

Opis raziskovalnega dela (Research work description)

1. Članica UL (UL member):

Medicinska fakulteta

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

Jure Derganc, jure.derganc@mf.uni-lj.si

3. Raziskovalno področje (Research field):

Biofizika (Biophysics)

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.: Na Inštitutu za biofiziko Medicinske fakultete iščemo mladega raziskovalca ali mlado raziskovalko z diplomo ali magisterijem iz fizike, ki ima željo raziskovati na področju ved o življenju. Naše raziskovalne tematike so povezane z razumevanjem delovanja celičnih toksinov, z uporabo umetnih celičnih membran v sintezni biologiji ter z analizo in manipulacijo velikega števila posameznih sesalskih celic, kar postaja vse pomembnejše pri personalizirani medicini in sodobnih celičnih terapijah. Vsebina naloge bo prilagojena predznanju in interesom kandidatke oz. kandidata. Pri raziskavah bomo uporabljali najnovejše mikroskopske tehnike, optično pinceto, sodobne metode za strojno razpoznavanje slik ter razvijali nove mikrofluidične metode za uporabo v biomedicini. Več informacij o naših raziskavah je na naslovu <https://biophysics.splet.arnes.si/jure-derganc/>

Eng.: We are looking for an open-minded student with a BSc MSc in Physics who is interested in conducting research at the intersection between biophysics and medicine. Our research topics include the study of cellular toxins, artificial cell membranes in synthetic biology, and high-throughput analysis of individual mammalian cells, which is becoming increasingly important for personalized medicine and advanced cell therapies. The PhD project will be tailored to the candidate's interests and prior expertise. Our work involves cutting-edge microscopy techniques, optical tweezers, advanced image recognition methods, and the development of novel biomedical microfluidic techniques. For more information about our research, visit <https://biophysics.splet.arnes.si/jure-derganc/>

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):

Medicinska fakulteta

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

Mateja Erdani Kreft, mateja.erdani@mf.uni-lj.si

3. Raziskovalno področje (Research field):

Celična biologija

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.: Rak sečnega mehurja je ena najpogostejših malignih bolezni z naraščajočo incidenco v Evropi. Pogosteje prizadene moške, a ženske imajo pogosto slabšo prognozo. Človeška amnijska membrana (hAM) izkazuje imunomodulatorne in protitumorske lastnosti. Nedavne raziskave so pokazale, da njeni pripravki selektivno zavirajo proliferacijo rakavih celic mehurja, ne da bi vplivali na zdrave celice. Delujejo na signalno pot FAK/PI3K/Akt/mTOR, zavirajo epitelno-mezenhimski prehod (EMT) ter omejujejo migracijo in invazijo rakavih celic. Namen doktorskega dela bo preučiti celično-biološke mehanizme protitumorskega delovanja pripravkov hAM in njihovo uporabo pri zdravljenju raka mehurja. Raziskava bo osredotočena na vpliv hAM na avtofagijo in makropinocitozo ter oceno učinka kombinacije hAM z molekularnimi inhibitorji. Uporabljeni bodo biomimetični in vitro modeli urotelija sečnega mehurja, tumorski eksplantati in organoidi raka sečnega mehurja iz pacientov, različne mikroskopske metode ter tehnike molekularne biologije in funkcionalne analize. Rezultati raziskave bodo prispevali k razumevanju protirakavih mehanizmov delovanja hAM, kar bo omogočilo ne le iskanje novih terapevtskih tarč, temveč tudi boljše razumevanje celično-bioloških mehanizmov raka sečnega mehurja. Pri kandidatu/kandidatki za mladega raziskovalca/ko se pričakuje izkušnje z delom s celičnimi kulturami ter osnovne izkušnje s svetlobno in elektronsko mikroskopijo.

Eng.: Bladder cancer is one of the most common malignancies with a rising incidence in Europe. It more frequently affects men, but women often have a poorer prognosis. The human amniotic membrane (hAM) exhibits immunomodulatory and antitumor properties. Recent studies have shown that its preparations selectively inhibit the proliferation of bladder cancer cells without affecting healthy cells. They act on the FAK/PI3K/Akt/mTOR signaling pathway, suppress epithelial-mesenchymal transition (EMT), and limit the migration and invasion of cancer cells. The aim of the doctoral research will be to investigate the cell biological mechanisms underlying the antitumor effects of hAM and its potential use in bladder cancer treatment. The study will focus on the effects of hAM on autophagy and macropinocytosis, as well as the evaluation of the combined effects of hAM with molecular inhibitors. Biomimetic in vitro models of the bladder urothelium, tumor explants, and patient-derived bladder cancer organoids will be used, along with various microscopic methods, molecular biology techniques, and functional analyses. The research findings will contribute to the understanding of the antitumor mechanisms of hAM, which will not only facilitate the identification of new therapeutic targets but also improve the understanding of the cell biological mechanisms of bladder cancer. Candidates for the young researcher position are expected to have experience in cell culture work and basic experience in light and electron microscopy.

