Dear Editors:

We would like to submit the enclosed manuscript entitled “**Effects of mitochondrial fusion and fission regulation on mouse hippocampal primary cultures: relevance to Alzheimer's disease**”, which we wish to be considered for publication in “Aging Pathobiology and Therapeutics”. No conflict of interest exits in the submission of this manuscript, and manuscript is approved by all authors for publication. I would like to declare on behalf of my co-authors that the work described was original research that has not beenpublished previously, and not under consideration for publication elsewhere, in whole or in part. All the authors listed have approved the manuscript that is enclosed.

In this work we investigated the controlled effects on mitochondrial fusion and fission processes on primary mixed astro-neuronal cultures of mouse hippocampus. Altering the balance of fusion-division processes in native hippocampal cell cultures creates conditions under which an adult-formed neuronal culture in the absence of pathologies faces a forced disruption of cellular homeostasis. This allows us to study how such changes are reflected in the morphology of mitochondria and the cell culture as a whole. As part of this work, we used selective mitochondrial fission inhibitors and fusion promoters, as well as the administration of exogenous zinc at certain low concentrations, which allowed us to achieve activation of mitochondrial fission. In our work, we consider changes in mitochondrial morphology, astro-neuronal shifts and lipofuscin levels as a marker correlating with mitochondrial disorders and aging. Our goal was to select conditions where culture reproduces certain patterns characteristic of Alzhemier's disease - decreased astro-neuronal density, astrogliosis and lipofuscin accumulation. Thus, we are looking at whether mitochondrial abnormalities can lead to a cascade of specific senile pathologies.

I hope this paper is suitable for “Aging Pathobiology and Therapeutics”. We deeply appreciate your consideration of our manuscript, and we look forward to receivingcomments from the reviewers. If you have any queries, please don’t hesitate to contact me at the

Thank you and best regards.

Yours sincerely, corresponding author:

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