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ULYANOVSK STATE UNIVERSITY
Faculty of Medicine
Department of General and Clinical Morphology

**GUIDELINES FOR INDIVIDUAL WORK OF STUDENTS
FOR THE DISCIPLINE
«NANOTECHNOLOGIES IN MEDICINE»**

Specialty - 31.05.01 «General medicine»
Form of study: intramural

Developers:
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Reviewer: candidate of biological sciences, associate Professor O. A. Mironcheva

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Methodical instructions are prepared in accordance with the working program of the discipline "Nanotechnology in medicine". The structure of guidelines includes guidelines for students on each topic studied according to the plan of classroom work. Methodical instructions are intended for students of the faculty of medicine, trained in specialties 31.05.01- General medicine.

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1. GOALS AND OBJECTIVES OF THE DISCIPLINE

The purpose of the discipline is to form students ' knowledge about the essence of nanotechnology, taking into account the medical orientation of the subjects, with the specifics of NanoBio - and bionanotechnology.

Tasks of discipline development:

- 1.to form students ' knowledge about the main directions of nanotechnology in medicine, the main objects of nanotechnology development;
- 2.to know nanobiotechnological processes and their implementation in various branches of science, medicine and pharmacology;
- 3.to study the classification and properties of nanostructured materials; features of the influence of nanomaterials on living organisms.

2.REQUIREMENTS TO RESULTS OF MASTERING THE DISCIPLINE

The academic discipline "Nanotechnology in medicine" refers to the disciplines of choice of the professional cycle of disciplines.

The discipline "Nanotechnology in medicine" provides the formation of knowledge and ideas about nanomedicine, the purpose of which is to monitor, correct, construct and control human biological systems at the molecular level using the developed nanodevices and nanostructures. The unique properties and biological activity of nanomaterials cause wide opportunities for their use in biology and medicine, in particular, for targeted drug delivery, for the fight against cardiological and oncological diseases, for the purposes of genetic, molecular and tissue engineering, improving the quality of the environment and in many other areas.

The results of mastering the discipline will be necessary for the further learning process in the frame-work of the gradual formation of competencies in the study of the following special disciplines:

- Bioethics
- Physics, Mathematics
- Chemistry
- Biochemistry
- Philosophy
- Immunology
- Nanotechnology in medicine
- Medical rehabilitation
- Dialogue between a doctor and a patient (diseases of the cardiovascular system)
- Hygiene
- Practice on obtaining primary professional skills of a doctor of an inpatient institution
- Faculty therapy
- Diabetology and Emergency endocrinology
- Practice on obtaining primary professional skills and skills of an outpatient clinic doctor
- Current issues of hospital surgery medicine
- Current issues of HIV infection
- Clinical electrocardiography
- Preparation for passing and passing the state exam
- Surgical gastroenterology and endoscopy

- Palliative medicine
- Polyclinic therapy

3.THEMES OF THE INDIVIDUAL WORK

Unit 1. Introduction. Basic concepts of nanotechnology

The purpose of the lesson and its motivational characteristics

To master the methods of scanning probe microscopes, to look at biological objects-nanoparticles, to get acquainted with the scale of the nanoworld.

Questions for control knowledge in the classroom:

- 1.Nanotechnology instruments: electron microscope, scanning probe microscope. Optical tweezers.
- 2.General principles of scanning probe microscopes.
- 3.The main modes of operation of the atomic force microscope: contact, non-contact and semi-contact.
- 4.Biomedical applications of scanning probe microscopy: nanoscopy, nanodiagnostics and nanotechnology.

Type of individual work

Interdisciplinarity of nanotechnology. Prospects of nanotechnology development in Russia.

Form of control: Quiz, Interview

Unit 2. Methods and tools of nanotechnology.

The purpose of the lesson and its motivational characteristics

To study the classification and properties of nanomaterials, paying special attention to nanomaterials used in medicine.

Questions on the topic:

- 1.Classification of nanomaterials based on their shape, chemical composition, method of production.
- 2.Size effect.
- 3.Carbon nanostructures: fullerenes, graphene, single and multi-wall nanotubes, nanofibers.
- 4.Applications of nanomaterials. Nanomaterials in medicine.
- 5.Biological activity of nanomaterials.
- 6.Wound healing activity, regenerating and bactericidal properties of metal nanoparticles (silver, gold, magnesium, copper).

7. Magnetic nanoparticles in biological objects.

Type of individual work

Preparation of nanocrystalline powders and compact materials. Living organisms as bioreactors of nanoparticles.

Form of control: Quiz, Interview

Unit 4. Nanomaterials: classification and properties.

