

Relevance of the topic under study: The protection of the body from infectious agents, the performance of the immune system tasks of maintaining tissue homeostasis of the body depend on the adequacy of the immune response, which is impossible without adequate recognition of the antigen by T-lymphocytes. Each allelic variant of the MHC molecule binds peptides to certain "anchor" amino acid residues. Natural selection. Each individual is potentially able to develop a response only to those peptides that are able to bind the MHC glycoproteins of this individual. Specific variants of MHC are fixed in evolution by natural selection, and each individual is adapted to the regional species and strains of microorganisms, which were protected from the selection of MHC in the ancestors. Non-classical MHC genes are not polymorphic or not as polymorphic as classical MHC genes. The value of MHC polymorphism. Genetic polymorphism reflects the adaptive potential of a population and a species. The wider it is, the more likely it is that there are individuals within the species that can survive extreme changes in environmental conditions. Microorganisms, having a high rate of reproduction and the ability to change, represent a potential danger to the existence of highly organized living beings, whose MHC molecules are the main structures that present infectious antigens. Their ability to bind foreign peptides and activate T-lymphocytes largely determines the level of response of the adaptive immune system to an infectious agent. It is no coincidence that the pathogenic properties of viruses are due to the ability to inhibit the expression of MHC molecules. It was the diversity of microorganisms that led to the polymorphism of MHC, but the amount of hereditary information is limited by the capacity of the cell nucleus, and an individual is not able to have the entire possible spectrum of allelic diversity in the genome. Nature has distributed it among individuals within the species. Thus, the polymorphism of the HLA genes protects all of humanity from extinction, but not its individual representatives. Antigenic peptide – MHC complexes. The formation of complexes of antigenic peptides with MHC of different classes occurs in different cell compartments. MHC-I "serve" the zone of the cytosol communicating through the nuclear pores with the contents of the nucleus. MHC molecules are polymorphic products of genes of the major histocompatibility complex of classes I and II. HLA molecules encoded by MHC genes are divided into MHC class I glycoproteins (HLA-A, HLA-B, and HLA-C), which are present on the surface of all somatic cells except for the cells of the villous trophoblast and red blood cells, and HLA molecules encoded by MHC class II genes (HLA-DP, HLA-DQ, and HLA-DR) are expressed mainly on the membrane of antigen-presenting cells (DC, activated macrophages and B-lymphocytes), as well as on some T-helper cells. In addition to the role of leukocyte antigens in protecting against diseases, they can cause organ rejection after transplantation, can protect against cancer or increase its likelihood (if unregulated due to frequent infections); can affect the development of autoimmune diseases (e.g., type 1 diabetes, SLE, Bekhterev's disease). There are many variants of MHC class II membrane molecules, which is due, on the one hand, to the polygenism of the α - and β -chains, on the other hand, to their ability to combine not only within the haplotype, but also to form combinations of parent chains encoded within the same regions. The α 1 and α 2 domains form a groove for binding antigenic peptides with a length of 9–11 amino acids, presented for recognition to T-lymphocytes. Moreover, it was found that T-cells recognize the antigen only in combination with MHC molecules, in contrast to B-lymphocytes and immunoglobulins, which recognize epitopes in the composition of any protein molecules. T-lymphocytes

with the help of antigen-recognizing receptors are able to recognize antigens only in combination with MHC-I or MHC-II molecules on the cell surface of their body – the phenomenon of double recognition. In the immune system, these glycoproteins perform an important function: they are involved in the presentation of antigen-presenting cells (APC) of peptide antigens to T-lymphocytes. Initially, they were divided by the induction of their products mainly humoral (class II) or cellular (class I) immunity. Initially, human leukocyte antigen (HLA) genes were identified in successful organ transplants between people with similar HLA. Human leukocyte antigens (HLA) are glycoproteins encoded by the genes of the major histocompatibility complex – MHC. Unlike MHC-I, the peptide-binding cleft is open on both sides, which allows the binding of longer peptides (15–30 amino acids). The mechanism of their adaptation to an unlimited set of antigens lies in their genetic polymorphism (co-dominance, multiplicity of alleles, natural selection). The polymorphism of the classical MHC genes means that the population has many alleles – variants of the same gene in different individuals. HLA diversity in the human population is an aspect of disease defense, and therefore the chances of all HLA genes matching at all loci are very small. MHC-II class molecules are heterodimers of 2 transmembrane glycoproteins: α - and β -chains. The MHC I genes occupy a distal and MHC II genes occupy a proximal position with respect to the centromere. Both classical MHC molecules and non-classical structures are encoded in MHC class II and I clusters. Genes that carry information about the structure of classical MHC molecules are characterized by polymorphism and polygenism. Class I and II antigen products are involved in the rejection of incompatible implants and the presentation of antigen to T-cells. α and β encoding the corresponding polypeptide chains of the molecules are directly involved in the presentation of the antigen. The MHC-I have 3 genes (A, B, C) in each of the homologous chromosomes, and the MHC-II genes have also 3 of them (DP, DQ, DR). In addition to the genes encoding the 6 main antigens, there are many other genes involved in the functioning of the immune system, which are also found in the HLA complex. MHC-I class molecules consist of 2 polypeptide chains – α -chain and β 2-microglobulin. A light molecular chain, β 2-microglobulin, is non-covalently associated with extracellular β -domains. There are 3 sites in the MHC: a cluster encoding I class MHC, a cluster encoding II class MHC, a cluster encoding III class MHC. MHC I genes carry information about the structure of the α -chains of MHC I molecules, MHC II genes – about the structure of the α - and β -chains of MHC II proteins. The expression of histocompatibility genes occurs co-dominantly, i.e. both alleles are realized in the phenotype. As a result, 6 variants of classical MHC class I molecules can be simultaneously represented on the surface of a particular cell. MHC class III genes are not the part of histocompatibility molecules and their presentation. They encode some complement components, TNF-family cytokines, heat shock proteins. The genes of MHC complex (unlike the TCR or Ig genes) do not undergo recombination. Co-dominance is the simultaneous expression of the genes of the maternal and paternal chromosomes. The peptide-binding groove is formed together by the α 1- and β 1-domains. The first is formed by the genes A, B, and C, which are characterized by high polymorphism – several hundred of their allelic forms are known. Another group is formed by non-classical genes E, F, G, H (genes with limited polymorphism). There can be more than 100 allelic variants of individual MHC loci. HLA may be associated with some individual odors that play a role in the selection of sexual partners. Somatic cells do not express MHC-II molecules under normal conditions. The α -chain

has 3 extracellular domains (?1, ?2, ?3), a transmembrane site, and a cytoplasmic site. Genes of the major histocompatibility complex The complex is localized in the short arm of human chromosome 6. Polygenism is the coding of one characteristic by several genes. MHC class II genes also include several variants. Thus, if the mother and father do not have the same alleles, each person has 12 different alleles of the MHC genes. Therefore, the student needs to know the structure and functions of histocompatibility molecules. Transmembrane MHC molecules. Between them is a MHC class III cluster. The extracellular part of each chain has 2 domains. There are 2 groups of class I genes. The products of the genes DR (? Genes of the major histocompatibility complex. Multiplicity of alleles. They determine the biological identity of each person. Pic. These are classic class I genes. and ?), DP (? and .?), and DQ (? Pic. Genetic polymorphism. 1.2