

ОҢТҮСТІК-ҚАЗАҚСТАН MEDISINA AKADEMIASY «Оңтүстік Қазақстан медицина академиясы» АҚ		 SOUTH KAZAKHSTAN MEDICAL ACADEMY АО «Южно-Казахстанская медицинская академия»
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Lecture complex

Module: "Structural organization of human physiological processes"

Discipline: "Molecular Biology of the Cell"

Module code: SOFPCH 1203

Name of EP: 6B10115 "Medicine"

Study hours/credits: 24 hours/1.5 credits

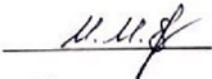
Course and semester of study: 1-I

Lecture volume: 3 h.

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The lecture complex was developed in accordance with the working curriculum of the EP "Structural organisation of human physiological processes", the discipline "Molecular Biology of the Cell" and discussed at the meeting of the department.

Protocol no. __17__ of «_26_» __05__ 2023 y.

Head of Department, Professor  Yessirkepov M.M.

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Lecture №1. Molecular biology of the cell

1. Topic. Molecular biology of the cell. Structure and functions of the main components of the cell. Transport of substances through bio membranes. Adhesive function of membranes. External signal transmission in the cell. Types of signaling pathways and signaling systems.

2. Purpose: To give an idea of the main cellular elements involved in the life activity of the cell, as well as the mechanisms of formation of intercellular contacts, adhesion, and extracellular matrix.

3. Lecture thesis: Molecular biology is a complex of biological sciences that study the mechanisms of storage, transmission and realization of genetic information, structure and functions of irregular biopolymers (proteins and nucleic acids). The three main components of a cell are: nucleus, cytoplasm and the surrounding cell membrane - plasmolemma. The cytoplasm (cytoplasm) of the cell includes hyaloplasm, its obligatory cellular components - organelles, as well as various non-permanent structures - inclusions. Hyaloplasm is a complex colloidal system that includes various biopolymers such as proteins, nucleic acids, polysaccharides. The hyaloplasm is mainly composed of various globular proteins. The most important enzymes in the hyaloplasm include enzymes for the metabolism of sugars, nitrogenous bases, amino acids, lipids, and other important compounds. Enzymes of amino acid activation during protein synthesis, transport (transfer) RNAs (tRNAs) are located in the hyaloplasm.

Organelles are the most important component of the cell, cell structures that have a strictly defined structure and functions.

According to the functional sign organelles are divided into:

- 1 - Organelles of general importance;
- 2 - Organelles of special significance;

According to the structural principle, organelles are divided into:

- 1 - Membrane organelles (mitochondria, EPS, CG, lysosomes, peroxisomes);
- 2 - Non-membrane organelles (fibrillar organelles (microtubules, microfilaments, cilia, flagella, centrioles) and granular organelles (ribosomes, polysomes).

Organelles are dynamic structures; they can change size but do not form. The formation of new organelles requires information in the form of a rudiment or matrix from an already existing organelle. Each organelle occupies in hyaloplasm a place optimal for fulfilment of its specialised function.

Biomembranes are lipoprotein formations that limit the cell from the outside and form some organelles, as well as the nuclear envelope - karyolemma.

There are several types of membranes, which differ in chemical composition, size and function, but have a common plan of structure.

The common feature of all cell membranes is that they are thin (6-10 nm) layers of lipoprotein nature (i.e. lipids in complex with proteins). The main chemical components of cell membranes are lipids (40%), proteins (60%) and carbohydrates (5-10%).

Lipids (Greek lipos - fat) are a group of natural substances insoluble in water, but soluble in non-polar solvents (chloroform, ether, etc.). Lipid molecules are amphiphilic, i.e. each lipid molecule has a hydrophilic (water-soluble) "head" and two hydrophobic (water-insoluble) "tails" (Fig.6,A). The molecules of the "tail" are a long hydrocarbon chain.

Membrane proteins account for 50% of the mass of cell membranes. Their role is that they provide functional activity of membranes, namely:

- 1 - Participate in the transport of substances;
- 2 - Are part of transport pumps and ion channels?
- 3 - Are enzymes and receptors, participating in the conduction of signals into the cell?
- 4 - Link the cytoskeleton to the extracellular matrix;
- 5 - Convert the energy of food substances into the chemical energy of macro energetic bonds of the ATP molecule.

