

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

1. Raziskovalna organizacija (*Research organisation*):

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

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

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

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

4.06 Biotehnologija (Biotechnology)

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 tujih jezikov, izkušnje z laboratorijskim delom, potrebne licence za usposabljanje...).

slo:

Za nevrodegenerativne bolezni je značilna selektivna disfunkcija in izguba nevronov, povezanih s patološko spremenjenimi proteini. Slednji se odlagajo v možganh v centralno živčnem sistemu, kot tudi v perifernih organih, ali pa gre za proteine, ki so povezani z vnetnimi procesi, posredovanimi preko aktivacije celic mikroglije in astrocitov. Ti proteini in njihove biokemijske spremembe so lahko potencialna tarča za načrtovanje strategij zdravljenja teh bolezni, ali pa se uporabljajo le kot označevalci bolezni. Mednje sodi tudi cisteniska peptidaza katepsin X. Po drugi strani molekule, kot so nevrotrofični faktorji, ki delujejo na specifične celične receptorje in s tem sprožijo kaskado signalnih poti, lahko vodijo v zmanjšano celično smrt ter spodbujeno proliferacijo in diferenciacijo celic, in tako predstavljajo pomembno orodje za načrtovanje novih strategij zdravljenja nevrodegenerativnih bolezni. Nevrotrofično aktivnost izkazuje tudi C-končni del glikolitičnega encima γ -enolaze, slednja pa je uravnavana s cisteinsko peptidazo katepsinom X, pri čemer le-ta s cepitvijo C-končnega dipeptida γ -enolaze iznici nevropotekativno delovanje γ -enolaze.

Kandidat/ka za mladega/o raziskovalca/o se bo osredotočil/a na proučevanje vloge γ -enolaze in njene regulacije pri spodbujanju preživetja, proliferacije in diferenciacije nevronov in vloge γ -enolaze in njene regulacije s katepsinom X v glja celicah z ozirom na zaščitno vlogo γ -enolaze pri zaščiti poškodovanih nevronov. Opredeljeni znanstveni problem bo obravnavan v okviru raziskovalnega dela mladega/e raziskovalca/e, ki vsebuje tri glavne raziskovalne cilje: 1) vloga γ -enolaze in njene regulacije s katepsinom X pri diferenciaciji nevronov v posamezen podtip; 2) vloga γ -enolaze in njene regulacije s katepsinom X pri vnetnem odzivu, posredovanim z glja celicami; 3) povečanje nevrotrofične in nevropotekativne aktivnosti γ -enolaze s ciljno usmerjenim delovanjem proti peptidazam. Tekom usposabljanja se bo kandidat/ka seznanil/a z *in vitro* celičnimi modeli in *in vivo* živalskimi modeli za proučevanje fizioloških kot tudi patoloških procesov ter povezanih mehanizmov nevrodegeneracije ter pri delu uporabil/a najnovejše tehnike in metode v biokemiji, celični in molekularni biologiji ter metode molekulskega kloniranja.

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

eng:

Neurodegenerative diseases are characterized by selective dysfunction and loss of neurons associated with pathologically altered proteins that deposit in the human brain but also in peripheral organs, and proteins secreted during neuroinflammatory processes, which are mainly mediated by activated microglia and astrocytes. These proteins and their biochemical modifications can be potentially targeted for therapy or be used as biomarkers. On the other hand, the alterations in levels and activities of neurotrophic factors, which act on specific cell receptors to trigger cellular pathways that prevent cell death and support the neuronal proliferation and maturation, also emerge as novel therapeutic strategies of neurodegeneration. Neurotrophic and neuroprotective activity has been reported for the C-terminal end of γ -enolase. This neuroprotective activity is regulated by the cysteine peptidase cathepsin X through proteolytic cleavage of the C-terminal dipeptide of γ -enolase.

The candidate will focus on the understanding of role and regulation of γ -enolase in supporting survival, proliferation and maturation of neuron subtypes and role and regulation of γ -enolase in glia cells during neuroinflammation with an emphasis on γ -enolase-mediated neuroprotection of intoxicated neurons. The identified scientific problem will be addressed in the research work of the Young Researcher containing three main research objectives: 1) role of γ -enolase and its regulation by cathepsin X in differentiation into neuronal-specific subtype; 2) role of γ -enolase and its regulation by cathepsin X in neuroinflammation mediated by glia cells; 3) enhancing neurotrophic and neuroprotective activity of γ -enolase by peptidase targeting. In the course of Young Researcher's training, the candidate will become acquainted with *in vitro* and *in vivo* models to follow their physiological and pathological mechanism related to neurodegeneration. The most recent techniques and methods in biochemistry, cell and molecular biology, and molecular cloning will be applied.

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