

**Federal State Autonomous Educational Institution of Higher Education "Moscow
Institute of Physics and Technology
(National Research University)"**

APPROVED

**Head of the Phystech School of
Biological and Medical Physics**

D.V. Kuzmin

Work program of the course (training module)

course: Tissue Engineering/Тканевая инженерия
major: Biotechnology
specialization: Medical Biotechnology/Медицинская биотехнология
Phystech School of Biological and Medical Physics
Chair of Physics of Living Systems
term: 1
qualification: Master

Semester, form of interim assessment: 2 (spring) - Grading test

Academic hours: 15 AH in total, including:

lectures: 15 AH.

seminars: 0 AH.

laboratory practical: 0 AH.

Independent work: 30 AH.

In total: 45 AH, credits in total: 1

Authors of the program:

K.I. Agladze, candidate of physics and mathematical sciences

V.A. Tsvelaya, candidate of biological sciences

S.R. Frolova

The program was discussed at the Chair of Physics of Living Systems 04.06.2020

Annotation

The aim of this discipline is to acquire theoretical and practical knowledge in the field of bioengineering and tissue engineering. As a result of the course, the student will master the basic problems of regenerative medicine, learn about attempts and prospects for solving these problems. The student will get acquainted with cell therapy, assess its effectiveness, learn how to combine genetic engineering methods to design testing systems and artificial organs. After mastering the course, the student will know the concepts of embryogenesis and master the basic principles of working with cell cultures and, in particular, with stem cells, will understand the fundamental concepts and methods of tissue engineering, the structure and functions of the main molecules of a living cell and whole organs, modern problems of molecular medicine, solved using modern methods of bioengineering and tissue engineering.

1. Study objective

Purpose of the course

Mastering by students of fundamental knowledge in the field of biology, biochemistry, human biophysics for the application of this knowledge in the field of regenerative medicine. Study of methods and methods for studying the processes of biophysics and medical physics, as well as engineering methods used for solutions and research in these areas. Gaining knowledge about the practical application of tissue engineering to maintain health and prolong human life.

Tasks of the course

- To form ideas about the principles and possibilities of tissue engineering from the point of view of physiology and cellular technologies.
- To form ideas about tissue engineering as an effective tool for regenerative medicine.
- To provide knowledge about the possibility of using cell technologies in regenerative medicine.
- Getting an idea of the direction of development of the regenerative medicine of the future.
- To give knowledge of the basic methods of cell technology and tissue engineering of organs.

2. List of the planned results of the course (training module), correlated with the planned results of the mastering the educational program

Mastering the discipline is aimed at the formation of the following competencies:

Code and the name of the competence	Competency indicators
UC-1 Use a systematic approach to critically analyze a problem and develop an action plan	UC-1.1 Systematically analyze the problem situation, identify its components and the relations between them
	UC-1.2 Search for solutions by using available sources
	UC-1.3 Develop a step-by-step strategy for achieving a goal, foresee the result of each step, evaluate the overall impact on the planned activity and its participants
Gen.Pro.C-2 Acquire an understanding of current scientific and technological challenges in professional settings, and scientifically formulate professional objectives	Gen.Pro.C-2.1 Assess the current state of mathematical research within professional settings
	Gen.Pro.C-2.2 Assess the relevance and practical importance of research in professional settings
	Gen.Pro.C-2.3 Understand professional terminology used in modern scientific and technical literature and present scientific results in oral and written form within professional communication

3. List of the planned results of the course (training module)

As a result of studying the course the student should:

know:

Fundamentals of cell technologies and their place in regenerative medicine.

Principles and capabilities of tissue engineering from the point of view of physiology and cellular technologies.

Basic concepts of tissue engineering as an effective tool for regenerative medicine.

be able to:

Apply and select, in accordance with the task, the main methods of cell technologies and tissue engineering of organs.

master:

Knowledge of the possibility of using cell technologies in regenerative medicine.
The main methods of cell technology and tissue engineering of organs.

