

Opis raziskovalnega dela (Research work description)

1. Članica UL (UL member):

Fakulteta za farmacijo (UL FFA)

2. Ime, priimek in elektronski naslov mentorja/ice (Mentor's name, surname and email):

Marko Anderluh, marko.anderluh@ffa.uni-lj.si

3. Raziskovalno področje (Research field):

Vede o življenju, LS7 Preprečevanje, diagnosticiranje in zdravljenje človeških bolezni

4. Opis raziskovalnega dela (Research work description):

Vključuje morebitne dodatne pogoje, ki jih mora izpolnjevati kandidat/ka za mladega raziskovalca/ko, ki niso navedeni v razpisu za mlade raziskovalce (It includes any additional conditions that the candidate for a young researcher must meet, which are not listed in the call to tender for young researchers.).

Slov.: Raziskovalno delo mladega raziskovalca (MR) bo temeljilo na nedavno pridobljenemu projektu Horizon EU MSCA-DN GlyCanDrug (ID: 101119601). V projektu sodeluje 9 akademskih institucij in 6 podjetij, kar predstavlja izjemno platformo za odlično raziskovalno delo, ki ne bi bilo mogoče v le enem laboratoriju. Predvideno delo MR bo segalo na področje glikoznanosti in sicer načrtovanje in vrednotenje ciljanih molekularnih prob za natančno zaviranje izražanja z rakom povezanih glikanov. Namreč, dosedanje preliminarne raziskave kažejo, da rakasta tkiva (prekomerno) izražajo različne glikane, kot so površinski glikoproteini in glikolipidi. Te pretvorbe potekajo prek različnih glikoziltransferaz, ki so membransko vezani encimi v Golgijevem aparatu (npr. fukoziltransferaze FT6, FT7 in FT8, in sialiltransferaze ST6Gal1 in ST6GalNAc1). Primera takih encimov sta GalNAc-T6 in GalNAc-T7 - specifični izoformi polipeptidnih N-acetilgalaktozaminiltransferaz (GalNAc-T), ki v Golgijevem aparatu katalizirata prenos N-acetilgalaktozamina (O-glikozilacijo) na različne substrate. GalNAc-T6 in GalNAc-T7 sta pogosto prekomerno izražena pri raku (npr. raku debelega črevesa), kar spodbuja displastično rast in zavira diferenciacijo. Substrati GalNAc-T6 vključujejo mucine (npr. MUC1), receptorje rastnih faktorjev in adhezijske molekule. Ti onkogeni ali pro-preživetveni proteini zahtevajo ustrezno O-glikozilacijo za stabilnost, ustrezno zlaganje in odpornost proti proteolizi. Poleg tega O-glikani uravnavajo adhezijo med celicami in interakcije med celicami in matriksom. Domnevamo, da zaviranje GalNAc-T6 in T7 lahko zmanjša potencial za metastaze, saj ovira ločevanje in invazijo tumorskih celic, na primer z zmanjšanjem interakcije tumorskih celic z endotelnimi selektini.

Da bi lahko proučevali oba encima v tumorju, potrebujemo majhne molekulske zaviralce obeh encimov. Naša hipoteza je, da bo zaviranje GalNAc-T6 in T7 spremenilo površinske lastnosti rakavih celic, s čimer bi zavirali njihovo invazivnost in sposobnost kolonizacije. MR bo načrtoval majhne nizkomolekularne zaviralce zgoraj navedenih glikoziltransferaz na podlagi obstoječih kristalnih struktur ciljnih encimov. Načrtovane spojine bo nato sintetiziral in karakteriziral. V sodelovanju s prof. Ramonom Hurtado-Guerrero in dr. Mattio Ghirardello z Univerze v Zaragoza (Španija) bomo pridobili tarčne encime v zadostni količini za izvedbo biokemijskih testov zaviranja encimske aktivnosti. Spojine bomo nato ovrednotili na zaviranje nastanka posebnih glikanov na površini človeških celičnih linij v sodelovanju z dr. Jennifer Munkley iz Univerze v Newcastlu (UK).

V okviru izobraževanja načrtujemo krajša gostovanja bodočega MR, ki bo na omenjenih partnerskih institucijah pridobil komplementarna znanja iz osnov biokemije in celične biologije. Njegovo raziskovalno delo bo tako ne le interdisciplinarno, temveč bo tudi mednarodno. MR bo omogočeno tudi izobraževanje iz prenosljivih spretnosti iz nabora izobraževanj projekta GlyCanDrug. S pridobljenimi znanji in ekspertizami bo MR izjemno konkurenčen za zaposlitev v raziskovalnih institucijah ali v slovenski farmacevtski industriji.

