Course: Immunology
Course Coordinator: Pero Lučin, MD, Ph.D., Full Professor
Department: Department of Physiology, Immunology, and Pathophysiology
Study: Integrated Undergraduate and Graduate University Study of Medicine in English
Year of the study: Second
Academic year: 2021/2022
Number of ECTS credits: 4

COURSE SYLLABUS

Course information (basic description, general information, teaching overview, required equipment, and preparation, etc.

The main aim of this course is to introduce students to the normal and pathological function of the immune system. The focus is on the explanation of physiological processes that enable normal functioning of certain subtypes of immune cells in a non-specific and specific immune response, as well as on the explanation of pathophysiological mechanisms leading to disorders of normal immune processes, as well as on the possibilities for therapeutic action to the immune response. Teaching tasks imply enabling the student to connect basic knowledge of immunology and pathophysiology of the immune system with the teaching of physiology and pathophysiology, microbiology and parasitology, pathology, infectious disease, oncology, and epidemiology (vaccination), therefore, qualifying the student to apply immunological cognition in clinical medicine.

Course content:

Class organization:
Class attendance is mandatory. The course consists of 24 hours of lectures, 18 hours of seminars, and 8 hours of practicals, which totals 50 class hours. Students are obligated to wear lab coats during practicals and have exercise protocols, where they will write measured and obtained values. Throughout seminars and practicals, the student actively discusses immune mechanisms with the lecturer. The student is obligated to prepare the material that is being discussed in seminars and practicals. The teacher evaluates student participation throughout seminars and practicals (demonstrated knowledge, understanding, the ability to set up a problem, concluding, etc.). There will be two midterm exams during the course, and a written and an oral part of the final exam at the end of classes. After completing all class activities and the final exam, the student acquires 4 ECTS credits.

Required textbooks:

Recommended for additional reading:
Course Syllabus 2021/2022 – Immunology – Study of Medicine in English

Course teaching plan

List of lectures (with titles and learning outcomes)

Lecture 1: Introduction to the immune system. Congenital and acquired immunity. Cells and tissues of the immune system, Overview of immune responses to microorganisms

Learning outcomes:
- To describe immunology as biomedical science, the concept of immunity, immune system, and immune response.
- To explain the phylogenetic relationship between innate and adaptive immunity, their physiological functions, and features.
- To name and explain the classification of adaptive immunity according to the mode of acquisition and executive mechanisms (humoral and cellular immunity).
- To explain forms of immune activity (immune response, immune non-reactivity).
- To describe the morphological, physical, and biological properties of cells of the immune system.
- To describe the anatomy and function of lymphatic tissues (bone marrow, thymus, lymphatic system, lymph nodes, spleen, and regional lymphatic systems).
- To name the subtypes of lymphocytes, primary differentiation markers for individual subtypes of immune cells, and to describe their function.
- To name the subtypes of T and B lymphocytes and to describe their function.
- To describe the distribution and recirculation of lymphocytes in the body.
- To describe the function of chemokines, chemokine receptors, and adhesion molecules on leukocytes and endothelial cells.

MATERIAL:

Lecture 2: Major Histocompatibility Complex Molecules and Antigen Presentation to T Lymphocytes

Learning outcomes:
- To describe the mechanisms of antigen capture and the function of precursor cells.
- To explain the intercellular interactions of immune cells, especially precursor cells, and T lymphocytes.
- To name the classification and to explain the function of adhesion, coreceptor, and costimulatory molecules.
- To describe the system of tissue antigens, their classification, structure, and function of MHC group I and II antigens, and distribution in the organism.
- To understand the MHC gene structure (polygeny and polymorphism).
- To describe the role of the MHC gene in determining immunoreactivity characteristics (in controlling the response to individual antigens, in the appearance of autoimmune diseases, in the appearance of high alloreactivity).
- To explain the processing of another’s antigen and the mechanism of its binding to MHC class I and II molecules.

