UČNI NAČRT PREDMETA / COURSE SYLLABUS	
Predmet:	MOLEKULARNA HUMANA GENETIKA
Course Title:	MOLECULAR HUMAN GENETICS

Študijski program in stopnja Study Programme and Level	Študijska smer Study Field	Letnik Academic Year	Semester Semester
MAG Biokemija, 2. stopnja	**/**	**1.**	**2.**
USP Biochemistry, 2nd Cycle	**/**	**1st**	**2nd**

Vrsta predmeta / Course Type: obvezni / Mandatory

Univerzitetna koda predmeta / University Course Code: BI216

Predavanja Lectures	Seminar Seminar	Vaje Tutorial	Klinične vaje Work	Druge oblike študija	Samost. delo Individual Work	ECTS
40	**20**	**15 LV**	**/**	**/**	**75**	**5**

Nosilec predmeta / Lecturer: prof dr. Boris Rogelj / Dr. Boris Rogelj, Full Professor
doc. dr. Vera Župunski / Dr. Vera Županski, Assistance Professor

Jeziki / Languages:

Predavanja / Lectures:	**slovenski / Slovenian**
Vaje / Tutorial:	**slovenski / Slovenian**

Pogoji za vključitev v delo oz. za opravljanje študijskih obveznosti:

Študent oz. kandidat mora imeti predmet opredeljen kot študijsko obveznost.

Prerequisites:

The course has to be assigned to the student.

Vsebina:

1. Mehanizmi podvojevanja DNA in rekombinacije pri človeku
2. Nestabilni genom: mutacije in popravljanje mutacij
3. Proces transkripcije pri človeku in stopnje uravnavanja izražanja
4. Regulacijski elementi cis in trans, delovanje aktivatorjev in represorjev
5. Uravnavanje izražanja z razgradnjo RNA
6. Signalne kaskade, ki vplivajo na izražanje genov
7. Alternativna transkripcija in epigenetski dejavniki

Content (Syllabus outline):

1. Mechanisms of human DNA replication and recombination.
2. Instable genome: mutations and mutation repair.
3. Transcription and regulation of human gene expression.
4. Cis and trans regulatory elements, mechanism of activation and repression.
5. Regulation of expression through RNA degradation.
6. Signal cascades influencing gene expression.
7. Alternative transcription and epigenetic factors.

8. Biosinteza proteinov 9. Človekov kariotip 10. Organizacija človekovega genoma 11. Molekulska zgradba centromerov in telomerov 12. Ponovljena zaporedja in transpozicijski elementi pri človeku 13. Preoblikovanje kromatina 14. Genetika celičnega cikla 15. Evolucija mitohondrijskega in jedrnega genoma 16. Imunogenetika 17. Projekt Človeški genom in njegovo nadaljevanje s funkcijsko genomiko 18. Iskanje in kloniranje človekovih genov 19. Monogenske bolezni: molekularna patologija in diagnostika z analizo DNA 20. Molekularna patologija kompleksnih genskih sistemov 21. Uravnavanje delovanja genov med razvojem osebka 22. Genetika in diferenciacija celic 23. Molekularna onkologija: onkogeni in antionkogeni 24. Analiza DNA za tipizacijo tkiv in za osebno identifikacijo 25. Osnove funkcijske genomike in biologije sistemov 26. Gensko zdravljenje 27. Koncept osebne medicine 28. Molekularna genetika in družba: etični, sociološki in politični vidiki 29. Funkcionalna genetika nevrodegenerativnih bolezni.	8. Human protein expression. 9. Karyotype. 10. Organization of the human genome. 11. Molecular structures of centromeres and telomeres. 12. Repeated regions and transposition elements in the human genome. 13. Chromatin rearrangements. 14. Genetics of the cell cycle. 15. Evolution of the mitochondrial and nuclear genome. 16. Immunogenetics. 17. Human genome project and functional genomics. 18. Identification and cloning of human genes. 19. Monogenic diseases: molecular pathology and diagnostics by DNA analysis. 20. Molecular pathology of complex genetic systems. 21. Gene regulation in development of a human being. 22. Genetics and cell differentiation. 23. Molecular oncology: oncogenes and antioncogenes. 24. DNA analysis for tissue typing and personal identification. 25. Fundamentals of functional genomics and systems biology. 26. Gene therapy. 27. Concept of personal medicine. 28. Molecular genetics and society: ethical, social and legal issues. 29. Functional genetics of neurodegenerative diseases