Glede na naravo dela in interdisciplinarnost zastavljene naloge imajo pri izboru prednost kandidati, ki so končali enovite ali magistrske študijske programe farmacija, kemija in biokemija.

Eng.: The young researcher's (YR) research work will be based on the recently awarded Horizon EU MSCA-DN GlyCanDrug project (ID: 101119601). This project involves nine academic institutions and six companies, providing an exceptional platform for research that would not be possible in a single laboratory. The YR's work will extend to the field of glycoscience, specifically the development and evaluation of targeted molecular probes to inhibit the expression of cancer-associated glycans with precision. Preliminary studies have previously shown that cancer tissue over-expresses various glycans, such as surface glycoproteins and glycolipids. These conversions occur via various glycosyltransferases, which are membrane-bound enzymes in the Golgi apparatus, such as fucosyltransferases (FT6, FT7 and FT8) and sialyltransferases (ST6Gal1 and ST6GalNAc1). Examples of such enzymes include GalNAc-T6 and GalNAc-T7, which are specific isoforms of the polypeptide N-

acetylgalactosaminyltransferase (GalNAc-T) family that initiate mucin-type O-glycosylation in the Golgi apparatus. GalNAc-T6 and GalNAc-T7 are often overexpressed in cancers (e.g. colon cancer), promoting dysplastic growth and inhibiting differentiation. GalNAc-T6 substrates include mucins (e.g. MUC1), growth factor receptors and adhesion molecules. These oncogenic or pro-survival proteins require proper O-glycosylation for stability, proper folding, and resistance to proteolysis. Furthermore, O-glycans regulate cell-cell adhesion and cell-matrix interactions. We presume that inhibiting GalNAc-T6 and T7 may reduce metastatic potential by impairing tumour cell detachment and invasion, for example by decreasing tumour cell interaction with endothelial selectins, among other mechanisms.

In order to study both enzymes in a tumour environment, we require small-molecule inhibitors of both enzymes. We hypothesise that inhibiting GalNAc-T6 and T7 will alter the surface properties of cancer cells, thereby inhibiting their invasiveness and ability to colonise the environment. YR will design small-molecule inhibitors of the aforementioned glycosyltransferases, based on existing crystal structures of the target enzymes. The designed compounds will then be synthesised and characterised. In collaboration with Professor Ramon Hurtado-Guerrero and Dr Mattia Ghirardello from the University of Zaragoza in Spain, we will obtain sufficient quantities of the target enzymes to carry out biochemical tests to inhibit enzyme activity. The compounds will then be studied in collaboration with Dr Jennifer Munkley from Newcastle University (UK) to investigate their inhibition of the formation of specific glycans on the surface of human cell lines.

As part of the training programme, the future YR will make short visits to the above-mentioned partner institutions to acquire complementary knowledge in the basics of biochemistry and cell biology. Their research will therefore be both interdisciplinary and international. As part of the GlyCanDrug project's training package, the YR will also be trained in transferable skills. With this knowledge and experience, the YR will be highly competitive for employment in research institutions or the Slovenian pharmaceutical industry.

Given the nature of the work and the interdisciplinary nature of the tasks, preference is given to candidates who have completed bachelor's and/or master's degree programs in pharmacy, chemistry, and biochemistry.

5. Priloge, ki jih je treba priložiti ob prijavi (*Documents required to be submitted with the application*):

potrdilo o doseženi izobrazbi (*proof of completed education*)

- kandidat z zaključenim magistrskim študijskim programom (2. bolonjska stopnja) (*candidate who has completed a Master's degree (2nd Bologna level)*):
 - o diplomska listina / potrdilo o zaključku študijskega programa (*diploma certificate / certificate of completion of the study programme*)
 - o priloga k diplomi / potrdilo o opravljenih obveznostih (*diploma supplement / official transcript of records containing all grades obtained in the study programme*)
- kandidat, ki še ni zaključil študija na 2. stopnji (*candidate who has not yet completed a Master's degree*):
 - o potrdilo o do sedaj opravljenih obveznostih z ocenami magistrskega študijskega programa, s katerim se bo kandidat prijavil na doktorski študij (*official transcript of records listing all courses and grades obtained so far in the Master's degree programme on the basis of which the candidate will apply for enrollment in a doctoral degree programme.*)

nagrade – univerzitetna Prešernova nagrada ali Prešernova nagrada članice Univerze v Ljubljani oz. druga enakovredna nagrada (*awards, e.g. Prešeren Prize of the University of Ljubljana, Prešeren Prize of a University of Ljubljana member and/or another equivalent award*)

bibliografija (*bibliography*)