MATERIAL:

Lecture 3: Antigen Recognition in The Adaptive Immune System

Learning outcomes:
- To define and describe the immune receptor family.
- To describe the structure of the receptor for the T lymphocyte antigen.
- To understand the basic principles of antigen-antibody binding, the affinity and avidity of binding recognition molecules to an antigen, electrostatic forces in the antigen-antibody reaction.
- To describe the term antigen, classification of antigens, antigen determinant (epitope), and its forms.
- To define the term immunogenicity, the factors that affect the antigen immunogenicity.
- To describe the principles of antigen recognition.
- To describe the principles of cytosolic and vesicular antigen recognition.
- To describe the course of clone specialization of B lymphocytes for a particular bone marrow specificity.

MATERIAL:

Lecture 4: T Cell-Mediated Immunity

Learning outcomes:
- To understand the mechanisms of T lymphocyte activation (signal transduction to the cell and their effects upon antigen receptor stimulation).
- To describe the inhibitory receptors of T and B lymphocytes and NK cells.
To describe the structure and classification of cytokine receptors, the mechanism of signal transduction by cytokine receptors.
To describe the processes of T lymphocyte development and the role of the thymus in them.
To understand the multigenic organization of antigen receptor genes, the rearrangement mechanisms, and the assembly of functioning genes for the variable receptor region.

**MATERIAL:**

**Lecture 5: Effector Mechanisms of T Cell-Mediated Immunity**

Learning outcomes:
To explain the mechanisms and main features of cellular immunity.
To describe the subgroups of effector CD4+ T cells.
To explain macrophage activation by sensitized T lymphocytes of TH1 subtype.
To explain the development and function of T lymphocytes of TH2 subtype.
To explain the development and function of T lymphocytes of the TH17 subtype.
To explain the characteristics and function of T-γδ cells and NKT cells.
To describe the characteristics and to explain the executive roles of cytotoxic T lymphocytes and the mechanism of target-cell killing.

**MATERIAL:**

**Lecture 6: Humoral Immune Responses**

Learning outcomes:
To describe the mechanisms of antigen recognition and antigen activation of B lymphocytes.
To describe the morphology of B lymphocyte differentiation, plasma cell, and memory cell formation in T lymphocyte-dependent responses.
To understand the gene mechanism for heavy-chain class switching.
To understand the genetic mechanisms that are the source of antibody diversity (creating a repertoire of antibody specificity).
To understand the affinity immunoglobulin maturation and the switching of IgM to IgG, and the mechanism by which a single plasma cell produces one type of immunoglobulin (allelic exclusion).
To explain the kinetics of antibody formation in primary and secondary immune response, distribution in the organism, and dynamics of antibody degradation.

**MATERIAL:**

**Lecture 7: Effector Mechanisms of Humoral Immunity**

Learning outcomes:
To explain the functions and biological properties of individual antibody classes.
To explain the mechanism of antibody-dependent cellular cytotoxicity.
To describe the natural killer (NK) activity, receptors on the surface of NK cells, and killer activity activated by lymphokines (LAK).
To describe the classical, lectin, and alternative complement activation pathway.
To describe the biological role of the complement and regulation of complement activation.

**MATERIAL:**

**Lecture 8: Specialized Immunity at Epithelial Barriers and in Immune Privileged Tissues**

Learning outcomes:
To describe the structure of the immune system at the epithelial barriers.
To describe the immunity of the digestive system and other mucous membranes.
To describe the function of Microfold (M) cells.
To explain the induction of the mucosal TH2 immune response.
To explain the induction of the mucosal inflammatory TH1 immune response.
To explain the structure, function, and secretion of IgA antibodies.
To explain the function of γδ T lymphocytes.
To explain the function of immunoregulatory cytokines (TGF-β, IL-10) and regulatory T lymphocytes in mucosal immunity.
To describe the immunity of the skin and immune-privileged tissues.
Material:

Lecture 9: Immunologic Tolerance and Autoimmunity
Learning outcomes:
To explain the term immunologic tolerance, the mechanisms for establishing tolerance at birth, and in adulthood.
To describe the factors that affect tolerance (maturity of the immune system, antigen features, antigen dose, and antigen intake pathway).
To explain the mechanisms of central (perinatal) and peripheral immunologic tolerance (disappearance of clones, clonal anergy, immune neglect, immune-privileged sites, redirection of the immune response, facilitative antibodies, and blocking factors), and mechanisms of immunologic tolerance termination.
To describe the active suppressive mechanism at the periphery, the suppressive cells, and the activity of suppressive cytokines.
To describe the immunologic relationship between a mother and a child and the mechanisms that prevent fetal rejection.
To explain the term autoimmunity, mechanisms for autoimmunity occurrence (the role of autoantigen, the role of external antigen as an immunogenic carrier, to describe the cross-reaction).
To describe the features of autoreactive T and B lymphocyte occurrence at the periphery.
To explain the pathogenic mechanisms of autoimmunity and the mechanisms of tissue and organ damage by antibodies, antigen-antibody complexes, and T lymphocytes.
To describe autoimmune diseases and their classification, genetic factors of autoimmunity, the influence of gender, age, infections, and immunologic disorders on the occurrence of autoimmunity.
To name the principles of treating autoimmune diseases.

Material:

Lecture 10: Hypersensitivity Disorders
Learning outcomes:
To define the term immunologic hypersensitivity, to name the classification of immunologic hypersensitivity, and to describe their main characteristics.
To explain the immune diseases caused by antibodies.
To explain hypersensitivities caused by immunocomplexes.
To explain diseases caused by T lymphocytes.
To explain cell-dependent hypersensitivity features, tuberculin response, and contact hypersensitivity.
To describe the pathogenesis and treatment strategies of selected immune diseases (SLE, RA, multiple sclerosis, type 1 diabetes, inflammatory bowel diseases).

Material:

Lecture 11: Allergy
Learning outcomes:
To define the term allergy.
To describe the formation of IgE-class antibodies.
To explain the role of TH2 cells, mast cells, basophils, and eosinophils in allergic reactions.
To explain anaphylactic hypersensitivity and its forms.
To describe IgE-class antibodies and receptors for the Fc fragment of IgE, to describe target cell degranulation, as well as secretion and function of mediator substances (primary and secondary mediators).
To describe allergic diseases in humans and the principles of their treatment.

Material:

Lecture 12: Immunity to Tumors
Learning outcomes:
To describe tumor antigens, their subtypes, properties, and methods for demonstrating tumor antigens and human tumor antigens.
To describe the immune response to the tumor, and subtypes of immune resistance to a tumor (cellular and humoral immunity).
To understand the theory of immune surveillance over tumor cells, and tumor suppression mechanisms to immune defense.
To describe the tumor immunotherapy and its subtypes.
To describe the role of innate and adaptive immunity in promoting tumor growth.

MATERIAL:

Lecture 13: Congenital and Acquired Immunodeficiencies
Learning outcomes:
To define immunodeficiency and its classification.
To explain primary immunodeficiencies and disorders of their immune effectors (deficiency of B lymphocytes, T lymphocytes, phagocytes, complement system, and associated T and B lymphocyte deficiencies).
To explain secondary immunodeficiencies and the reasons for their occurrence.
To describe the structure and biological behavior of HIV, the way of transmission, the mechanism by which it causes AIDS, AIDS (incubation, seroconversion, symptoms, and the course of the disease).

MATERIAL:

List of seminars (with titles and learning outcomes)

Big seminar 1: Innate Immunity
Learning outcomes:
To describe the development and the mechanisms for innate immunity (anatomical, physiological, cellular, inflammatory obstacles).
To name the cellular receptors for molecular pattern recognition and their function in innate immunity.
To describe the mechanism of chemotaxis, endocytosis, and phagocytosis, and decomposition of phagocytic particles.
To describe classical, lectin, and alternative complement activation pathways.
To describe the biological role of the complement.
To describe the regulation of complement activation.
To define inflammation and to describe the mechanism of inflammatory response.
To describe the mechanism of innate antiviral response.

MATERIAL:

Big seminar 2: Immunity to Microbes
Learning outcomes:
To explain the terms parasitism, pathogenicity, virulence, and infection.
To describe the features of the immune response (non-specific and specific immunity) to pathogenic microbes.
To explain the features of specific immunity in infections, specific active immunity acquired naturally, and artificially triggered specific active immunity, the concept, and principle of vaccination and forms of specific passive immunity (acquired naturally and artificially triggered specific passive immunity).
To describe the basic features of viruses, bacteria, single-cell and multiple-cell parasites, and infections caused by these parasites.
To explain the features of innate and adaptive immunity to extracellular and intracellular bacteria, fungi, viruses, and single-cell and multiple-cell parasites.

