

**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: Genetic and Genomic Engineering/Генная и геномная инженерия
major: Applied Mathematics and Physics
specialization: Applied Bioinformatics/Прикладная биоинформатика
Phystech School of Biological and Medical Physics
Center for educational programs in bioinformatics
term: 1
qualification: Master

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

Academic hours: 30 AH in total, including:

lectures: 0 AH.

seminars: 30 AH.

laboratory practical: 0 AH.

Independent work: 15 AH.

In total: 45 AH, credits in total: 1

Authors of the program:

D.Y. Gushchin, candidate of biological sciences

A.V. Melerzanov, candidate of medical sciences

The program was discussed at the Center for educational programs in bioinformatics 04.06.2020

Annotation

The purpose of this discipline is to master the basic concepts, modern knowledge and principles, as well as research methods, the implementation of hereditary information in living systems, to understand the use of approaches and techniques of genetic and genomic engineering in the context of solving bioinformatics problems. After mastering the course, the student will understand the fundamental concepts and principles of the implementation of hereditary information in living systems, modern principles and problems of the application of genetic and genomic engineering methods to solve various biological and medical problems, legal and ethical aspects of the application of genetic and genomic engineering to solve medical and biotechnological problems ... Features of legal regulation in Russia and abroad.

1. Study objective

Purpose of the course

mastering the basic concepts, modern knowledge and principles, as well as research methods, the implementation of hereditary information in living systems, to understand the use of approaches and techniques of genetic and genomic engineering in the context of solving bioinformatics problems.

Tasks of the course

- mastering by students of basic knowledge (concepts, concepts, methods and models) of genetic and genomic engineering used in biology;
- acquisition of theoretical knowledge and practical skills and knowledge in the field of genetic and genomic engineering technologies and their application in biology and medicine;
- providing advice to students in the course of solving model problems on the application of bioinformatics in fundamental biology and medicine.

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-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-4.1 Apply ICT knowledge and skills to find and study scientific literature and use software products
	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
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-1.2 Make hypotheses, build mathematical models of the studied phenomena and processes, evaluate the quality of the developed model
	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-3 Use research and testing equipment (devices and installations, specialized software) in a selected subject field	Pro.C-3.1 Understand the operating principles of the equipment and specialized software
	Pro.C-3.3 Evaluate the accuracy of the experimental (numerical) results
	Pro.C-3.2 Conduct an experiment (simulation) using research equipment (software)

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

As a result of studying the course the student should:

know:

- ☐ fundamental concepts and principles of the implementation of hereditary information in living systems;
- ☐ modern principles and problems of application of genetic and genomic engineering methods for solving various biological and medical problems;
- ☐ legal and ethical aspects of the application of genetic and genomic engineering for solving medical and biotechnological problems. Features of legal regulation in Russia and abroad.

be able to:

- ☐ set goals and objectives for research using genetic and genomic engineering technologies in biology and medicine, understand the goals and objectives;
- ☐ use their knowledge to solve problems and apply the technology of applying genetic and genomic engineering in biology and medicine;
- ☐ evaluate the correctness of the problem formulations and build algorithms for achieving their optimal solution in various living systems;
- ☐ set goals and objectives for research using genetic and genomic engineering technologies in biology and medicine, understand the goals and objectives;
- ☐ use your knowledge to solve problems and apply the technology of applying genetic and genomic engineering in biology and medicine;
- ☐ evaluate the correctness of the problem formulations and build algorithms for achieving their optimal solution in various living systems;
- ☐ to apply the obtained fundamental knowledge for applied purposes of applying genetic and genomic engineering technologies for solving fundamental problems and problems of practical medicine.

master:

- ☐ skills of mastering a large amount of information and approaches to solving problems in molecular biology and medicine;
- ☐ skills of independent work and mastering new knowledge, abilities and skills;
- ☐ principles and approaches to solving biological and medical problems related to genomics;
- ☐ terminology, including working terms sufficient to understand the scientific literature.

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	Realization of genomic information in a cell		4		2
2	Genetic engineering techniques		4		2
3	Polymerase chain reaction and its modifications		4		2
4	Methods for cloning and creating DNA libraries		6		3
5	Genomic engineering in eukaryotes		4		2
6	Application of the CRISPR system in cell biology		4		2
7	DNA structure		4		2
AH in total			30		15
Exam preparation		0 AH.			

Total complexity	45 AH., credits in total 1
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4.2. Content of the course (training module), structured by topics (sections)

Semester: 2 (Spring)

1. Realization of genomic information in a cell

Analogy: Software and Hardware.

Features of the implementation of hereditary information in living systems. Maintaining the integrity of the genome: replication, recombination and repair of genomic DNA. Central dogma of biology. Gene expression: transcription and translation.

