

**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: Microbiology and Metagenomics/Микробиология и метагенетика
major: Biotechnology
specialization: Medical Biotechnology/Медицинская биотехнология
Phystech School of Biological and Medical Physics
Chair of Bioinformatics and Systems Biology
term: 1
qualification: Master

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

Academic hours: 30 AH in total, including:

lectures: 30 AH.

seminars: 0 AH.

laboratory practical: 0 AH.

Independent work: 60 AH.

In total: 90 AH, credits in total: 2

Authors of the program:

V.N. Danilenko, doctor of biological sciences, full professor

A.V. Tyakht, candidate of biological sciences

The program was discussed at the Chair of Bioinformatics and Systems Biology 04.06.2020

Annotation

The purpose of this discipline is give the essential mechanisms on human microbiome in health and disease, modern methods for analyzing the microbial diversity. After completing the course, the student will understand general concepts, current views and perspectives related to the diversity of human microbiome, role of microbiome in health and disease, potential microbial biomarkers, methods for profiling microbiome composition, formats and specifications of metagenomic data, bioinformatic algorithms for analyzing metagenomic data, experimental methods of work with microorganisms.

1. Study objective

Purpose of the course

Give the essential mechanisms on human microbiome in health and disease, modern methods for analyzing the microbial diversity.

Tasks of the course

- establish basic knowledge about the interactions between structure and functions of microbiome, their interactions with the host and effect on immune, nervous and other organ systems;
- hands-on development of skills to analyze human microbiome data;
- establishing basic experimental skills and getting experience required for independent research in the field of microbial diversity.

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
Gen.Pro.C-2 Acquire an understanding of current scientific and technological challenges in professional settings, and scientifically formulate professional objectives	Gen.Pro.C-2.3 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-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
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-1.5 Has the ability to create software tools and databases used in bioengineering and bioinformatics
	Pro.C-1.3 Make hypotheses, build mathematical models of the studied phenomena and processes, evaluate the quality of the developed model
	Pro.C-1.2 Apply fundamental knowledge of mathematics, physics, chemistry, and biology in professional settings
	Pro.C-1.1 Locate, analyze, and summarize information on current research findings within a selected subject area
	Pro.C-1.4 Apply theoretical and/or experimental research methods to a specific scientific task and interpret the obtained results

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

As a result of studying the course the student should:

know:

- general concepts, current views and perspectives related to the diversity of human microbiome;
- role of microbiome in health and disease;
- potential microbial biomarkers;
- methods for profiling microbiome composition;
- formats and specifications of metagenomic data;
- bioinformatic algorithms for analyzing metagenomic data;
- experimental methods of work with microorganisms.

be able to:

- quickly find required data and concepts using Internet and scientific/applied literature on biology;
- compare structure, properties and functions of biological objects;
- apply basic bioinformatic methods for human microbiome data analysis in scientific research;
- apply basic experimental methods for work with microbes in laboratory.

master:

- skills of efficiently processing large volumes of information;
- standards of designing and modeling biological tasks for exploring human microbial diversity.

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	Human microbiome: discoveries and perspectives	2			4
2	Microbiome as a new “organ”; its functions in health and disease	4			8
3	Modulation of microbiome. Clinical trials and microbiome	4			8
4	Applications of omics-technologies for human microbiome research	4			8
5	Algorithms in metagenomics-I: taxonomic composition analysis	4			8
6	Algorithms in metagenomics-II: functional composition analysis	4			8
7	Comparative genomics of human gut microbes. Biotargets and mechanisms of toxin-antitoxin type II systems action	4			8
8	Statistical analysis of metagenomic data	4			8
AH in total		30			60
Exam preparation		0 AH.			
Total complexity		90 AH., credits in total 2			

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

Semester: 2 (Spring)

1. Human microbiome: discoveries and perspectives

Diversity of microbes in human gut and other sites. Structure and functions of human gut microbiome. Microbiome as a cornerstone of precision medicine. Recent discoveries obtained using metagenomics.

2. Microbiome as a new “organ”; its functions in health and disease

Links between human microbiome and clinical status: from associations to mechanisms. Major phyla relevant for human health. Dynamics of human microbiome during lifetime.

3. Modulation of microbiome. Clinical trials and microbiome

Metabolic interdependence of host and microbiome. Diet, probiotics, prebiotics and microbiome transplantation as key ways to manipulate human microbiome. Scientific-based evaluation of intervention efficacy.

