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

APPROVED
Head of Landau Phystech-School of Physics & Research
A.V. Rogachev

Work program of the course (training module)

course:	Basics of Molecular Gerontology/Основы молекулярной геронтологии
major:	Applied Mathematics and Physics
specialization:	General and Applied Physics/Общая и прикладная физика
	Landau Phystech-School of Physics & Research
	Chair of Biophysics
term:	1
qualification:	Master

Semester, form of interim assessment: 1 (fall) - Exam

Academic hours: 30 AH in total, including:
lectures: 15 AH.
seminars: 15 AH.
laboratory practical: 0 AH.

Independent work: 30 AH.

Exam preparation: 30 AH.

In total: 90 AH, credits in total: 2

Number of course papers, tasks: 2

Author of the program: I.V. Manukhov, doctor of biological sciences

The program was discussed at the Chair of Biophysics 19.06.2023

Annotation

The course introduces students to the basic molecular signs of cell aging, as well as dysfunctions at the level of human body systems. The relationship between different damages through signal cascades is shown. A critical review of interventions that slow down the development of aging is given.

1. Study objective

Purpose of the course

students mastering fundamental knowledge in the field of biology, biochemistry, biophysics of human aging, studying the ways and methods of their research, as well as practical application to influence the aging process and maintain health.

Tasks of the course

1) the formation of basic knowledge in the field of biophysics of aging as a discipline that integrates the biological, biochemical and general theoretical training of biophysicists and provides the technological foundations of modern innovative fields of activity;

2) Acquaintance of the students with the principles of functioning of the systems of the human body, identifying their age-related changes, leading to age-related degradation and death;

3) formation of approaches to the implementation of research by students in the field of biophysics in the framework of final works for a master's degree.

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-4 Use modern communication tools in the academic and professional fields, including those in a foreign language	UC-4.1 Exchange business information in oral and written forms in Russian and at least one foreign language
Gen.Pro.C-1 Gain fundamental scientific knowledge in the field of physical and mathematical sciences	Gen.Pro.C-1.2 Consolidate and critically assess professional experience and research findings
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
Gen.Pro.C-3 Select and/or develop approaches to professional problem-solving with consideration to the limitations and specifics of different solution methods	Gen.Pro.C-3.1 Analyze problems, plan research strategy to achieve solution(s), propose, and combine solution approaches
	Gen.Pro.C-3.2 Employ research methods to solve new problems and apply knowledge from various fields of science (technology)
	Gen.Pro.C-3.3 Gain knowledge of analytical and computational methods of problem-solving, understand the limitations of the implementation of the obtained solutions in practice
Gen.Pro.C-4 Successfully perform a task, analyze the results, and present conclusions, apply knowledge and skills in the field of physical and mathematical sciences and ICTs	Gen.Pro.C-4.2 Apply knowledge in the field of physical and mathematical sciences to solve problems, make conclusions, and evaluate the obtained results
	Gen.Pro.C-4.3 Justify the chosen method of scientific research

Gen.Pro.C-5 Undertake professional training, achieve professional growth, and become a team leader in a professional sphere, tolerant of social, ethnic, religious, and cultural differences	Gen.Pro.C-5.1 Tolerate social, ethnic, religious, and cultural differences in teamwork
	Gen.Pro.C-5.3 Apply new knowledge and achieve personal and professional growth
Pro.C-1 Assign, formalize, and solve tasks, develop and research mathematical models of the studied phenomena and processes, systematically analyze scientific problems and obtain new scientific results	Pro.C-1.1 Locate, analyze, and summarize information on current research findings within the subject area
	Pro.C-1.3 Apply theoretical and/or experimental research methods to a specific scientific task and interpret the obtained results
Pro.C-2 Organize and conduct scientific research and testing independently or as a member (leader) of a small research team	Pro.C-2.1 Plan and conduct scientific research independently or as part of a research team

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

As a result of studying the course the student should:

know:

1) basic theories of aging;
2) the main molecular sensors of the internal and external state of the cell;
3) the main stresses that damage the cell;
4) basic systems of quality control, protection and reparation;
5) major changes in the interaction of cells and body systems with age;
6) basic physical, biophysical and biochemical research methods in gerontology;
7) methods for critical analysis and evaluation of modern scientific achievements, as well as methods for generating new ideas in solving research and practical problems, including in interdisciplinary areas;
8) modern ways of using information and communication technologies.

