UČNI NAČRT PREDMETA / COURSE SYLLABUS	
Predmet:	Mehanizem in biološke implikacije agregacije proteinov
Course title:	Mechanism and Biological Implications of Protein Aggregation

Študijski program in stopnja Study programme and level	Študijska smer Study field	Letnik Academic year	Semester Semester
Nanoznanosti in nanotehnologije, 3. stopnja	Bioznanosti	1	1
Nanosciences and Nanotechnologies, 3rd cycle	Biosciences	1	1

Vrsta predmeta / Course type Izbirni / Elective

Univerzitetna koda predmeta / University course code: NANO3-810

Predavanja Lectures	Seminar Seminar	Vaje Tutorial	Klinične vaje work	Druge oblike študija	Samost. delo Individ. work	ECTS
30	**30**			**30**	**210**	**10**

**Navedena porazdelitev ur velja, če je vpisanih vsaj 15 študentov. Drugače se obseg izvedbe kontaktnih ur sorazmerno zmanjša in prenese v samostojno delo. / This distribution of hours is valid if at least 15 students are enrolled. Otherwise the contact hours are linearly reduced and transfered to individual work.*

Nosilec predmeta / Lecturer: Prof. dr. Eva Žerovnik

Jeziki / Languages:		
	Predavanja / Lectures:	Slovenščina, angleščina / Slovenian, English
	Vaje / Tutorial:	

Pogoji za vključitev v delo oz. za opravljanje študijskih obveznosti:	**Prerequisits:**
Končan študij druge stopnje biokemije, biologije, medicine, veterine ali katerekoli druge naravoslovne smeri.	Second cycle degree in biochemistry, biology, medicine, vet-medicine or any other natural sciences discipline.

Vsebina:

Poglavja:

1. Biofizikalne osnove agregacije proteinov. Modeli za amiloidno fibrilacijo proteinov
2. Struktura amiloidnih fibril
3. Eksperimentalne tehnike za študij termodinamike in kinetike procesa fibrilacije Študij primerov iz literature: A-beta, beta-microglobulin, alfa-sinuklein, stefin B.
4. Korelacija med zvijanjem proteinov in tvorjenjem amiloidnih fibril Vloga vmesnih stanj zvitja pri tvorbi amiloidov Vloga šaperonov pri obrambi pred agregati
5. Citotoksičnost amiloidnih fibril Interakcija z lipidi in tvorjenje por
6. Proteinska agregacija v celici Akumulacija in transport agregatov Čiščenje celice – razgradnja agregatov preko

Content (Syllabus outline):

Topics:

1. Biophysical background of protein aggregation Models describing amyloid-fibrillation of proteins
2. The structure of amyloid-fibrils
3. Experimental means to study thermodynamics and kinetics of the process of fibrillation. Case studies from the literature: A-beta, beta-microglobulin, alpha-synuclein, stefin B
4. Correlation between protein folding and amyloid-fibril formation Role of folding intermediates. of chaperones in defence against aggregates
5. Citotoxicity of amyloid fibrils. Interaction with lipids and pore formation
6. Protein aggregation in the cell Accumulation and transport of the aggregates.

ubikvitin proteasomalnega sistema in autofagije 7. Amiloidoze in nevrodegenerativne boleznim - Seminar	Means of clearance: ubiquitin proteasome system and autophagy 7. Amyloidoses and neurodegenerative diseases - Seminar

Temeljni literatura in viri / Readings:

Books:

Protein Folding-Misfolding: some current concepts of protein chemistry. Zbilut JP and Scheibel T (eds.), Nova Sci Publi., New York, 2007.

Protein misfolding diseases; current and emerging therapies. eds Raminez-Alvarado, J.W. Kelly, C.M. Dobson, Wiley Series in Protein and Peptide Science, Series Ed. V.N. Uversky. John Wiley & Sons, New Jersey 2010.

Review papers:

Žerovnik E (2002) Amyloid-fibril formation; Proposed mechanisms and relevance to conformational disease. Eur.J.Biochem. 269, 3362- 3371.

Lansbury PT, Lashuel HA. (2006) A century-old debate on protein aggregation and neurodegeneration enters the clinic. Nature 443: 774-779. Review.

Haass C, Selkoe DJ. 2007. Soluble protein oligomers in neurodegeneration: lessons from the Alzheimer's amyloid beta-peptide. Nat Rev Mol Cell Biol. 2007 Feb;8(2):101-12. Review.

M, Ueno T, Waguri S et al. 2007. Constitutive autophagy: vital role in clearance of unfavorable proteins in neurons. Cell Death Differ. 1-8.

Irvine CB, El-Agnaf OM, Shankar GM and Walsh DM (2008). Protein aggregation in the brain. The molecular basis for Alzheimer's and Parkinson's diseases. Mol.Med. 14, 451 – 464.

Žerovnik E. (2010).Protein conformational pathology in Alzheimer's and other neurodegenerative diseases; new targets for therapy. Curr Alzheimer Res. 7: 74-83. Review.

Žerovnik E, Stoka V, Mirtič A, Gunčar G, Grdadolnik J, Staniforth RA, Turk D, Turk V. (2011). Mechanisms of amyloid fibril formation--focus on domain-swapping. FEBS J. 278:2263-82. doi: 10.1111/j.1742-4658.2011.08149.x. Epub 2011 May 31. Review.