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)
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☒ **bibliografija** (*bibliography*)

☒ **življenjepis** (*CV*)

☒ **motivacijsko pismo** (*motivation letter*)

Opis raziskovalnega dela (Research work description)

1. Članica UL (UL member):

Univerza v Ljubljani, Medicinska fakulteta (University of Ljubljana, Faculty of Medicine)

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

Marko Goličnik, marko.golicnik@mf.uni-lj.si

3. Raziskovalno področje (Research field):

Naravoslovje - Biokemija in molekularna biologija (Natural sciences - Biochemistry and molecular biology)

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.:

Mladi raziskovalec (M/Ž) bo svoje delo opravljal na Inštitutu za biokemijo in molekularno genetiko UL MF v skupini Laboratorija za preučevanje encimov. Ob tem bo vključen tudi v raziskovalni program 'Molekulski mehanizmi uravnavanja celičnih procesov v povezavi z nekaterimi boleznimi pri človeku' (P1-170), v študijskem letu 2025/26 pa se bo vpisal na interdisciplinarni doktorski študijski program Biomedicina UL – smer Biokemija in molekularna biologija. Zaradi navedenega bi bil primeren kandidat z dokončanim magistrskim študijskim programom iz naravoslovnih ved oz. ved o življenju (biokemija, biologija, biotehnologija, laboratorijska biomedicina ipd).

V Laboratoriju za preučevanje encimov preučujemo predvsem kinetične in strukturne lastnosti encimov iz razreda hidrolaz s poudarkom na esterazah kot so holinesteraze in paraoksonaza 1. Znanstveno raziskovalno delo mladega raziskovalca bo zajemalo preučevanje encima paraoksonaza 1 (PON1). PON1 je od kalcija odvisen in evolucijsko nespecializiran encim, ki bi specifično kataliziral presnovo fiziološkega substrata ter je odgovoren za hidrolizo različnih vrst estrov kot so ciklični estri (laktoni), aril estri in fosfortriestri. Delo mladega raziskovalca bo obsegalo izražanje in čiščenje rekombinantnih encimov ter kinetično karakteriziranje njihovega delovanja pod različnimi eksperimentalnimi pogoji v prisotnosti različnih ligandov. Vsebina naloge bo prilagojena predznanju in predhodni izobrazbi kandidata. Izkušnje z različnimi računalniškimi programi ter predhodne izkušnje z raziskovalnim delom v laboratoriju je dobrodošlo, ni pa pogoj.

Eng.:

The young researcher (M/F) will work at the Institute of Biochemistry and Molecular Genetics, UL MF, in the Laboratory for Enzyme Research. He/she will also be included in the research program 'Molecular mechanisms of regulation of cellular processes related to some human diseases' (P1-170), and in the academic year 2025/26 he will enroll in the interdisciplinary doctoral study program Biomedicine UL - Biochemistry and Molecular Biology major. For this reason, a suitable candidate would be a completed master's study program in natural sciences or life sciences (biochemistry, biology, biotechnology, laboratory biomedicine, etc.).

In the Laboratory for Enzyme Research, we primarily study the kinetic and structural properties of enzymes from the class of hydrolases, with an emphasis on esterases such as cholinesterases and paraoxonase 1. The young researcher's scientific research work will include the study of the enzyme paraoxonase 1 (PON1). PON1 is a calcium-dependent and evolutionarily unspecialized enzyme that specifically catalyzes the metabolism of a physiological substrate and is responsible for the hydrolysis of various types of esters such as cyclic esters (lactones), aryl esters and phosphotriesters. The work of the young researcher will include the expression and purification of recombinant enzymes and the kinetic characterization of their activity under various experimental conditions in the presence of various ligands. The content of the assignment will be adapted to the candidate's prior knowledge and education. Experience with various computer programs and previous experience with research work in a laboratory is welcome, but not a requirement.

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

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☒ **motivacijsko pismo** (*motivation letter*)

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

Opis raziskovalnega dela (Research work description)

1. Članica UL (UL member):

Univerza v Ljubljani, Medicinska fakulteta, Vrazov trg 2, 1000 Ljubljana, Slovenija

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

Marko Kreft, marko.kreft@mf.uni-lj.si

3. Raziskovalno področje (Research field):

3.03. Medicinske vede. Nevrobiologija

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.:

Astrociti so najpogostejše ne-nevronske celice v osrednjem živčnem sistemu. Idealno so pozicionirani za zaznavanje sinaptične dejavnosti v možganih, uravnavanje pretoka krvi ter interakcijo z nevroni in endotelijskimi celicami. Otekanje astrocitov lahko ovira njihovo sposobnost podpiranja energetskega metabolizma možganov. V predhodni raziskavi smo odkrili, da so spremembe v volumnu astrocitov posledica razgrinjanja plazemske membrane in ne vstavljanja nove membrane. To smo ugotovili s pomočjo elektronske mikroskopije, ki sicer omogoča visoko ločljivostno analizo, vendar ne omogoča opazovanja živih celic v realnem času. Astrociti imajo pomembno vlogo pri uravnavanju homeostaze spanja s sproščanjem adenoizina, ki deluje na presinaptične receptorje A1 ali A2A, kar sproži spremembe v njihovi celični morfologiji. Ta komunikacija je dvosmerna, saj lahko na funkcijo astrocitov vplivajo tudi zunajcelični signali, kot so adenzin in laktat, mehanski dražljaji ter aktivacija receptorjev sirot, sklopljenih z G-proteini, kot na primer GPR27. V naših nedavnih raziskavah smo pokazali, da astrociti igrajo ključno vlogo v energetskem metabolizmu možganov, pri čemer nanje vplivajo noradrenalin, signalizacija preko kanabinoidnih receptorjev in adenoizinska signalizacija. Že prej je bilo znano, da astrociti sodelujejo pri odstranjevanju metabolitov iz možganov med spanjem. Tako imenovana glimfatična pot, ki temelji na akvaporinu-4 v astrocitih, je ključna pri tem procesu, vendar mehanizmi nadzora celičnega volumna še niso raziskani.

