

Main Report

Awardee: Mychael Lourenco, PhD student

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Supervisors: Sergio T. Ferreira, PhD and Fernanda G. De Felice, PhD

Institute of Medical Biochemistry Leopoldo de Meis, Federal University of Rio de Janeiro

Host Supervisor: Ottavio Arancio, MD, PhD

Host Institution: Taub Institute for Research on Alzheimer's Disease and the Aging Brain, Columbia University – New York (NY)

Dear Dr. Roberto Cappai,

I was awarded a 2014 ISN/CAEN Travel Award 1A for a scientific visit to another lab. For this sake, I have been kindly hosted by Dr. Ottavio Arancio in his lab at Columbia University in New York, USA. I was very pleased to join his lab during the weeks of October and November of 2014. Dr. Arancio was a very kind and helpful host and many members of his team were equally supportive to my planned activities. The University staff was very efficient in scheduling all training sessions and putting together all the resources I needed to comply with Columbia requirements. I am thankful to Dr. Arancio, his team and also to Columbia staff in this regard.

I should here disclose that our initial plans comprised a collaborative visit to Dr. William L. Klein laboratory at Northwestern University (Evanston, IL, USA) to perform part of the experiments prior to Arancio lab visit. However, in order to optimize time and experimental conditions and given the availability of APP/PS1 mice kindly allocated by Dr. Arancio at Columbia, all planned experiments have been conducted in Dr. Arancio's lab, without any detriment or delay to any of the experiments. I then apologize for any inconvenient that might be found by ISN for this change of plans. Experiments comprised biochemical preparations of amyloid-beta oligomers, electrophysiology in hippocampal slices and expression of adenovirus in the hippocampus of APP/PS1 mice, a murine model of Alzheimer's disease (AD).

The visit to Arancio's lab provided me with the opportunity to interact and exchange scientific ideas with the talented and engaged scientists that compose his team. Moreover, this was an outstanding experience of working in a renowned research centre in AD and the vibrant scientific atmosphere was quite evident and exciting.

During my stay in Arancio's lab, I was able to get in touch with electrophysiology (field recordings for LTP purposes in hippocampal slices) and behavioural experiments (Radial Arm Water Maze and Fear Conditioning memory tests). This was my first contact with electrophysiology experiments and I was able to learn the theory underlying the procedures employed for LTP measurements as well as to get initial hands-on aspects of electrophysiology recordings in slices. I further performed stereotaxic injections and behavioural experiments in WT and APP/PS1 mice to assess spatial and fear memory as inferred from radial arm water maze and fear conditioning tasks, respectively. Although I was already versed in some memory tests in mice, this was the first time I was trained to use these behavioural protocols, which I found very useful for testing memory impairment in AD mouse models. I am now able to spread this knowledge in the lab here in Brazil.

The labs run by my supervisors Sergio Ferreira and Fernanda De Felice have as their main goals: (1) to dissect the molecular mechanisms that lead to brain damage and memory impairment in AD and (2) to find strategies of neuroprotection with translational impact to treat AD. My previous work identified a molecular pathway mediated by inflammation and cellular stress mechanisms that causes defective memory and brain insulin signalling in AD models (Lourenco et al, *Cell Metabolism*, 2013). Going through the second lab aim, we have turned out to investigate potential roles for neuroprotective molecules in AD.

By performing the designed sets of experiments in Arancio's lab, I found is that overexpressing a recently described neuromodulatory molecule is able to counteract APP/PS1-related memory and LTP deficits. This goes in line with previous in vitro and in vivo experiments that we performed in this project. These results I obtained in this short visit are quite interesting and exciting and will be included in a manuscript in preparation. Further, these results have stimulated novel ideas for experiments that I long

to perform in the next months to get mechanistic insights into how neuroprotection develops in this case.

Finally, as part of Columbia requirements, I have received a high-standard training for animal ethics, care and handling that included interactive on-line courses, presential lectures and hands-on training and verifications. Please see enclosed my certificates of approval in animal training. Considering that a this complete training is still unavailable at my home University, I am sure that this training will help improve my skills and knowledge over animal research and use.

In summary, this was a very productive and rewarding scientific visit, as I had a unique chance to develop my scientific and technical skills in my field of study and to spend some time in an exciting scientific environment such as Columbia. Given the complexity of memory and of the diseases that affect it, I feel that researchers in the field should pursue complete approaches, ranging from cellular/molecular studies to physiology/behavioural assessment. And this is what ISN and the CAEN helped me keep pursuing now, at this early stage of my science path. The possibility of facing different ideas and challenges, as well as the practical issue of improving my English (as a non-native speaker), are other features that resulted as benefits from this scientific visit. Hence I am truly grateful to ISN/CAEN for supporting my career development through this award.

Kind regards,



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Enclosed lab photograph