be able to:

1) build relationships between different lesions in the cell;
2) evaluate the effectiveness of interventions in a certain aging mechanism to influence the state of the system as a whole;
3) use the basic laws of natural science disciplines in professional activities;
4) work with scientific and technical information;
5) identify and systematize the main ideas in scientific texts;
6) critically evaluate any incoming information, regardless of the source;
7) when solving research and practical problems, generate new ideas.

master:

1) skills in choosing methods and means for solving research problems;
2) methods of theoretical and experimental research;
3) search skills (including using information systems and databases), processing, analysis and systematization of information;
4) the skills of critical analysis and evaluation of modern scientific achievements.

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	Overview of signs of aging	1	1		2
2	Violation of the stability of the genome	1	1		2
3	Telomere theory of aging	1	1		2
4	Age-related epigenetic changes	1	1		2

5	Loss of proteostasis	1	1		2
6	Loss of mitochondrial functionality	1	1		2
7	Age-related dysregulation of the work of molecular sensors of nutrition and energy	1	1		2
8	Senescent cells	2	2		4
9	Depletion of stem cells	2	2		4
10	Change in intercellular interactions	2	2		4
11	Long-lived animals on the example of a naked mole rat	2	2		4
AH in total		15	15		30
Exam preparation		30 AH.			
Total complexity		90 AH., credits in total 2			

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

Semester: 1 (Fall)

1. Overview of signs of aging

molecular markers of cell aging, age-related systemic changes in the body, basic theories about the mechanisms of aging, anti-aging interventions with an assessment of side effects.

2. Violation of the stability of the genome

chemical structure of DNA, spatial arrangement of DNA in the metaphase and interphase nucleus, mitochondria. Sources of DNA damage (oxidative, reductive stresses). Sensory and executive proteins that respond to DNA damage. The principle of the PARP1 protein in the repair of DNA breaks, experimental approaches to assessing the activity of PARP1. Theories of accumulation of mutations, activation of retrotransposons as a mechanism of aging, genes that determine lifespan, the influence of miRNAs.

3. Telomere theory of aging

Chromosome shortening process (terminal underreplication effect, stress-accelerated shortening), replicative stress, replicative aging, telomere theory of aging, T-loop, effect of telomere shortening on the expression of spatially close genes. Interventions to maintain genome stability. mechanism of telomerase and alternative telomere elongation (DNA recombination), Cytofluorimetric and PCR methods for assessing cell telomere length, approaches to assessing telomerase activity.

4. Age-related epigenetic changes

age-related epigenetic changes, their heritability, NADH metabolism in relation to the maintenance of redox balance, stress response. Epigenetic reprogramming during the development of a new organism. Yamanaki cocktail to restore the "young" epigenetic DNA profile. The epigenetic clock as a marker of aging. How SIRT1 works as a NAD-dependent epigenetic modulator. Geroprotective mechanism of resveratrol, nicotinamide adenine dinucleotide NAD supplementation, microRNA influence.

5. Loss of proteostasis

Proteinopathies, liquid-liquid phase transition, stress granules, protein quality control system, pathways for catabolism transition induction. ER-stress, reducing environment in the ER as a cause of misfolded proteins. Active carbonyl compounds and protein carbonylation. Damage to biological membranes and isolation of important proteins in aggregates. Approaches for assessing the efficiency levels of the autophagy process by a two-color fluorescent probe and the expression level of a set of proteins (ATG5, ATG12, LC3, LAMP1, p62). Geroprotective mechanism of calorie restriction, rapamycin and rapologists, metforman and calorie restriction mimetics.

6. Loss of mitochondrial functionality

disorders of oxidative phosphorylation; mechanism of flip-flop transfer of fatty acids between the inner and outer surface of the membrane; mitochondrial release of free radicals, including in response to oxidative stress, mitohormesis, proton gradient adjustment mechanisms, mitochondrial-lysosomal axis, mitophagy, lipofuscin, mitochondrial telomerase function.

7. Age-related dysregulation of the work of molecular sensors of nutrition and energy

mTORC1, AMPK, SIRT1, metabolic restructuring from anabolism to catabolism with calorie restriction. Excessive chemical activity of metabolites as an aging factor.