Doktorski kandidat bo uporabljal napredno super-ločljivo optično mikroskopijo in mikroskopijo atomskih sil za spremljanje morfoloških sprememb astrocitov, ki spremljajo spremembe v energetskem metabolizmu. Metabolite, kot so glukoza, laktat in piruvat, bomo spremljali z uporabo znotrajceličnih nanosenzorjev na osnovi fluorescenčnega resonančnega prenosa energije (FRET). Raziskava kandidata bo osredotočena na razumevanje mehanizmov, ki povezujejo energetski metabolizem astrocitov, dinamiko celičnega volumna in morfološke spremembe astrocitnih izrastkov kot odziv na zunajcelične in znotrajcelične signale.

Zaželeno je, da ima kandidat predhodne izkušnje na področju raziskav celične fiziologije. Prav tako je priporočljivo poznavanje sistema kakovosti v laboratorijskem okolju. Doktorski projekt bo prispeval k boljšemu razumevanju energetskega metabolizma astrocitov in spremljajočih morfoloških sprememb, kar bo nudilo nove vpoglede v njihovo vlogo pri delovanju možganov.

Eng.:

Astrocytes are the most abundant non-neuronal cell type in the central nervous system. They are ideally positioned to sense synaptic activity in the brain, regulate blood flow, and interact with neurons and endothelial cells. Astrocyte swelling can impair their ability to support brain energy metabolism. Our previous research has shown that changes in astrocytic volume result from plasma membrane unfolding rather than the insertion of new membrane. This conclusion was drawn from electron microscopy studies, which, while highly detailed, do not allow real-time imaging of live cells.

Astrocytes are believed to modulate sleep homeostasis by releasing adenosine, which acts on presynaptic A1 and A2A adenosine receptors and triggers changes in their own cell morphology. However, this communication appears to be bidirectional, as astrocytic function can also be influenced by extracellular signals such as adenosine and lactate, mechanical stimuli, and the activation of orphan G protein-coupled receptors, including GPR27. Our recent findings indicate that astrocytes play a significant role in brain energy metabolism, particularly through regulation by noradrenaline, cannabinoid signaling, and adenosine signaling. It was previously known that astrocytes contribute to the clearance of metabolic waste from the brain during sleep. The so-called glymphatic pathway, which depends on astrocytic aquaporin-4, is critical in this process; however, the mechanisms governing astrocyte volume control remain unknown.

The PhD candidate will utilize advanced super-resolution optical microscopy and atomic force microscopy to monitor morphological changes in astrocytes associated with shifts in energy metabolism. Metabolites such as glucose, lactate, and pyruvate will be tracked using intracellular nanosensors based on fluorescence resonance energy transfer (FRET).

The candidate's research will focus on elucidating the mechanisms linking astrocyte energy metabolism, cell volume dynamics, and morphological changes in astrocyte processes in response to extracellular and intracellular signaling.

Prior experience in cell physiology research is preferred. Additionally, familiarity with quality systems in a laboratory environment is desirable. This PhD project will contribute to a deeper understanding of astrocyte energy metabolism and the associated morphological changes, providing new insights into their role in brain function.

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 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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☒ **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*):

MEDICINSKA FAKULTETA (FACULTY OF MEDICINE)

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

ANDREJA KUKEC andreja.kukec@mf.uni-lj.si

3. Raziskovalno področje (*Research field*):

JAVNO ZDRAVJE (PUBLIC HEALTH)

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.:

Raziskovanje na področju aktualnih izzivov s področja javnega zdravja (opazovanih zdravstvenih izidov, izpostavljenosti, metodologije – razvoj in validacija orodji ter oblikovanje/vpeljava javnozdravstvenih intervencij). Raziskovalno delo se bo izvajalo v akademskem in kliničnem okolju.

Eng.:

Research on current public health challenges (observed health outcomes, exposures, methodologies - development and validation of tools and design/implementation of public health interventions). The research will be carried out in academic and clinical environment.

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

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☒ **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*)

Opis raziskovalnega dela (Research work description)

1. Članica UL (UL member):

Medicinska fakulteta

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

Tea Lanišnik Rižner, tea.lanisnik-rizner@mf.uni-lj.si

3. Raziskovalno področje (Research field):

3.07 Medicina, Metabolne in hormonske motnje,

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.:

