

## 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*):

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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 angleškega jezika, izkušnje z laboratorijskim delom, potrebne licence za usposabljanje...).

*slo:*

Nevroni jedra Locus coreuleus (LC) izločajo difuzno po možganih noradrenalin (NA). Glavna tarča delovanja NA v možganih pa so astrociti, kjer NA pospeši glikolizo in nastanek laktata. Laktat stimulira izločanje noradrenalina, hkrati pa je laktat signalna molekula in deluje prek receptorjev na plazemski membrani in v astrocitih spodbuja nastajanje laktata. Razvoj demence je označen v veliki meri s propadanjem nevronov jedra LC, zaradi česar je porušen tudi velik del metabolne in neurotransmitske signalizacije v možganih. Usposabljanje mladega raziskovalca bo vključevalo proučevanje mehanizmov aktivacije glikolize in nastajanja laktata z agonisti za laktatne receptorje. Ti bi lahko nadomestili učinke noradrenalina, ki se s starostjo in z nevrološkiimi boleznimi zmanjšuje. Usposabljanje bo konkretno vključevalo tudi: dobro laboratorijsko prakso, izolacijo tkiva iz živali, pripravo primarnih celičnih kultur nevronov jedra LC in astrocitov novorojenih podgan, tehniko transfekcije plazmida z zapisom za molekule nanosenzorjev za zaznavanje znotrajceličnega nivoja različnih metabolitov; imunocitokemično označevanje celic, tehniko prenosa energije z resonanco fluorescence (FRET) v posamezni celici, fluorescenčno mikroskopijo, in druge metode in postopke. Znotrajcelične spremembe energetske metabolitov (glukoza, laktat) še niso bile pokazane v posameznem nevronu jedra LC. Zaželeno so izkušnje kandidata z raziskavami celične energijske presnove in poznavanje sistema kakovosti pri laboratorijskem delu. Rezultati dela bodo omogočili vpogled v odzive in dogajanja na nivoju posameznega nevrona ter na nivoju medceličnih interakcij z astrociti.

*eng:*

Neurons of the nucleus Locus coreuleus (LC) secrete noradrenaline (NA) diffusely in the brain. The main targets of NA activity in the brain are astrocytes, where NA accelerates glycolysis and lactate formation. Lactate stimulates the secretion of noradrenaline, at the same time lactate is a signalling molecule and acts via plasma membrane receptors and stimulates the formation of lactate in astrocytes. The development of dementia has been marked to a large extent by the decay of neurons of the LC, causing a disruption of a metabolic and neurotransmitter signalling in the brain. The training of a young researcher will include the study of glycolysis activation

mechanisms and the formation of lactate with lactate receptor agonists. These lactate receptor agonists could replace the effects of noradrenaline, which is decreasing with age and neurological diseases. The training will also include: good laboratory practice, isolation of tissue from the animals, preparation of primary cell cultures of neurons of the LC nucleus and astrocytes of new-born rats, plasmid transfection technique with a sequence for nanosensor molecules to detect intracellular levels of different metabolites; immunocytochemical staining of cells, the technique of fluorescence resonance energy transfer (FRET) in a single cell, fluorescence microscopy, and other methods and processes. Intracellular changes in energy metabolites (glucose, lactate) have not yet been shown in a single neuron of the LC. Experiences of the candidate in the research of cell physiology and laboratory quality management are preferred. The results of the work will provide insight into the responses and events at the level of individual neurons and on the level of intracellular interactions with astrocytes.