2. Genetic engineering techniques

Major milestones in the creation of recombinant DNA technology. Vectors and enzymes in genetic engineering. Restriction enzymes, DNA manipulation enzymes. Cloning techniques

3. Polymerase chain reaction and its modifications

PCR, gene isolation by PCR, primer design - gene-specific primers, nested primers, degenerate primers, optimization of PCR components and temperature conditions, PCR controls, PCR types - reverse PCR, nested PCR, TAIL PCR, LAMP, semi-quantitative PCR, RT-PCR in real time with SYBR and Taqman probe, site-directed mutagenesis.

4. Methods for cloning and creating DNA libraries

Sticky end cloning, blunt end cloning, cloning using adapters, linkers and homopolymer tail, GATYWAY cloning, Gibson assembly cloning, cDNA library construction, cDNA subtraction libraries, normalized cDNA libraries, genomic libraries

5. Genomic engineering in eukaryotes

Genomic engineering in yeast. Genomic engineering in mice. Programmable artificial nucleases: Meganucleases, ZFN, TALN, CRISPR system. Use of the CRISPR system in knockouts, gene insertions, genomic editing, transcriptional regulation, and epigenomics. Radix editors CBE and ABE. Genome-wide CRISPR screening. Cellular Engineering. Genomic engineering of animals and plants.

6. Application of the CRISPR system in cell biology

Varieties of CRISPR nucleases. Cas nickases and Cas inactivated proteins. Application of the CRISPR system in cell biology. RNA editing. Radix editors CBE and ABE. CRISPR detection of specific DNA and RNA. The problem of the specificity of the CRISPR system. Delivery of nucleases into cells and tissues. Gene therapy. Social and ethical problems of genome editing in higher organisms.

7. DNA structure

DNA structure. DNA analysis. Assembly. Genetic mutations in DNA. Double helix formation.

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

Standard classroom. Projector.

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

Main literature

Provided by the department in translation

Genetic and Genomic Engineering Courses and Materials:

1. Lectures on the course
2. D. Krebs, S. Kilpatrick, E. Goldstein "Genes according to Lewin" Publisher: Laboratory of Knowledge, 2017
3. R. Schmidt "Visual Biotechnology and Genetic Engineering" Knowledge Laboratory, 2015

Additional literature

Provided at the department:

1. Singer, M. Genes and genomes: in 2 volumes / M. Singer, P. Berg. - M.: Mir, 1998.
 2. Zhimulev I.F. General and Molecular Genetics. 2003
 3. Zavilgelsky G.B., Manukhov I.V. Genetic engineering. - M.: ed. MIPT, 2012.
1. Recommended articles from scientific journals on the topic of lectures (will be offered after each lecture)

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

www.molbiol.ru

<http://www.biosyn.com/Gizmo/Tools/Oligo/Oligonucleotide%20Properties%20Calculator.htm>

<http://www.ncbi.nlm.nih.gov/>

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

The lectures use multimedia technologies, including the demonstration of presentations. Zoom is required for some of the lessons. 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

1. Attend seminars
2. To prepare for the final attestation in the subject, use the materials of the seminars and the recommended literature.

Assessment funds for course (training module)

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Authors:

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A.V. Melerzanov, candidate of medical 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
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	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-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-4.1 Apply ICT knowledge and skills to find and study scientific literature and use software products
	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
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-1.2 Make hypotheses, build mathematical models of the studied phenomena and processes, evaluate the quality of the developed model
	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-3 Use research and testing equipment (devices and installations, specialized software) in a selected subject field	Pro.C-3.1 Understand the operating principles of the equipment and specialized software
	Pro.C-3.3 Evaluate the accuracy of the experimental (numerical) results
	Pro.C-3.2 Conduct an experiment (simulation) using research equipment (software)

2. Competency assessment indicators

As a result of studying the course the student should:

know:

- ☐ fundamental concepts and principles of the implementation of hereditary information in living systems;
- ☐ modern principles and problems of application of genetic and genomic engineering methods for solving various biological and medical problems;
- ☐ legal and ethical aspects of the application of genetic and genomic engineering for solving medical and biotechnological problems. Features of legal regulation in Russia and abroad.

be able to:

- ☐ set goals and objectives for research using genetic and genomic engineering technologies in biology and medicine, understand the goals and objectives;
- ☐ use their knowledge to solve problems and apply the technology of applying genetic and genomic engineering in biology and medicine;
- ☐ evaluate the correctness of the problem formulations and build algorithms for achieving their optimal solution in various living systems;
- ☐ set goals and objectives for research using genetic and genomic engineering technologies in biology and medicine, understand the goals and objectives;
- ☐ use your knowledge to solve problems and apply the technology of applying genetic and genomic engineering in biology and medicine;
- ☐ evaluate the correctness of the problem formulations and build algorithms for achieving their optimal solution in various living systems;
- ☐ to apply the obtained fundamental knowledge for applied purposes of applying genetic and genomic engineering technologies for solving fundamental problems and problems of practical medicine.

master:

- ☐ skills of mastering a large amount of information and approaches to solving problems in molecular biology and medicine;
- ☐ skills of independent work and mastering new knowledge, abilities and skills;
- ☐ principles and approaches to solving biological and medical problems related to genomics;
- ☐ terminology, including working terms sufficient to understand the scientific literature.

