

Reasoning of dissertation topic and competency of potential supervisor for admission onto joint LSU and TU doctoral studies in 2019

Area of research (title and code)	
Field of research (title and code)	
Topic of research	
Institution	LSU

Potential supervisor

Pedagogical and scientific degree	Name, surname	Academic position
PhD	Audrius Kilikevičius	Scientist

Short reasoning of proposed dissertation topic

Title
Intracellular response of small RNA-machinery to exercise training.
<p>Summary</p> <p>Exercise → Gene expression change → Phenotype, is a central dogma how our body adapt to physical training. Understanding how distinct exercises drives specific genes program can have beneficial role in health care, injury regeneration and therapeutic fields.</p> <p>Small RNAs (sRNAs) emerged as potential expression regulators, however their role in exercise adaptation process is still enigmatic. The sport scientists' community still publishing junk papers identifying sRNAs expression changes induced by training, however it is only conceptual evidence about their role in adaptation. Another limitation of these papers is thinking "in box" that sRNAs regulate gene post-transcriptionally in cytoplasm and that only differently expressed sRNAs can have significant effect.</p> <p>The goal of thesis to determine whether protein complex rearrangement and intracellular translocation of sRNAs regulatory machinery is potential mechanism how skeletal muscle regulate adaptation to exercise training. The rationale for this experiment is that sRNAs:</p> <p>(I) function as part of large protein complex; La Rocca et al. (1) published that sRNAs predominantly is in low molecular weight, non-functional, protein complex in resting muscle fibers. In the same paper they shown that PI3K-Akt-mTOR signaling promotes assembly into larger functional complex in T cells. Because this signaling pathway is highly activated by resistance and suppressed by endurance training (2), it let us hypothesize that PI3K-Akt-mTOR stimulating exercise will increase number of large complexes in muscle cells. This would suggest that instead of synthesizing new sRNAs, the primary adaptation expression program to exercise is triggered by recruiting resting sRNAs.</p> <p>(II) do cell compartment specific gene regulation. The previous works on myoblasts transition to differentiated cells, suggest that specific genes expression can be launched by translocating sRNAs-protein complex to different cell compartments. For instance, sRNA, miR-1, during myogenesis from cytoplasm efficiently enters the mitochondria where regulate mitochondrial genome transcript (3). While another sRNA, miR-181a, get into nucleus to down regulate inhibitor of myoblast differentiation (4). The recent paper released by Castanotto et al. (5) demonstrated that in cancer cells sRNAs transport to the nucleus increase by oxidative stress and DNA damage. Because these two stressors occur especially during endurance exercise (6), the hypothesis is that exercise training will induce translocation of sRNA machinery among cell compartments.</p>

1. doi: 10.1073/pnas.1424217112.
2. doi: 10.1371/journal.pone.0149082
3. doi.org/10.1016/j.cell.2014.05.047
4. doi: 10.1038/celldisc.2017.2
5. doi.org/10.1073/pnas.1721346115
6. doi:10.3390/antiox7090119

Please indicate the links between the proposed topic for the doctoral thesis and health promotion / physical therapy / sports study programs.

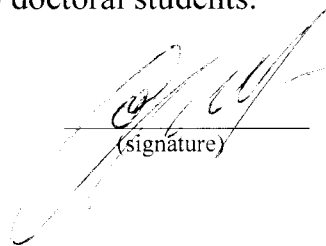
This topic land into molecular level of adaptation to physical training.

Is the proposed topic for the doctoral thesis related to currently funded research projects?
NO

Is the proposed topic for the doctoral thesis related to joint research with a foreign institution?
NO

Currently I am supervisor of 0 doctoral students.

Supervisor



(signature)

Audrius Kilikevičius

(Name, surname)

Date 2018 03 14