Izhodišče raziskovalne naloge MR: Rak jajčnikov je najbolj smrtonosen ginekološki rak. Najpogostejši rak jajčnikov je serozni rak jajčnikov visokega gradusa, ki se razvršča v štiri molekularne podtippe. Število na novo ugotovljenih primerov raka jajčnikov vsako leto narašča, vendar se preživetje bolnic v zadnjih letih ni bistveno izboljšalo. Pri večini bolnic rak diagnosticirajo v kasnejši fazi, ko ima bolezen že slabo prognozo. Poleg citoreduktivnega operativnega zdravljenja se za zdravljenje raka jajčnikov običajno uporablja kemoterapija z derivati platine in taksanov. Čeprav je prvi odziv na to zdravljenje ugoden, pa se kar v 2/3 primerov razvije na kemoterapevtsko rezistentna oblika raka. Trenutno le 30-40% bolnic preživi pet let. Študije naše raziskovalne skupine so razkrile, da so v kemorezistenco vpleteni tudi steroidni hormoni. Pred kratkim smo pri seroznem raku jajčnikov visokega gradusa opisali razlike v izražanju genov in v metabolizmu estrogenov glede na odzivnost na kemoterapevtske. Pokazali smo, da se nekateri geni vpleteni v sintezo in delovanje estrogenov statistično značilno različno izražajo pri različnih molekularnih podtipih raka jajčnikov in predstavljajo možne prognostične označevalce. Objavljene študije kažejo, da so v kemorezistenco vpleteni tudi drugi steroidni hormoni, tako androgeni kot progesteron, vendar molekularni mehanizmi vpletenosti steroidnih hormonov v kemorezistenco še niso raziskani. Podrobno razumevanja biosinteze/metabolizma steroidnih hormonov in njihovega delovanja v povezavi s kemorezistenco bi tako lahko prispevalo k odkrivanju novih možnosti zdravljenja na kemoterapijo neodzivnega raka jajčnikov.

V okviru raziskovalne naloge želimo razjasniti mehanizme vpletenosti izbranih steroidnih hormonov, predvsem progesterona, v kemorezistenco raka jajčnikov. Raziskava bo potekala v sodelovanju z Ginekološko kliniko, UKC Ljubljana in Katholic University Leuven, Belgija. **Delovna hipoteza:** Spremembe v lokalni biosintezi/metabolizmu in delovanju progesterona so povezane z napredovanjem in kemorezistenco raka jajčnikov. Javno dostopni omski podatki

kemosenzitivnega/kemorezistentnega raka jajčnikov, v kombinaciji študijami metabolizma, transkriptomskimi ter proteomskimi podatki kemosenzitivnih/kemorezistentnih modelnih celičnih linij in vzorcev tkiv, omogočajo opredelitev novih tarč zdravljenja in lahko prispevajo k prepoznavanju novih možnosti zdravljenja.

Metode: Zastavljeno hipotezo bomo preverili z analizo prostodostopnih podatkov, študijo izražanja celotnega genoma (RNA sekvenciranje), s pristopom tarčne transkriptomike in proteomike, z uporabo tkivnih mikromrež in imunohistokemijskega barvanja, s študijami metabolizma progesterona z uporabo LC-MS/MS, z utišanjem genov s pristopom siRNA in študijami proliferacije, invazivnosti in migracije v realnem času. Vlogo progesterona bomo proučili v vzorcih tkiva bolnic in v modelnih celičnih linijah kemorezistentnega in kemosenzitivnega seroznega raka jajčnikov visokega gradusa. Proučili bomo: 1. razlike v transkriptomu in proteomu kemorezistentnega in kemosenzitivnega rakavega tkiva in modelnih celičnih linij, 2. razlike v sintezi in metabolizmu progesterona in 3. pomen receptorja za progesteron in ključnih encimov biosinteze in metabolizma progesterona pri kemorezistenci. Na osnovi teh rezultatov bomo postavili model vpletenosti progesterona v kemorezistenco raka jajčnikov. Z raziskovalno nalogo želimo prispevati k razjasnitvi mehanizmov kemorezistence in možnosti uporabe hormonske terapije kot novega pristopa zdravljenja kemorezistentnih oblik raka.

Eng:

Background of the research project: Ovarian cancer is the deadliest type of gynaecological cancer. The most common ovarian cancer is high-grade serous ovarian cancer, which is categorised into four molecular subtypes. The number of newly diagnosed cases of ovarian cancer is increasing every year, but the survival rate of patients has not improved significantly in recent years. In most patients, the cancer is diagnosed at a later stage when the disease already has a poor prognosis. In addition to cytoreductive surgical treatment, chemotherapy with platinum

derivatives and taxanes is usually used to treat ovarian cancer. Although the initial response to this treatment is favourable, a form of cancer resistant to chemotherapy develops in up to 2/3 of cases. Currently, only 30-40% of patients survive five years. Studies by our research group have shown that steroid hormones are also involved in chemoresistance. Recently, we have described differences in gene expression and oestrogen metabolism in high-grade serous ovarian cancer in relation to response to chemotherapy. We have shown that some genes involved in the synthesis and action of oestrogens are statistically significantly differentially expressed in different molecular subtypes of ovarian cancer and represent potential prognostic markers. Published studies suggest that other steroid hormones, both androgens and progesterone, are also involved in chemoresistance, but the molecular mechanisms of steroid hormone involvement in chemoresistance have not yet been investigated. A detailed understanding of the biosynthesis/metabolism of steroid hormones and their effect in the context of chemoresistance could thus contribute to the discovery of new treatment options for chemotherapy-refractory ovarian cancer. **As part of the research project**, we aim to clarify the mechanisms of the involvement of selected steroid hormones, in particular progesterone, in the chemoresistance of ovarian cancer. The research will be conducted in collaboration with the Department of Gynaecology, the University Medical Centre Ljubljana and the Katholic University Leuven, Belgium. **Working hypothesis:** Changes in local biosynthesis/metabolism and the action of progesterone are associated with the progression and chemoresistance of ovarian cancer. Publicly available omics data from chemosensitive/chemoresistant ovarian cancer in combination with metabolism studies, transcriptomic and proteomic data from chemosensitive/chemoresistant tissue samples and model cell lines will allow the identification of new drug targets and may contribute to the identification of new treatment options. **Methods:** The hypothesis will be tested by analysing publicly available data, whole genome expression studies (RNA sequencing), targeted transcriptomics and proteomics, tissue microarrays and immunohistochemical staining, studies of progesterone metabolism by LC-MS/MS, gene silencing by siRNA and real-time studies of proliferation, invasiveness and migration. The role of progesterone will be investigated in tissue samples from patients and in model cell lines of chemoresistant and chemosensitive high-grade serous ovarian cancer. We will investigate: 1) the differences in the transcriptome and proteome of chemoresistant and chemosensitive cancer tissue and model cell lines, 2) the differences in progesterone metabolism, and 3) the role of the progesterone receptor and key enzymes of progesterone biosynthesis and metabolism in chemoresistance. Based on these results, we will develop a model for the involvement of progesterone in ovarian cancer chemoresistance. With this research project we aim to contribute to the elucidation of the mechanisms of chemoresistance and the possibility of using hormone therapy as a new approach for the treatment of chemoresistant forms of cancer.