življenjepis (*CV*)

motivacijsko pismo (*motivation letter*)

opis dosedanjega sodelovanja pri raziskovalnem delu (*description of the candidate's research work*)

osnutek idejne zasnove raziskovalnega dela (*preliminary research proposal*)

priporočilno pismo (*letter of recommendation*)

druge priloge (*other attachments*):

Kandidati so vabljeni, da preberejo članek na povezavi <https://www.nature.com/articles/s42004-025-01458-6> ter napišejo povzetek članka z identifikacijo ključnega prispevka k znanosti.

Candidates are invited to read the article at <https://www.nature.com/articles/s42004-025-01458-6> and write a summary of the article identifying the key contribution to science

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Fakulteta za farmacijo

2. Ime, priimek in elektronski naslov mentorja/ice (*Mentor's name, surname and email*):

izr. prof. dr. Barbara Ostanek – barbara.ostanek@ffa.uni-lj.si

3. Raziskovalno področje (*Research field*):

3.07.00 Medicina	Metabolne in hormonske motnje
1.09.00 Naravoslovje	Farmacija

4. Opis raziskovalnega dela (*Research work description*):

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Stov.: Staranje prebivalstva predstavlja enega ključnih izzivov sodobne medicine in družbe, saj se s tem povečuje pojavnost starostno pogojenih bolezni. Med pomembnejšimi sta osteoporoza in sarkopenija, ki izrazito vplivata na kakovost življenja starajoče se populacije. Doktorski projekt mladega raziskovalca (m/ž) je usmerjen v raziskave njunega molekularnega ozadja in funkcionalno ovrednotenje novih genomskih in epigenomskih označevalcev, ki bodo omogočili razvoj bolj personaliziranih pristopov za oceno kostnih in mišičnih sprememb pri starostnikih ter prispevali k razvoju ustrezne preventive.

Raziskovalno delo bo potekalo v interdisciplinarnem okolju raziskovalne skupine na Katedri za klinično biokemijo, v tesnem sodelovanju z uveljavljenimi domačimi in tujimi kliničnimi ter temeljno-raziskovalnimi strokovnjaki. Doktorski študent bo vključen v celoten raziskovalni proces – od zbiranja kliničnih vzorcev do poglobljenih analiz OMIK na nivoju DNA, RNA, proteinov in mezenhimskih matičnih celic. Posebej pomembna bo vzpostavitev in vrednotenje celičnih modelov z utišanim ali povečanim izražanjem genov, ki bodo izbrani za funkcijsko vrednotenje.

K prijavi vabimo visoko motivirane kandidate z interesom za laboratorijsko delo na področju molekularne genetike in celične biologije ter bioinformatike. Izkušnje na področju bioinformatike in molekularne biologije predstavljajo pomembno prednost. Znanje angleškega jezika je obvezno. Od kandidata pričakujemo samoiniciativnost, zanesljivost, sposobnost kritičnega razmišljanja, veselje do timskega dela ter pozitiven in raziskovalno naravn pristop k delu.

Eng.: Population aging represents one of the key challenges of modern medicine and society, as it is accompanied by an increasing prevalence of age-related diseases. Among the most significant are osteoporosis and sarcopenia, which markedly impair the quality of life of the aging population. The doctoral project of the young researcher (m/f) is focused on investigating the molecular background these two diseases and on the functional evaluation of novel genomic and epigenomic biomarkers that will enable the development of more personalized approaches for the assessment of bone and muscle alterations in older adults and will contribute to the development of appropriate preventive strategies.

The research work will be conducted in an interdisciplinary environment within the research group at the Department of Clinical Biochemistry, in close collaboration with established

national and international clinical and basic science research experts. The doctoral student will be involved in the entire research process—from the collection of clinical samples to in-depth OMICS analyses of DNA, RNA, proteins, and mesenchymal stem cells. Particular emphasis will be placed on the establishment and evaluation of cellular models with silenced or increased gene expression of selected genes for functional validation.