MATERIAL:

Big seminar 3: Transplantation Immunology
Learning outcomes:
To define levels of immunogenic compatibility.
To explain the mechanisms of transplant response, to name the evidence that transplant response is an immune response.
To name and describe the forms of transplant response depending on the rate and the rejection mechanism, and to describe the reaction of mixed lymphocytes.
To explain the features of non-lymphatic tissue and organ transplantation and xenogeneic organ transplantation.
To explain the features of lymphatic tissue transplantation (bone marrow), the reaction of the graft against the receiver, and the transplant disease.

MATERIAL:
Big seminar 4: Immunosuppression; Vaccination

Learning outcomes:
- To describe the possibilities for action on the intensity of the immune response (immunosuppression, immunostimulation).
- To explain immunosuppression, mechanisms for inducing specific (suppression of immune response by antigens, antibodies, antilymphocyte serum, monoclonal antibodies) and non-specific (corticosteroids, cytostatics) immunosuppression.
- To explain immunostimulation procedures by vaccination for protection against infection.
- To name the properties of vaccines and their types.
- To explain vaccination by weakened pathogens.
- To explain vaccination by conjugated vaccines.
- To explain vaccination against bacterial toxins.
- To explain vaccination by recombinant, alive viral, and DNA vaccines.
- To describe the methods of genetic engineering in methods of preparing antitumor vaccines and enhancement of antitumor immune response.
- To name the types of adjuvants and to explain the principles of their action.

MATERIAL:

List of practicals (with titles and learning outcomes)


Learning outcomes:
- Discussion: Content of Lecture 1 and Big seminar 1
- Focussed discussion: Coronavirus infections

MATERIAL:

Seminar 2 + Practical 2 (2:1): Antibodies and Antigens; Lymphocyte Development and Antigen Receptor Gene Rearrangement;

Learning outcomes:
- Discussion: Content of Lecture 3
- Focussed discussions: Immunofluorescence and immunodiagnostics; Enzyme-linked immunosorbent assay (ELISA); Flow cytometry

MATERIAL:

Seminar 3 + Practical 3 (2:1): Major Histocompatibility Complex Molecules and Antigen Presentation to T Lymphocytes; Immune Receptors and Signal Transduction; Activation of T Lymphocytes; Differentiation and Functions of CD4+ and CD8+ Effector T Cells

Learning outcomes:
- Discussion: Content of Lecture 2, 4, and 5
- Focussed discussion: Cross presentation, activation of pre-cytotoxic T lymphocytes, and activation of immune memory

MATERIAL:

Seminar 4 + Practical 4 (2:1): Infection immunity

Learning outcomes:
- Discussion: Content of Big seminar 2
Focussed discussion: **Immunopathogenesis of hepatitis B infection**
To define the principles of primary and secondary response to viral infection. Kinetics of IgM and IgG antibody responses.
To understand and explain the principles of the occurrence of acute and chronic responses to viral infection.
To list, understand, and describe the immune mechanisms in the acute and chronic course of hepatitis B infection.
To understand the principles of immune exhaustion and the transition of the disease into a chronic course.
**MATERIAL:**

**Seminar 5 + Practical 5 (1:2): Hypersensitivity Disorders; Allergy**
Learning outcomes:
- Discussion: Lecture 10, and 11
- Focussed discussions: **Anaphylactic reaction; Serum sickness**
  - To define the term anaphylactic hypersensitivity.
  - To know, list and describe the immune effects of the immune mechanisms involved in anaphylactic hypersensitivity (cells, primary and secondary mediators).
  - To explain the mechanisms of immune hypersensitivity to penicillin.
**MATERIAL:**

**Seminar 6 + Practical 6 (1:2): Immunologic Tolerance and Autoimmunity; Specialized Immunity at Epithelial Barriers and in Immune Privileged Tissues**
Learning outcomes:
- Repetition: Lecture 8, and 9
- Focussed discussion: **Inflammatory bowel disease; Systemic lupus erythematosus; Rheumatoid arthritis; Insulin-dependent diabetes mellitus**
**MATERIAL:**
Exam (exam taking, detailed exam description of the oral/written/practical part, point distribution, grading criteria):

ECTS grading system

Student grading will be conducted according to the current Ordinance on Studies of the University of Rijeka and the Ordinance on Student Grading at the Faculty of Medicine in Rijeka.

