

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 molekularskih 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. Mehanizem teh pretvorb poteka tudi preko fukoziiltransferaz (encimi FT6, 7 in 8) in sialiltransferaz (encima ST6Gal1 in ST6GalNAc1), ki so membransko vezani encimi v Golgijevem aparatu ter skrbijo za z rakom povezano prekomerno pripenjanje fukoziilnih in sialilnih ostankih na površinskih glikanih. Domnevamo, da bi z zaviranjem omenjenih encimov lahko spreminjali površinske lastnosti rakastih celic tako, da zaviramo možnost njihovega ugnezdjenja v okolje in olajšamo njihovo prepoznavo imunskemu sistemu. MR bo načrtoval nizkomolekularne zaviralce omenjenih glikoziltransferaz na osnovi obstoječih kristalnih struktur tarčnih encimov. Temu bo sledila sinteza načrtovanih spojin in njihova karakterizacija. V sodelovanju s prof. Ramonom Hurtado-Guerrero z Univerze v Zaragozi (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 ter rakavih sferoidov in tumoroidov iz kliničnih izolatov v sodelovanju s prof. Celso Reisom iz Univerze v Portu (Portugalska). 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.

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.

Eng.: The research work of the young researcher (YR) will be based on the recently awarded Horizon EU MSCA-DN GlyCanDrug project (ID: 101119601). The project involves 9 academic institutions and 6 companies, providing an exceptional platform for excellent research work that would not be possible in a single laboratory. YR's planned work extends to the field of glycoscience, namely the development and evaluation of targeted molecular probes to precisely inhibit the expression of cancer-associated glycans. Previous preliminary studies have shown that cancer tissue (over)expresses various glycans such as surface glycoproteins and glycolipids. The mechanism of these conversions occurs via fucosyltransferases (enzymes FT6, 7 and 8) and sialyltransferases (enzymes ST6Gal1 and ST6GalNAc1), which are membrane-bound enzymes in the Golgi apparatus that are responsible for the cancer-associated excessive accumulation of fucosyl and sialyl residues on surface glycans. We hypothesize that by inhibiting these enzymes, we can alter the surface properties of cancer cells to inhibit their ability to colonize the environment and facilitate their recognition by the immune system. YR will develop small molecule inhibitors of the above-mentioned glycosyltransferases based on the existing crystal structures of the target enzymes. Subsequently, the developed compounds will be synthesized and characterized. In collaboration with Prof. Ramon Hurtado-Guerrero from the University of Zaragoza (Spain), we will obtain the target enzymes in sufficient quantities to carry out biochemical tests to inhibit enzyme activity. The compounds will then be studied in collaboration with Prof. Celso Reis from the University of Porto (Portugal) for their inhibition of the formation of specific glycans on the surface of human cell lines as well as cancer spheroids and tumoroids from clinical isolates. As part of the training, we are planning short visits by the future YR, who will acquire complementary knowledge in the basics of

biochemistry and cell biology at the above-mentioned partner institutions. Her/his research work will therefore not only be interdisciplinary, but also international. The YR will also be trained in transferable skills as part of the GlyCanDrug project's training package. With the acquired knowledge and experience, YR will be highly competitive for employment in research institutions or in the Slovenian pharmaceutical industry. 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.

5. Priloge, ki jih kandidat priloži k prijavi (*Documents that the candidate submits with the application*):

- ☒ **diplomska listina/potrdilo o zaključku študijskega programa** (*diploma certificate for study programme, with which the candidate has enrolled/ will enroll in a doctoral degree programme*)
- ☒ **priloga k diplomi/ potrdilo o opravljenih obveznostih** (*official transcript of all the grades for study programme, with which the candidate has enrolled/will enroll in a doctoral degree programme*)
- ☒ **potrdilo o do sedaj opravljenih obveznostih z ocenami študijskega programa, s katerim se bo kandidat prijavil na študij** (*official transcript of all the grades the candidate has received so far for the study programme, with which the candidate will enroll to a doctoral degree programme*)
- ☒ **nagrade** (*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

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

Rok Frlan, rok.frlan@ffa.uni-lj.si

3. Raziskovalno področje (Research field):

1.09 Farmacija

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.: Protimikrobna odpornost predstavlja enega izmed desetih največjih svetovnih javnozdravstvenih izzivov. Ena najučinkovitejših strategij za premagovanje protimikrobne odpornosti je ciljanje specifičnih bakterijskih encimov in mehanizmov, ki prispevajo k odpornosti patogenih bakterij.