Temeljna literatura in viri / Readings:

- Trent R.J.: Molecular Medicine, 4th ed., Academic Press (2012) https://www.elsevier.com/books/molecular-medicine/trent/978-0-12-381451-7
- Strachan T. & Read A.: Human Molecular Genetics, 4th ed., Garland (2010) http://www.garlandscience.com/product/isbn/9780815341499
- Tom Strachan, Judith Goodship, Patrick Chinnery: Genetics and Genomics in Medicine, 2015

Obseg gradiv za izpit: ~300 strani.

Cilji in kompetence: | **Objectives and Competences:**

Študenti bodo znali razložiti molekulske mehanizme ohranjanja genetske informacije pri človeku ter prenosa informacije z genoma na proteine. Razumeli bodo delovanje signalnih kaskad, ki se končajo v jedru in kako poteka uravnavanje izražanja genov na različnih ravneh. Kromosomsko zgradbo človekovega genoma bodo razumeli na citološki in molekulski ravni, hkrati pa bodo vedeli, kako se struktura kromosomskega zapisa spreminja v procesih podvojevanja in prepisovanja genov. Razen jedrnega genoma bodo razumeli tudi pomen mitohondrijskega genoma in njegovo evolucijo. Vedeli bodo, kako je mogoča izjemna heterogenost proteinov imunskega sistema kljub relativno majhnemu številu genov za te proteine. Opisati bodo znali, kako so določili zaporedje človekovega genoma in kakšne so njegove lastnosti, kako je mogoče identificirati točno določen gen in ga analizirati. Poznali bodo več primerov dednih bolezni in naravo njihovega prenosa med generacijami. Hkrati bodo razumeli, kako se v procesu diferenciacije celic ali razvoja osebka spreminja aktivnost določenih genov. Aplikativna znanja bodo vključevala metode za molekulsko diagnostiko bolezni in tipizacijo tkiv, pristope h genskemu zdravljenju, poznali pa bodo tudi genetsko naravo sprememb, povezanih z razvojem rakavih obolenj. S seminarji bodo študenti spoznali novosti pri raziskavah človekovega genoma, bolezni zaradi genetskih sprememb in pri razvoju novih metod za raziskovanje človekovega genoma. Za seminarje bodo uporabljali vire v angleškem jeziku, s čimer se bodo urili v uporabi literature in prevajanju. Z vodenimi razpravami na seminarjih bodo pridobili izkušnje v oblikovanju relevantnih vprašanj in	Students will be able to explain molecular mechanisms of preservation of human genetic information and the transfer of information from the genome to proteins. They will understand the signalling cascades that lead to nucleus and different levels of regulation of gene expression. Students will understand cytological and molecular aspects of the human genome, and know how the structure of the chromosome changes in the processes of replication and translation. They will also comprehend the role and evolution of the mitochondrial genome. They will have insight into the mechanisms that from a relatively small number of genes give rise to substantial heterogeneity of proteins in the immune system. They will be able to describe procedures to determine the sequence and properties of the human genome and how to identify and analyse individual genes. They will know several hereditary diseases and how they are transferred between generations. At the same time they will understand changes in gene expression during development. They will know applications involving molecular diagnostics and tissue typing and methods of gene therapy. They will also comprehend the genetic changes involved in oncogenesis. With seminars, the students will get acquainted with current research of the human genome and genetic diseases as well as development of new research methods for analysis of the human genome. The resources for the seminar will be in English, which will provide training in use of literature and translation. With guided discussion following presentations, the students will gain experience in shaping of relevant questions and discussion of viewpoints.

zagovarjanju stališč.	