Student work and achievement are assessed and graded during the course, which is the basis for the final grade. Student work and competencies are evaluated during classes with a maximum of 70-grade points and up to 30-grade points at the final exam, which totals 100-grade points. Students are graded according to the ECTS (A-E) and numerical system (1-5). Grading, according to the ECTS system, is conducted according to the absolute redistribution, as well as according to the graduate grading criteria.

I. The following components are evaluated during the course (maximum of 70-grade points):

1) Attendance (up to 6-grade points)

Attendance at all forms of teaching (lectures, training seminars, practicals):

<table>
<thead>
<tr>
<th>Attendance</th>
<th>Grade points</th>
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</thead>
<tbody>
<tr>
<td>95-100%</td>
<td>6-grade points</td>
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<tr>
<td>90%-94,9%</td>
<td>5-grade points</td>
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<tr>
<td>85%-89,9%</td>
<td>4-grade points</td>
</tr>
<tr>
<td>80%-84,9%</td>
<td>3-grade points</td>
</tr>
<tr>
<td>75%-79,9%</td>
<td>2-grade points</td>
</tr>
<tr>
<td>70%-74,9%</td>
<td>1-grade points</td>
</tr>
</tbody>
</table>

2) Adopted knowledge (up 64 points)

During classes, acquired knowledge will be evaluated by two midterm exams (MTE) comprising 70 questions, which will take place on April 16th, 2021 (first midterm exam), and on June 1st, 2021 (second midterm exam). A student may obtain up to 32-grade points on each exam:

<table>
<thead>
<tr>
<th>Correct answers</th>
<th>Grade points</th>
<th>Correct answers</th>
<th>Grade points</th>
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<tr>
<td>68-70</td>
<td>32</td>
<td>68-70</td>
<td>32</td>
</tr>
<tr>
<td>65-67</td>
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<td>62-64</td>
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<td>57-58</td>
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<td>57-58</td>
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<td>55-56</td>
<td>27</td>
<td>55-56</td>
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<tr>
<td>51-52</td>
<td>25</td>
<td>51-52</td>
<td>25</td>
</tr>
</tbody>
</table>

Students who fail to earn a minimum number of points one or both MTEs can repeat one or both MTEs, which will be organized in February, between the first and second term of the Final exam. At repeated MTEs, a student can acquire grade points according to the above table and correct/improve the final score.

Improvement of the overall performance during the course. Students who have achieved sufficient points on a regular MTEs can improve their final score at the repeated MTE/MTEs. The repeated MTEs (writing the test) will be organized at the Faculty of Medicine under controlled conditions: either using traditional printed tests or using the Merlin platform in the Faculty's computer classroom.

Additional acquisition of minimum conditions for the Final exam. Students who failed to acquire a minimum score on one of the MTEs can earn minimum grades required to access the Final exam. This will be organized in early September. The acquisition of minimum grade points will be carried out by writing one or both tests covering the material of the first and/or second MTE. The acquisition of minimum grade points (writing a test) will be organized at the Faculty of Medicine under controlled conditions: either using traditional printed tests or using the Merlin platform in the Faculty's computer classroom. On tests for the acquisition of minimum conditions, students cannot earn additional grade points. With a positive test result (more than 50%), a student can earn the minimum number of grade points (17.5+17.5) and can access the Final exam. If it is not possible to approach the Faculty due to the
Epidemiologic situation, additional acquisition of minimum conditions will be carried out by oral examination of the required materials using MS teams or Google Meets. At the oral check, students can achieve a positive result and earn the minimum number of points needed to enter the Final exam.