Usposabljanje mladega raziskovalca ali raziskovalke bo potekalo na Katedri za farmacevtsko kemijo Fakultete za farmacijo Univerze v Ljubljani, kjer že vrsto let raziskujemo in razvijamo nove zaviralce pomembnih bakterijskih tarč. Mladi raziskovalec bo sodeloval pri načrtovanju in sintezi zaviralcev bakterijskih tarč, kot so InhA, FtsQ, BamA in iztočne črpalke. InhA je že dolgo prepoznana tarča za zdravljenje tuberkuloze, medtem ko predstavljajo ostale tarče povsem nove pristope k boju proti odpornim bakterijam in do danes še nimajo klinično uporabnih antibiotikov.

Glavni cilj raziskovalnega dela bo načrtovanje selektivnih zaviralcev omenjenih tarč, njihova sinteza in karakterizacija. Pri razvoju novih zaviralcev bomo uporabili kombinacijo računalniškega modeliranja (virtualno reševanje, molekulske sidranje, modeliranje QSAR), kemijske sinteze in bioloških testiranj. Sintetizirane spojine bomo nato biokemijsko, mikrobiološko in toksikološko ovrednotili, kar bo omogočilo nadaljnjo optimizacijo njihovih lastnosti.

Zahtevane kompetence kandidata:

- Znanje organske sinteze in farmacevtske kemije
- Poznavanje analiznih metod za karakterizacijo organskih spojin

Zaželene kompetence kandidata:

- Poznavanje osnov računalniškega načrtovanja zdravilnih učinkovin (molekulske sidranje, QSAR, virtualno reševanje).
- Osnovno znanje programiranja v programskem jeziku Python in pripravljenost na učenje novih računalniških metod, kot je strojno učenje.

- Interes za interdisciplinarno delo, ki zajema kemijo, biokemijo in mikrobiologijo.

Raziskovalec bo pridobil celovit nabor znanj s področja načrtovanja zdravil, kemijske sinteze, strukturne biologije in vrednotenja biološke aktivnosti novih protibakterijskih spojin. Delo bo potekalo v sodelovanju z domačimi in mednarodnimi partnerji, kar bo omogočilo prenos znanja in nadgradnjo raziskovalnih kompetenc mladega raziskovalca.

Eng.: Antimicrobial resistance is one of the biggest global public health challenges. One of the most effective strategies for overcoming antimicrobial resistance is targeting specific bacterial enzymes and mechanisms that contribute to the resistance of pathogenic bacteria.

The training of the young researcher will take place at the Department of Pharmaceutical Chemistry at the Faculty of Pharmacy, University of Ljubljana, where we have been researching and developing new inhibitors of important bacterial targets for many years. The young researcher will participate in the design and synthesis of inhibitors targeting bacterial proteins such as InhA, FtsQ, BamA, and efflux pumps. InhA has long been recognized as a target for tuberculosis treatment, while the other targets represent entirely new approaches to combating resistant bacteria and currently lack clinically approved antibiotics.

The main objective of the research will be the design, synthesis, and characterization of selective inhibitors for these targets. The development of new inhibitors will involve a combination of computational modeling (virtual screening, molecular docking, QSAR modeling), chemical synthesis, and biological testing. The synthesized compounds will be biochemically, microbiologically, and toxicologically evaluated to enable further optimization of their properties.

Required competencies of the candidate:

- Knowledge of organic synthesis and pharmaceutical chemistry
- Familiarity with analytical methods for characterizing organic compounds

Preferred competencies of the candidate:

- Understanding the basics of computational drug design (molecular docking, QSAR, virtual screening).
- Basic programming skills in Python and a willingness to learn new computational methods, such as machine-learning.
- Interest in interdisciplinary work, including chemistry, biochemistry, and microbiology.

The researcher will acquire a comprehensive set of skills in drug design, chemical synthesis, structural biology, and the evaluation of the biological activity of novel antibacterial compounds. The research will be conducted in collaboration with domestic and international partners, enabling knowledge transfer and the enhancement of the young researcher's scientific competencies.