Predvideni študijski rezultati:	**Intended Learning Outcomes:**
Znanje in razumevanje **Znanje:** Prenos genetske informacije pri človeku. Nastanek in odpravljanje mutacij. Mesta in načini uravnavanja izražanja genov. Mehanizmi aktivacije in represije pri transkripciji. Utišanje genov z razgradnjo RNA. Značilnosti kariotipa in organizacije človekovega genoma. Tipi ponavljajočih se zaporedij in delovanje transpozonov. Lastnosti mitohondrijskega genoma in njegova evolucija. Rekombinacije pri nastanku zapisov za proteine imunskega sistema. Postopki pri določanju zaporedja sesalskih genomov. Genetska narava monogenskih in kompleksnih dednih bolezni. Razvojna genetika: spremembe v aktivnosti genov med razvojem celice in človeka. Genetska osnova rakavih sprememb. Sodobne metode za analizo genoma in transkriptoma. Načini genskega zdravljenja. **Razumevanje:** Primerjava prokariontskih in evkariontskih procesov prenosa genetske informacije – razumevanje razlik med podobnosti. Raznolikost v uravnavanju izražanja genov pri človeku. Prenosi signalov iz okolice in iz notranjosti celice se lahko končajo v jedru in vplivajo na prepisovanje genov. Kemične spremembe nukleotidov lahko vplivajo na raven prepisovanja genov. Mikroskopski in molekulski ustroj kromosomov. Pomen ponavljajočih se zaporedij v genomu. Spremembe kromatina aktivnih regij kromosoma. Pomen poznavanja genomskih zaporedij in nadgradnja s spoznanji funkcijske genomike. Način identifikacije posameznih genov v genomu.	Knowledge and Comprehension **Knowledge:** Transfer of genetic information in humans. Genesis and treatment of mutations. Methods and targets of regulation of gene expression. Mechanisms of activation and repression of transcription. RNA silencing. Karyotype characteristics and organisation of the human genome. Types of repeat sequences and function of the transposons. Evolution and characteristics of the mitochondrial genome. Recombination of genes of immune system. Modern sequencing methods of the genome and the transcriptome. Genetic basis of monogenic and complex hereditary diseases. Developmental genetics: gene regulation during cell and organism development. Genetics of oncogenesis. Gene therapy methods. **Comprehension:** Comparison of prokaryotic and eukaryotic processes of transfer of genetic information – understanding of similarities and differences. Different pathways of gene regulation in humans. Environmental and internal signals can be transferred to the nucleus and influence translation. Chemical modifications of nucleotides can influence levels of transcription. Microscopic and molecular makeup of the chromosomes. The importance of repeat sequences for the genome. Chromatin changes in the active regions of chromosomes. Importance of the overview of the genome sequence. Methods of identification of individual genes.
Uporaba Poosebljena medicina – skorajšnja uporaba v	Application Personalised medicine - the perspectives for

medicinski praksi. Povezava spoznanj s sorodnih področij znanosti (genetika, molekularna genetika in molekularna biologija). Metode za analizo genoma in transkriptoma ter molekularnogenetske diagnostične metode.	general use. Connection with state-of-the-art in other fields of research (genetics, molecular genetics and molecular biology). Methods of genome and transcriptome analysis and molecular genetic diagnostics.
Refleksija Navidezni razkorak med stabilnostjo človekovega genoma in raznolikostjo njegovega izražanja. Smisel nekodirajočih zaporedij v genomu – pojem sebičnega gena. Širjenje lastnosti polipeptidov kot posledica alternativnih procesov v prenosu genetske informacije (mesta začetka transkripcije, alternativno izrezovanje intronov, urejanje mRNA ipd.). Celični cikel in življenjski cikel – spremembe v aktivnosti genov na ravni celice in organizma. Dedne bolezni so posledica različnih genskih okvar. Zakaj se nekatere mutacije popravljajo, druge pa ne? Vsak človek lahko zboli za rakom – kaj lahko naredi posameznik, da ne bi zbolel? Zakaj prve generacije genskih zdravil niso bile učinkovite in kaj je treba izboljšati, da bi lahko prišlo do širše uporabe? Molekularna biologija in genetika lahko vplivata na kakovost življenja in segata od posameznika v družbo.	Analysis The dichotomy of stability of the human genome and the variability of expression. The sense of the noncoding sequences in the genome and the concept of the selfish gene. Increase of the characteristics of polypeptides as a result of alternative processes in the transfer of genetic information (alternative start of transcription, alternative splicing, RNA editing). Cellular and life cycle – changes in gene expression on the cellular and organism level. Hereditary disease are the consequence of different genetic mutations. Why are some mutations repaired while others are not? Everyone can get cancer – what can one do to reduce this possibility? Why the first generation of gene therapies was not successful and what needs to be improved? Molecular biology and genetics influence the quality of life, therefore the reach the individual as well as the society.
Prenosljive spretnosti Predstavitve strokovnih vsebin na osnovi angleškega izvirnika; uporaba terminološkega slovarja.	Skill-transference Ability Presentation of specialist state-of-the art findings from English resources; use of technical dictionary.