8. Senescent cells

method for detecting the senescent state by increased activity of the enzyme beta-galactosidase, overexpression of p16INK, the principle of antagonistic pleiotropy, senescence bypass, crisis, autophagy-induced cell death, cytosolic telomeric DNA, the mechanism of the cGAS-STING system of intracellular immune response, cytostatics, senolytics, physical limitations for the survival of tumor cells.

9. Depletion of stem cells

division asymmetry, quinescence, molecular sensors of the state of the cell, mechanisms of immortality of stem (including sex), tumor cells, tumor stem cells.

10. Change in intercellular interactions

connexins, intercellular matrix, exosomes, immunosenescence. Inflammaging, the main players in inflammation processes (senescent cells, hypothalamus, interleukin (IL)-1, tumor necrosis factors (TNF), NF-kB mechanism), insulin resistance, hormone therapy, age-related changes in circadian rhythms, melatonin against aging and cancer. Microbiota and its influence on immunity, susceptibility to diseases.

11. Long-lived animals on the example of a naked mole rat

model of a short-lived killifish organism, mechanisms that prolong the life of a naked mole rat.

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

Classroom with a media projector and screen, Internet access.

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

Main literature

1. Молекулярные и физиологические механизмы старения [Текст]. В 2 т. Т. 1/В. Н. Анисимов, Molecular fnd Physiological Mechanisms of Aging, -СПб., Наука, 2008

2. Молекулярные и физиологические механизмы старения [Текст]. В 2 т. Т. 2/В. Н. Анисимов, Molecular fnd Physiological Mechanisms of Aging, -СПб., Наука, 2008

Фонд базовой кафедры:
3. Textbook Vijg, Campisi, Lithgow Molecular and cellular biology of aging, Geron, 2015

Additional literature
Фонд базовой кафедры:
1. Голубев А. Г. Биология продолжительности жизни и старения. – 2009.
2. Fahy, Gregory M., et al. The Future of Aging. Springer, 2010

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

http://serious-science.org/?s=aging
http://www.senescence.info/
https://www.cellsenescence.info/
http://gerontology.bio.msu.ru/links.htm

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

Not used

9. Guidelines for students to master the course

A student studying the discipline must, on the one hand, master the general conceptual apparatus, and on the other hand, must learn to apply theoretical knowledge in practice.
As a result of studying the discipline, the student must know the basic definitions and concepts, be able to apply the knowledge gained to solve various problems.
Successful completion of the course requires:
- attendance of all classes provided for by the curriculum for the discipline;
- keeping a synopsis of classes;
- student's intense independent work.
Independent work includes:
- reading recommended literature;
- study of educational material, preparation of answers to questions intended for independent study;
- solving problems offered to students in the classroom;
- preparation for the performance of tasks of the current and intermediate certification.
An indicator of mastery of the material is the ability to answer questions on the topics of the discipline without a synopsis.
It is important to achieve an understanding of the material being studied, not its mechanical memorization. If a student finds it difficult to study certain topics, questions, he/she should seek advice from a teacher.
Intermediate control of students' knowledge is possible in the form of solving problems in accordance with the topic of classes.

SUPPLEMENT

Assessment funds for course (training module)

major:	Applied Mathematics and Physics
specialization:	General and Applied Physics/Общая и прикладная физика Landau Phystech-School of Physics & Research Chair of Biophysics
term:	1
qualification:	Master

