Faculty of Medicine in Rijeka

**Curriculum**
**2026/2027**

For course

# The Role of HLA Genes in Organ Transplantation and Diagnostics of Autoimmune Diseases

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|---|---|
| Study program: | **Medical Studies in English (R)** (elective)<br>University integrated undergraduate and graduate study |
| Department: | **Department of Clinical Laboratory Diagnostics** |
| Course coordinator: | **doc. dr. sc. Katalinić Nataša, dr. med.** |
| Year of study: | **3** |
| ECTS: | **1.5** |
| Incentive ECTS: | **0 (0.00%)** |
| Foreign language: | **Possibility of teaching in a foreign language** |

## Course information:

Kolegij **Uloga gena HLA u transplantaciji organa i dijagnostici autoimunih bolesti** je izborni kolegij na trećoj godini Integriranog preddiplomskog i diplomskog sveučilišnog studija Medicina i sastoji se od 5 sati predavanja, 5 sati vježbi i 15 sati seminara, ukupno 25 sati, 1,5 ECTS. Kolegij se izvodi u prostorijama Medicinskog fakulteta i Laboratorija za tipizaciju tkiva Kliničkog bolničkog centra Rijeka.

**Cilj kolegija** je usvajanje osnovnih znanja o glavnom sustavu tkivne podudarnosti u čovjeka odnosno sustavu HLA (Hum Leucocyte Antygen) koji predstavlja najpolimorfniji genski sustav u čovjeka.

**Sadržaj kolegija:**

Upoznati sustav HLA i njegovu ulogu u presadbi organa i koštane srži, u genetici, u određivanju spornog očinstva, u sudsk medicini, u ispitivanju nasljeđivanja, u ispitivanju sklonosti prema različitim bolestima, u transfuzijskom liječenju.

**Izvođenje nastave:**

**Nastava se izvodi u obliku predavanja, seminara i vježbi. Predviđeno vrijeme trajanja nastave je ukupno 1 - tjedna ovisno o slobodnim terminima studenata. Tijekom seminara i vježbi nastavnik sa studentima raspravl o temama vezanim uz kolegij i izvodi različite vježbe kako bi im približio složenost i polimorfizam sustava HLA. Na kraju nastave održat će se obavezni pismeni (prema potrebi usmeni) završni ispit. Izvršavanjem svi nastavnih aktivnosti te pristupanjem obveznom kolokviju i završnom ispitu student stječe 1,5 ECTS bodova**

## List of assigned reading:


NK Mehra (ed.). The HLA Complex in Biology and Medicine: A Resource Book. New Delhi: Jaypee Brothers Medical Publisher Ltd, 2010

Janeway C.A., Travers P., Walport M., Shlomchik M.J. Immunobiology 5, The Immune system in health and disease. New York: Garland Publishing, 2001.


## List of optional reading:


Choo SY. The HLA System: Genetics, Immunology, Clinical Testing, and Clinical Implications. Yonsei Med J. 2007 Feb 28;48(1):11-23.

Batool Mutar Mahdi BM. A Glow of HLA Typing in Organ Transplantation. Clin Transl Med. 2013 Feb 23;2(1):6.

Mosaad YM. Clinical Role of Human Leukocyte Antigen in Health and Disease. Scand J Immunol. 2015 Oct;82(4):283-306.

Brown CJ, Navarrete CV. Clinical Relevance of the HLA System in Blood Transfusion. Vox Sang. 2011 Aug;101(2):93-105.

Časopisi: HLA, Human Immunology, Clinical Kidney Journal

## Curriculum:

### Practicals list (with titles and explanation):

#### V1. Isolation of lymphocytes

Principles of cell isolation, practical performance of the test using density gradient, determination of the number and viability of lymphocytes, adjustment of lymphocyte suspension for testing, freezing and storage of cell suspension.

#### V2. Complement-dependent lymphocytotoxicity test – HLA typing

Practical performance of HLA class I antigen typing, interpretation of results.