The purpose of the lesson and its motivational characteristics

To study new approaches using nanomaterials and nanotechnology to the treatment of cancer.

Questions on the topic:

1. New approaches of cell and molecular biology to solving problems of Oncology.
2. Immunotherapy, RNA interference, epigenetic regulation of genes.
3. Inhibition of angiogenesis in tumors by gold nanoparticles.
4. Photodynamic therapy of malignant neoplasms.
5. Passive targeting.
6. Functionalization of nanoparticles by tumor-specific antibodies.

Type of individual work

Properties of bulk and nanostructured materials. Nanoporous substances, nanostructured films. Carbon-encapsulated nanomaterials. Metal-polymer nanocomposites. Nanocrystals for biomedical research. Supramolecular complexes of the type "guest-host". Silver and bismuth nanobiocomposites. Water-soluble derivatives of fullerenes.

Form of control: Quiz, Interview

Unit 5. Biochips in biomedical research.

The purpose of the lesson and its motivational characteristics

To study the structure and characteristics of biochips used in biomedical research.

Questions on the topic:

1. Prospects for the use of biological microchips.
2. Oligonucleotide Protein biochips.
3. Determination of nucleotide sequences (sequencing) of DNA.
4. Mapping of genetic information of DNA and RNA, determination of mutations and level of expression of genetic material.
5. Enzyme-based biochips.
6. Cell biosensors: creation, characterization, application.

Type of individual work

The study of the topic begins with the historical background of the development of biochips.

Form of control: Quiz, Interview

Unit 6. Nanotechnology in medicine: a panorama of directions

The purpose of the lesson and its motivational characteristics

To study the basic technologies of obtaining and transferring genes; to know the concepts of "gene therapy" and "gene targeting". To study the main methods of obtaining, properties and prospects of application of nanoconstructions based on DNA.

Questions on the topic:

1. Obtaining genes for transplantation.
2. Technologies of gene transfer into the cell.
3. Achievements and prospects of genetic engineering.
4. Gene therapy and gene targeting.
5. DNA is a universal component for creating nanostructured devices. Branched DNA. "Sticky ends."
6. Prospects of creation and application of nanoconstructions based on double-stranded DNA molecules.
7. Two-dimensional nanoscale DNA lattices are the basis for the creation of new types of catalysts, molecular sieves, biochips.

Type of individual work

Regenerative medicine

At the beginning of the study of the topic with the active participation of students, the definition of "genetic engineering" is discussed as "the construction in vitro of functionally active genetic structures (recombinant DNA), i.e. the creation of artificial genetic programs" (Baev A. A.). According To E. S. Piruzyan, genetic engineering is a system of experimental techniques that allow to construct artificial genetic structures in the form of so-called recombinant or hybrid DNA molecules by laboratory means (in vitro). As a result of studying this topic, the student should have an idea about the directed, according to a predetermined program, construction of molecular genetic systems outside the body, followed by their introduction into a living organism. In this case, recombinant DNA becomes an integral part of the genetic apparatus of the recipient organism and gives it new unique genetic, biochemical, and therefore physiological properties. Students should know that the purpose of applied genetic engineering is to design such recombinant DNA molecules, which, when introduced into the genetic apparatus, would give the body properties useful for the human body. Further, the methods of recombinant DNA technology are briefly considered: specific DNA cleavage by limiting nucleases, accelerating the isolation and manipulation of individual genes; rapid sequencing of all nucleotides in the purified DNA fragment, which allows to determine the boundaries of the gene and the amino acid sequence encoded by it; construction of recombinant DNA; hybridization of nucleic acids, allowing to identify specific sequences of RNA or DNA with greater accuracy and sensitivity, based on their ability to bind complementary sequences of nucleic acids; DNA cloning: amplification in vitro by chain polymerase reaction or the introduction of a DNA fragment in a

bacterial cell, which after such transformation reproduces this fragment in millions of copies; cells or organisms. This knowledge is necessary to understand further material devoted to the study of gene therapy.