Metode poučevanja in učenja:	**Learning and Teaching Methods:**
Predavanja in seminarji (individualne predstavitve, vodena razprava).	Lectures and seminars (individual presentation, guided discussion).

Načini ocenjevanja:	Delež (v %) / Weight (in %)	**Assessment:**
Seminar Pisni izpit Ocene: 6-10 (pozitivno), 1-5 (negativno).	30 % 70 %	Seminar Written exam Grades: 6-10 (positive), 1-5 (negative)

Reference nosilca / Lecturer's references:

- HUDLER Petra, KOČEVAR Nina, **KOMEL Radovan**: Proteomic approaches in biomarker discovery : new perspectives in cancer diagnostics. The Scientific World Journal, ISSN 1537-744X; 2014, vol.
- Režen T, Kovanda A, Eiken O, Mekjavic IB, **Rogelj B.** 2014, Expression changes in human skeletal muscle miRNAs following 10 days of bed rest in young healthy males. Acta Physiologica (Oxf), [Epub ahead of print]
- Bratkovic T, Glavan G, Strukelj B, Zivin M and **Rogelj B**, 2012, Exploiting microRNAs for cell engineering and therapy. Biotechnology Advances, 30:753-765.
- Tollervey JR, Curk T, **Rogelj B**, Briese M, Cereda M, Kayikci M, König J, Hortobágyi T, Nishimura AL, Zupunski V, Patani R, Chandran S, Rot G, Zupan B, Shaw CE and Ule J, 2011, Characterizing the RNA targets and position-dependent splicing regulation by TDP-43. Nature Neuroscience, 14:452-458.
- Nishimura AL, Župunski V, Troakes C, Kathe C, Fratta P, Howell M, Gallo J-M, Hortobágyi T, Shaw CE and **Rogelj B**, 2010, Nuclear import impairment causes cytoplasmic TDP-43 accumulation and is associated with frontotemporal lobar degeneration, Brain, 133:1763-1771.
- Vance C, **Rogelj B**, Hortobagyi T, De Vos KJ, Sreedharan J, Hu X, Wright P, Nishimura AL, Ganesalingam J, Tripathi V, Smith B, Ruddy D, Al-Saraj S, Al-Chalabi A, Leigh PN, Blair IP, Nicholson G, de Belleroche J, Gallo J-M, Miller CC and Shaw CE, 2009. Mutations in FUS, an RNA processing protein, cause familial amyotrophic lateral sclerosis type 6. Science, 323:1208-1211.
- Lee YB, Chen HJ, Peres JN, Gomez-Deza J, Attig J, Stalekar M, Troakes C, Nishimura AL, Scotter EL, Vance C, Adachi Y, Sardone V, Miller JW, Smith BN, Gallo JM, Ule J, Hirth F, **Rogelj B**, Houart C, Shaw CE. 2013, Hexanucleotide repeats in ALS/FTD form length-dependent RNA foci, sequester RNA binding proteins, and are neurotoxic. Cell Reports, 5:1178-1186.