Di Scala e tal., (2016) Common molecular mechanism of amyloid pore formation by Alzheimer's b- amyloid peptide and a-synuclein Scien. Reports, DOI: 10.1038/srep28781

Sengupta U, Nilson N.A., Kayed R., The role of amyloid-b oligomers in toxicity, propagation, and immunotherapy EBioMedicine , 2016, vol6, 42-49

Cilji in kompetence:	**Objectives and competences:**
CILJI: Razumeti proces agregacije proteinov do amiloidnih fibril. Ti procesi se pojavljajo v nevrodegenerativnih boleznih, kot so Alzheimerjeva, Parkinsonova, razne demence in prionske bolezni. Z boljšim razumevanjem molekularnih in celičnih osnov proteinske agregacije bo možno priti do novih terapij za nevrodegenerativne bolezni. Predmet bo vključeval molekularne, celične in izbrane klinične vidike. KOMPETENCE: Spoznavanje z interdisciplinarnimi področji molekularne in celične biologije, biokemije in biofizike. Samostojno mišljenje, formuliranje problemov in vprašanj.	OBJECTIVES: To understand the phenomenon of protein ordered aggregation into amyloid fibrils. These processes are involved in neurodegenerative diseases such as Alzheimer's, Parkinson's, various dementias and prion diseases. Additional understanding of molecular and cellular bases of protein aggregation will help in search for new therapies for neurodegenerative diseases. The course will cover molecular, cellular and selected clinical aspects. COMPETENCES: get to know interdisciplinary fields of molecular and cell biology, biochemistry and biophysics. Independent and creative thinking; be able to formulate problems and open questions.

Predvideni študijski rezultati:	**Intended learning outcomes:**
Znanje in razumevanje: • Študent bo razumel osnove fenomena urejene agregacije proteinov do amiloidnih fibril • Študent bo pridobil razumevanje, kako se ta osnovna znanja prenašajo v prakso, t.j. v iskanje novih terapij za nevrodegenerativne bolezni • Pridobil bo dodatno razumevanje molekularnih in celičnih vidikov proteinske agregacije. Splošni rezultati: • poznavanje raziskovalnih metod, postopkov in procesov, ki se uporabljajo na področju zvijanja in agregacije proteinov, ki obsegajo biofizikalne metode, mikroskopije (AFM, TEM, fluorescence in konfokalni m), biokemijske metode frakcioniranja oligomer, kot npr. SEC in DLS, in spektroskopije, kot npr. CD, FTIR, NMR in fluorescenca, • razvoj kritične in samokritične presoje, • razvoj komunikacijskih sposobnosti in spretnosti, posebej predstavitve raziskovalnih rezultatov, • kooperativnost, delo v skupini v stimulativnem okolju; možna mednarodna izmenjava. Predmetnospecifični rezultati: • Predmet pripravlja študente za delo na interdisciplinarnih bazičnih projektih • Povezanost z biomedicino • Uporabna znanja tudi za biotehnologijo in živilsko tehnologijo	Knowledge and Understanding • The student will understand basics of the phenomenon of protein ordered aggregation into amyloid fibrils. • He also will get to know ways, how this basic knowledge is being used in search for therapy of neurodegenerative diseases • Additional understanding of molecular and cellular aspects of protein aggregation General Ouitcomess: • The student will get to know research methods, procedures and processes used in the field of protein folding and aggregation, which comprise biophysical methods, microscopies: AFM and TEM, fluorescent and confocal m., biochemical methods of oligomer fractionation, such as SEC and DLS and spectroscopies, such as CD, FTIR, NMR and fluorescence. • The student will develop critical thinking • The student will develop communication skills to present research achievenment • Cooperation, team work in competitive environment; possible international exchange Course Specific Results: • This course prepares students to work on interdisciplinary projects • Is connected to biomedicine • Useful for biotechnology and food technology

Metode poučevanja in učenja:	**Learning and teaching methods:**
• Predavanja • Konzultacije • Individualno delo • Laboratorijsko delo (samo v primeru mentorstva)	• Lectures • Consultations • Individual work • Laboratory work (If supervising the student)

Načini ocenjevanja:	Delež (v %) / Weight (in %)	**Assessment:**
• ustno preverjanje	50 %	• oral assessment
• pisni e-seminar	50 %	• written e-seminar

Reference nosilca / Lecturer's references:

• Polajnar M, Zerovnik E. Impaired autophagy: a link between neurodegenerative and neuropsychiatric diseases. J Cell Mol Med. 2014 Sep;18(9):1705-11. doi: 10.1111/jcmm.12349. Epub 2014 Aug 19.
• Polajnar M, Zavašnik-Bergant T, Škerget K, Vizovišek M, Vidmar R, Fonović M, Kopitar-Jerala N, Petrovič

U, Navarro S, Ventura S, Žerovnik E. Human stefin B role in cell's response to misfolded proteins and autophagy. PLoS One. 2014 Jul 21;9(7):e102500. doi: 10.1371/journal.pone.0102500. eCollection 2014.

- Polajnar M, Zavašnik-Bergant T, Kopitar-Jerala N, Tušek-Žnidarič M, Zerovnik E. Gain in toxic function of stefin B EPM1 mutants aggregates: correlation between cell death, aggregate number/size and oxidative stress. Biochim Biophys Acta. 2014 Sep;1843(9):2089-99. doi: 10.1016/j.bbamcr.2014.05.018. Epub 2014 Jun 5.
- Taler-Verčič A, Kirsipuu T, Friedemann M, Noormägi A, Polajnar M, Smirnova J, Znidarič MT, Zganec M, Skarabot M, Vilfan A, Staniforth RA, Palumaa P, Zerovnik E. The role of initial oligomers in amyloid fibril formation by human stefin B. Int J Mol Sci. 2013 Sep 5;14(9):18362-84. doi: 10.3390/ijms140918362.
- Žganec M, Žerovnik E. Amyloid fibrils compared to peptide nanotubes. Biochim Biophys Acta. 2014 Sep;1840(9):2944-52. doi: 10.1016/j.bbagen.2014.05.019. Epub 2014 Jun 5. Review.