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, Medicinska fakulteta (*University of Ljubljana, Faculty of Medicine*)

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

doc. dr. Polona Maver Vodičar, dr. med.; polona.maver@mf.uni-lj.si

3. Raziskovalno področje (Research field):

3.01 Mikrobiologija in imunologija (*Microbiology and immunology*)

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.:

Kandidat za mladega raziskovalca se bo vključil v raziskovalno delo programske skupine P30083, ki preučuje odnose parazitskega obstajanja med povzročitelji bolezni in gostiteljem, načini prenosa, življenjskimi krogi mikroorganizmov in dejavniki, ki vplivajo na nastanek in klinični potek bolezni ter zdravljenje. Usposabljanje kandidata bo obsegalo aktivno vključitev v strokovni proces laboratorija, spoznavanje diagnostičnih in raziskovalnih metod, izvajanje različnih delovnih procesov pod mentorstvom in postopno uvajanje v samostojno opravljanje raziskovalnega dela. Raziskovalno področje bo obsegalo razvoj, implementacijo in evalvacijo različnih diagnostičnih mikrobioloških metod, preučevanje etiologije in prevalence infektivnih bolezni, imunski odziv na okužbo s patogenimi mikroorganizmi ter preučevanje odpornosti proti protimikrobnim zdravilom. Uporabljene metode dela bodo vključevale predvsem molekularne metode in metode sekvenciranja naslednje generacije z bioinformacijsko analizo genomskega podatkov z ovrednotenjem kvalitete podatkov.

Kandidat mora izkazati aktivno znanje angleškega jezika in osnovno znanje uporabe programskega orodja Microsoft Office. Zaželeno je, da ima kandidat izobrazbo iz naravoslovne smeri, predvsem pridejo v poštev kandidati s področja mikrobiologije, biotehnologije, medicine, veterinarske medicine in sorodnih ved. Zaželeno so vsaj minimalne izkušnje z laboratorijskim delom na področju mikrobiologije, biologije, kemije ali farmacije.

Eng.:

The candidate for the position of Junior Researcher will be involved in the research activities of the Research Programme Group P30083, covering a broad area of research that includes host-parasite relationships, pathogen transmission routes, the life cycle of microorganisms, and factors influencing the development and clinical course of disease and its treatment. The candidate's training will include active participation in the laboratory work process, learning about diagnostic and research methods and performing various work tasks under supervision, as well as gradual introduction to independent research work.

The field of research includes the development, implementation and evaluation of diagnostic microbiological methods, the study of the aetiology and prevalence of infectious diseases, the immune response to the infection and antimicrobial resistance. Research methods used will

primarily include molecular and next-generation sequencing methods with bioinformatic analysis of genomic data and assessment of data quality.

The candidate must be fluent in English and have a basic knowledge of Microsoft Office software. A degree in the natural sciences, particularly in microbiology, biotechnology, medicine, veterinary medicine or related fields, is highly desirable, as is at least minimal experience in laboratory work in the field of microbiology, biology, chemistry or pharmacy.

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*)
- ☐ **priporočilno pismo** (*letter of recommendation*)
- ☐ **druge priloge** (*other attachments*)

Opis raziskovalnega dela (Research work description)

1. Članica UL (UL member):

Medicinska fakulteta (Medical faculty)

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

Marija Petek Šter, marija.petek-ster@mf.uni-lj.si

3. Raziskovalno področje (Research field):

Družinska medicina (Family medicine)

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.: Srčno-žilne bolezni predstavljajo velik javnozdravstveni problem, ki se v zadnjih letih močno povezuje s problemom multimorbidnosti v starajoči se populaciji. V kolikor kandidat ne bo zdravnik, je mogoče temo prilagoditi iz klinično usmerjene v širše področje obvladovanja srčno-žilnih bolezni in z zdravjem povezanih problemov starajoče se populacije (javno-zdravstveni vid, ekonomska analiza, zdravstvena politika, edukacija...)

Eng.: Cardiovascular disease represents a major public health problem, which in recent years has been strongly associated with the problem of multimorbidity in the aging population. If the candidate is not a physician, the topic can be adapted from a clinically oriented one to a broader area of cardiovascular disease management and health-related problems of the aging population (public health perspectives, economic analysis, health policy, education, etc.)