4. Applications of omics-technologies for human microbiome research

Metagenomics. Comparative functional genomics. Metatranscriptomics. Metaproteomics. Metabolomics. Culturomics.

5. Algorithms in metagenomics-I: taxonomic composition analysis

Approaches for metagenomic reads classification. Composition, phylogeny and similarity-based methods. Processing of amplicon and shotgun sequencing data. Reference databases related to microbiome. Analytical metagenomic pipelines and online platforms.

6. Algorithms in metagenomics-II: functional composition analysis

Metagenomic assembly de novo. Metabolic potential profiling. Reconstruction of strain gene content and analysis of polymorphisms from shotgun metagenomic data. Correlation-based methods for reconstructing genomes from metagenomes. Prediction of functional potential from 16S rRNA sequencing data.

7. Comparative genomics of human gut microbes. Biotargets and mechanisms of toxin-antitoxin type II systems action

Comparative genomics of bifidobacteria, lactobacilli and other major gut phylotypes. Classification of toxin-antitoxin bacterial systems. Toxin-antitoxin type II systems in human gut microbes. MazE-MazF and RelB-RelE toxin-antitoxin systems.

8. Statistical analysis of metagenomic data

Statistical specifics of microbial composition features derived from metagenomic data. Concepts of significance and statistical power in metagenomics. Parametric and non-parametric statistical tests for metagenomic data. Integrated pipelines for meta-analysis of microbiome data.

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

Equipment needed for lectures and seminars: computer and multimedia equipment (projector, sound system)

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

Main literature

1. Гены [Текст] = Genes IX : [учебник для вузов] / Б. Льюин ; пер. с 9-го англ. изд. И. А. Кофиади [и др.] ; под ред. Д. В. Ребрикова .— М. : БИНОМ. Лаб. знаний, 2012 .— 896 с.

Provided at the department:

2. S.Schloissnig, M.Arumugam, S.Sunagawa, M.Mitreva, J.Tap, A.Zhu, A.Waller, D.Mende, J.Kultima, J.Martin, K.Kota, S.Sunyaev, G.Weinstock, P.Bork. 2013. Genomic variation landscape of the human gut microbiome. *Nature*. V.493. №7430. P.45–50.
3. S.Bengmark. 2012 Gut microbiota, immune development and function. *Pharmacol Res*. pii: S1043-6618(12)00166-1.
4. J.Nicholson, E.Holmes, J., R.Burcelin, G.Gibson, W.Jia, S.Pettersson. 2012 Host-gut microbiota metabolic interactions. *Science*. V.336. N6086. P.1262–7.
5. H.Flint, K.Scott, P.Louis, S.Duncan. 2012 The role of the gut microbiota in nutrition and health. *Nat Rev Gastroenterol Hepatol*. V.10. N5. P.577–89.
6. J.Kelsen, G.Wu. 2012. The gut microbiota, environment and diseases of modern society. *Gut Microbes*. V.3. N4. P.374–82.
7. H.Tilg, A.Kaser. 2011 Gut microbiome, obesity, and metabolic dysfunction. *J.Clin Invest*. V.121. N6. P.2126–32.
8. C.Thum, A.Cookson, D.Otter, W.McNabb, A.Hodgkinson, J.Dyer, N.Roy. 2012. Can Nutritional Modulation of Maternal Intestinal Microbiota Influence the Development of the Infant Gastrointestinal Tract. *J.Nutr*. V.142. N11. P.1921–1928.
9. Y.Yamaguchi, J.Park, M.Inouye. 2011. Toxin-antitoxin systems in bacteria and archaea. *Annu Rev Genet*. V.45. P.61–79.
10. V.Danilenko, O.Averina, M.Alekseeva, K.Klimina, E.Poluektova. 2012. The Toxin-Antitoxin System Gene Polymorphism As a Marker for Species and Strain Identification of the Probiotic Component of Human Microbiome. Abstracts of International Human Microbiome Congress. Paris. P.19–21.
11. Structure, function and diversity of the healthy human microbiome. 2012. *Nature*. V.486. P.207–214.
12. M.Arumugam, J.Raes, E.Pelletier, D.LePaslier. 2011. Enterotypes of the human gut microbiome. *Nature*. V.473. N7346. P.174–180.
13. X.Morgan, N.Segata, C.Huttenhower. 2013. Biodiversity and functional genomics in the human microbiome. *Trends in Genetics*. V.29. N1. P.51–58.
14. N.Segata, L.Waldron, A.Ballarini, V.Narasimhan, O.Jousson, C.Huttenhower. 2012. Metagenomic microbial community profiling using unique clade-specific marker genes. *Nat.Methods*. V.9. N8. P.811–814.
15. Klimenko, Natalia, et al. "Microbiome responses to an uncontrolled short-term diet intervention in the frame of the citizen science project." *Nutrients* 10.5 (2018): 576.
16. Tyakht, Alexander V., et al. "Human gut microbiota community structures in urban and rural populations in Russia." *Nature communications* 4 (2013): 2469.