5. Priloge, ki jih kandidat priloži k prijavi (*Documents that the candidate submits with the application*):

☒ **potrdilo o do sedaj opravljenih obveznostih z ocenami študijskega programa, s katerim se bo kandidat prijavil na študij** (*official transcript of all the grades the candidate has received so far for the study programme, with which the candidate will enroll to a doctoral degree programme*)

☒ **nagrade** (*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*)

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

Opis raziskovalnega dela (Research work description)

1. Članica UL (UL member):

Fakulteta za farmacijo (Faculty of pharmacy)

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

Martina Gobec, martina.gobec@ffa.uni-lj.si

3. Raziskovalno področje (Research field):

Onko-imunologija (oncoimmunology)

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.: Proteasom je večkatalitični encim in osrednja komponenta ubikvitin-proteasomskega sistema (UPS). Predstavlja ključni regulator znotrajcelične razgradnje beljakovin in posledično uravnava številne celične procese, vključno s proliferacijo, diferenciacijo, procesiranjem antigenov in tvorbo vnetnih molekul. Različne podenote proteasoma ($\beta 1$, $\beta 2$, $\beta 5$, $\beta 1i$, $\beta 2i$, $\beta 5i$) imajo specifične katalitične funkcije, ki edinstveno prispevajo k celični biologiji. Vloga proteasoma v tumorskih in imunskih celicah je dobro raziskana, zaradi česar je proteasom uveljavljena terapevtska tarča pri hematoloških malignih obolenjih. Številni zaviralci proteasoma so trenutno tudi v kliničnih testiranjih za zdravljenje različnih imunskih bolezni.

Čeprav je proteasom v imunskih in tumorskih celicah obsežno raziskan, pa ostaja njegova vloga v trombocitih, zlasti v kontekstu oblikovanja tumorskega mikrookolja, slabo razumljena. Trombociti, majhni delci celic brez jedra, so vse bolj prepoznani kot ključni akterji pri zaščiti rakavih celic pred imunskim sistemom in spodbujanju njihove invazivnosti. Znano je, da lahko trombociti prevzamejo različne tumorsko izločene komponente in posledično spremenijo svoje lastnosti, kar dodatno spodbuja zaviranje imunskega odziva, invazivnost rakavih celic in angiogenezo. Na podlagi tega se poraja vprašanje, ali bi lahko zaradi ključne vloge proteasoma v uravnavanju imunskega sistema z njegovim selektivnim zaviranjem v trombocitih spremenili njihovo funkcionalnost do te mere, da ne bi več nudili zaščite tumorskim celicam.

Kandidat/ka za mladega/o raziskovalca/o bo tako poskušal/a odgovoriti na vprašanje s sistematičnim vrednotenjem vloge posameznih podenot proteasoma v delovanju trombocitov in njihovem vplivu na napredovanje raka dojke. Z uporabo naprednih orodij molekularne biologije, modelov tumorjev, pridobljenih od pacientov, in mikrofluidnih sistemov bo:

- razjasnil/a, kako selektivno zaviranje posameznih podenot proteasoma v trombocitih vpliva na interakcije med tumorji in trombociti ter na oblikovanje tumorskega mikrookolja;
- ocenil/a klinični pomen proteasomsko moduliranih trombocitov na primarnih kulturah raka dojke, pridobljenih iz tumorskih eksplantov bolnic;
- raziskal/a učinke snovi, sproščenih iz trombocitov, na imunski sistem in angiogenezo

Zaželeno je, da ima kandidat/ka znanje angleškega jezika ter predhodno metodološko znanje s področja celične oz. molekularne biologije.

Eng.: The proteasome is a multicatalytic enzyme and a central component of the ubiquitin-proteasome system (UPS). It serves as a key regulator of intracellular protein degradation, thereby controlling numerous cellular processes, including proliferation, differentiation, antigen processing, and the production of inflammatory molecules. Different proteasome subunits ($\beta 1$, $\beta 2$, $\beta 5$, $\beta 1i$, $\beta 2i$, $\beta 5i$) perform specific catalytic functions, uniquely contributing to cellular biology. The role of the proteasome in tumor and immune cells has been well-studied, establishing it as a validated therapeutic target in

hematological malignancies. Numerous proteasome inhibitors are also currently undergoing clinical trials for the treatment of various immune-related diseases.

Although the proteasome is extensively studied in tumor and immune cells, its role in platelets—particularly in the context of shaping the tumor microenvironment (TME)—remains poorly understood. Platelets, small anucleate cell fragments, are increasingly recognized as key players in protecting tumor cells from the immune system and promoting their invasiveness. It is well-documented that platelets can take up various tumor-secreted components, subsequently altering their properties to further suppress immune responses, enhance tumor cell invasiveness, and promote angiogenesis. This raises the question of whether selective inhibition of proteasomes in platelets, given their key role in regulating immune responses, could modify their functionality to the extent that they no longer provide protection to tumor cells.