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)

☒ **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)

Opis raziskovalnega dela (Research work description)

1. Članica UL (UL member):

Medicinska fakulteta

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

Izr. prof. dr. Tadeja Režen, tadeja.rezen@mf.uni-lj.si

3. Raziskovalno področje (Research field):

1.05 Biokemija in molekularna biologija/ 3.00 Medicinske vede

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.).

Rak jeter ima visoko smrtnost zaradi omejenih terapevtskih pristopov in pozne diagnoze. Njegova incidenca se povečuje zaradi staranja prebivalstva in tudi zaradi naraščanja etiologije povezane z metabolično zamaščenostjo jeter. Bolezni jeter so kompleksne večfaktorske bolezni, ki zahtevajo interdisciplinaren pristop k preučevanju in razumevanju molekularnih mehanizmov patologije razvoja in progresije bolezni. Krožne RNA imajo dokazano vlogo v patogenezi različnih rakov in vplivajo tako na razvoj progresijo raka kot tudi na odziv na zdravljenje. Ključno pa je, da lahko preko eksosomov vplivajo na druge celice v telesu in da se tudi izmenjujejo med tumorskimi celicami in imunskimi celicami.

Mladi raziskovalec/mlada raziskovalka bo s posameznoceličnimi omskimi pristopi analiziral/a vzorce bolnikov in tako določil/a celično-specifično izražanje krožnih RNA v tumorjih jeter. Molekularno funkcijo in onkogeni potencial izbranih krožnih RNA bo potrjeval/a na 3D celičnem modelu z molekularnimi in biokemijskimi metodami. Usposabljanje bo obsegalo sodelovanje pri klinični študiji in delo z vzorci bolnikov, različne pristope k transkriptomskim analizam, učenje izbranih statističnih in orodij funkcijske genomike, delo s celičnimi linijami in razvoj celičnega modela raka jeter ter številne različne molekularne in biokemijske metode. Usposabljanje bo potekalo na Centru za funkcijsko genomiko in bio-čipe, ki je del Inštituta za biokemijo in molekularno genetiko, na Medicinski fakulteti UL.

Iščemo visoko motiviranega kandidata/kandidatko, ki si želi usposabljati tako v laboratoriju kot tudi v analizah podatkov. Od kandidata/kandidatke pričakujemo željo po raziskovanju nepoznanega, ustvarjalnost, samoiniciativnost in sposobnost timskega dela v interdisciplinarni in mednarodni skupini.

Liver cancer has a high mortality rate due to limited therapeutic approaches and late diagnosis. Its incidence is increasing due to the ageing population and increasing aetiology associated with metabolic fatty liver disease. Liver diseases are complex, multifactorial diseases that require an interdisciplinary approach to study and understand the molecular mechanisms of disease development and progression. Circular RNAs have been shown to play a role in the development of various cancers and influence both the development and progression of cancer and the response to treatment. The key point is that they can affect other cells in the body via exosomes and that they also vary between tumour cells and immune cells.

The young researcher will use single-cell omics approaches to analyse patient samples to determine the cell-specific expression of circular RNAs in liver tumours. The molecular function and oncogenic potential of selected circRNA will be confirmed using molecular and biochemical methods on 3D liver cell model. The training includes participation in a clinical study, working with patient samples, different approaches to transcriptome analysis, learning selected statistical and functional genomics tools, working with cell lines and developing a cell model for liver cancer, as well as different molecular and biochemical methods. The training will take place at the Centre for Functional Genomics and Bio-chips, which is part of the Institute of Biochemistry and Molecular Genetics at the UL Faculty of Medicine.

We are looking for a highly motivated candidate who is willing to be trained both in the laboratory and in data analysis. We expect the applicant to have a desire to explore the unknown, creativity, initiative and the ability to work in a team in an interdisciplinary and international group.

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*)

☒ **druge priloge** (*other attachments*)

Opis raziskovalnega dela (Research work description)

1. Članica UL (UL member):

Medicinska fakulteta

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

Rok Romih rok.romih@mf.uni-lj.si

3. Raziskovalno področje (Research field):

Celična biologija

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.: Med mikcijskimi cikli mora stena sečnega mehurja zaznavati spremembe v napetosti in raztegnjenosti ter te informacije posredovati centralnemu živčnemu sistemu. Kadar sistem zaznavanja in sporočanja ne deluje, pride do simptomov, kot je na primer intersticijski cistitis, povezan s sindromom bolečega mehurja. Medtem ko razumemo delovanje senzornih živcev, pa se zelo malo ve o vlogah ne-živičnih celic pri teh dogodkih. Raziskovalno delo se bo osredotočalo na proučevanje celic urotelija, ki gradijo pregrado med steno sečnega mehurja in urinom, ter celic v vezivnem tkivu mehurja. Namen dela je analiza izražanja in subcelične lokalizacije mehanosenzornih proteinov v celicah zdravega sečnega mehurja in med intersticijskim cistitisom ter moduliranje ionskih in membranskih transportov med mikcijskim ciklom. Uporabljene bodo mikroskopske metode, metode molekularne biologije in funkcionalne analize. Rezultati dela bodo prispevali k razumevanju mehanosenzorne vloge različnih celic v steni sečnega mehurja in njihovega prispevka k razvoju sindroma bolečega mehurja med intersticijskim cistitisom.
Od kandidat/ka za mladega raziskovalca/ko se pričakujejo osnovne izkušnje z delom na svetlobnih in elektronskih mikroskopih.