Semester, form of interim assessment: 1 (fall) - Exam

Author: I.V. Manukhov, doctor of biological sciences

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-4 Use modern communication tools in the academic and professional fields, including those in a foreign language	UC-4.1 Exchange business information in oral and written forms in Russian and at least one foreign language
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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
Gen.Pro.C-3 Select and/or develop approaches to professional problem-solving with consideration to the limitations and specifics of different solution methods	Gen.Pro.C-3.1 Analyze problems, plan research strategy to achieve solution(s), propose, and combine solution approaches
	Gen.Pro.C-3.2 Employ research methods to solve new problems and apply knowledge from various fields of science (technology)
	Gen.Pro.C-3.3 Gain knowledge of analytical and computational methods of problem-solving, understand the limitations of the implementation of the obtained solutions in practice
Gen.Pro.C-4 Successfully perform a task, analyze the results, and present conclusions, apply knowledge and skills in the field of physical and mathematical sciences and ICTs	Gen.Pro.C-4.2 Apply knowledge in the field of physical and mathematical sciences to solve problems, make conclusions, and evaluate the obtained results
	Gen.Pro.C-4.3 Justify the chosen method of scientific research
Gen.Pro.C-5 Undertake professional training, achieve professional growth, and become a team leader in a professional sphere, tolerant of social, ethnic, religious, and cultural differences	Gen.Pro.C-5.1 Tolerate social, ethnic, religious, and cultural differences in teamwork
	Gen.Pro.C-5.3 Apply new knowledge and achieve personal and professional growth
Pro.C-1 Assign, formalize, and solve tasks, develop and research mathematical models of the studied phenomena and processes, systematically analyze scientific problems and obtain new scientific results	Pro.C-1.1 Locate, analyze, and summarize information on current research findings within the subject area
	Pro.C-1.3 Apply theoretical and/or experimental research methods to a specific scientific task and interpret the obtained results
Pro.C-2 Organize and conduct scientific research and testing independently or as a member (leader) of a small research team	Pro.C-2.1 Plan and conduct scientific research independently or as part of a research team

2. Competency assessment indicators

As a result of studying the course the student should:

know:

1) basic theories of aging;
2) the main molecular sensors of the internal and external state of the cell;
3) the main stresses that damage the cell;
4) basic systems of quality control, protection and reparation;
5) major changes in the interaction of cells and body systems with age;
6) basic physical, biophysical and biochemical research methods in gerontology;
7) methods for critical analysis and evaluation of modern scientific achievements, as well as methods for generating new ideas in solving research and practical problems, including in interdisciplinary areas;
8) modern ways of using information and communication technologies.

be able to:

1) build relationships between different lesions in the cell;
2) evaluate the effectiveness of interventions in a certain aging mechanism to influence the state of the system as a whole;
3) use the basic laws of natural science disciplines in professional activities;
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7) when solving research and practical problems, generate new ideas.

master:

1) skills in choosing methods and means for solving research problems;
2) methods of theoretical and experimental research;
3) search skills (including using information systems and databases), processing, analysis and systematization of information;
4) the skills of critical analysis and evaluation of modern scientific achievements.

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

In order to control the students' mastery of the training material, an oral questioning is conducted at the beginning of the lesson on the topic of the last session.

4. Evaluation criteria

Checking questions:

1) Epigenetic reprogramming during the development of a new organism. Yamanaki cocktail to restore the "young" epigenetic DNA profile.

2) Inflammaging, the main players in the processes of inflammation (senescent cells, hypothalamus, interleukin (IL)-1, tumor necrosis factors (TNF), the mechanism of NF-kB),

3) Proteinopathy, liquid-liquid phase transition, stress granules, protein quality control system, ways to induce the transition to catabolism.

4) The principle of the PARP1 protein in the repair of DNA breaks, experimental approaches to assessing the activity of PARP1.

5) Loss of mitochondrial functionality: disorders of oxidative phosphorylation; the mechanism of flip-flop transfer of fatty acids between the inner and outer surface of the membrane.

6) How can you explain the benefits of NAD+ supplementation for the cell (or the organism as a whole).

7) Why HIV (AIDS) drugs may have some effectiveness in reducing problems caused by the retrobiome.

8) Write what kind of stress sensor is the telomeric regions of chromosomes.

9) Why does a stem cell need to change its epigenetic profile in order to become a cell of a certain type (tissue, organ).

10) How does catabolism help fight age-related changes in the cell? Name the positive effect of catabolism on proteostasis, mitochondrial dysfunction.

Examples of exam question papers:

Question paper 1.

1. What are the positive and negative aspects of the use of antioxidants.

Hormesis through mild hypoxia-reoxygenation (oxygen preconditioning).

2. Activation of what mechanism is needed for the transformation of an old cell into a tumor one? How does this mechanism help the cancer cell divide indefinitely?

Question paper 2.

1. Describe the mechanisms of anti-aging action of metformin, resveratrol, rapamycin and calorie restriction. What mechanism of cell aging is targeted by these interventions.

2. Can a eukaryotic cell live without mitochondria (possibly under special conditions)? Describe what she will lose and gain without mitochondria.

Question paper 3.

1. Tell us what are the positive and negative aspects of the appearance of senescent cells in the body. Is their presence in the body justified?

2. Tell us about the telomeric theory of aging.

Question paper 4.