Additional literature

Provided at the department:

Additional literature (optional)

1. C.Palmer, E.Bik, D.Digiulio, D.Relman, P.Brown. 2007. Development of the Human Infant Intestinal Microbiota. *PLoS Biol* 5:e177.
2. F.Turroni, A.Ribbera, E.Foroni, Douwe van Sinderen, M.Ventura. 2008. Human gut micribiota and bifidobacteria: from composition to functionality. *Antonie van Leeuwenhoek*. V.94. P.35–50.
3. M.Ventura, S.O’Flaherty, M.Claesson, F.Turroni, T.Klaenhammer, D.van Sinderen, and P.O’Toole. 2009. Genome-scale analyses of health-promoting bacteria: probiogenomics. *Nat.Rev.Microbiol*. V.7. P.61–71.
4. Efimova, Daria, et al. "Knomics-Biota-a system for exploratory analysis of human gut microbiota data." *BioData mining* 11.1 (2018): 25

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

Scientific bibliographic and patent databases in the field of physico-chemical biology, available on the Internet in free mode - Science Citation Index (Web of Science), Medline (PubMed), Scientific Electronic Library (NEB), Russian Patent DB of FGU FIPS and American USPAFULL patent database; email addresses of major scientific publishers who provide access to the full text of current and archival issues of these journals.

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

Internet access. For some of the lessons, you 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 studies discipline must, on the one hand, master a 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 should know the basic definitions of the discipline, be able to apply this knowledge to solve various problems.

Successful learning requires:

- visits to all classes provided by the curriculum for the discipline;
- conducting the abstract of occupations;
- intense independent work of the student.

Independent work includes:

- reading recommended literature;
- study of educational material, preparation of answers to questions intended for self-study;
- solving problems offered to students in the classroom;
- preparation for performance of tasks of the current and intermediate certification.

An indicator of possession of the material is the ability to answer questions on discipline topics without an outline.

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

Intermediate control of students' knowledge in the form of problem solving in accordance with the subject of classes is possible

Assessment funds for course (training module)

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Authors:

V.N. Danilenko, doctor of biological sciences, full professor
A.V. Tyakht, candidate of biological sciences

1. Competencies formed during the process of studying the course

Code and the name of the competence	Competency indicators
Gen.Pro.C-2 Acquire an understanding of current scientific and technological challenges in professional settings, and scientifically formulate professional objectives	Gen.Pro.C-2.3 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-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
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-1.5 Has the ability to create software tools and databases used in bioengineering and bioinformatics
	Pro.C-1.3 Make hypotheses, build mathematical models of the studied phenomena and processes, evaluate the quality of the developed model
	Pro.C-1.2 Apply fundamental knowledge of mathematics, physics, chemistry, and biology in professional settings
	Pro.C-1.1 Locate, analyze, and summarize information on current research findings within a selected subject area
	Pro.C-1.4 Apply theoretical and/or experimental research methods to a specific scientific task and interpret the obtained results

2. Competency assessment indicators

As a result of studying the course the student should:

know:

- general concepts, current views and perspectives related to the diversity of human microbiome;
- role of microbiome in health and disease;
- potential microbial biomarkers;
- methods for profiling microbiome composition;
- formats and specifications of metagenomic data;
- bioinformatic algorithms for analyzing metagenomic data;
- experimental methods of work with microorganisms.

be able to:

- quickly find required data and concepts using Internet and scientific/applied literature on biology;
- compare structure, properties and functions of biological objects;
- apply basic bioinformatic methods for human microbiome data analysis in scientific research;
- apply basic experimental methods for work with microbes in laboratory.

master:

- skills of efficiently processing large volumes of information;
- standards of designing and modeling biological tasks for exploring human microbial diversity.

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. Structure and functions of human gut microbiome.
2. Major phyla relevant for human health.
3. Dynamics of human microbiome during lifetime.
4. Metabolic interdependence of host and microbiome.