4. Content of the course (training module), structured by topics (sections), indicating the number of allocated academic hours and types of training sessions

4.1. The sections of the course (training module) and the complexity of the types of training sessions

№	Topic (section) of the course	Types of training sessions, including independent work			
		Lectures	Seminars	Laboratory practical	Independent work
1	Introduction: tissue engineering and regenerative medicine.	1			2
2	Cell culture. The main methods of working with them, the specifics of working with cells of different types.	1			2
3	Methods for working with primary cell cultures: working with laboratory animals, methods for isolating cardiomyocytes and hepatocytes	1			2
4	Cell lines.	1			2
5	Using stem cells, methods of directed differentiation.	1			2
6	The concept of cellular reprogramming, induced pluripotent stem cells (iPSCs). Direct reprogramming.	1			2
7	Methods for the structural organization of cell cultures: hydrogels, electrospinning, three-dimensional printing.	1			2
8	Tissue engineering of the heart, the main features of working with cardiomyocytes	1			2
9	Electrophysiological methods and optical mapping.	1			2
10	The main directions of development of tissue engineering of the heart	1			2
11	Tissue engineering of the liver.	1			2
12	Cellular technologies in bone tissue regeneration.	1			2
13	Tissue Engineering of Nerve Tissue	1			2
14	Retinal regeneration	1			2
15	Combination of tissue engineering methods with methods of genetic modification of cells and tissues.	1			2
AH in total		15			30
Exam preparation		0 AH.			
Total complexity		45 AH., credits in total 1			

4.2. Content of the course (training module), structured by topics (sections)

Semester: 2 (Spring)

1. Introduction: tissue engineering and regenerative medicine.

Introduction: the main events in the history of the study of the cell: the invention and development of microscopic technology, the discovery of the cell and the main cellular components. Subject of the study of modern cell biology; basic methods of cytological analysis (light and electron microscopy, fluorescence microscopy, immunocytochemistry, autoradiography, cytochemistry, molecular hybridization, cell culture, cell hybridization); connection of cell biology with other branches of biology.

2. Cell culture. The main methods of working with them, the specifics of working with cells of different types.

Universal cell features. Cell theory. The main postulates of modern cell theory: a single plan of the structure of cells, the law of cell reproduction, totipotency of cells of multicellular organisms; the concept of cell differentiation; the concept of a cell as a single integrated system of components, a cell as a unit of structure, functioning, development and pathology of organisms. The main components of the cell: nucleus, hyaloplasm, ribosomes, cytoskeleton; vacuolar system (EPR, AH, lysosomes, endosomes), mitochondria, plastids, plasma membrane.

Cell culture methods, cell specification, peculiarities of working with different types of cells

3. Methods for working with primary cell cultures: working with laboratory animals, methods for isolating cardiomyocytes and hepatocytes

Working with laboratory animals, rules for conducting operations, primary cultures, cultivation methods, methods for isolating cell cultures, features of protocols for isolating various types of cells

4. Cell lines.

Types of cell lines. Immortalization of cell lines and their characterization. Properties of immortalized cultures. Induced and embryonic pluripotent stem cells. Line cultivation methods. Methods for obtaining lines.

5. Using stem cells, methods of directed differentiation.

Embryogenesis. Stem cell concept. The concept of pluripotency. Hematopoietic cells. Embryonic stem cells. Their allocation. Features and rules for their use. The use of stem cells in tissue engineering, regenerative medicine, pharmaceuticals.

6. The concept of cellular reprogramming, induced pluripotent stem cells (iPSCs). Direct reprogramming.

Induced pluripotent stem cells. Their difference from embryonic. Cellular reprogramming. The concept of reprogramming and genetic modifications of cells. Chimeras. Direct reprogramming. Features of differentiation of IPSC. Open questions about the use of IPSC.

7. Methods for the structural organization of cell cultures: hydrogels, electrospinning, three-dimensional printing.

Formation of substrates. Biomaterials in Tissue Engineering. Methods for the structural organization of cell cultures: hydrogels, electrospinning, three-dimensional printing. Bioprinting. Features of the methods and limitations of applicability.

8. Tissue engineering of the heart, the main features of working with cardiomyocytes

The heart as an organ. Heart from the point of view of electrophysiology. Heart tissue. Cardiac tissue culture. Cultivation of cardiomyocytes. Construction of heart tissue with materials. 2 D and 3D models of the heart. Action potential. A wave of excitement. Arrhythmias. Features of conducting excitation waves in cell culture. Heart failure. Myocardial infarction and its consequences.