1. Epigenetic reprogramming during the development of a new organism. Yamanaki cocktail to restore the "young" epigenetic DNA profile.

2. Inflammaging, the main players in inflammation processes (senescent cells, hypothalamus, interleukin (IL)-1, tumor necrosis factors (TNF), NF-kB mechanism)

Question paper 5.

1. Proteinopathy, liquid-liquid phase transition, stress granules, protein quality control system, pathways for catabolism transition induction.

2. The principle of the PARP1 protein in the repair of DNA breaks, experimental approaches to assessing the activity of PARP1.

Assessment “excellent (10)” is given to a student who has displayed comprehensive, systematic and deep knowledge of the educational program material, has independently performed all the tasks stipulated by the program, has deeply studied the basic and additional literature recommended by the program, has been actively working in the classroom, and understands the basic scientific concepts on studied discipline, who showed creativity and scientific approach in understanding and presenting educational program material, whose answer is characterized by using rich and adequate terms, and by the consistent and logical presentation of the material;

Assessment “excellent (9)” is given to a student who has displayed comprehensive, systematic knowledge of the educational program material, has independently performed all the tasks provided by the program, has deeply mastered the basic literature and is familiar with the additional literature recommended by the program, has been actively working in the classroom, has shown the systematic nature of knowledge on discipline sufficient for further study, as well as the ability to amplify it on one’s own, whose answer is distinguished by the accuracy of the terms used, and the presentation of the material in it is consistent and logical;

Assessment “excellent (8)” is given to a student who has displayed complete knowledge of the educational program material, does not allow significant inaccuracies in his answer, has independently performed all the tasks stipulated by the program, studied the basic literature recommended by the program, worked actively in the classroom, showed systematic character of his knowledge of the discipline, which is sufficient for further study, as well as the ability to amplify it on his own;

Assessment “good (7)” is given to a student who has displayed a sufficiently complete knowledge of the educational program material, does not allow significant inaccuracies in the answer, has independently performed all the tasks provided by the program, studied the basic literature recommended by the program, worked actively in the classroom, showed systematic character of his knowledge of the discipline, which is sufficient for further study, as well as the ability to amplify it on his own;

Assessment “good (6)” is given to a student who has displayed a sufficiently complete knowledge of the educational program material, does not allow significant inaccuracies in his answer, has independently carried out the main tasks stipulated by the program, studied the basic literature recommended by the program, showed systematic character of his knowledge of the discipline, which is sufficient for further study;

Assessment “good (5)” is given to a student who has displayed knowledge of the basic educational program material in the amount necessary for further study and future work in the profession, who while not being sufficiently active in the classroom, has nevertheless independently carried out the main tasks stipulated by the program, mastered the basic literature recommended by the program, made some errors in their implementation and in his answer during the test, but has the necessary knowledge for correcting these errors by himself;

Assessment “satisfactory (4)” is given to a student who has discovered knowledge of the basic educational program material in the amount necessary for further study and future work in the profession, who while not being sufficiently active in the classroom, has nevertheless independently carried out the main tasks stipulated by the program, learned the main literature but allowed some errors in their implementation and in his answer during the test, but has the necessary knowledge for correcting these errors under the guidance of a teacher;

Assessment “satisfactory (3)” is given to a student who has displayed knowledge of the basic educational program material in the amount necessary for further study and future work in the profession, not showed activity in the classroom, independently fulfilled the main tasks envisaged by the program, but allowed errors in their implementation and in the answer during the test, but possessing necessary knowledge for elimination under the guidance of the teacher of the most essential errors;

Assessment “unsatisfactory (2)” is given to a student who showed gaps in knowledge or lack of knowledge on a significant part of the basic educational program material, who has not performed independently the main tasks demanded by the program, made fundamental errors in the fulfillment of the tasks stipulated by the program, who is not able to continue his studies or start professional activities without additional training in the discipline in question;

Assessment “unsatisfactory (1)” is given to a student when there is no answer (refusal to answer), or when the submitted answer does not correspond at all to the essence of the questions contained in the task.

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

The course is graded at an exam. The questioning starts with a random task assigned to each student and time given for completion of the task. No aids are allowed. The student then proceeds to a chat with the examiner, at which he/she presents his/her solution to the assigned task. The examiner then asks the student several questions that evenly cover the course content. A final grade is assigned based on the quality of answers and demonstrated level of understanding.