The study of the topic "Nanotechnology based on nucleic acids" begins with a discussion of the structure of DNA. The basic principles of the structure of the DNA double helix are recalled and analyzed. The student should be fluent in this information, because this knowledge is the basis for understanding and studying the formation of spatial DNA nanoconstructions with adjustable parameters. The questions of self-Assembly of DNA bispiral, principles of replication, transcription, processing, translation as examples of molecular nanomachines are discussed in detail. Special attention is paid to the methods of creating nanoconstructions based on double-stranded nucleic acids, which allow to control the structure of the obtained materials with molecular precision: "step by step" design, "all at once" design. The student must understand the essence of creating nanoconstructions. Within the framework of the topic, the possibilities of practical application of nanoconstructions in combining the properties of nucleic acids and antibiotics are considered. Nanoconstructions, the concentration of DNA in which exceeds 200 mg / ml, can be used as carriers of genetic material or biologically active compounds introduced into their composition. Nanostructures based on nucleic acids can serve as sensitive elements of optical sensor devices that react to the presence of biologically active compounds. To do this, a compound is embedded in the nanomastic, which is destroyed upon contact with the analyzed substance. Nanomastic and all nanoconstructs collapse, falls anomalous optical activity. It is possible to introduce nanostructures with controlled physical and chemical properties into the polymer film without disturbing their anomalous optical properties. This opens the possibility for the use of such polymer matrices in Photonics as optical filters with adjustable optical parameters.

Form of control: Quiz, Interview

Unit 7. Directed transport of medicines.

The purpose of the lesson and its motivational characteristics

Study of Structure of phosphatidylcholine. Physicochemical and dynamic properties of lipids. Lipid phase transitions. Self-assembling lipid nanotubes as a tool for delivering nucleic acids to cells. Using bacteria for intracellular drug delivery

Questions on the topic:

1. Liposomes. The principles of organization of the lipid bilayer.
2. Formation of micelles. Reverse micelles.
3. The advantages and prospects of application of liposomal forms of drugs.
4. Capsules on the basis of polymeric materials.
5. Dendrimers. Structure and dimensions of macromolecules of dendrimers.
6. Properties and application of dendrimers in biology and medicine: directed drug transport, molecular sieves, contrast agents.
7. Preparation of dendrimers with adjustable internal cavity for catalytic reactions.

Type of individual work

Structure of phosphatidylcholine. Physicochemical and dynamic properties of lipids. Lipid phase transitions. Self-assembling lipid nanotubes as a tool for delivering nucleic acids to cells. Using bacteria for intracellular drug delivery.

Form of control: Quiz, Interview

Unit 8. Nanotechnology in the diagnosis and treatment of cancer.

The purpose of the lesson and its motivational characteristics

Study of Nanoparticles with a dielectric core surrounded by an ultrathin metal shell.

"Optical transparency window" of biological tissues. Mechanism of action of General and local hyperthermia.

Questions on the topic:

1. New approaches of cell and molecular biology to the solution of ontology problems.
2. Immunotherapy, RNA interference, epigenetic regulation of genes.
3. Inhibition of angiogenesis in tumors by gold nanoparticles.
4. Photothermal therapy of malignant neoplasms.
5. Passive targeting.
6. Functionalization of nanoparticles by tumor-specific antibodies.

Type of individual work

Nanoparticles with a dielectric core surrounded by an ultrathin metal shell. "Optical transparency window" of biological tissues. Mechanism of action of General and local hyperthermia.

Form of control: Quiz, Interview

Unit 9. Biochips in biomedical research.

The purpose of the lesson and its motivational characteristics

Study of Hybridization of nucleic acids.

The amplification of the DNA. Polymerase chain reaction: new possibilities.

Properties of immobilized cells

Questions on the topic:

1. Prospects for the use of biological microchips.
2. Oligonucleotide Protein biochips.
3. Determination of nucleotide sequences (sequencing) of DNA.
4. Mapping of genetic information of DNA and RNA, determination of mutations and level of expression of genetic material.
5. Enzyme-based biochips.
6. Cell biosensors: creation, characterization, application.

Type of individual work

Hybridization of nucleic acids. The amplification of the DNA. Polymerase chain reaction: new possibilities. Properties of immobilized cells

Form of control: Quiz, Interview

Unit 10. Nano-technology in the field of Transplantology and implantology.

The purpose of the lesson and its motivational characteristics

Study of Methods of creation and application of artificial nanofibers in biology and medicine.

The use of nanotechnology to improve the biocompatibility of transplants.

Nanostructured titanium in dental implantology. Ultra-fine-grained biocomposites. Nanomaterials that mimic natural bone tissue..Preparation and use of hydroxyapatite for medical purposes. Nanodisperse preparations of calcium.

Questions on the topic:

1. Obtaining genes for transplantation.
2. Technologies of gene transfer in a cell.
3. Achievements and prospects of genetic engineering.
4. Gene therapy and gene targeting.

Type of individual work

Methods of creation and application of artificial nanofibers in biology and medicine. The use of nanotechnology to improve the biocompatibility of transplants. Nanostructured titanium in dental implantology. Ultra-fine-grained biocomposites. Nanomaterials that mimic natural bone tissue. Preparation and use of hydroxyapatite for medical purposes. Nanodisperse preparations of calcium

Form of control: Quiz, Interview

Unit 11. Nanotechnology in gene, cell and tissue engineering

The purpose of the lesson and its motivational characteristics

Study of Technology of recombinant DNA production.