We invite highly motivated candidates interested in laboratory work in molecular genetics, cell biology, and bioinformatics to apply. Experience in bioinformatics and molecular biology is highly advantageous. Proficiency in English is required. The successful candidate is expected to demonstrate self-initiative, reliability, critical thinking skills, enthusiasm for teamwork, and a positive, research-oriented attitude.

5. Priloge, ki jih je treba priložiti ob prijavi (*Documents required to be submitted with the application*):

potrdilo o doseženi izobrazbi (*proof of completed education*)

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druge priloge (*other attachments*):

Opis raziskovalnega dela (*Research work description*)

1. Članica UL (*UL member*):

Univerza v Ljubljani, Fakulteta za farmacijo (University of Ljubljana, Faculty of Pharmacy)

2. Ime, priimek in elektronski naslov mentorja/ice (*Mentor's name, surname and email*):

Anja Pišlar (anja.pislar@ffa.uni-lj.si)

3. Raziskovalno področje (*Research field*):

4.06 Biotehnologija (Biotechnology), 1.09. Farmacija (Pharmacy)

4. Opis raziskovalnega dela (*Research work description*):

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Slov.: Cisteinski katepsini so lizosomske peptidaze, katerih izražanje in aktivnost sta izrazita v celicah tumorskega mikrookolja, zlasti v s tumorjem povezanih makrofagih (TAM, »*tumor associated macrophages*«). Poleg njihove uveljavljene vloge pri preoblikovanju zunajceličnega matriksa, invaziji in angiogenezi vedno več dokazov kaže, da lahko katepsini vplivajo tudi na uravnavanje imunskega odziva in celični metabolizem. V tumorskem mikrookolju so TAM podvrženi obsežnemu metabolnemu reprogramiranju in pogosto privzamejo fenotip, ki podpira imunosupresivno delovanje, pro-tumorski M2 fenotip. Čeprav je znano, da takšno polarizacijo spodbujajo dejavniki, kot so imunosupresivni citokini, hipoksija in metabolit laktat, še vedno ni jasno, ali so cisteinski katepsini zgolj posledični označevalci fenotipa M2 makrofagov ali pa aktivno uravnavajo metabolno reprogramiranje in polarizacijo makrofagov v imunosupresivni fenotip.

Kandidat/ka za mladega/o raziskovalca/ko bo sistematično ovrednotil/a, ali cisteinski katepsini predstavljajo ključne dejavnike M2 polarizacije v povezavi z metabolizmom TAM in avtofagijo. Predmet raziskovanja bodo povezave med izražanjem in aktivnostjo katepsinov na polarizacijo TAM v imunosupresivni fenotip ter preučevanje njihove vloge v presnovnih poteh in avtofagiji v makrofagih, izpostavljenih tumorsko pridobljenim signalom. Z razjasnitvijo vloge cisteinskih katepsinov v tumorskem mikrookolju in njihovim vplivom na polarizacijo TAM ter njihov metabolizem, bo kandidat/ka naslovil/a pomembno vrzel na presečišču biologije peptidaz in imunometabolizma. Mehanistično razumevanje osi katepsini–avtofagija–metabolizem–polarizacije v TAM bi lahko prispevalo k razvoju novih strategij za reprogramiranje makrofagov proti protitumorskemu fenotipu ter k razvoju kombiniranih terapevtskih pristopov, ki hkrati ciljajo lizosomsko funkcijo in presovne poti pri raku.

Za kvalitetno usposabljanje mladega/e raziskovalca/ke je zaželeno, da ima kandidat/ka znanje angleškega jezika ter predhodno metodološko znanje s področja biokemije in biotehnologije.

Eng.: Cysteine cathepsins are lysosomal peptidases that are highly expressed in the tumour microenvironment, particularly in tumour-associated macrophages (TAMs). In addition to their established roles in extracellular matrix remodelling, invasion, and angiogenesis, growing evidence suggests that cathepsins may also influence immune regulation and cellular metabolism. TAMs undergo significant metabolic reprogramming in tumours, often adopting phenotype that support immunosuppressive, pro-tumoral M2 phenotype. Although factors such as immunosuppressive cytokines, hypoxia and tumour-derived lactate are known to drive this polarization, it remains unclear whether cysteine cathepsins are merely downstream markers of M2-like states or active regulators of macrophage metabolic rewiring and functional polarization.