Eng.: During micturition cycle, the degree of tension and distension of the bladder wall must be sensed and relayed to the central nervous system, otherwise bladder dysfunction ensues as in interstitial cystitis/bladder pain syndrome. While we understand the function of sensory neurons, the roles of non-neuronal cells in these events is not clear. Research work focuses on urothelial cells, which form the barrier between the bladder wall and urine, and bladder's connective tissue cells. The aims of the research are detection and localization of mechanosensory proteins in cells of normal bladder and in interstitial cystitis and analyses of ion transports and membrane traffic as responses to changes during micturition cycles. Microscopy and molecular biology methods as well as functional analyses will be applied. The results will contribute to understanding of mechanosensory role of bladder wall constituent cells and their contribution to interstitial cystitis/bladder pain syndrome.
The candidate for a young researcher must be acquainted with work with light and electron microscopes.

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)
- ☐ **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*)

Opis raziskovalnega dela (Research work description)

1. Članica UL (UL member):

Medicinska fakulteta

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

Uroš Tkalec, uros.tkalec@mf.uni-lj.si

3. Raziskovalno področje (Research field):

Fizika

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.).

Usposabljanje mladega raziskovalca bo potekalo v okviru programske skupine »Biofizika polimerov, membran, gelov, koloidov in celic« na Inštitutu za biofiziko in v sodelovanju z eksperimentalnimi skupinami in teoretiki, ki delujejo na povezanih vsebinah tako v Sloveniji kot v tujini. Raziskovalno se bo ukvarjal z dinamičnimi pojavi na odzivnih mehkih površinah na osnovi tekočih kristalov, ki so del aktualnih interdisciplinarnih raziskav na preseku biofizike, mikrofluidike in fizike kondenzirane snovi. Posvetil se bo pripravi in karakterizaciji vodnih kapljic in emulzij v stiku s tekočokristalnimi mezofazami na mikrostrukturiranih površinah. Pri tem bo uporabljal najsodobnejše eksperimentalne metode, kot so kapljična mikrofluidika, optična polarizacijska in interferenčna mikroskopija, visokoločljive hitre kamere, mikromanipulatorji, vrhunski merilnik kontaktnih kotov in površinske napetosti ter zunanja polja. Realizacija predlagane tematike bo pomembno prispevala k razumevanju dinamike kompleksnih tekočin, kapilarnih pojavov in transporta mikrodlecev na novih tipih mehkih površin ter s tem k razvoju naprednih materialov za senzorske aplikacije.

Pri kandidatih so zaželeno poglobljena znanja iz fizike, optike in programiranja, analitičen pristop k reševanju problemov, motiviranost za učenje novih konceptov, izkušnje z eksperimentalnim delom v laboratoriju ter solidne pisne in govorne sposobnosti v angleškem jeziku. Pomemben del nalog mladega raziskovalca bo tudi pregled relevantne literature, priprava publikacij za mednarodno uveljavljene znanstvene revije, sodelovanje pri prijavih projektov ter udeležba na strokovnih konferencah in poletnih šolah v tujini. Na ta način bo mladi raziskovalec pridobil kvalitetno podlago za nadaljevanje bolj samostojne znanstvene poti ali za delovanje v interdisciplinarnih raziskovalnih skupinah v industriji.

The young researcher will be educated and trained in the group "Biophysics of Polymers, Membranes, Gels, Colloids and Cells" at the Institute of Biophysics and in collaboration with experimental groups and theoreticians working on related topics in Slovenia and abroad. His/her research will focus on dynamic phenomena on responsive liquid crystal-based surfaces, which are part of the current interdisciplinary research at the interface of biophysics, microfluidics and condensed matter physics. He/she will focus on the preparation and characterization of aqueous droplets and emulsions in contact with liquid crystalline mesophases on microstructured surfaces. He/she will use state-of-the-art experimental methods such as droplet microfluidics, optical polarization and interference microscopy, high-speed digital cameras, micromanipulators, contact angle goniometry and external field applications. The realisation of the proposed topic will significantly contribute to the understanding of complex fluid dynamics, capillary phenomena and microparticle transport on novel soft surfaces and thus to the development of advanced materials for sensor applications.

Applicants should have a sound knowledge of physics, optics and programming, an analytical approach to problem solving, the motivation to learn new concepts, experience with experimental work in the laboratory and fluency in English. An important part of the young researcher's tasks will be to review relevant literature, prepare publications for international scientific journals, contribute to project proposals and participate in conferences and summer schools abroad. This will provide the young researcher with a good basis for an independent academic career or for working in interdisciplinary research teams in industry.

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 doktorski 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)
- ☐ 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):

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

Maja Zorović, maja.zorovic@mf.uni-lj.si

3. Raziskovalno področje (Research field):

3. Medicina (3.03. Nevrobiologija) / 3. Medicine (3.03 Neurobiology)
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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.: Mladi raziskovalec oz. mlada raziskovalka (v nadaljevanju: MR) se bo priključil/-a Laboratoriju za raziskave možganov na Inštitutu za patološko fiziologijo, kjer na živalskih modelih nevrodegenerativnih bolezni in duševnih motenj preučujemo vpliv farmakoloških intervencij in/ali neinvazivne možganske stimulacije na spremembe v možganski plastičnosti. Z vedenjskimi testi spremljamo vpliv potencialno terapevtskih postopkov na vedenjske kazalnike bolezni oz. motenj, z naborom biokemijskih raziskav pa ugotavljamo spremembe v izražanju posameznih genov na ravni mRNA in proteinov ter spremembe v aktivnosti izbranih encimov.

