

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

1. Raziskovalna organizacija (*Research organisation*):

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

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

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

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

3.03. Medicinske vede. Neurobiologija

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:*

Astroцити so številčne ne-nevronske celice v centralnem živčnem sistemu. Astroцити so v možgansko tkivo primerno umeščeni, da lahko zaznavajo sinaptično dejavnost, nadzorujejo pretok krvi in komunicirajo z nevroni in endotelijskimi celicami. Otekanje astroцитов lahko prepreči njihovo vlogo pri zagotavljanju energijske presnove možganov. Ugotovili smo, da so spremembe v volumnu astroцитов posledica odvijanja nagubane plazemske membrane, ne pa vgrajevanja nove membrane. To smo odkrili z elektronsko mikroskopijo, ki pa ne omogoča slikanja živih celic v realnem času.

Astroцити so vpleteni v homeostazo spanja s sproščanjem adenočina, ki deluje na adenočinske receptorje A1 ali A2A na presinaptični membrani nevronov. Komunikacija je lahko dvosmerna in zunajcelični adenočin lahko vpliva tudi na astroците. Pred kratkim se je pokazalo, da so adenočinski receptorji na astroцитih vključeni v protivnetno aktivnost resveratrola. Astroцити igrajo tudi vlogo pri izpiranju metabolitov iz možganov med spanjem. Tako imenovana glimfatična pot temelji na astroцитnem akvaporinu 4.

Kandidat ali kandidatka bo uporabila nove super-ločljivostne optično-mikroskopske pristope in mikroskopijo na atomsko silo za meritve sprememb morfologije astroцитов, ki nastanejo ob spremenjeni energijski presnovi. Aktivnost presnovkov (na primer glukoze, laktata, piruvata) v posamezni celici bo spremljal z znotrajceličnimi nanosenzorji, ki temeljijo na prenosu energije z resonanco fluorescence (FRET). Dinamiko površine plazmaleme bomo spremljali z elektrofiziološko tehniko »patch-clamp«.

Kandidat ali kandidatka se bo osredotočila na odkrivanje mehanizma povezave med spremembami energijske presnove astroцитов in dinamike površine membrane kot posledice zunajceličnih in znotrajceličnih signalov in spremembe geometrije izrastkov astroцитов.

Zaželeno so izkušnje kandidata z raziskavami celične fiziologije in poznavanje sistema kakovosti pri laboratorijskem delu. Ta doktorski projekt bo prispeval k razumevanju energetske presnove in spremljajočih sprememb morfologije astroцитов.

*eng:*

Astrocytes are abundant non-neuronal cell type in the central nervous system. They are ideally positioned to sense synaptic activity in the brain; they control blood flow and interact with neurons

and endothelial cells. Swelling of astrocytes may prevent their function in providing support for brain energy metabolism. We have determined previously, that changes in astrocytic volume are due to plasma membrane unfolding rather than new membrane insertion. This was determined by electron microscopy, which prevents imaging of live cells in real time.

Astrocytes are thought to modulate the process of sleep homeostasis through the release of adenosine which acts on adenosine A1 or A2A receptors on the presynaptic membrane. However, the communication may be bidirectional and extracellular adenosine may affect also astrocytes. It has been recently shown, that adenosine receptors on astrocytes are involved in the anti-inflammatory activity of resveratrol. Astrocytes also play roles in flushing metabolites from the brain during sleep. A so called glymphatic pathway relies on astrocytic aquaporin 4.

The candidate will employ new super-resolution optical microscopy and atomic force microscopy to monitor morphology changes of astrocytes which accompany changes in energy metabolism. The metabolites (such as glucose, lactate, pyruvate) will be monitored by intracellular nanosensors based on fluorescence resonance energy transfer. Dynamics of the plasma membrane surface area will be monitored by patch clamp electrophysiology.

The candidate will focus on determining the mechanism of association between changes of astrocyte energy metabolism and cell membrane dynamics as a result of extracellular and intracellular signalling and changes in geometry of astrocyte processes.

Experiences of the candidate in the research of cell physiology are preferred. The candidate should be acquainted with the quality system in the laboratory environment. This PhD project will contribute to the understanding of energy metabolism and accompanying morphology changes in astrocytes.