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

During the current control, the student should be able to answer the following questions:

1. Experiments by G. Mendel and T. Morgan, the concept of dominance, incomplete dominance, codominance.
2. Multiple allelism, inter-allelic compliment, multiple allelism, inter-allelic compliment, negative dominance.
3. Enzymes used in genetic engineering.
4. Restriction-modification systems.
5. RNA polymerase. DNA polymerase.
6. Alkaline phosphatase and polynucleotide kinase.
7. Nucleases.
8. Topoisomerase.
9. DNA ligase.
10. Replication, transcription, translation: main differences in pro- and eukaryotes.
11. Autonomous units of replication (plasmids, bacteriophages, chromosomes). Replicons.
12. Incompatibility of plasmids. Mobilization of plasmids.
13. Markers used for selection.
14. Construction of hybrid plasmids.
15. Isolation of plasmid DNA. Isolation of total DNA. Isolation of RNA.
16. Separation of DNA fragments by electrophoresis in agarose and polyacrylamide gels.
17. Principle of amplification of DNA fragments using PCR.
18. Cloning of fragments obtained by PCR. Cloning into a T-vector.
19. Transformation of bacterial cells. Transfection.
20. Blotting and hybridization.
21. DNA sequencing.
22. Isolation of eukaryotic mRNA. RT-PCR (RT-PCR). PCR cloning of eukaryotic genes.
23. Spontaneous mutagenesis. The main types of DNA damage.
24. DNA repair systems in bacteria on the example of E. coli.
25. Homologous DNA recombination.
26. Site-directed mutagenesis.
27. Obtaining mutations in the E. coli chromosome.
28. Transcription of bacterial genes.
29. Regulation of E. coli lactose operon.
30. Regulation of transcription of the target gene in strain BL21 (DE3) on vectors of the pET series.
31. Transcription of eukaryotic genes.
32. Translation in bacteria and eukaryotes.
33. Post-translational level of regulation of protein activity.
34. Chimeric proteins.
35. Vectors: pBR322, pUC18 / 19, pACYC184, pET15b.
36. Vectors with a wide range of hosts and shuttle vectors for gram-negative and gram-positive bacteria.
37. Yeast vectors and vectors for cloning large DNA fragments: Yac, Bac.
38. Indicators of microbial fermentation.
39. Genes encoding metabolism.
40. Minimization of the genome.
41. Economical and efficient ways of synthesis.
42. Metabolomics and flows.

43. Flow cytometry.
44. Robotic screening.
45. Direct and reverse genetics.
46. Methods for increasing and decreasing gene expression.
47. Fine tuning of promoters.
48. Scaffolds.
49. Changes in the substrate specificity of enzymes.
50. Inhibition and desensitization.
51. The principle of conjugation of synthesis with vital functions.

During the lesson, you can conduct interactive discussions in the course chats, which is a homework assignment. It is possible to perform patent search as an independent task. Successful completion of all tasks of the course and completion of the control slices of knowledge gives an advantage on differential credit.

4. Evaluation criteria

List of typical control tasks:

Describe the concept of genetic and genomic engineering. List the main areas of application of genetic and genomic engineering technologies in fundamental research and medicine.

List and describe the main enzymes used in genetic engineering.

List and describe the main platforms and proteins used in genomic engineering, describe the advantages and disadvantages of each approach.

Describe the main objectives for the use of genetic engineering.

Describe the main objectives for the use of genomic engineering.

Describe specificity problems in genomic engineering. Describe approaches to address the specificity problem.

Describe the problems of delivery of constructs in genomic engineering. Describe the different approaches for the delivery of constructs and proteins used in genomic engineering.

DNA. Describe the structure of DNA. Describe the structure of the gene in pro- and eukaryotes.

Describe the packaging of DNA in eukaryotes. Describe the structure of the chromosome. Describe the current understanding of the packaging of chromosomes in the cell nucleus.

Formulate the central dogma of biology. Describe exceptions to the central dogma of biology.

Describe the process of implementing hereditary information in living systems.

Describe the basic concepts: transcription, translation. Enzymes involved in the processes of transcription and translation.

Describe the processes of regulation of transcription. Describe transcriptional and post-transcriptional, translational and post-translational control.

Describe the process of amplifying DNA regions using PCR (polymerase chain reaction). Describe the main directions of the use of PCR in molecular biology.

