Mitochondrial Dynamics: impact on adult neural stem cell fate

Rita Soares^{1,2,3}, Diogo M. Lourenço^{1,2}, Jonathan Verduyck⁴, Ana M. Sebastião^{1,2}, Sara Xapelli^{1,2*}, Vanessa A. Morais^{1,3*}

¹Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina, ULisboa, Lisboa, Portugal; ²Instituto de Farmacologia e Neurociência, Faculdade de Medicina, ULisboa, Lisboa, Portugal; ³Instituto de Biologia Molecular, Faculdade de Medicina, ULisboa, Lisbon, Portugal; ⁴UC Leuven Limburg, 3000 Leuven, Belgium. ritasoares@medicina.ulisboa.pt; *Corresponding authors.

INTRODUCTION

Neural stem cells (NSCs) are a powerful tool to treat disease-related neural loss. Several studies hypothesised that NSC differentiation depend on mitochondrial dynamics and bioenergetics. Identifying which mitochondrial processes are involved in the modulation of NSC fate will contribute to finding effective therapies for brain repair.

METHODS

RESULTS

1. Optimization of neurosphere culture parameters: number of passages

1.1. Characterization of SVZ and DG neurospheres

Note: The effect of the neurosphere passage in cell death was also evaluated, being high in passages 3, 4 and 5.

1.2. SVZ- and DG-derived NSPCs differentiation

2. Mitochondrial biogenesis during SVZ- and DG-derived NSPC differentiation

Expression levels of AMPK α , phospho-AMPK α , AMPK β 1, phospho-AMPK β 1, AMPK β 2 and mTOR were also evaluated with no significant changes.

3. Mitochondrial fusion and fission during SVZ- and DG-derived NSPC differentiation

Overall, fusion and fission are altered throughout differentiation.

4. Mitochondrial morphology of SVZ-derived cells

Both the number of individual mitochondria and the mitochondria which belong to a network significantly change with SVZ-derived NSPC differentiation.

CONCLUSIONS

- ❖ Primary/passaged neurospheres present no significant differences in the NSC yields and proliferative capacity. Moreover, NSPCs show to be multipotent.
- ❖ Expression of proteins involved in fusion/fission significantly change during NSPC differentiation, in cells with different passages.
- ❖ Mitochondria morphology significantly alters during NSPC differentiation.

FUTURE PERSPECTIVES

- ❖ Assess the impact of mitochondrial modulation on differentiation of SVZ- and DG-derived NSPCs.
- ❖ Determine the mitochondrial function in different cell types.