9. Electrophysiological methods and optical mapping.

Currents and action potential of cardiomyocytes. Electrophysiological methods for the study of a single cardiomyocyte. Patch Clamp as Voltage clamp and current clamp. Method configurations. Electromechanical syncytium. Visualization of excitation waves. 2D and 3D optical mapping methods.

10. The main directions of development of tissue engineering of the heart

The main directions of development of tissue engineering of the heart. Simulation of cardiac tissue and conduction of excitation waves. Artificial heart. Test systems for drugs. Cell therapy.

11. Tissue engineering of the liver.

The liver as an organ. Liver function. Features of the structure of the liver. Artificial liver. Failure treatment methods now. Tissue Engineering as a Treatment Method.

12. Cellular technologies in bone tissue regeneration.

Bone marrow. Mesenchymal stem cells. Self-regeneration of tissues. Bone tissue regeneration. Immunity. Types of bones. Cellular technologies for trauma treatment.

13. Tissue Engineering of Nerve Tissue

Нейроны. Виды нейронов. Синапсы. Проведение возбуждения по нейрональным сетям. Регенерация нервных клеток. Тканевая инженерия для регенерации нервной ткани.

14. Retinal regeneration

Features of the structure of the eye. The first attempts at cell therapy. Artificially grown cornea and retina. Retinal regeneration. Application of tissue engineering for the treatment of eye diseases.

15. Combination of tissue engineering methods with methods of genetic modification of cells and tissues.

Genetic and genomic engineering methods. Combination of tissue engineering and genetic engineering techniques. Application problems. Channel rhodopsin. Crispr-Cas9 method. Data processing. CAGE analysis.

5. Description of the material and technical facilities that are necessary for the implementation of the educational process of the course (training module)

Necessary equipment for lectures: classroom equipped with a computer and multimedia equipment (projector, sound system)

Additional equipment for demonstrations:

Biosafety class II laminar flow cabinets, incubators, refrigeration equipment, low and high speed centrifuges

6. List of the main and additional literature, that is necessary for the course (training module) mastering

Main literature

Alberts B. et al. Molecular biology of the cell Garland //New York. – 2002. – T. 2.
Stem Cells - from Hype to Real Hope. K. H. Haider, S. M. Aziz. De Gruyter, 2018.
Ionic channels of excitable membranes.: By Bertil Hille. Sunderland, Massachusetts: Sinauer.(1991).
607 pp. – 1992.

Additional literature

Drubin DA, Way JC, Silver PA. Designing biological systems. Genes Dev. 2007 21:242-54.

7. List of web resources that are necessary for the course (training module) mastering

<https://www.isscr.org/>
<https://www.escardio.org/>
<https://www.nia.nih.gov/health/alzheimers-disease-fact-sheet>
<https://nyscf.org/>
<http://www.ncbi.nlm.nih.gov>
<http://bioscience.jbpub.com/cells/>

8. List of information technologies used for implementation of the educational process, including a list of software and information reference systems (if necessary)

For some of the lessons, you will need Zoom. Google Drive to access course materials. The presence of smartphones / laptops during classes is encouraged to participate in interactive exercises.

9. Guidelines for students to master the course

A student who has attended the course must, on the one hand, master the theoretical apparatus of bioengineering, and on the other hand, must learn to apply the knowledge gained in practice. Successful mastering of the course requires independent student work. In the program of the course, the minimum time is allocated for the student's independent work on the topic.

Independent work includes:

- study of educational material (based on lecture notes, educational and scientific literature),
- reading and taking notes of additional literature,
- preparation of answers to questions intended for self-study,
- solving problems offered to students at lectures,
- preparation for differential credit.

The management and control of the student's independent work is carried out in the form of individual consultations. An indicator of mastery of the material is the ability to solve problems. To form the ability to apply theoretical knowledge in practice, the student needs to solve as many problems as possible. When solving problems, each action must be argued, referring to the previously discussed theoretical apparatus.