#### V3. Isolation of DNA

Manual isolation of DNA from peripheral blood samples with a commercial kit. Determination of DNA concentration and purity by spectrophotometer.

#### V4. HLA typing by PCR-SSP method

Low resolution HLA-typing using commercial diagnostic kits.

#### V5. HLA typing by PCR-SSP method – gel electrophoresis, interpretation of results

Electrophoresis of DNA samples amplified by PCR-SSP reaction in agarose gel - principle, practical execution of the test. Interpretation of HLA class I and class II typing results.

### Lectures list (with titles and explanation):

#### P1 . Introduction to the HLA System and Historical Review

Objectives:

- To understand the basic role of the immune system
- To define MHC and HLA systems
- To explain the main functions of HLA molecules
- To describe the basic principles of HLA inheritance (genotypes, haplotypes, co-dominant expression)
- To get familiar with HLA nomenclature (antigen vs. allele designation)

#### P2. Structure and Organization of the HLA System

**Objectives:**

- to distinguish between HLA Class I, II, and III
- to explain genetic organization
- to understand molecular (antigenic) structure

#### P5. HLA associated diseaseas

**Objectives:**

- to understand the role of HLA system in disease susceptibility
- to explain the mechanisms linking HLA molecules to autoimmune and other diseases
- to describe common HLA-associated diseases (e.g., autoimmune, infectious, pharmacogenetic associations)
- to understand the role of HLA typing in disease diagnostics and risk assessment
- to interpret basic clinical relevance of HLA-disease associations
- to recognize the importance of HLA in personalized medicine

#### P3. HLA Typing Methods

**Objectives:**

- to understand the differences between serological and molecular HLA typing methods
- to explain the basic principles of laboratory testing used in HLA typing
- to describe the workflow of key serological methods (e.g., complement-dependent cytotoxicity, CDC)

to describe the principles of major molecular techniques (PCR-SSP, PCR-SSO, qPCR, SBT)
- to compare the advantages and limitations of serological versus molecular approaches
- to interpret basic results of HLA typing assays (e.g., positive/negative reactions, allele identification)
- to recognize the clinical relevance of different typing methods in transplantation and diagnostics

**P4. HLA in Organ Transplantation**

**Objectives:**

- to understand the importance of HLA matching in organ transplantation
- to explain the immunological mechanisms of graft rejection (cellular and humoral)
- to describe the concept of HLA mismatches and their impact on graft survival
- to analyze the relationship between the number of mismatches and transplant outcomes
- to explain the role of HLA antibodies in transplant rejection
- to describe the components of pre-transplant evaluation (HLA typing, antibody screening, crossmatch)
- to recognize strategies used to improve transplant success (e.g., matching, desensitization, allocation systems)
- to understand the role of international organizations (e.g., Eurotransplant) in organ allocation

**Seminars list (with titles and explanation):**

**SEM 1. Clinical Role of HLA in Health and Disease**

By the end of this seminar, student will be able to:

- Describe the structure, function, and genetic diversity of the human leukocyte antigen (HLA) system.
- Explain the role of HLA in immune recognition, transplantation, and disease susceptibility.
- Analyze clinical scenarios where HLA typing and antibody testing inform diagnosis, treatment, and patient management.
- Apply knowledge of HLA in interpreting laboratory results and making evidence-based clinical decisions.

**SEM 2. Role of HLA in Autoimmune Disease**

By the end of this seminar, student will be able to:

- Explain the association between specific HLA alleles and susceptibility to autoimmune diseases.
- Describe the immunological mechanisms by which HLA molecules contribute to autoimmunity.
- Analyze clinical cases where HLA typing informs diagnosis, risk assessment, or therapeutic decisions in autoimmune conditions.
- Evaluate current research on HLA-disease associations and their implications for personalized medicine.