Questions on the topic:

1. DNA is a universal component for creating nanostructured devices.
2. Branched DNA. "Sticky ends."
3. Prospects of creation and application of nanoconstructions based on double-stranded DNA molecules.
4. Two-dimensional nanoscale DNA lattices are the basis for the creation of new types of catalysts, molecular sieves, biochips.

Type of individual work

Technology of recombinant DNA production.

Form of control: Quiz, Interview

Unit 12. Nanotechnologies based on nucleic acids

The purpose of the lesson and its motivational characteristics

Study of Design strategy: "step by step" (N. Seaman), "all at once" (Y. M. Yevdokimov).

Questions on the topic:

1. Methodological approaches to assessing the safety of nanomaterials.
2. The main components of the nanomaterials risk assessment system.
3. The problem of determining the "dose "and" dose-effect " dependence for nanoparticles.
4. The main ways of nanoparticles entering the human body.
5. Distribution and accumulation of nanoparticles in various organs and tissues.
6. Influence of carbon nanomaterials on respiratory organs.
7. Neuro -, cardio-and hepatotoxicity of nanomaterials

Type of individual work

Design strategy: "step by step" (N. Seaman), "all at once" (Y. M. Yevdokimov).

Form of control: Quiz, Interview

Unit 13. Risk assessment of nanomaterials

The purpose of the lesson and its motivational characteristics

Study of Dependence of the degree of toxicity on the extent of nanostructures. Physico-chemical basis of the biological action of nano-objects. Penetration of nanoparticles through the blood-brain barrier. Effect of fullerenes, single-and multi-layer carbon nanotubes on the blood coagulation system. The use of nanotechnology methods in the field of ecology and energy. Nanomaterials and wastewater treatment. Composite nanofilters

Questions on the topic:

1. Methodological approaches to assessing the safety of nanomaterials.
2. The main components of the nanomaterials risk assessment system.
3. The problem of determining the "dose "and" dose-effect " dependence for nanoparticles.
4. The main ways of nanoparticles entering the human body.
5. Distribution and accumulation of nanoparticles in various organs and tissues.
6. Influence of carbon nanomaterials on respiratory organs.
7. Neuro -, cardio-and hepatotoxicity of nanomaterials

Type of individual work

Dependence of the degree of toxicity on the extent of nanostructures. Physico-chemical basis of the biological action of nano-objects. Penetration of nanoparticles through the blood-brain barrier. Effect of fullerenes, single-and multi-layer carbon nanotubes on the blood coagulation

system. The use of nanotechnology methods in the field of ecology and energy. Nanomaterials and wastewater treatment. Composite nanofilters

Form of control: Quiz, Interview

4. CONTROL QUESTIONS ON DISCIPLINE

(QUESTIONS FOR A CREDIT)

1. Definition of concepts "nanotechnology", "nanobiotechnology", "nanomedicine".
2. Application of technical methods in biological nanosystems and use of biological strategies in technical nanosystems.
3. Interdisciplinarity of nanotechnology.
4. Prospects of nanotechnology development in Russia.
5. The main approaches to the creation of nanoobjects.
6. Nanotechnology instruments: electron microscope, scanning probe microscope, optical tweezers.
7. Methods of obtaining nanostructures.
8. Methods of nanoparticle stabilization: matrix isolation, nanoparticle surface functionalization, localization of nanoparticles on the surface of carriers of different nature.
9. Living organisms as bioreactors of nanoparticles.
10. Classification of nanomaterials based on their shape, chemical composition, method of production.
11. Properties of bulk and nanostructured materials. Dimensional effects.
12. Carbon nanostructures: fullerenes, graphene, single- and multi-wall nanotubes, nanofibers.
13. Nanoporous substances, nanostructured films.
14. Applications of nanomaterials. Nanomaterials in medicine.
15. Wound healing activity, regenerating and bactericidal properties of metal nanoparticles (silver, gold, magnesium, copper).
16. Magnetic nanoparticles in biological objects.
17. Definition of concepts "self-Assembly", "self-organization".
18. Using the principles of self-organization in nanotechnology.
19. The work "molecular motors": ATP synthetase, actinomyosin-St complex, and kinesin.
20. Nanotechnology in medicine today. Drug nanopreparations in Oncology, neurology, immunology.
21. Regenerative medicine.
22. Liposomes. The advantages and prospects of application of liposomal forms of drugs.