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According to their location in the membrane, proteins are divided into integral and surface (peripheral) proteins.

According to their functions, membrane proteins are divided into:

- 1 - Structural;
- 2 - Transport;
- 3 - Adhesive (providing intercellular interactions);
- 4 - Involved in the transmission of signals from one cell to another;
- 5 - Catalytic.

Molecular biology historically emerged as a branch of biochemistry. By the beginning of the XXI century, data on the primary structure of the entire DNA of humans and a number of other organisms, most important for medicine, agriculture and scientific research, were obtained, which led to the emergence of several new areas in biology: genomics, bioinformatics and others.

Membrane transport is the transport of substances through the cell membrane into or out of the cell by various mechanisms - simple diffusion, facilitated diffusion and active transport. The most important property of the biological membrane is its ability to allow various substances to pass into and out of the cell. Membrane transport (transport of substances through the lipid bilayer): passive and active. Active membrane transport - against the (electro) chemical gradient, i.e. energy expenditure is required (coupling with an energetically favorable process): primary and secondary. Passive membrane transport - along the (electro) chemical gradient, does not require energy expenditure: diffusion or facilitated diffusion. Energy sources for active membrane transport: ATP hydrolysis, light, redox reactions, (electro) chemical gradient.

The energy for primary active transport comes from a source other than the chemical gradient already presents (electro). Channel proteins (protein channels), a type of transport protein, and acts as a pore in the membrane that rapidly allows water molecules or small ions to pass through. Water channel proteins (aquaporin's) allow water to diffuse through the membrane very quickly. Ion channel proteins allow ions to diffuse across the membrane. In most cases, signal transduction within the cell is a chain of sequential biochemical reactions carried out by enzymes, some of which are activated by secondary mediators. Such processes are usually fast: their duration is of the order of milliseconds in the case of ion channels and minutes in the case of activation of protein kinases and lipid-mediated kinases. However, in some cases it may take hours or even 24 hours (in the case of gene expression) from the cell receiving a signal to responding to it. Signal transduction pathways, or signaling pathways, are often organized as signal cascades: the number of protein molecules and other substances involved in signal transduction increases at each successive step as the distance from the initial stimulus increases. Thus, even a relatively weak stimulus can elicit a significant response. This phenomenon is called signal amplification. The original term signal transduction first appeared in refereed journals in 1974, and appeared in the title of the article in 1979.

4. Illustrative material: Overview, video training, presentation

https://www.youtube.com/watch?v=j0sEi_Dscd8&feature=youtu.be Cage

<https://www.youtube.com/watch?v=QSfntmjVtpQ&feature=youtu.be> Transport

<https://www.youtube.com/watch?v=V6YC97Dj5E0&feature=youtu.be>. Contact

5. Literature: see appendix 1

6. Control questions: (feedback)

1. Structure of biomembranes
2. Function of biomembranes
3. Adhesive function of biomembranes
4. Active transport.
5. Passive transport.
6. Structure and function of cell organoids

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7. Structure and functions of the nucleus
8. Structure and functions of the cell membrane
9. Structure and functions of the Golgi apparatus
10. Structure and Functions of Mitochondria
11. Structure and functions of the lysosome

Lecture №2

1. Topic: Molecular biology of the cell. Adhesive function of membranes. External signal transduction in the cell.

2. Purpose: To give an idea of adhesive function of membranes. Transmission of external signal into the cell.

3. Lecture Abstracts: For most regulatory molecules, a complex series of events - specific signal transduction pathways, otherwise known as signal transduction pathways - intervene between their binding to a membrane receptor and the final response of the cell, i.e., a change in its function. Depending on the nature of the ligand, three pathways of signal transduction into the cell are considered. 1. Endocrine regulators (hormones) are secreted by endocrine cells into the blood and transported by it to target cells, which may be located anywhere in the body. 2. Neurocrine regulators are secreted by neurons in close proximity to target cells. 3. Paracrine substances are released somewhat further away from their targets, but still close enough to them to reach receptors. Paracrine substances are secreted by one cell type and act on another, but in some cases the regulators are destined for the cells that secreted them or for neighboring cells of the same type. In some cases, the final step in signal transduction consists of phosphorylation of certain effector proteins, leading to enhancement or inhibition of their activity, which in turn determines the cellular response required by the organism. Protein kinases are responsible for protein phosphorylation, and protein phosphatases are responsible for dephosphorylating. Changes in protein kinase activity occur as a result of binding of a regulatory molecule (generally referred to as a ligand) to its membrane receptor, which triggers a cascade of events.