The candidate will systematically evaluate whether cysteine cathepsins are key determinants of M2 polarization in relation to TAM metabolism and autophagy. The candidate will further investigate the relationship between cathepsin expression and activity on TAM polarization into immunosuppressive phenotype, and their involvement in metabolic pathway engagement and autophagic flux in macrophages exposed to tumour-derived signals. By clarifying the role of cysteine cathepsins in the tumour microenvironment and their impact on TAM polarization and metabolism, the candidate will address an important gap at the intersection of peptidase biology and immunometabolism. A mechanistic understanding of the cathepsin–autophagy–metabolism–polarization axis in TAMs could contribute to the development of new strategies for reprogramming macrophages toward an anti-tumour phenotype, as well as to the development of combinatorial therapeutic approaches that simultaneously target lysosomal function and metabolic pathways in cancer.

For quality training of a Young Researcher, it is desirable that the candidate has knowledge of English language and has prior knowledge in the field of biochemistry and biotechnology.

5. Priloge, ki jih je treba priložiti ob prijavi (*Documents required to be submitted with the application*):

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bibliografija (*bibliography*)

življenjepis (*CV*)

motivacijsko pismo (*motivation letter*)

opis dosedanjega sodelovanja pri raziskovalnem delu (*description of the candidate's research work*)

osnutek idejne zasnove raziskovalnega dela (*preliminary research proposal*)

priporočilno pismo (*letter of recommendation*)

druge priloge (*other attachments*):

Opis raziskovalnega dela (*Research work description*)

1. Članica UL (*UL member*):

Univerza v Ljubljani, Fakulteta za farmacijo (University of Ljubljana, Faculty of Pharmacy)

2. Ime, priimek in elektronski naslov mentorja/ice (*Mentor's name, surname and email*):

Robert Roškar (robert.roskar@ffa.uni-lj.si)

3. Raziskovalno področje (*Research field*):

1.09. Farmacija (Pharmacy)

4. Opis raziskovalnega dela (*Research work description*):

Vključuje morebitne dodatne pogoje, ki jih mora izpolnjevati kandidat/ka za mladega raziskovalca/ko, ki niso navedeni v razpisu za mlade raziskovalce (*It includes any additional conditions that the candidate for a young researcher must meet, which are not listed in the call to tender for young researchers.*).

Slov.:

Razpisano mesto mlade raziskovalke oz. raziskovalca (MR) je usmerjeno na področje nečistot oziroma kontaminantov v zdravilih, s posebnim poudarkom na genotoksičnih nitrozaminih. Ti so po številnih globalnih odpoklicih zdravil v zadnjih letih postali ena osrednjih tem v regulativi zdravil in farmacevtski industriji. Sprva so bili v ospredju nizkomolekularni nitrozamini, v zadnjem času pa se bolj usmerjamo k strukturnim nitrozaminom, ki predstavljajo številne raziskovalne izzive.

MR bo v okviru doktorskega usposabljanja razvijal in optimiziral napredne analizne metode za določanje nitrozaminov v sledovih ter se poglobljeno ukvarjal z raziskovanjem mehanizmov njihovega nastanka ter z razvojem pristopov za njihovo zaviranje v zdravilnih učinkovinah. Raziskave bodo osredotočene na zdravila, dodatno pa bomo preverjali prisotnost nitrozaminov tudi v drugih izdelkih, kot so prehranska dopolnila, kozmetični izdelki in vodni vzorci, s ciljem širšega razumevanja izpostavljenosti.

Pri delu bo MR uporabljal sodobno analitsko opremo, predvsem tekočinsko kromatografijo sklopljeno z masno spektrometrijo visoke ločljivosti ter napredne postopke priprave vzorcev. Raziskovalno delo MR predstavlja nadaljevanje in nadgradnjo obstoječega raziskovalnega dela na Fakulteti za farmacijo ter dosedanjega uspešnega sodelovanja s farmacevtsko industrijo na tem področju. Projekt bo temeljil na že vzpostavljeni raziskovalni infrastrukturi, strokovnem znanju in sodelovanju z industrijskimi partnerji. Pridobljena znanja in kompetence s področja napredne analitike, regulative ter obravnave nečistot bodo doktorandu kasneje omogočila široke zaposlitvene možnosti tako v akademskem okolju kot tudi v farmacevtski industriji, kjer je za tovrstne strokovnjake zelo veliko povpraševanje.