**SEM 3. Relevance of the HLA system in blood transfusion**

By the end of this seminar, student will be able to:

- Describe the role of the HLA system in immune recognition relevant to blood transfusion.
- Explain how HLA incompatibility can contribute to transfusion-related complications, including platelet refractoriness and alloimmunization.
- Analyze clinical scenarios where HLA typing improves transfusion safety and efficacy.
- Evaluate strategies to prevent and manage HLA-mediated transfusion reactions.
- Apply HLA knowledge to interpret laboratory results and optimize transfusion therapy for patients.

**SEM 4. The HLA System and Histocompatibility Testing for Organ Transplantation**

By the end of this seminar, student will be able to:

- Describe the role of HLA compatibility in organ and tissue transplantation.
- Explain how HLA mismatches and donor-specific antibodies affect graft survival and rejection risk.
- Analyze clinical cases to understand the impact of HLA typing on donor selection and post-transplant management.
- Evaluate laboratory strategies for HLA antibody detection and their application in transplant immunology.
- Apply HLA knowledge to optimize patient outcomes and minimize immunological complications after transplantation.

**SEM 5. HLA and Kidney Transplantation**

By the end of this seminar, student will be able to:

Describe the role of the HLA system in kidney transplantation and graft survival.
- Explain how HLA compatibility and donor-specific antibodies influence rejection risk and patient outcomes.
- Analyze clinical scenarios to interpret HLA typing results for donor selection and post-transplant management.
- Evaluate laboratory methods for HLA antibody detection and their application in kidney transplant immunology.
- Apply knowledge of HLA in kidney transplantation to optimize patient care and minimize immunological complications.

**SEM 6. HLA and Hematopoietic Stem Cell Transplantation**

By the end of this seminar, student will be able to:

- Describe the role of HLA compatibility in hematopoietic stem cell transplantation (HSCT) and its impact on graft-versus-host disease and transplant outcomes.
- Explain the processes of HLA matching for both related and unrelated donor registries, including international stem cell donor banks.
- Analyze clinical cases to understand how HLA typing guides donor selection, transplantation strategy, and post-transplant monitoring.
- Evaluate laboratory techniques for HLA typing and antibody detection specific to HSCT.
- Apply knowledge of HLA and donor registries to optimize patient outcomes and reduce immunological complications in HSCT.

**SEM 7. HLA and Liver Transplantation**

By the end of this seminar, participants will be able to:

- Describe the role of HLA compatibility in liver transplantation and its impact on graft survival and rejection risk.
- Analyze clinical scenarios to interpret HLA typing results for donor selection and post-transplant management.
- Evaluate laboratory methods for HLA and antibody detection specific to liver transplantation.
- Apply knowledge of HLA in liver transplant immunology to optimize patient care and minimize immunological complications.

**SEM 8. Cardiothoracic Transplantation**

By the end of this seminar, participants will be able to:

- Describe the role of HLA compatibility in heart and lung transplantation and its impact on graft survival and rejection.
- Explain how donor-specific HLA antibodies contribute to antibody-mediated rejection and long-term outcomes in cardiothoracic transplant recipients.
- Analyze clinical scenarios to interpret HLA typing and antibody testing results for optimal donor selection and post-transplant management.
- Evaluate laboratory methods for HLA and antibody detection specific to heart and lung transplantation.
- Apply knowledge of HLA immunology to improve patient care and minimize immunological complications in cardiothoracic transplantation.

**SEM 9. Immunogenetics of xenotransplantation**

By the end of this seminar, student will be able to:

- Describe the immunogenetic principles relevant to xenotransplantation and species-specific HLA-like antigens.
- Explain the role of preformed and induced antibodies in xenograft rejection.
- Analyze strategies for immunogenetic matching and genetic modification to reduce immune-mediated rejection in xenotransplantation.
- Evaluate laboratory techniques for detecting antibodies and immune responses in xenotransplant models.
- Apply knowledge of immunogenetics to anticipate and manage immunological challenges in clinical and experimental xenotransplantation.