Usually they adhere to the following scheme: study of the material of the lecture by synopsis on the same day when the lecture was listened to (10-15 minutes); repetition of the material on the eve of the next lecture (10-15 minutes), study of educational material based on lecture notes, educational and scientific literature, preparation of answers to questions, problem solving (1 hour).

It is important to achieve an understanding of the studied material, and not its mechanical memorization. If you find it difficult to study individual topics, questions, you should seek advice from the lecturer.

Assessment funds for course (training module)

major: Biotechnology
specialization: Medical Biotechnology/Медицинская биотехнология
Phystech School of Biological and Medical Physics
Chair of Physics of Living Systems
term: 1
qualification: Master

Semester, form of interim assessment: 2 (spring) - Grading test

Authors:

K.I. Agladze, candidate of physics and mathematical sciences
V.A. Tsvelaya, candidate of biological sciences
S.R. Frolova

1. Competencies formed during the process of studying the course

Code and the name of the competence	Competency indicators
UC-1 Use a systematic approach to critically analyze a problem and develop an action plan	UC-1.1 Systematically analyze the problem situation, identify its components and the relations between them
	UC-1.2 Search for solutions by using available sources
	UC-1.3 Develop a step-by-step strategy for achieving a goal, foresee the result of each step, evaluate the overall impact on the planned activity and its participants
Gen.Pro.C-2 Acquire an understanding of current scientific and technological challenges in professional settings, and scientifically formulate professional objectives	Gen.Pro.C-2.1 Assess the current state of mathematical research within professional settings
	Gen.Pro.C-2.2 Assess the relevance and practical importance of research in professional settings
	Gen.Pro.C-2.3 Understand professional terminology used in modern scientific and technical literature and present scientific results in oral and written form within professional communication

2. Competency assessment indicators

As a result of studying the course the student should:

know:

Fundamentals of cell technologies and their place in regenerative medicine.

Principles and capabilities of tissue engineering from the point of view of physiology and cellular technologies.

Basic concepts of tissue engineering as an effective tool for regenerative medicine.

be able to:

Apply and select, in accordance with the task, the main methods of cell technologies and tissue engineering of organs.

master:

Knowledge of the possibility of using cell technologies in regenerative medicine.

The main methods of cell technology and tissue engineering of organs.

3. List of typical control tasks used to evaluate knowledge and skills

During the current control, the student must be able to answer the questions of the current material:

- 1) Tissue Engineering and Regenerative Medicine. Scope of tissue engineering, the main methods on which it is based. Biomedical Engineering Concept.
- 2) Cell culture. The main methods of working with them, the specifics of working with cells of different types.
- 3) Methods of working with primary cell cultures: working with laboratory animals, methods of isolating cardiomyocytes and hepatocytes.
- 4) Cell lines.
- 5) The use of stem cells, methods of directed differentiation.
- 6) The concept of cellular reprogramming, induced pluripotent stem cells (iPSCs). Direct reprogramming.
- 7) Methods of structural organization of cell cultures: hydrogels, electrospinning, three-dimensional printing.
- 8) Tissue engineering of the heart, the main features of working with cardiomyocytes.
- 9) Electrophysiological methods and optical mapping.
- 10) The main directions of development of tissue engineering of the heart.
- 11) Tissue engineering of the liver.
- 12). Cellular technologies in bone tissue regeneration.
- 13) Tissue engineering of nervous tissue
- 14). Retinal regeneration

15) Combination of tissue engineering methods with methods of genetic modification of cells and tissues.

During the class, interactive discussions can take place in the course chats, where additional materials, articles for analysis and homework will be published. Successful completion of all tasks in the course and the completion of control slices of knowledge gives an advantage on differential credit.

4. Evaluation criteria

Certification for the course is carried out by differential credit. The test consists of an answer to one of the typical tickets presented below:

Ticket 1.

- 1) Explain the features of working with a primary culture and with a cell line.
- 2) Explain the differences between totipotent, pluripotent and multipotent stem cells.

Ticket 2.

- 1) What is cellular reprogramming and its main methods.
- 2) What are the main physiological functions of cardiomyocytes?

