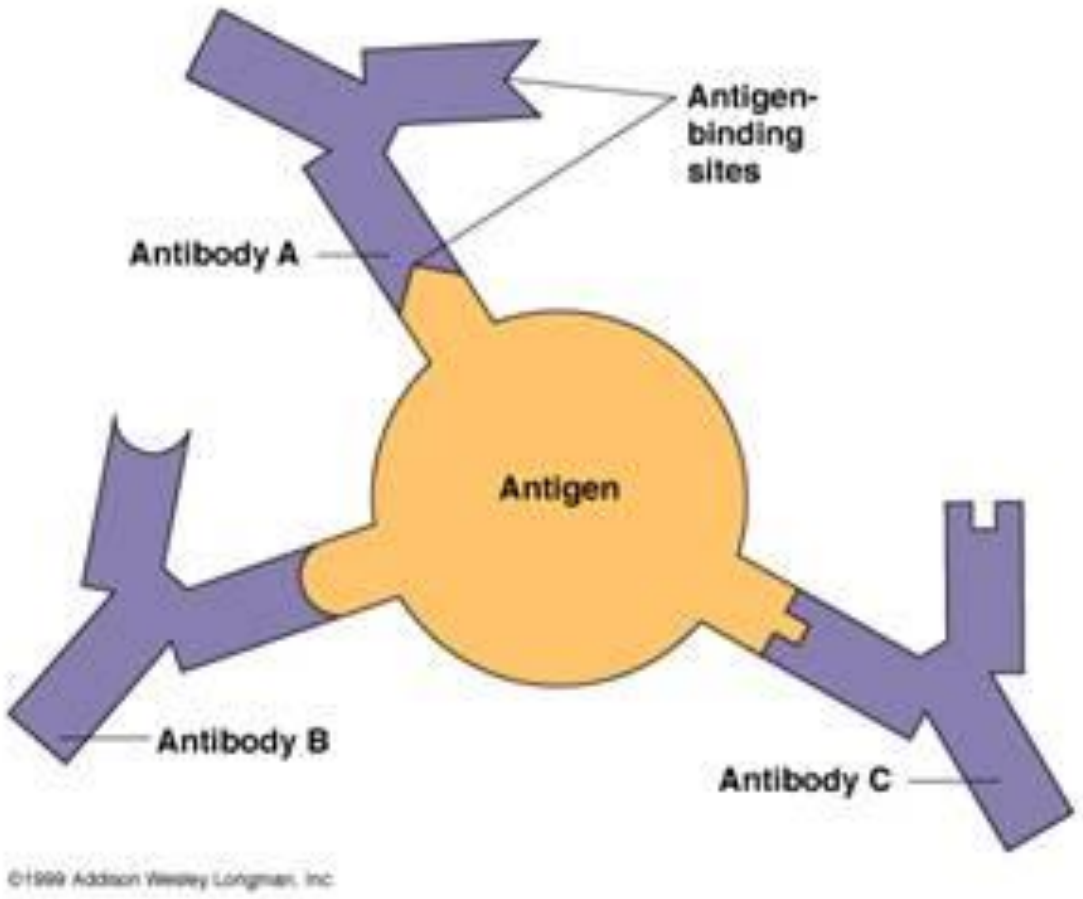
Immunoglobulin classes

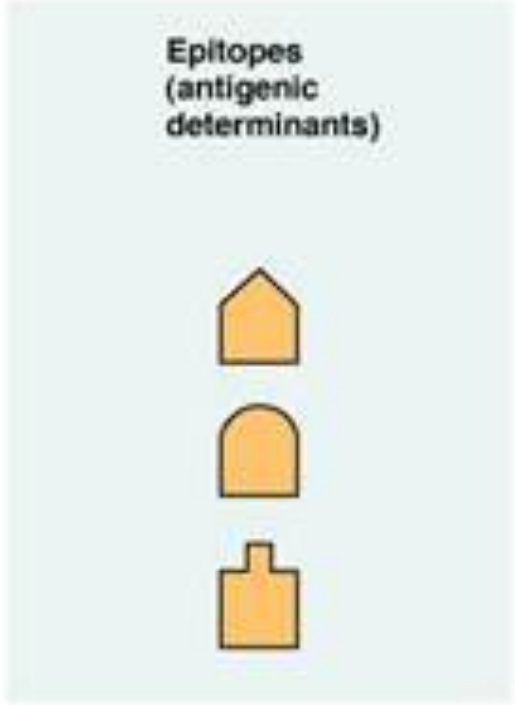


Immunoglobulin classes

Immuno-globulin Class	Structure	Molecular Weight	Percent in Blood	Location	Crosses Placenta?	Fixes Complement?
IgG		150,000	75–80	Blood and tissue fluids	Yes	Yes
IgM		900,000	6–7	Blood and tissue fluids	No	Yes
IgA		170,000*	15–21	Saliva, mucus, and secretions	No	No
IgE		200,000	<1	Skin, respiratory tract, and tissue fluids	No	No
IgD		180,000	<1	Serum	No	No