**SEM 10. HLA Genetics – Celiac Disease**

By the end of this seminar, participants will be able to:

- Describe the genetic basis of celiac disease, with emphasis on HLA-DQ2 and HLA-DQ8 alleles.
- Explain how HLA genotype contributes to susceptibility and pathogenesis of celiac disease.
- Analyze the role of HLA testing in the diagnosis, risk assessment, and family screening for celiac disease.
- Evaluate current research on HLA associations and their implications for personalized management of celiac patients.
- Apply HLA genetic knowledge to interpret laboratory results and inform clinical decision-making in celiac disease.

**SEM 11. HLA Genetics – Rheumatoid arthritis**

By the end of this seminar, participants will be able to:

- Describe the role of HLA genes, particularly HLA-DR alleles, in susceptibility to rheumatoid arthritis (RA).
- Explain the immunogenetic mechanisms by which HLA contributes to disease pathogenesis and severity.
- Analyze the use of HLA typing in risk assessment, diagnosis, and prognosis of RA patients.
- Evaluate current research on HLA associations with RA and their implications for personalized therapy.
- Apply HLA genetic knowledge to interpret laboratory findings and support clinical decision-making in rheumatoid arthritis.

**SEM 12. HLA Genetics – Type 1 diabetes mellitus**

By the end of this seminar, participants will be able to:

- Describe the role of HLA genes, particularly HLA class II alleles, in susceptibility to type 1 diabetes mellitus (T1DM).
- Explain the immunogenetic mechanisms by which HLA contributes to autoimmune beta-cell destruction.
- Analyze the use of HLA typing in assessing risk, early diagnosis, and prediction of type 1 diabetes in at-risk individuals.
- Evaluate current research on HLA associations with T1DM and their implications for prevention and personalized medicine.
- Apply HLA genetic knowledge to interpret laboratory and genetic testing results in the clinical management of T1DM.

**SEM 13. HLA Genetics – Ankylosing Spondylitis**

By the end of this seminar, participants will be able to:

- Describe the role of HLA genes, particularly HLA-B27, in susceptibility to ankylosing spondylitis (AS).
- Explain the immunogenetic mechanisms linking HLA-B27 to disease pathogenesis.
- Analyze the use of HLA typing in diagnosis, risk assessment, and family screening for ankylosing spondylitis.
- Evaluate current research on HLA associations with AS and their implications for personalized patient management.
- Apply HLA genetic knowledge to interpret laboratory results and support clinical decision-making in ankylosing spondylitis.

**SEM 14. HLA Genetics – Multiple Sclerosis**

By the end of this seminar, student will be able to:

- Describe the role of HLA genes, particularly HLA-DR and HLA-DQ alleles, in susceptibility to multiple sclerosis (MS).
- Explain the immunogenetic mechanisms by which HLA contributes to autoimmune demyelination in MS.
- Analyze the use of HLA typing in risk assessment, prognosis, and understanding disease heterogeneity in MS patients.
- Evaluate current research on HLA associations with MS and their implications for personalized medicine and therapeutic strategies.
- Apply HLA genetic knowledge to interpret laboratory and genetic data in the clinical management of multiple sclerosis.

**SEM 15. HLA and HIV infection**

By the end of this seminar, participants will be able to:

- Describe the role of HLA genes in susceptibility, progression, and immune response to HIV infection.
- Explain how specific HLA alleles influence viral control, disease progression, and treatment outcomes.
- Analyze clinical and research data to understand the impact of HLA variability on HIV pathogenesis.
- Evaluate laboratory methods for HLA typing relevant to HIV studies and patient management.
- Apply knowledge of HLA in interpreting patient immunogenetic profiles and informing personalized treatment strategies in HIV infection.

## Student obligations:

Studenti su obvezni redovito pohađati i aktivno sudjelovati u svim oblicima nastave.