The candidate will try to answer this question by systematically evaluating the role of individual proteasome subunits in platelet function and their impact on breast cancer progression. Using advanced molecular biology tools, patient-derived tumor models, and microfluidic systems, the candidate will:

- elucidate how selective inhibition of individual proteasome subunits in platelets influences tumor-platelet interactions and the shaping of the TME;
- assess the clinical relevance of proteasome-modulated platelets using primary breast cancer cultures derived from patient tumor explants;
- investigate the effects of platelet-released factors on the immune system and angiogenesis.

It is desirable for the candidate to have knowledge of the English language and prior methodological knowledge in the field of cellular or molecular biology.

5. Priloge, ki jih kandidat priloži k prijavi (*Documents that the candidate submits with the application*):

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☒ **priloga k diplomii/ potrdilo o opravljenih obveznostih** (*official transcript of all the grades for study programme, with which the candidate has enrolled/will enroll in a doctoral degree programme*)

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☒ **nagrade** (*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):

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):

Prof. dr. Žiga Jakopin (ziga.jakopin@ffa.uni-lj.si)

3. Raziskovalno področje (Research field):

Po klasifikaciji ARIS: 1.09 Farmacija (Pharmacy) oziroma po klasifikaciji ERC: LS6 Imunost, infekcije in imunoterapija (Immunity, Infection, and Immunotherapy)

4. Opis raziskovalnega dela (Research work description):

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V svetu trenutno vlada akutno pomanjkanje novih adjuvansov in imunoterapevtikov. Adjuvansi povečajo imunogenost cepiv, zaradi česar so njihove ključne komponente. Potrebni so ne le, da povečajo jakost samega odziva ampak tudi, da vplivajo na sam tip odziva, ki bi privedel do najbolj učinkovite zaščitne imunosti proti določenemu patogenu/tumorju. Imunoterapevtiki so sposobni modulacije lastnega imunskega sistema in so uporabni predvsem pri zdravljenju rakavih obolenj, pa tudi vnetnih bolezni in alergij. Napredek v razumevanju prirojene imunosti je odprl nove možnosti za razvoj tovrstnih imunomodulatorjev. Prirojeni imunski sistem sestavljajo imunske celice, ki vsebujejo vrsto receptorjev za prepoznavanje vzorcev (PRR), med drugimi tudi receptorje NOD1. Agonisti PRR stimulirajo te celice in zagotovijo nepogrešljive začetne signale, ki določajo tip, jakost in trajnost imunskega odziva, zato predstavljajo obetavne spojine vodnice za razvoj novih adjuvansov/imunoterapevtikov. Hkratna aktivacija različnih PRR omogoča ojačanje signala. Kovalentna povezava več agonistov PRR pa le še poveča njihovo adjuvantno aktivnost, zato so tudi konjugirani dvojni agonisti postali predmet raziskav. Cilj usposabljanja bo torej raziskati in pripraviti nove imunomodulatorje za ustvarjanje ustreznih imunskih odzivov.

Mladi raziskovalec bo v prvi fazi vključen v razvoj novih agonistov NOD1 in konjugiranih dvojnih agonistov prirojene imunosti. Nato bo z uporabo celičnih testov na primarnih imunskih celicah in celičnih linijah proučil mehanizem delovanja spojin ter imunomodulatorno delovanje sintetiziranih spojin. V sklopu sodelovanja med skupino prof. Jakopina in prof. Slütterja (Leiden University) bomo proučevali ex vivo adjuvantno delovanje sintetiziranih spojin na uveljavljenih modelih, in sicer na mišjih dendritičnih celicah in jih ovrednotili v smislu vpliva na izločanje citokinov, izražanje površinskih označevalcev in sposobnosti indukcije proliferacije T celic CD4 in CD8. Najboljše spojine bodo kot adjuvansi ovrednotene na mišjem modelu vakcinacije. Izbrane spojine bomo kot imunoterapevtike dali ovrednotiti tudi v singenskem mišjem tumorskem modelu. Vzporedno bo mladi raziskovalec pod somentorstvom izr. prof. Janje Zupan (UL FFA, Katedra za klinično biokemijo) ovrednotil agoniste prirojene imunosti tudi na mezenhimskih matičnih/stromalnih celicah (MSC), in sicer s poudarkom na vplivu na polarizacijo, fenotip, sekretorni citokinski profil ter vplivu na interakcije MSC z imunskimi celicami in rakavimi celicami.