Specificity of immunoglobulins

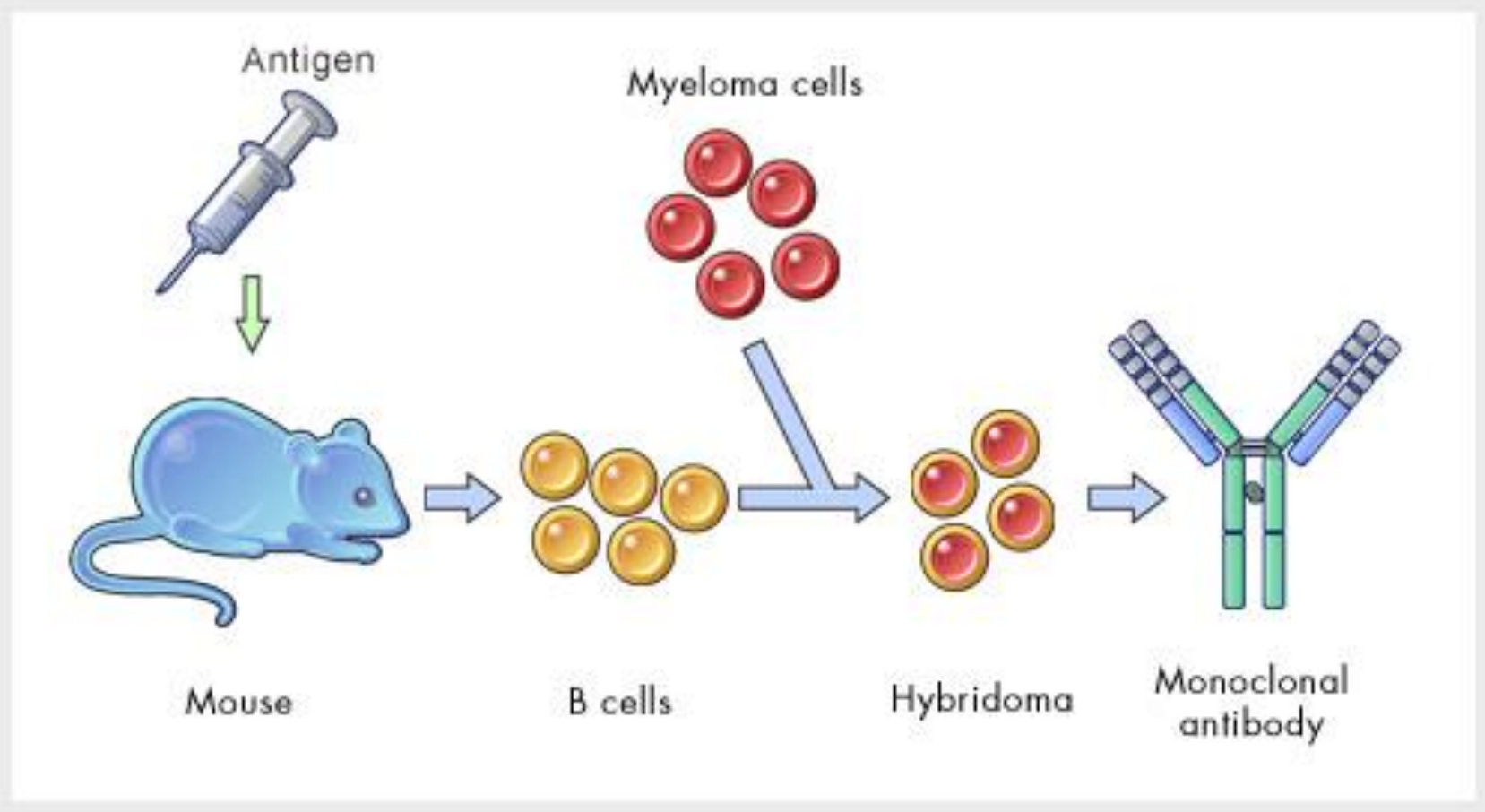




Diversity of antibodies

- Normal or natural antibodies.
- Receptor immunoglobulins
- Polyclonal antibodies
- Monoclonal antibodies were obtained by D. Keller and C. Milstein (1975) by fusing immune B-lymphocytes with a myeloma (tumor) cell. The resulting hybrids had the specific properties of an antibody producer and the "immortality" of a cancer-transformed cell.
- Incomplete or blocking antibodies.