23. The principles of organization of the lipid bilayer. Structure of phosphatidyl choline.
24. Formation of micelles. Reverse micelles.
25. Physico-chemical and dynamic properties of lipids. Phase transitions of lipids.
26. Dendrimers. Structure and size of macromolecules of dendrimers.
27. Properties and application of dendrimers in biology and medicine: directed drug transport, molecular sieves, contrast agents.
28. Self-assembling lipid nanotubes as a tool for getting nucleic acids into cells.
29. Using bacteria for intracellular drug delivery.
30. Photothermal therapy of malignant neoplasms.
31. Nanoparticles with a dielectric core surrounded by an ultrathin metal shell.
32. Passive targeting.
33. Functionalization of nanoparticles with tumor-specific antibodies.
34. Mechanism of action of General and local hyperthermia.
35. Prospects for the use of biological microchips.
36. Oligonucleotide Protein and protein biochips.
37. Determination of nucleotide sequences (sequencing) of DNA.
38. Hybridization of nucleic acids.
39. The amplification of the DNA. Polymerase chain reaction: new possibilities.
40. Enzyme-based biochips.
41. Cell biosensors: creation, characterization, application. Properties of immobilized cells.
42. Technology of recombinant DNA production.
43. Achievements and prospects of genetic engineering.
44. Gene therapy and gene targeting.
45. Methods of creation and application of artificial nanofibers in biology and medicine.
46. The use of nanotechnology to improve the biocompatibility of transplants.
47. Nanomaterials that mimic natural bone tissue.
48. DNA is a universal component for creating nanostructured devices. Branched DNA. "Sticky ends."
49. Design strategy: "step by step" (N. Seaman), "all at once" (Y. M. Yevdokimov).
50. Prospects of creation and application of nanoconstructions based on double-stranded DNA molecules.
51. Medical nanorobots R. Fritsa: respirocyte, clothecity, microporosity.
52. Problems of designing nanorobots.

53. Methodological approaches to assessing the safety of nanomaterials.
54. The problem of determining the "dose" and the "dose-effect" relationship for nanoparticles.
55. Influence of carbon nanomaterials on respiratory organs.
56. Dependence of the degree of toxicity on the extent of nanostructures.
57. Neuro-, cardio- and hepatotoxicity of nanomaterials.
58. Effect of fullerenes, single- and multi-layer carbon nanotubes on the blood coagulation system.
59. Physico-chemical bases of biological action of nanoobjects.
60. The main ways of nanoparticles entering the human body.
61. Distribution and accumulation of nanoparticles in various organs and tissues.
62. Penetration of nanoparticles through the blood-brain barrier.
63. The main components of the nanomaterials risk assessment system.
64. Application of nanotechnology methods in the field of ecology and energy.
65. Nanomaterials and wastewater treatment. Composite nano-filters.

5. THE LIST OF RECOMMENDED LITERATURE

Core reading

1. Remizov, A. N. Medical and biological physics : textbook / A. N. Remizov. - Moscow : GEOTAR-Media, 2022. - 576 с. - ISBN 978-5-9704-7102-9. - Текст : электронный // ЭБС "Консультант студента" : [сайт]. - URL : <https://www.studentlibrary.ru/book/ISBN9785970471029.html>
2. Medical informatics for medical school students in EnglishL: lecture course / compiled by S. V. Ponomarev, N. M. Pirova. — Ижевск : ИГМА, 2020. — 56 с. — Текст : электронный // Лань : электронно-библиотечная система. — URL: <https://e.lanbook.com/book/245366>

Supplementary reading

1. Medical informatics = Информатика в медицине : пособие для студентов учреждений высшего образования, обучающихся по специальности 1-79 01 01 «Лечебное дело» [на англ. яз.] : manual for students of higher education institutions studying in the specialty 1-79 01 01 "General Medicine" / С. И. Клинецвич, Е. П. Наумюк, В. М. Завадская и др. - Гродно : ГрГМУ, 2020. - 108 с. - ISBN 9789855952979. - Текст : электронный // ЭБС "Букар" : [сайт]. - URL : <https://www.books-up.ru/ru/book/medical-informatics-13570186/>
2. Guidelines for students to practical lessons for the discipline "Modern medical information systems" Specialty - 31.05.01 «General medicine» Form of study: intramural / J. F. Zerkalova, M. V. Vorotnikova; Ulyanovsk State University, Faculty of Medicine. - Ulyanovsk : UISU, 2019. - Загл. с экрана; На англ. яз.; Неопубликованный ресурс. - Электрон. текстовые дан. (1 файл : 369 Кб). - Текст : электронный. <http://lib.ulsu.ru/MegaPro/Download/MObject/5609>