Od kandidata pričakujemo zelo dobro znanje angleškega jezika, visoko stopnjo motiviranosti, samoiniciativnost ter interes za predlagano raziskovalno delo. Zaželeno je predhodno znanje s področja analitike (zlasti kromatografskih tehnik in masne spektrometrije) ter izkušnje z laboratorijskim delom.

Eng.:

The open position for an Early-Stage Researcher (PhD candidate) is focused on the field of impurities in medicinal products, with particular emphasis on genotoxic nitrosamines. Following numerous global medicines recalls in recent years, these impurities have become one of the central topics in pharmaceutical regulation and the

pharmaceutical industry. Initially, low-molecular-weight nitrosamines were the main focus; more recently, attention has shifted toward structural nitrosamines, which present several research challenges.

Within the doctorate, the PhD candidate will develop and optimize advanced analytical methods for the determination of nitrosamines at trace levels and will conduct in-depth research into the mechanisms of their formation, as well as the development of approaches for their mitigation in active pharmaceutical ingredients. The research will focus primarily on medicinal products, while the presence of nitrosamines will also be investigated in other products, such as food supplements, cosmetic products, and water samples, with the aim of achieving a broader understanding of their exposure.

The PhD candidate will use state-of-the-art analytical instrumentation, particularly liquid chromatography coupled with high-resolution mass spectrometry, as well as advanced sample preparation techniques. The research represents a continuation and advancement of existing research activities at the Faculty of Pharmacy and builds upon previously successful collaborations with the pharmaceutical industry in this field. The project will be based on already established research infrastructure, expertise, and collaboration with industrial partners. The knowledge and competencies acquired in advanced analytics will provide the doctoral candidate with broad employment opportunities in both academia and the pharmaceutical industry, where there is strong demand for such experts. Applicants are expected to demonstrate excellent proficiency in English, a high level of motivation, initiative, and interest in the proposed research work. Previous knowledge in analytical chemistry (especially chromatographic techniques and mass spectrometry) as well as laboratory experience are desirable.

5. Priloge, ki jih je treba priložiti ob prijavi (*Documents required to be submitted with the application*):

potrdilo o doseženi izobrazbi (*proof of completed education*)

- kandidat z zaključenim magistrskim študijskim programom (2. bolonjska stopnja) (*candidate who has completed a Master's degree (2nd Bologna level)*):
 - o diplomska listina / potrdilo o zaključku študijskega programa (*diploma certificate / certificate of completion of the study programme*)
 - o priloga k diplomi / potrdilo o opravljenih obveznostih (*diploma supplement / official transcript of records containing all grades obtained in the study programme*)
- kandidat, ki še ni zaključil študija na 2. stopnji (*candidate who has not yet completed a Master's degree*):
 - o potrdilo o do sedaj opravljenih obveznostih z ocenami magistrskega študijskega programa, s katerim se bo kandidat prijavil na doktorski študij (*official transcript of records listing all courses and grades obtained so far in the Master's degree programme on the basis of which the candidate will apply for enrollment in a doctoral degree programme.*)

nagrade – univerzitetna Prešernova nagrada ali Prešernova nagrada članice Univerze v Ljubljani oz. druga enakovredna nagrada (*awards, e.g. Prešeren Prize of the University of Ljubljana, Prešeren Prize of a University of Ljubljana member and/or another equivalent award*)

bibliografija (*bibliography*)

življenjepis (*CV*)

motivacijsko pismo (*motivation letter*)

opis dosedanjega sodelovanja pri raziskovalnem delu (*description of the candidate's research work*)

osnutek idejne zasnove raziskovalnega dela (*preliminary research proposal*)

priporočilno pismo (*letter of recommendation*)

druge priloge (*other attachments*):

Opis raziskovalnega dela (Research work description)

1. Članica UL (UL member):

Fakulteta za farmacijo; UL-FFA

2. Ime, priimek in elektronski naslov mentorja/ice (Mentor's name, surname and email):

Anamarija Zega; anamarija.zega@ffa.uni-lj.si

3. Raziskovalno področje (Research field):

1.09 Farmacija (Pharmacy); LS7 Preprečevanje, diagnosticiranje in zdravljenje človeških bolezni (Prevention, Diagnosis and Treatment of Human Diseases)

4. Opis raziskovalnega dela (Research work description):

Vključuje morebitne dodatne pogoje, ki jih mora izpolnjevati kandidat/ka za mladega raziskovalca/ko, ki niso navedeni v razpisu za mlade raziskovalce (It includes any additional conditions that the candidate for a young researcher must meet, which are not listed in the call to tender for young researchers.).

