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

1. Raziskovalna organizacija (*Research organisation)*:

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

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

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| Katja Goričar, katja.goricar@mf.uni-lj.si |

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

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| 1.05.00 Naravoslovje Biokemija in molekularna biologija<br>1.05.00 Nature sciences Biochemistry and molecular biology |

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…).

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| *slo:*<br>Mladi raziskovalec se bo posvetil preučevanju molekularnih mehanizmov, ki vplivajo na razvoj in potek blage kognitivne motnje (BKM) in Alzheimerjeve demence (AD). AD je najpogostejša nevrodegenerativna bolezen, neznane etiopatogeneze, a z močnim genetskim ozadjem. AD je vzrok za 60-70% demenc. Ponavadi se začne z predklinično fazo, ki se imenuje BKM. Ljudje z BKM imajo do 15-krat večjo verjetnost za razvoj AD kot ljudje brez BKM. Namen raziskovanja je poiskati in preučiti možne prognostične označevalce prehoda iz BKM v AD. Študije celotnega genoma in kandidatnih genov so identificirale več kandidatnih genov v poteh, ki so povezane s tveganjem za AB. Opisan je bil tudi poligenski indeks za napoved tveganja za razvoj AB.<br>Kandidat bo preverjal hipotezo, da genetski in epigenetski dejavniki, ki prispevajo k tveganju za razvoj AD, lahko služijo kot prognostični označevalec prehoda med BKM in AD. Kandidat bo analiziral prisotnost genetskih, epigenetskih in tudi drugih potencialnih molekularnih označevalcev (protein, eksosomski označevalci) v cerebrospinalni tekočini in krvni plazmi bolnikov z BKM in AD ter jih skupaj s kliničnimi in slikovnimi podatki vključil v napovedne modele prehoda med BKM in AD. Identificirani prognostični označevalci prehoda med BKM in AB bi omogočili zgodnje odkrivanje bolnikov s povečanim tveganjem za razvoj AB in omogočilo razvoj novih pristopov za upočasnitev ali tudi obrat procesa napredovanja bolezni z morebitnim cepljenjem bolnikov dovzetnih za AB, zdravljenjem z nevroprotektivnimi ali bolezen-modulirajočimi zdravili ali z razširitvijo indikacij za že obstoječa zdravila.<br>Raziskovalno delo bo potekalo v tesnem sodelovanju med Laboratorijem za farmakogenetiko Inštituta za biokemijo, UL MF in Nevrološko kliniko UKC Ljubljana. Pri raziskavah bo mladi raziskovalec uporabljal širok razpon molekularno genetskih pristopov, metode za izolacijo in analizo DNA, RNA, proteinov in zunajceličnih veziklov iz likvorja in krvi, kot tudi različna bioinformacijska in biostatistična orodja. V času opravljanja doktorskega dela se bo mladi raziskovalec udeležil tudi več strokovnih izpopolnjevanj doma in v tujini, zato je potrebno aktivno znanje angleškega jezika. |

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The young researcher will focus on the studies of molecular mechanisms that influence the development and the course of mild cognitive impairment (MCI) and Alzheimer's dementia (AD). AD is the most frequent neurodegenerative disease, with unknown etiopathogenesis, although with a very strong genetic background. AD is the cause of 60–70% of dementias. It usually starts with a preclinical stage, called MCI. People with MCI are up to 15-times more likely to develop AD than those with normal cognition. Our aim is to identify and evaluate potential prognostic biomarkers of transition from MCI to AD. Genome wide and candidate gene studies identified several candidate genes in pathways that may be involved in AD susceptibility and a polygenic score index was proposed for prediction of risk for AD.

The following hypothesis will be tested: Genetic and epigenetic factors contributing to the risk for AD may serve as prognostic biomarkers of transition from MCI to AD. The young researcher will therefor investigate genetic, epigenetic as well as other molecular biomarkers (proteins, exosome-derived biomarkers) in cerebrospinal fluid and peripheral venous blood of patients with MCI and AD. These biomarkers will be incorporated together with the clinical and imaging data in the predictive models for transition from MCI to AD. The identified prognostic biomarkers of transition from MCI to AD will enable early detection of patients with a high risk to develop AD. This could provide the opportunity to reverse or at least slow down the progression with vaccination of susceptible patients. It may also support identification of new drug targets and consequently new neuroprotective or disease modulating drugs, or enable drug repositioning.

Research work will be performed in collaboration between the Pharmacogenetics Laboratory at the Institute of Biochemistry, UL MF and Neurology clinic, University Clinical Centre Ljubljana. The young researcher will use a wide range of molecular genetics research techniques, methods for the isolation and analysis of DNA, RNA, proteins and extracellular vesicles, as well as bioinformatic and biostatistic tools. In the course of his/her PhD studies the young researcher will participate at international research and professional meetings, training courses and collaborative studies, therefore fluent knowledge of the English language is required.