The activity of various protein kinases is regulated by the receptor not directly, but through secondary messengers (secondary mediators), such as cAMP, cGMP, Ca²⁺, inositol-3-phosphate (IP₃) and diacylglycerol (DAG). Thus ligand binding to a membrane receptor alters the intracellular level of the secondary messenger, which in turn affects protein kinase activity. Many regulatory molecules influence cellular processes through signal transduction pathways involving heterotrimeric GTP-binding proteins (heterotrimeric G-proteins) or monomeric GTP-binding proteins (monomeric G-proteins). When ligand molecules bind to membrane receptors that interact with heterotrimeric G-proteins, there is a transition of the G-protein to an active state by binding to GTP. The activated G protein can then interact with many effector proteins, primarily enzymes such as adenylate cyclase, phosphodiesterase, and phospholipase. This interaction sets off a chain of reactions that culminate in the activation of protein kinases. In general terms, the signal transduction pathway involving G-proteins - protein kinases includes the following steps.

1. ligand binds to the receptor on the cell membrane.

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4. Illustrative material: Overview, presentation

<https://www.youtube.com/watch?v=BmAq-EolVCc&feature=youtu.be> contacts

<https://www.youtube.com/watch?v=G7-hNjwCwaw&feature=youtu.be> signals

<https://www.youtube.com/watch?v=iv-025Dx8LE&feature=youtu.be> adhesion

5. Literature: see appendix 1

6. Control questions: (feedback)

1. Families of adhesive membrane proteins.
2. adhesive function of membranes
3. basic steps of signal transduction.
4. Signals transmitted through signalling molecules
5. Cyclic nucleotides
6. Secondary messengers
7. Cyclic adenosine monophosphate
8. Cyclic guanosine monophosphate

Lecture №3

1. Topic. Molecular structure of cells and diseases arising from their dysfunction.

2. Purpose: Definition of the concept of organoids and their classification. Diseases of lysosomes, peroxisomes, protein sorting disorders in EPS, mitochondrial diseases. Definition and mechanism of development.

3. Lecture theses: Lysosomal Storage Diseases is the common name for a group of very rare inherited diseases caused by dysfunction of intracellular organelles of lysosomes. These single-membrane organoids are part of the endomembrane system of the cell and specialise in the intracellular breakdown of substances: glycogen, glycosaminoglycans, glycoproteins and others. Lysosomal accumulation diseases are caused by genetically determined deficiency of lysosomal enzymes, which

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leads to accumulation of macromolecules, which are the substrate of these enzymes, in various organs and tissues of the body.

The clinical picture of the first hereditary disease from the group of lysosomal accumulation diseases (Tay-Sachs disease) was described in 1881. Then, in 1882, the disease named after the French physician Philippe Gaucher, who first described it, was described. In 1932, Dutch physician John Pompe described glycogenosis type 2, later called Pompe disease after his name. In the late 1950s and early 1960s, Belgian biochemist Christian de Duve et al, using cell fractionation techniques, discovered lysosomes as cell organelles responsible for the breakdown and utilisation of macromolecules. This scientific discovery soon made it possible to identify the pathophysiological basis of lysosomal accumulation diseases. Pompe disease was the first inherited disease identified as a lysosomal accumulation disease. In 1963, the Belgian physiologist and biochemist Henri G. Hers published a paper in which he linked the cause of this symptom complex to α -glucosidase deficiency and suggested that other genetic diseases, including mucopolysaccharidoses, were associated with deficiencies of a particular enzyme. Mitochondrial diseases are caused by genetic, structural, and biochemical defects of mitochondria leading to disorders of tissue respiration.

They are transmitted only through the female line to children of both sexes, as the spermatozoa transfer half of the nuclear genome to the zygote, while the ovum supplies the other half of the genome and mitochondria. Pathological disorders of cellular energy metabolism can manifest themselves as defects in various links in the Krebs cycle, in the respiratory chain, beta-oxidation processes, and so on. Not all enzymes and other regulators necessary for the efficient functioning of mitochondria are encoded by mitochondrial DNA. Most mitochondrial functions are controlled by nuclear DNA. Two groups of mitochondrial diseases can be distinguished:

Pronounced hereditary syndromes caused by mutations of genes responsible for mitochondrial proteins (Barth syndrome, Kearns-Sayre syndrome, Pearson syndrome, MELAS syndrome, MERRF syndrome and others). Secondary mitochondrial diseases, including disorder of cellular energy exchange as an important link in the formation of pathogenesis (connective tissue diseases, chronic fatigue syndrome, glycogenosis, cardiomyopathy, migraine, liver failure, pancytopenia, as well as hypoparathyroidism, diabetes, rickets and others).

