Kratek opis usposabljanja mladega raziskovalca (*Short description of the Young Researcher's training)*

1. Raziskovalna organizacija (*Research organisation)*:

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

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

Izr. prof. dr. Alja Videtič Paska, alja.videtic@mf.uni-lj.si

3. Šifra in naziv raziskovalnega področja (*Research field*):

3.09 Psihiatrija *3.09 Psychiatry*

4. Kratek opis usposabljanja mladega raziskovalca (*Short description of the Young Researcher's training*):

Navedite tudi morebitne druge zahteve, vezane na usposabljanje mladega raziskovalca (npr. znanje angleškega jezika, izkušnje z laboratorijskim delom, potrebne licence za usposabljanje…).

slo: Na globalni ravni samomori predstavljajo 50 % vseh nasilnih smrti med moškimi in 71 % med ženskami in po podatkih Svetovne zdravstvene organizacije vsako leto zaradi samomora umre milijon ljudi. Slovenija sodi v svetu med države z najvišjim samomorilnim količnikom. Samomor je kompleksen fenomen, pri katerem se prepletajo različni dejavniki, kot so npr. genetski dejavniki in dejavniki okolja. Najpomembnejši dejavniki tveganja za samomor so predhodni poskus samomora in duševne motnje. Depresivna motnja prizadane več kot 350 milijonov ljudi na svetu in je eden od glavnih vzrokov invalidnosti; kar 16 % bolnikov z depresivno motnjo pa poskuša storiti samomor. Genetska komponenta naj bi k samomoru prispevala pomemben delež, med 30% in 40%. V naši raziskovalni skupini smo so sedaj že pokazali, da bi pomembno vlogo lahko igrali polimorfizmi posameznih nukleotidov, v zadnjem času pa se posvečamo proučevanju epigenetike, predvsem metilacije DNA. Namen dela mladega raziskovalca je proučevanje drugih epigenetskih mehanizmov, kot so miRNA in posttranslacijske modifikacije histonov, ki bi lahko bili povezani s samomorilnim vedenjem ali duševno motnjo, predvsem depresijo. Pomembna komponenta zastavljene naloge je povezovanje že obsotječih podatkov o metilaciji DNA z novimi epigenetskimi podatki, saj večina do sedaj objavljenih študij raziskuje le posamezne dejavnike tveganja, z globalno oceno le-teh, predvsem pa sovplivanja med njimi, pa bi lažje napredovali k celostnemu razumevanju in obravnavanju samomorilnega vedenja. Pomembno mesto v raziskovanju molekularnih osnov samomorilnega vedenja imajo študije, ki omogočajo vzporejanje med sicer nedosegljivimi ali težko dostopnimi tkivi (možgani in cerebrospinalna tekočina) in perifernimi tkivi (kri, serum), ki pa bi v prihodnosti lahko omogočile razvoj orodij za pomoč pri obravnavi bolnikov. Metodologija dela bo temeljila na delu z možganskimi in krvnimi vzorci žrtev samomora in kontrol, pa tudi oseb z depresivno motnjo, kjer bomo preučevali različne epigenetske mehanizme z metodo sekvenciranja naslednje generacije, izražanja genov, biooinformatiko... Glavni cilj raziskave je s pridobljenimi podatki, ki bodo obsegali tako fenotip kot epigenetski

status, omogočiti celovitejši in globlji vpogled ne samo v samomor, temveč tudi v različna psihična stanja (predispozicije). Boljše poznavanje diagnostičnih in prognostičnih genomskih biooznačevacev predstavlja dober potencial za nadaljnje raziskovanje morebitnih tarč za zdravila, lahko pa služi tudi kot izhodišče za oblikovanje postopkov za pravočasne oblike intervencije.

Od kandidata/ke pričakujemo veliko motiviranost za raziskovalno delo, natačnost, samostojnost, iznajdljivost in odličen študijski uspeh. Predhodne izkušnje z laboratorijskim delom na področju biokemije in molekularne biologije so potrebne. Prednost bodo imeli kandidati s predhodnimi izkušnjami na področju bioinformatike in obdelave podatkov in tisti, ki se želijo dela s podatki sekvenciranja naslednje generacije priučiti.

Kandidat/ka se bo vključil/a v majhno in dinamično skupino, ki se ukvarja s študijem (epi)genetike samomora in drugih duševnih motenj, katere rezultati dosegajo pomembno odmevnost v svetovnem merilu.

eng:
On the global level, suicides represent 50% of all violent deaths among men and 71% among women, and according to the World Health Organization, millions of people die each year due to suicide. Slovenia is among the countries with the highest suicide rate. Suicide is a complex phenomenon, involving a variety of factors, such as genetic and environmental factors. The most important risk factors for suicide are previous suicide attempt and mental disorder. Depression affects more than 350 million people in the world and is one of the main causes of disability; 16% of patients with depressive disorder try to commit suicide. It has been shown that genetic component contributes a significant proportion to suicide, between 30% and 40%. In our research team, we have already shown that the single nucleotide polymorphisms could play an important role, but recently we are oriented on the study of epigenetics, in particular methylation of DNA.
The purpose of the proposed doctoral work is to study other epigenetic mechanisms, such as miRNA and posttranslational modifications of histones, which may be associated with suicidal behaviour or mental disorder, particularly depression. An important component of the work will be linking the already acquired data on methylation of DNA with new epigenetic data since most of the studies so far published explore only individual risk factors. With a global assessment of risk factors and interactions between them, it could become possible to progress towards a holistic understanding and treatment of suicidal behaviour. An important position among the studies of molecular bases of suicidal behaviour have studies that allow the association of otherwise hardly accessible tissues (brain and cerebrospinal fluid) and peripheral tissues (blood, serum), which in the future could enable the development of new tools for better patients examinations.
The methodology of the proposed work will be based on the analysis of samples from brain and blood of suicide of victims and controls, as well as from patients with depressive disorder, where we will study various epigenetic mechanisms using next generation sequencing, gene expression, bioinformatics... The main aim of the research is to obtain comprehensive and deeper insight into the acquired data, which will include both the phenotype and the epigenetic status, not only in suicide, but also in different psychological states (predispositions). A better knowledge of diagnostic and prognostic genomic biomarkers represents a good potential for further exploration of potential drug targets, but it can also serve as a starting point for the design of procedures for timely forms of intervention.

From the candidates we expect to be highly motivated for research work, accurate, independent, ingenious and have excellent grades. Previous experience with laboratory work in the field of biochemistry and molecular biology is required. Priority will be given to candidates with previous

experience in the field of bioinformatics and data computation, and those who would like to learn the analysis of the next generation sequencing data.

The candidate will be included in a small and dynamic group studying the (epi)genetics of suicide and other mental disorders, whose results already achieved a significant global impact.