Ticket 3

- 1) What are the main methods for studying the electrical activity of cells?
- 2) What methods can be used to provide the necessary architecture of cultured tissue in 2D and 3D?

Ticket 4

- 1) What are the main physiological functions of hepatocytes?
- 2) What are the main areas of application of tissue-engineered cardiac flaps?

Ticket 5

- 1) What objects in which cellular reprogramming of the nervous tissue is used do you know?
- 2) What ethical principles and regulations do you know when working with animals and human cells?

The teacher also has the right to ask a number of additional questions from the topics of the passed material:

- 1) Tissue Engineering and Regenerative Medicine. Scope of tissue engineering, the main methods on which it is based. Biomedical Engineering Concept.
- 2) Cell culture. The main methods of working with them, the specifics of working with cells of different types.
- 3) Methods of working with primary cell cultures: working with laboratory animals, methods of isolating cardiomyocytes and hepatocytes.
- 4) Cell lines.
- 5) The use of stem cells, methods of directed differentiation.
- 6) The concept of cellular reprogramming, induced pluripotent stem cells (iPSCs). Direct reprogramming.
- 7) Methods of structural organization of cell cultures: hydrogels, electrospinning, three-dimensional printing.
- 8) Tissue engineering of the heart, the main features of working with cardiomyocytes.
- 9) Electrophysiological methods and optical mapping.
- 10) The main directions of development of tissue engineering of the heart.
- 11) Tissue engineering of the liver.
- 12). Cellular technologies in bone tissue regeneration.
- 13) Tissue engineering of nervous tissue
- 14). Retinal regeneration
- 15) Combination of tissue engineering methods with methods of genetic modification of cells and tissues.

The mark is excellent (10 points) - given to a student who has shown comprehensive, systematized, deep knowledge of the curriculum of the discipline, who is interested in this subject area, who has demonstrated the ability to confidently and creatively apply them in practice when solving specific problems, free and correct justification of the decisions made.

The mark is excellent (9 points) - given to a student who has shown comprehensive, systematized, in-depth knowledge of the curriculum of the discipline and the ability to confidently apply them in practice when solving specific problems, free and correct justification of decisions made.

The mark is excellent (8 points) - given to a student who has shown comprehensive, systematized, deep knowledge of the curriculum of the discipline and the ability to confidently apply them in practice when solving specific problems, the correct justification of the decisions made, with some drawbacks.

The mark is good (7 points) - given to a student if he firmly knows the material, expresses it competently and in essence, knows how to apply the knowledge gained in practice, but does not correctly justify the results obtained.

The mark is good (6 points) - given to the student if he firmly knows the material, expresses it competently and in essence, knows how to apply the knowledge gained in practice, but makes some inaccuracies in the answer or in solving problems.

A good grade (5 points) is given to a student if he basically knows the material, expresses it competently and in essence, knows how to apply the knowledge gained in practice, but admits a fairly large number of inaccuracies in the answer or in solving problems.

The mark is satisfactory (4 points) - given to a student who has shown a fragmentary, scattered nature of knowledge, insufficiently correct formulations of basic concepts, violation of the logical sequence in the presentation of the program material, but at the same time he has mastered the main sections of the curriculum necessary for further education, and can apply the obtained knowledge modeled on a standard situation.

The mark is satisfactory (3 points) - given to a student who has shown a fragmentary, scattered nature of knowledge, makes mistakes in the formulation of basic concepts, disruptions in the logical sequence in the presentation of program material, has little command of the main sections of the curriculum necessary for further education and has difficulty applying the obtained knowledge even in a standard situation.

The mark is unsatisfactory (2 points) - given to a student who does not know most of the main content of the curriculum of the discipline, makes gross errors in the formulation of basic principles and does not know how to use the knowledge gained in solving typical problems.

The mark is unsatisfactory (1 point) - given to a student who does not know the main content of the curriculum of the discipline, makes gross errors in the formulation of the basic concepts of the discipline, and generally does not have the skills to solve typical practical problems.

5. Methodological materials defining the procedures for the assessment of knowledge, skills, abilities and/or experience

When conducting an oral differential test, the student is given 30 minutes to prepare. The survey of a student with a ticket should not exceed one astronomical hour.