MR bo v svoji raziskavi na podganjem modelu za depresijo kombiniral/-a neinvazivno možgansko stimulacijo (repetitivno transkranijsko magnetno stimulacijo (rTMS)) s farmakološkim tretmajem s psihoaktivno substanco psilocibin. V zadnjem času se povečuje zanimanje za uporabo psihedelikov za zdravljenje duševnih motenj, predvsem depresije, pri čemer številne študije poudarjajo potencial psilocibina (psihoaktivne snovi, ki jo najdemo v halucinogenih gobah iz rodu *Psilocybe*), medtem ko se rTMS že nekaj časa uporablja za zdravljenje depresije pri bolnikih, ki jim običajna antidepresivna zdravila ne pomagajo. Pokazalo se je, da ima rTMS trajne učinke na možganske funkcije, ki blažijo depresivne simptome in izboljšajo razpoloženje.

Tako rTMS kot terapija s psilocibinom imata svoje prednosti in pomanjkljivosti in nobena od njiju ni učinkovita pri vseh pacientih. rTMS ima zaradi svoje neinvazivnosti nič ali pa zelo malo neželenih učinkov, a je za antidepresivni učinek potrebnih veliko ponovitev, medtem ko pri psilocibinu za antidepresivno delovanje zadostuje en sam odmerek, a lahko njegov akutni psihedelični učinek pri pacientih privede do anksioznosti ali paničnih napadov, ki negativno vplivajo na rezultat zdravljenja. Na podlagi dognanj dosedanjih predkliničnih in kliničnih raziskav mehanizmov delovanja posamezne od obeh terapij predvidevamo, da bi lahko predhodna nevrostimulacija z rTMS zmanjšala neželene akutne psihedelične učinke psilocibina in izboljšala njegovo antidepresivno delovanje, hkrati pa bi se ob dodatku psilocibina zmanjšala potreba po ponovitvah terapij z rTMS.

MR bo doktorsko nalogo predvidoma opravljal/-a v okviru Doktorskega študija Biomedicina – smer nevroznanost Univerze v Ljubljani. Raziskovalno delo bo potekalo na Inštitutu za patološko fiziologijo in v Medicinskem eksperimentalnem centru, oba MF UL, in bo obsegalo predklinično raziskavo z uporabo modelnih poskusnih živali ter laboratorijsko delo z možganskimi vzorci poskusnih živali. Od kandidata/-ke pričakujemo zainteresiranost za znanstveno-raziskovalno delo na področju nevroznanosti, pripravljenost za usposabljanje in delo z živalmi v poskusih ter aktivno znanje angleškega jezika.

Eng.: The young researcher (hereafter: MR) will join the Brain Research Laboratory at the Institute of Pathological Physiology, where we study the impact of pharmacological interventions and/or non-invasive brain stimulation on changes in brain plasticity in animal models of neurodegenerative diseases and mental disorders. Behavioural assays are used to monitor the impact of treatments on behavioural indicators of the studied disease/disorder, and a range of biochemical techniques are employed to detect changes in the expression of individual genes at the mRNA and protein level, as well as changes in the activity of selected enzymes.

MR will combine non-invasive brain stimulation (repetitive transcranial magnetic stimulation (rTMS)) with pharmacological treatment using the psychoactive substance psilocybin in the rat model of depression. Recently, there has been an increasing interest in the use of psychedelics for the treatment of mental disorders, especially depression, with a number of studies highlighting the potential of psilocybin (a psychoactive substance found in hallucinogenic mushrooms of the genus *Psilocybe*). rTMS has been used for some time to treat depression in patients who do not respond to conventional antidepressant drugs. rTMS has been shown to have lasting effects on brain functions, alleviating depressive symptoms and improving mood.

Both rTMS and psilocybin therapy have their advantages and disadvantages, and neither is effective for every patient. rTMS has no or very few side effects due to its non-invasiveness, but many repetitions are needed for an antidepressant effect. In contrast, with psilocybin, a single dose is sufficient for antidepressant action. Still, its acute psychedelic effect can lead patients to experience anxiousness or panic attacks, which negatively affect the outcome of treatment. Based on the findings of preclinical and clinical studies on the mechanisms of action of each of the two therapies, we hypothesise that pre-treatment with rTMS could reduce the adverse acute psychedelic effects of psilocybin and improve its antidepressant activity while reducing the need for repeat rTMS treatments when psilocybin is added.

MR is expected to carry out his PhD thesis in the framework of the Doctoral Programme in Biomedicine - Neuroscience at the University of Ljubljana. The research will be carried out at the Institute of Pathological Physiology and the Medical Experimental Centre, both at the Faculty of Medicine, UL, and will include preclinical research using model experimental animals and laboratory work with brain samples from experimental animals. We expect the candidate to have an interest in scientific research, a willingness to train and work with experimental animals, and an active knowledge of the English language.

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*)

☒ **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*)

☒ **življenjepis (CV)**

☒ **motivacijsko pismo** (*motivation letter*)