## Exam (exam taking, description of the written/oral/practical part of the exam, point distribution, grading criteria):

Ocjenjivanje studenata provodi se prema važećem Pravilniku o studijima Sveučilišta u Rijeci (odobrenog od Senata Sveučilišta u Rijeci), te prema **Pravilniku o ocjenjivanju studenata na Medicinskom fakultetu u Rijeci** (usvojenom na Fakultetskom vijeću Medicinskog fakulteta u Rijeci).
Rad studenata vrednovat će se i ocjenjivati tijekom izvođenja nastave, te na završnom ispitu. Od ukupno 100 bodova, tijekom nastave student može ostvariti **70 bodova**, a na završnom ispitu **30 bodova.**
Ocjenjivanje studenata vrši se primjenom ECTS (A-E) i brojčanog sustava (1-5). Ocjenjivanje u ECTS sustavu izvodi se apsolutnom raspodjelom, te prema diplomskim kriterijima ocjenjivanja.

Od maksimalnih 70 ocjenskih bodova koje je moguće ostvariti tijekom nastave, student mora sakupiti minimum od 40 ocjenskih bodova da bi pristupio završnom ispitu. Studenti koji sakupe manje od 40 ocjenskih bodova imat će priliku za jedan popravni međuispit te, ako na tom međuispitu ispitu zadovolje, moći će pristupiti završnom ispitu. Studenti koji sakupe između 40 i 49,9 ocjenskih bodova (FX ocjenska kategorija) imaju pravo izaći na završni ispit, koji se tada smatra popravnim ispitom i ne boduje se, i u tom slučaju završna ocjena može biti jedino dovoljan 2E (50%). Studenti koji sakupe 39,9 i manje ocjenskih bodova (F ocjenska kategorija) moraju ponovno upisati kolegij.

Ocjenske bodove student stječe aktivnim sudjelovanjem u nastavi, izvršavanjem postavljenih zadataka i izlascima na međuispite na sljedeći način
Ocjenske bodove student stječe na sljedeći način:
I. Tijekom nastave vrednuje se (maksimalno do 70 bodova):
a) obvezni pismeni test
Pohađanje nastave se posebno ne boduje. Student može izostati s 30% nastave zbog zdravstvenih razloga što opravdava liječničkom ispričnicom.
Ukoliko student neopravdano izostane s više od 30% nastave ne može nastaviti praćenje kolegija te gubi mogućnost izlaska na završni ispit. Time je prikupio 0 ECTS bodova i ocijenjen je ocjenom F.

a) Obvezni test (do 70 bodova)

Pismeni test sastoji se od 35 pitanja, te nosi 70 ocjenskih bodova (kriterij za dobivanje ocjenskih bodova je 50% točno riješenih pitanja).

| ocjena | ocjenski bodovi | točni odgovori |
|---|---|---|
| Nedovoljan | 0 | 0-17 |
| Dovoljan (E) | 25-29 | 18-19 |
| Dovoljan (D) | 30-40 | 21-24 |
| Dobar(C) | 41-49 | 25-27 |
| Vrlo dobar(B) | 50-61 | 28-31 |
| Izvrstan(A) | 62-70 | 32-35 |

**Završni ispit (ukupno 30 ocjenskih bodova)**
Studenti koji su na obaveznom testu ostvarili više od 30 ocjenskih bodova obavezno pristupaju završnom ispitu na kojem mogu ostvariti maksimalno 30 bodova.
Studenti koji su na obaveznom testu ostvarili manje od 25 ocjenskih bodova (pripadaju kategoriji FX) mogu izaći na završni ispit, s time da moraju nadoknaditi od 0-10% ocjene i prema Pravilniku mogu dobiti samo ocjenu 2E.
**Tko <u>ne može</u> pristupiti završnom ispitu:**
Studenti koji nisu pristupili obaveznom pismenom testu, nemaju pravo izlaska na završni ispit (upisuju kolegij druge godine).
Završni ispit je usmeni ispit. Nosi 30 ocjenskih bodova (raspon od 15-30).