Mitochondria are inherited differently from nuclear genes. Nuclear genes in each somatic cell are usually represented by two alleles (with the exception of most sex-linked genes in heterogametic sex). One allele is inherited from the father, the other from the mother. However, mitochondria contain their own DNA, with each human mitochondrion typically containing 5 to 10 copies of a circular DNA molecule (see Heteroplasmy), and all mitochondria are inherited from the mother. When a mitochondrion divides, copies of DNA are randomly distributed among its descendants. If only one of the original DNA molecules contains a mutation, such mutant molecules may accumulate in some mitochondria as a result of the random distribution. Mitochondrial disease begins to manifest itself when an appreciable number of mitochondria in many cells of a given tissue acquire mutant copies of DNA (threshold expression). Mutations in mitochondrial DNA occur, for various reasons, much more frequently than in nuclear DNA. This means that mitochondrial diseases are quite often manifested due to spontaneous newly arising mutations. Sometimes the mutation rate is increased due to mutations in nuclear genes encoding enzymes that control mitochondrial DNA replication.

4. Illustrative material: Overview, video training, presentation

<https://www.youtube.com/watch?v=agLNVS3BM3w&feature=youtu.be> cell

<https://www.youtube.com/watch?v=Xyy3ODuaQjQ&feature=youtu.be> diseases

<https://www.youtube.com/watch?v=LtEiV110bZg&feature=youtu.be> mitochondrial disease

<https://www.youtube.com/watch?v=wwe2bJtRxgQ&feature=youtu.be> lysosomal disease

5. Literature: see appendix 1

6. Control questions: (feedback)

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1. Mitochondrial diseases
2. Lysosomal disease
3. Peroxisome diseases
4. Disorders of protein sorting in the ER
5. Definition and mechanism of disease development

Appendix 1

5. Literature:

English language:

Basic:

1. Jorde L. B., Carey J.C., Bamshad M. J. Medical Genetics, Elsevier, 2015
2. Cooper G. M., Hausman R. E. The Cell: a Molecular Approach. - Sinauer Associates, 2015
3. Genetics [Текст] = Генетика : textbook / D. K. Aydarbaeva [and etc.]. - Almaty : Association of higher educational institutions of Kazakhstan, 2016. - 244 p
4. Alberts B. [et al.]. Molecular Biology of the CELL - 3th ed., 2014
5. Batyrova, K. I. Introduction to biology [Текст] = Введение в биологию : textbook / K. I. Batyrova, D. K. Aydarbaeva. - Almaty : Association of higher educational institutions of Kazakhstan, 2016. - 316 p.

Additional:

1. Schumm, Dorothy E. Core Concepts in clinical Molecular biology [Текст] : монография / Dorothy E. Schumm. - First Edition. - New York : Lippincott - Raven Publishers Philadelphia, 1997. - 74 p.

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1. Lodich, H. Molecular cell [Электронный ресурс]: научное издание / H. Lodich. - Электрон. текстовые дан. (10,4 Мб). - Б. м. : Б. и., 2003
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5. Watson, J. D. Molecular Biology of the gene [Электронный ресурс] : научное издание / J. D. Watson. - Fifth edition. - Электрон. текстовые дан. (30,2 Мб). - Б. м. : Б. и., 2004

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2	Republican interuniversity electronic library	http://rmebrk.kz/
3	Electronic library of the Medical University "Student Advisor"	http://www.studmedlib.ru
4	"Paragraph" information system "Medicine" section	https://online.zakon.kz/Medicine
5	Scientific electronic library	https://elibrary.ru/
6	Electronic library "BuxMed"	http://www.booksmed.com
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8	«Science Direct» (Elsevier)	https://www.sciencedirect.com
9	«Scopus» (Elsevier)	www.scopus.com
10	PubMed	https://www.ncbi.nlm.nih.gov/pubmed