Če povzamemo, mladi raziskovalec bo v okviru doktorske disertacije načrtoval in sintetiziral agoniste NOD1 in konjugirane dvojne agoniste PRR ter vrednotil njihovo biološko aktivnost z različnimi celičnimi testi. Zaželeno je, da ima kandidat za mladega raziskovalca osnovna znanja s področja farmacevtske/organske kemije (načrtovanje, sinteza in analitika spojin) in celične imunologije (biološko vrednotenje spojin z in vitro testi), ki pa jih bo tekom doktorata ponovno osvežil in tudi poglobil.

Currently, there is an acute shortage of new adjuvants and immunotherapeutics in the world. Adjuvants enhance the immunogenicity of vaccines, making them essential components. They are necessary not only to increase the strength of the immune response but also to influence the specific type of response that would lead to the most effective protective immunity against a particular pathogen or tumor. Immunotherapeutics are capable of modulating the body's immune system and are primarily used for the treatment of cancer, as well as inflammatory diseases and allergies. Advances in understanding innate immunity have opened new opportunities for developing such immunomodulators. The innate immune system consists of immune cells that contain various pattern recognition receptors (PRRs), including NOD1 receptors. PRR agonists stimulate these cells and provide crucial initial signals that determine the type, strength, and duration of the immune response, making them promising lead compounds for the development of new adjuvants and immunotherapeutics. Simultaneous activation of different

PRRs enhances the signal, while covalent binding of multiple PRR agonists further increases their adjuvant activity. As a result, conjugated dual agonists have also become a subject of research. The goal of the training will be to investigate and develop new immunomodulators to generate appropriate immune responses.

In the first phase, the young researcher will be involved in the development of new NOD1 agonists and conjugated dual agonists of innate immunity. Subsequently, using cellular assays on primary immune cells and cell lines, they will study the mechanism of action of these compounds and their immunomodulatory effects. As part of the collaboration between the research groups of Prof. Jakopin and Prof. Slütter (Leiden University), we will investigate the ex vivo adjuvant activity of the synthesized compounds using established models, specifically on murine dendritic cells. These studies will assess their impact on cytokine secretion, the expression of surface markers, and their ability to induce CD4 and CD8 T cell proliferation. The most promising compounds will be evaluated as adjuvants in a murine vaccination model. Selected compounds will also be assessed as immunotherapeutics in a syngeneic murine tumor model. In parallel, the young researcher will evaluate innate immunity agonists on mesenchymal stem/stromal cells (MSCs) under supervision of co-supervisor Assoc. Prof. Janja Zupan (UL FFA, Department of Clinical Biochemistry), focusing on their effects on polarization, phenotype, secretory cytokine profile, and their interactions with immune cells and cancer cells.

In summary, in the scope of doctoral dissertation the young researcher will design and synthesize NOD1 agonists and conjugated dual PRR agonists and then investigate their activity profile in various cell-based assays. It is therefore desirable that the candidate for the young researcher has basic knowledge of medicinal/organic chemistry (design, synthesis and analysis of compounds) as well as cell immunology (i.e., practical skills for conducting biological evaluation in vitro). However, these skills will be refreshed and further deepened during the PhD program.

5. Priloge, ki jih kandidat priloži k prijavi (*Documents that the candidate submits with the application*):

☒ **diplomska listina/potrdilo o zaključku študijskega programa** (*diploma certificate for study programme, with which the candidate has enrolled/ will enroll in a doctoral degree programme*)

☒ **priloga k diplomi/ potrdilo o opravljenih obveznostih** (*official transcript of all the grades for study programme, with which the candidate has enrolled/will enroll in a doctoral degree programme*)

☒ **potrdilo o do sedaj opravljenih obveznostih z ocenami študijskega programa, s katerim se bo kandidat prijavil na študij** (*official transcript of all the grades the candidate has received so far for the study programme, with which the candidate will enroll to a doctoral degree programme*)

☐ **nagrade** (*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):