5. Diet, probiotics, prebiotics and microbiome transplantation as key ways to manipulate human microbiome.
6. Scientific-based evaluation of intervention efficacy.
7. Omics-technologies for human microbiome analysis.
8. Approaches for metagenomic reads classification.
9. Processing of amplicon and shotgun sequencing data.
10. Reference databases related to microbiome.
11. Analytical metagenomic pipelines and online platforms
12. Metagenomic assembly de novo.
13. Metabolic potential profiling.
14. Reconstruction of strain gene content and analysis of polymorphisms from shotgun metagenomic data.
15. Correlation-based methods for reconstructing genomes from metagenomes.
16. Prediction of functional potential from 16S rRNA data
17. Comparative genomics of gut microbes.
18. Toxin-antitoxin bacterial systems.
19. Statistical specifics of microbial composition features derived from metagenomic data.
20. Concepts of significance and statistical power in metagenomics.
21. Parametric and non-parametric statistical tests for metagenomic data.

During the class, interactive discussions can take place in the course chats, which will be homework. It is possible to perform patent search as an independent task. Successful completion of all tasks in the course and the completion of control slices of knowledge gives an advantage in the differential credit.

4. Evaluation criteria

1. Structure and functions of human gut microbiome.
2. Major phyla relevant for human health.
3. Dynamics of human microbiome during lifetime.
4. Metabolic interdependence of host and microbiome.
5. Diet, probiotics, prebiotics and microbiome transplantation as key ways to manipulate human microbiome.
6. Scientific-based evaluation of intervention efficacy.
7. Omics-technologies for human microbiome analysis.
8. Approaches for metagenomic reads classification.
9. Processing of amplicon and shotgun sequencing data.
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17. Comparative genomics of gut microbes.
18. Toxin-antitoxin bacterial systems.
19. Statistical specifics of microbial composition features derived from metagenomic data.
20. Concepts of significance and statistical power in metagenomics.
21. Parametric and non-parametric statistical tests for metagenomic data.

Can be left unchanged

The mark is excellent (10 points) - it is given to a student who has shown comprehensive, systematic, deep knowledge of the curriculum of the discipline, who has an interest in this subject area, has demonstrated the ability to confidently and creatively put them into practice in solving specific problems, and a free and proper substantiation of decisions.

The mark is excellent (9 points) - it is given to a student who has shown comprehensive, systematic, in-depth knowledge of the curriculum of the discipline and the ability to confidently put them into practice in solving specific problems, free and proper substantiation of the decisions made.

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

A mark is good (7 points) - it is put up for a student, if he knows the material firmly, sets it up competently and in essence, knows how to apply the knowledge gained in practice, but does not competently substantiate the results obtained.

Evaluation is good (6 points) - it is put up to a student, if he knows the material firmly, sets it up correctly and in essence, knows how to apply this knowledge in practice, but admits some inaccuracies in the answer or in solving problems.

A mark is good (5 points) - it is given to a student, if he basically knows the material, correctly and essentially sets it out, knows how to apply this knowledge in practice, but allows a sufficiently large number of inaccuracies to answer or solve problems.

Grade satisfactorily (4 points) is given to a student who has shown the fragmented, fragmented nature of knowledge, insufficiently correct formulations of basic concepts, violations of the logical sequence in the presentation of program material, but at the same time he has mastered the main sections of the curriculum necessary for further education and can apply knowledge is modeled in a standard situation.

Grade satisfactorily (3 points) - given to a student who showed the fragmented, scattered nature of knowledge, making mistakes in formulating basic concepts, disrupting the logical sequence in presenting program material, poorly masters the main sections of the curriculum required for further education and even applies the knowledge gained in a standard situation.

The rating is unsatisfactory (2 points) - 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 wording of the basic principles and does not know how to use this knowledge when solving typical tasks.

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

Can be left unchanged

The mark is excellent (10 points) - it is given to a student who has shown comprehensive, systematic, deep knowledge of the curriculum of the discipline, who has an interest in this subject area, has demonstrated the ability to confidently and creatively put them into practice in solving specific problems, and a free and proper substantiation of decisions.

The mark is excellent (9 points) - it is given to a student who has shown comprehensive, systematic, in-depth knowledge of the curriculum of the discipline and the ability to confidently put them into practice in solving specific problems, free and proper substantiation of the decisions made.

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

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The rating is unsatisfactory (2 points) - 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 wording of the basic principles and does not know how to use this knowledge when solving typical tasks.

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

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

The student is given 30 minutes to prepare. Interview with a student on a differential oral test should not exceed one astronomical hour.