II. Final exam (up to 30-grade points)
Students who obtained 35-70 grade points during classes are obligated to access the final exam at which they may obtain additional grade points. The final exam consists of a multiple-choice questions test and an oral part. Students who obtained less than 35-grade points during classes or were absent for more than 30% of classes are not allowed to access the Final exam (insufficient F).
Students can obtain 15-30 grade points at the final exam. The final exam consists of an oral and a written part, where students are expected to show at least 50% of knowledge, skills, and competencies. A student who demonstrates at least 50% of knowledge, skills, and competencies at the written and the oral part of the exam is credited with points according to the achieved result, which is added to the grade points obtained during classes.

At the written part of the final exam, a student can obtain 13-25 grade points according to the table:

<table>
<thead>
<tr>
<th>Correct answers</th>
<th>Grade points</th>
<th>Correct answers</th>
<th>Grade points</th>
</tr>
</thead>
<tbody>
<tr>
<td>96-100%</td>
<td>25</td>
<td>74-75,9%</td>
<td>18</td>
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<td>92-95,9%</td>
<td>24</td>
<td>70-73,9%</td>
<td>17</td>
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<tr>
<td>88-91,9%</td>
<td>23</td>
<td>66-69,9%</td>
<td>16</td>
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<tr>
<td>84-87%</td>
<td>22</td>
<td>62-65,9%</td>
<td>15</td>
</tr>
<tr>
<td>80-83,9%</td>
<td>21</td>
<td>56-61,9%</td>
<td>14</td>
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<td>78-79,9%</td>
<td>20</td>
<td>55-55,9%</td>
<td>13</td>
</tr>
<tr>
<td>76-77,9%</td>
<td>19</td>
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</tr>
</tbody>
</table>

At the oral part of the final exam, a student can obtain 1-5 grade points that are divided into 5 categories (1, 2, 3, 4, 5).

III. The final grade (maximum of 100-grade points)
The final grade represents the sum of all grade points obtained during classes and at the final exam. It is based on the absolute redistribution according to the following scale:

| 90-100 grade points | A | excellent (5) |
| 75-89,99 grade points | B | very good (4) |
| 60-74,99 grade points | C | good (3) |
| 50-59,99 grade points | D | sufficient (2) |
| less than 50-grade points | E | insufficient (1) |

Other important information regarding the course:

Course content and all information regarding the course, including exam dates, can be found on the SharePoint platform of the Department of Physiology and Immunology on the following website: [https://spp.uniri.hr/ss_medri/katedre/427](https://spp.uniri.hr/ss_medri/katedre/427) - can be accessed via an AAI address.
## Course Syllabus 2021/2022 – Immunology – Study of Medicine in English

### COURSE SCHEDULE for the academic year 2020/2021

<table>
<thead>
<tr>
<th>Date</th>
<th>Course type</th>
<th>Time</th>
<th>Place</th>
<th>Lecturer</th>
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<tbody>
<tr>
<td>28. 2. 2022</td>
<td>L1</td>
<td>9,15-11,00</td>
<td>online</td>
<td>Prof. dr. sc. Pero Lučin</td>
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<tr>
<td>7. 3. 2022</td>
<td>BS1</td>
<td>9,15-11,00</td>
<td>online</td>
<td>Prof. dr. sc. H. Mahmutefendić Lučin</td>
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<tr>
<td>9.3. 2022</td>
<td>S1/P1 A</td>
<td>13,15-16,00</td>
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<td>Doc. dr. sc. Tamara Gulić</td>
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<td>9.3. 2022</td>
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<td>Doc. dr. sc. Zlatko Trobonjača</td>
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<tr>
<td>14. 3. 2022</td>
<td>L2</td>
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<td>Prof. dr. sc. H. Mahmutefendić Lučin</td>
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<tr>
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<td>online</td>
<td>Prof. dr. sc. Pero Lučin</td>
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<td>6. 4. 2022</td>
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<tr>
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<td>2. 5. 2022</td>
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### FINAL EXAM DATES

1. 13. 06. 2022.
2. 27. 06. 2022.
3. 11. 07. 2022.
4. 07. 09. 2022.
5. 21. 09. 2022.