Uspjeh na završnom ispitu pretvara se u ocjenske bodove na sljedeći način:

| ocjena | ocjenski bodovi |
|---|---|
| Nedovoljan | 0 |
| Dovoljan | 15 |
| Dobar | 20 |
| Vrlo dobar | 25 |
| Izvrstan | 30 |

Za prolaz na završnom ispitu i konačno ocjenjivanje (uključujući pribrajanje prethodno ostvarenih ocjenskih bodova tijekom nastave), student na završnom ispitu mora biti pozitivno ocijenjen i ostvariti minimum od 15 ocjenskih bodova (50%).

Ocjenjivanje u ECTS sustavu vrši se apsolutnom raspodjelom, odnosno na temelju konačnog postignuća:
A – 90 - 100% bodova
B – 80 - 89,9%
C – 70 - 79,9%
D – 60 - 69,9%
E – 50 - 59,9%

Ocjene u ECTS sustavu prevode se u brojčani sustav na sljedeći način:
A = izvrstan (5)
B = vrlo dobar (4)
C = dobar (3)
D i E = dovoljan (2)
F i FX = nedovoljan (1)

### Other notes (related to the course) important for students:

Nastavni sadržaj i sve obavijesti vezane uz kolegij kao i ispitni termini nalaze se na mrežnim stranicama Medicinskog fakulteta u Rijeci, Katedre za kliničko-laboratorijsku dijagnostiku.

### COURSE HOURS 2026/2027

The Role of HLA Genes in Organ Transplantation and Diagnostics of Autoimmune Diseases

| **Lectures**<br>(Place and time or group) | **Practicals**<br>(Place and time or group) | **Seminars**<br>(Place and time or group) |
|---|---|---|

### List of lectures, seminars and practicals:

| LECTURES (TOPIC) | Number of hours | Location |
|---|---|---|
| P1 . Introduction to the HLA System and Historical Review | 1 | |
| P2. Structure and Organization of the HLA System | 1 | |
| P5. HLA associated diseaseas | 1 | |
| P3. HLA Typing Methods | 1 | |
| P4. HLA in Organ Transplantation | 1 | |

| PRACTICALS (TOPIC) | Number of hours | Location |
|---|---|---|
| V1. Isolation of lymphocytes | 1 | |
| V2. Complement-dependent lymphocytotoxicity test – HLA typing | 1 | |
| V3. Isolation of DNA | 1 | |
| V4. HLA typing by PCR-SSP method | 1 | |
| V5. HLA typing by PCR-SSP method – gel electrophoresis, interpretation of results | 1 | |

| SEMINARS (TOPIC) | Number of hours | Location |
|---|---|---|
| SEM 1. Clinical Role of HLA in Health and Disease | 1 | |
| SEM 2. Role of HLA in Autoimmune Disease | 1 | |
| SEM 3. Relevance of the HLA system in blood transfusion | 1 | |
| SEM 4. The HLA System and Histocompatibility Testing for Organ Transplantation | 1 | |

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| SEM 5. HLA and Kidney Transplantation | 1 | |
| SEM 6. HLA and Hematopoietic Stem Cell Transplantation | 1 | |
| SEM 7. HLA and Liver Transplantation | 1 | |
| SEM 8. Cardiothoracic Transplantation | 1 | |
| SEM 9. Immunogenetics of xenotransplantation | 1 | |
| SEM 10. HLA Genetics – Celiac Disease | 1 | |
| SEM 11. HLA Genetics – Rheumatoid arthritis | 1 | |
| SEM 12. HLA Genetics – Type 1 diabetes mellitus | 1 | |
| SEM 13. HLA Genetics – Ankylosing Spondylitis | 1 | |
| SEM 14. HLA Genetics – Multiple Sclerosis | 1 | |
| SEM 15. HLA and HIV infection | 1 | |

**EXAM DATES (final exam):**

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