Describe the main modifications of the polymerase chain reaction. Describe the types of PCR: reverse PCR, nested PCR, TAIL PCR, LAMP, semi-quantitative RT-PCR, real-time PCR.

Describe the main approaches to creating mutations in genes in genetic engineering. Describe directed mutagenesis.

Describe the main approaches to creating mutations in the genome. Describe the difference in using homologous recombination and base editing with base editors. Describe the types of datum editors.

Describe and substantiate the ethical issues of genetic and genomic engineering.

List of possible model tickets:

1. Experiments by G. Mendel and T. Morgan, the concept of dominance, incomplete dominance, codominance.
2. Multiple allelism, inter-allelic compliment, multiple allelism, inter-allelic compliment, negative dominance.
3. Enzymes used in genetic engineering.

4. Restriction-modification systems.
5. RNA polymerase. DNA polymerase.
6. Alkaline phosphatase and polynucleotide kinase.
7. Nucleases.
8. Topoisomerase.
9. DNA ligase.
10. Replication, transcription, translation: main differences in pro- and eukaryotes.
11. Autonomous units of replication (plasmids, bacteriophages, chromosomes). Replicons.
12. Incompatibility of plasmids. Mobilization of plasmids.
13. Markers used for selection.
14. Construction of hybrid plasmids.
15. Isolation of plasmid DNA. Isolation of total DNA. Isolation of RNA.
16. Separation of DNA fragments by electrophoresis in agarose and polyacrylamide gels.
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22. Isolation of eukaryotic mRNA. RT-PCR (RT-PCR). PCR cloning of eukaryotic genes.
23. Spontaneous mutagenesis. The main types of DNA damage.
24. DNA repair systems in bacteria on the example of *E. coli*.
25. Homologous DNA recombination.
26. Site-directed mutagenesis.
27. Obtaining mutations in the *E. coli* chromosome.
28. Transcription of bacterial genes.
29. Regulation of *E. coli* lactose operon.
30. Regulation of transcription of the target gene in strain BL21 (DE3) on vectors of the pET series.
31. Transcription of eukaryotic genes.
32. Translation in bacteria and eukaryotes.
33. Post-translational level of regulation of protein activity.
34. Chimeric proteins.
35. Vectors: pBR322, pUC18 / 19, pACYC184, pET15b.
36. Vectors with a wide range of hosts and shuttle vectors for gram-negative and gram-positive bacteria.
37. Yeast vectors and vectors for cloning large DNA fragments: Yac, Bac.
38. Indicators of microbial fermentation.
39. Genes encoding metabolism.
40. Minimization of the genome.
41. Economical and efficient ways of synthesis.
42. Metabolomics and flows.
43. Flow cytometry.
44. Robotic screening.
45. Direct and reverse genetics.
46. Methods for increasing and decreasing gene expression.
47. Fine tuning of promoters.
48. Scaffolds.
49. Changes in the substrate specificity of enzymes.
50. Inhibition and desensitization.
51. The principle of conjugation of synthesis with vital functions.
52. Directed evolution and breeding in a fermenter.

- the mark "excellent (10)" is 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, free and correct justification of the chosen approaches

- the mark "excellent (9)" is given to a student who has shown comprehensive, systematized, in-depth knowledge of the curriculum of the discipline and the ability to apply them in practice in solving specific problems, free and correct justification of the chosen approaches
- the mark "excellent (8)" is given to a student who has shown comprehensive systematized, deep knowledge of the curriculum of the discipline and the ability to apply them in practice in solving specific problems, and the correct justification of the chosen approaches
- the mark "good (7)" is given to a student if he firmly knows the material, expresses it competently and to the point, knows how to apply the knowledge gained in practice, but makes some inaccuracies in the answer or in solving problems;
- the mark "good (6)" is given to the student if he knows the material, presents 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;
- the mark "good (5)" is given to a student if he knows the material, and essentially expounds it, knows how to apply the knowledge gained in practice, but makes some inaccuracies in the answer or in solving problems;
- the mark "satisfactory (4)" is given to a student who has shown a fragmented, 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 owns the main sections of the curriculum necessary for further education and can apply the obtained knowledge by model in a standard situation;
- the mark "satisfactory (3)" is 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 program material, but at the same time he has fragmentary knowledge of the main sections of the curriculum necessary for further education and can apply the knowledge gained by the model in a standard situation;
- the mark "unsatisfactory (2)" is given to a student who does not know most of the main content of the curriculum of the discipline, makes gross mistakes in the formulation of the basic concepts of the discipline and does not know how to use the knowledge gained in solving typical practical problems
- grade "unsatisfactory (1)" is given to a student who does not know the formulations of the basic concepts of the discipline.

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. Interrogation of a student on a ticket on a differential oral test should not exceed one astronomical hour.