Slov.: Naraščajoča bakterijska odpornost na obstoječe antibiotike predstavlja eno največjih sodobnih groženj javnemu zdravju. Razvoj novih protibakterijskih učinkovin z inovativnimi mehanizmi delovanja je zato ključen za zagotavljanje učinkovitega zdravljenja ter omejevanje širjenja rezistentnih sevov.

*Raziskovalno delo mladega raziskovalca bo usmerjeno na področje načrtovanja in sinteze novih protibakterijskih učinkovin, predvsem učinkovin proti povzročitelju tuberkuloze (*Mycobacterium tuberculosis*) ter proti ostalim klinično pomembnim netuberkuloznim mikobakterijam. Mikobakterije predstavljajo poseben terapevtski izziv zaradi svoje kompleksne celične stene, ki omejuje prehajanje zdravilnih učinkovin, dodatno težavo pa predstavlja njihova sposobnost preživetja in razmnoževanja znotraj celic gostitelja, zlasti makrofagov, kar zahteva razvoj učinkovin, ki učinkovito prodirajo v celice ter delujejo v specifičnem znotrajceličnem okolju.*

Na osnovi preliminarnih rezultatov vrednotenja predhodno sintetiziranih spojin na izoliranih mikobakterijskih tarčah, bakterijah, okuženih makrofagih in biofilmih, bo mladi raziskovalec načrtoval in sintetiziral nizkomolekularne zaviralce DNA giraze in modulatorje drugih izbranih mikobakterijskih tarč. Sintetizirane spojine bomo nato tudi v sklopu mednarodnega sodelovanja biokemijsko, mikrobiološko in toksikološko ovrednotili, kar bo omogočilo nadaljnjo optimizacijo njihovih lastnosti.

Mladi raziskovalec bo pridobil celovit nabor znanj s področja načrtovanja zdravilnih učinkovin, kemijske sinteze in analitike, strukturne biologije ter vrednotenja aktivnosti protibakterijskih spojin. Delo bo potekalo v sodelovanju z mednarodnimi partnerji.

Zaželeno je, da ima kandidat z metodološko znanje s področja organske sinteze in farmacevtske kemije ter poznavanje analiznih metod za karakterizacijo organskih spojin. Zaželen je tudi interes za interdisciplinarno delo, ki zajema kemijo, biokemijo in mikrobiologijo.

Eng.: The increasing prevalence of bacterial resistance to existing antibiotics represents one of the most serious contemporary threats to public health. The development of novel antibacterial agents with innovative mechanisms of action is therefore essential to ensure effective treatment and to limit the spread of resistant strains.

*The research activities of the junior researcher will focus on the design and synthesis of new antibacterial agents, particularly compounds targeting the causative agent of tuberculosis (*Mycobacterium tuberculosis*) as well as other clinically relevant non-tuberculous mycobacteria. Mycobacteria pose a specific therapeutic challenge due to their*

complex and highly impermeable cell wall, which restricts the penetration of drug molecules. An additional obstacle is their ability to survive and proliferate within host cells, especially macrophages, necessitating the development of compounds capable of efficient cellular uptake and activity within the specific intracellular environment.

Based on preliminary evaluation of previously synthesized compounds against isolated mycobacterial targets, whole bacterial cells, infected macrophages, and biofilms, the junior researcher will design and synthesize small-molecule inhibitors of DNA gyrase as well as modulators of other selected mycobacterial targets. The synthesized compounds will subsequently undergo biochemical, microbiological, and toxicological evaluation within the framework of international collaborations, enabling further optimization of their pharmacological and pharmacokinetic properties.

The junior researcher will acquire comprehensive expertise in drug design, chemical synthesis and analytical characterization, structural biology, and the evaluation of antibacterial activity. The research will be conducted in collaboration with international partners.

Candidates are expected to possess methodological knowledge in organic synthesis and medicinal chemistry, as well as familiarity with analytical techniques for the characterization of organic compounds. An interest in interdisciplinary research encompassing chemistry, biochemistry, and microbiology is also desirable.

5. Priloge, ki jih je treba priložiti ob prijavi (*Documents required to be submitted with the application*):

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 - o diplomska listina / potrdilo o zaključku študijskega programa (*diploma certificate / certificate of completion of the study programme*)
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priporočilno pismo (*letter of recommendation*)

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