Univerza v Ljubljani, Fakulteta za farmacijo

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

Mitja Kos, e-pošta: mitja.kos@ffa.uni-lj.si

3. Raziskovalno področje (Research field):

1.09 Farmacija

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.: Dokazi iz realnega okolja za vrednotenje učinkovitosti in varnosti zdravstvenih tehnologij ter na vrednosti temelječa zdravstvena obravnava

Dokazi iz realnega okolja (real-world evidence, RWE) lahko zagotovijo dragocen vpogled v varnost in učinkovitost zdravil in drugih zdravstvenih tehnologij dejanski klinični praksi. Kombinacija RWE in na vrednosti temelječe zdravstvene obravnave (Value-Based Healthcare, VBHC), ki v ospredje postavlja k pacientu osredotočene zdravstvene izide, in stroškovno učinkovitost, lahko pomaga oblikovati zdravstvene politike in ukrepe, ki spodbujajo trajnostno naravnani sistem zdravstvenega varstva.

Dokazi iz realnega okolja so postali ključni element pri vrednotenju učinkovitosti in varnosti zdravil ter zdravstvenih storitev. Dopolnjujejo podatke klasičnih kliničnih študij, in s tem pomembno osvetlijo delovanje zdravstvenih tehnologij v dejanskem okolju. Dokazi iz realnega okolja so še posebej koristni pri boljšem razumevanju farmakoterapije v različnih zdravstvenih sistemih in v primeru posameznih populacij bolnikov, zlasti pri starejših odraslih, bolnikih s kroničnimi boleznimi in pri sočasni uporabi več zdravil.

Koncept na vrednosti temelječe zdravstvene obravnave temelji na razvoju merljivih zdravstvenih izidov, ki imajo največjo vrednost za pacienta, ob upoštevanju stroškovne učinkovitosti znotraj zdravstvenih storitev. VBHC poudarja na pacienta osredotočeno obravnavo in izide, zaradi česar predstavlja obetavno spodbudo za trajnostni dostop do inovativnih zdravil, zlasti ob naraščajočih stroških zdravstvenega varstva.

Rezultati raziskav bodo opredelili strategije za izboljšanje cenovne dostopnosti in samega dostopa do zdravil ob ohranjanju visoke kakovosti oskrbe. Prav tako bodo rezultati omogočali bolj informirano odločanje in podpirali razvoj novih pristopov v zdravstvu, ki dajejo prednost vrednosti pred obsegom, kar bo koristilo bolnikom, ponudnikom zdravstvenih storitev in sistemu zdravstvenega varstva.

Pri kandidatih so zaželenne kompetence in vpogledi na naslednjih področjih: poznavanje zdravstvenega sistema, vrednotenje zdravstvenih tehnologij, farmakoekonomika in/ali zdravstvena ekonomika, na vrednosti temelječe zdravstvene obravnave, znanje angleškega jezika.

Eng.: Real-World Evidence and Value-Based Healthcare for Sustainable Medication Access

Real-world evidence (RWE) can provide valuable insights into the safety and effectiveness of medicines and other health technologies in real-world settings. When combined with a value-based healthcare (VBHC) approach that prioritizes patient-centered outcomes and cost-effectiveness, RWE can inform policies and interventions that promote sustainable healthcare systems.

Real-world evidence has become a crucial asset in the assessment of the efficacy and safety of medicines and healthcare services. It complements the traditional clinical trial data by offering valuable insights into the performance of health technologies in real-world settings. RWE is particularly useful in gaining a better understanding of pharmacotherapy in various healthcare systems and patient populations, especially in the case of older adults, patients with chronic illnesses, and when multiple medications are used concomitantly.

The concept of Value-Based Healthcare provides a methodology for measurable healthcare outcomes that make the biggest difference to patients, while driving cost-efficiencies within health services. VBHC emphasizes patient-centered care and outcomes, making it a promising approach for promoting sustainable access to innovative medicines, particularly in the face of rising healthcare costs.

This research will identify strategies to improve the affordability and accessibility of medicines while maintaining high-quality care. It will also inform policy decisions and support the development of new approaches to healthcare that prioritize value over volume, benefiting patients, healthcare providers, and the healthcare system.

It is desirable from candidates to have competencies and insights into the following themes: healthcare systems, health technology assessment, pharmacoeconomics and/or health economics, value-based healthcare, English language.

5. Priloge, ki jih kandidat priloži k prijavi (*Documents that the candidate submits with the application*):

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☒ **priporočilno pismo** (*letter of recommendation*)

☒ **druge priloge** (*other attachments*): priloge, ki so argumentirano smiselne