Obtaining monoclonal antibodies



Dynamics of antibody formation

- The primary immune response develops after the initial exposure to the antigen. After 4-5 days. (sometimes 7-10 days) IgM is detected in the blood serum, and then IgG, memory T-lymphocytes are formed.
- A secondary immune response develops when the antigen is re-introduced. Due to previously formed memory lymphocytes, there is practically no latent period of antibody production. With a secondary immune response due to memory lymphocytes, the rate of formation, quantity and affinity for the antigen significantly increase.
- (affinity).

Obtaining hyperimmune sera

- The phenomenon of intense antibody formation upon repeated contact with an antigen is widely used for practical purposes, for example, in vaccination.
- The effect of immune memory is the basis of vaccination of many infectious diseases. For this, a person is vaccinated and then (after a certain time interval) is revaccinated.
- The same phenomenon is used to obtain highly active therapeutic and diagnostic immune sera (hyperimmune). To do this, animals or donors are given multiple injections of antigen preparations according to a special scheme.

Immunodiagnostics

- Features of the interaction of an antibody with an antigen are the basis of diagnostic reactions in laboratories
- When antigens enter the body, specific antibodies are formed in the blood serum. These antibodies have the ability to specifically bind to antigens not only in the body (in vivo), but also outside the body (in vitro).
- The specificity of the interaction between antibodies and antigens makes it possible to identify an unknown antibody based on a known antigen, or vice versa.
- Immune reactions are used in diagnostic and immunological studies in sick and healthy people. For this purpose, serological methods are used (from Latin serum - serum and logos - teaching), i.e. methods for studying antibodies and antigens using antigen-antibody reactions, determined in blood serum and other fluids, as well as body tissues.

Application of serological reactions

- Serological reactions can be carried out in two directions:
- For identification of microbial antigens, various biologically active substances, blood groups, tissue and tumor antigens, immune complexes, cell receptors, etc.
- When a microbe is isolated from a patient, the pathogen is identified by studying its antigenic properties using immune diagnostic sera, i.e. blood sera of hyperimmunized animals containing specific antibodies. This is the so-called serological identification of microorganisms.

Application of serological reactions

- Serological tests use known antigens or microorganisms to identify unknown antibodies, i.e. diagnosticums
- Reference strains of microorganisms or their antigens are used as diagnosticums.
- The detection of antibodies against the antigens of the pathogen in the patient's blood serum makes it possible to diagnose the disease.
- (serological diagnosis).

Types of serological reactions

- Assessment of the results of serological reactions is carried out on the basis of the formation of an antigen-antibody complex
- The reactions differ in the registered effect and technique, however, they are all based on the reaction of the interaction of the antigen with the antibody and are used to detect both antibodies and antigens. Distinguish:
- - simple serological tests (involving two components)
- - complex serological reactions (involving three or more components).
- For the purpose of immunodiagnostics, agglutination, precipitation, neutralization reactions, reactions involving complement, using labeled antibodies and antigens (radioimmunological, enzyme immunoassay, immunofluorescent methods) are widely used.
- Immunity reactions are characterized by high sensitivity and specificity.

Phases of serological reactions

- The in vitro reaction between an antigen and an antibody consists of a specific and a non-specific phase.
- In the specific phase, there is a rapid specific binding of the active site of the antibody to the determinant of the antigen.
- The non-specific phase is a slower one, which is manifested by visible physical phenomena, for example, the formation of flakes (agglutination phenomenon) or a precipitate in the form of turbidity. This phase requires certain conditions (electrolytes, optimal pH of the medium).
- The binding of an antigen determinant (epitope) to the active site of an antibody Fab fragment is due to van der Waals forces, hydrogen bonds, and hydrophobic interactions. The strength and amount of antigen bound by antibodies depend on the affinity, avidity and valence of the antibodies.

Agglutination phenomenon