

Final Report: ISN-CAEN Award Category 1C: Return Home Grant



CV.

I was awarded the ISN-CAEN Award early 2015, following nearly 9 years of carrying out research at the UK. Half of this period I worked as a post-doc at Bristol University and the other half as a Lecturer in Pharmacology at the University of Reading. Alongside with the ISN-CAEN Return Home Grant, I was conferred an IBRO Return Home Fellowship and a Newton Advanced Fellowship. All these prestigious awards financially supported the establishment of my lab in Brazil, not mentioning their invaluable contribution to my

In March 2015 I was appointed Assistant Professor at the Department of Pharmacology, Federal University of Santa Catarina (UFSC), Brazil. The position here involves research, teaching and outreach, as well as administrative tasks. Below I briefly describe my activities in the past couple of years in the new job.

Teaching: As soon as I started I was responsible for the delivery of an average 8-hours/week of lectures on a number of Pharmacology areas (e.g. cardiovascular, renal, CNS, respiratory, gastro) to Pharmacy, Medicine, Odontology and Biological Sciences undergraduate students. I also contribute to the teaching in the Pharmacology and Neuroscience Postgraduate Programs, with courses varying from neurotransmission to respiratory therapeutics for Masters and PhD students.

Research: By mid-June 2015 I was given some office/laboratory space in the Department of Pharmacology, which has been named LINQ (*Laboratorio de Investigacao NeuroQuimica*, Laboratory of Neurochemistry Investigation). This space consists of a small laboratory for molecular biology/biochemistry experiments, an office that accommodates up to 6 students and another private office for me. I was then given the task to create the departmental cell culture room, which involved complete refurbishment of a former cell culture room that had been closed for quite some time. The newly arrived group members helped to leave both our laboratory and the communal culture room in fully working conditions.

So far the group consists of one post-doctoral research fellow (Ana Cristina G. de Souza) two PhD students (Camila A. Zanella and Stella C. Junqueira), one MSc student (Leticia C. Coelho), and two undergraduate students (Izi I. Floriano and Eduarda G. Centeno). All these projects are related to the understanding of the molecular mechanisms and functional consequences of a post-translational protein modification (SUMOylation) in neurodegenerative conditions, such as Alzheimer's disease and Parkinson's disease. There is also an ongoing project that examines the SUMOylation profile in brain samples from epileptic patients and implicates close collaboration with the Department of Clinical Medicine. I also have new and ongoing collaborations with colleagues in the Pharmacology, Biochemistry, Neuroscience and Immunology departments. All these are crucial for the optimization of research resources, both in terms of personnel and funding, especially considering emerging places like Brazil. In order to try to secure further funding for research I currently have grant proposals submitted to the Michael J. Fox Foundation, BBSRC Brazil Partnering Awards and CNPq (Brazil National Council for Scientific and Technological Development).

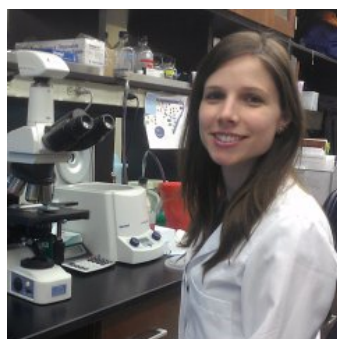
During this period (Mar 2015 – Ago 2017) I managed to publish two reviews on the roles of SUMOylation in Alzheimer's disease (Hoppe *et al.*, 2015; Martins *et al.*, 2016), one review on

SUMOylation in Parkinson's disease (Guerra de Souza *et al.*, 2016) and a further review on SUMOylation of calcium channels (Coelho-Silva *et al.*, *in press*). We also published a book chapter on the implications of SUMOylation in neurodegenerative diseases (Anderson *et al.*, 2017) and another one on the oxygen-glucose deprivation technique to mimic brain ischemia (Tasca *et al.*, 2015).

Outreach: In September I was involved in the organization of two international events held in Florianópolis. The first was a 4-day Newton Researcher Links Workshop followed by a 1-day FAPESC (Santa Catarina Research Foundation) conference on the same theme: *"Understanding and Advancing Therapies for CNS Disorders"*. The organization of both events was quite time-consuming and required a substantial amount of work, which, at the end, was compensated by their successes. The workshop was open only for early career researchers and had 40 delegates, half from the UK and the other half from different parts of Brazil (Image 1). The conference was open for a wider audience, with nearly 100 people subscribed, mostly postgraduate students from Santa Catarina and nearby states. Early in December I was invited to speak at the IV SIP-CCB, a local symposium designed to integrate all the postgraduate programs within the Biological Sciences Center of UFSC. In 2016 I also attended the FENS Meeting in Copenhagen and was an invited speaker at the FALAN Meeting in Buenos Aires. Earlier this year I was involved in the organization of the Joint Meeting of the Neurotoxicity Society and the International Neurotoxicology Association held in Florianópolis.

Administrative: Since March I have been invited to be the internal examiner for the vivas of several Master and PhD candidates. These opportunities have given me an overview of the wide range of research carried out at the Department and ideas for future collaborations. As I am under the 3-year probation period, I am required to attend several courses on administrative-related topics, varying from University legislation to how to use Moodle (virtual environment for teaching and learning). In January 2016 I was part of the committee responsible for the organization of two selection processes for new positions within the department. It was interesting to learn more about all the formalities involved and to participate to some extent in choosing my new colleagues.

Below my post-doc and PhD students contribute to this report by summarizing their achievements since they joined the lab.



Ana Cristina G. de Souza: Throughout the second semester of 2015, I worked reequipping the Cimarosti's lab, purchasing reagents, training PhD students, and implementing the essential techniques for our projects, such as neuronal cultures and Western blotting. In July 2015, I attended the 9th World Congress of IBRO in Rio de Janeiro, Brazil, where I presented a poster entitled *"Florianópolis' Brain Awareness Week 2015: outreaching children to elderly in the South of Brazil"*. In 2016, I spent 10 months working at Prof. Henley's lab in Bristol University, UK. The aim was to learn how to make viruses for overexpression / knockdown experiments, which are essential for efficient manipulation of SUMO levels. There I also learned co-

immunoprecipitation and confocal microscopy techniques. This key knowledge was shared with my colleagues upon my return and contributed greatly to the projects carried out in the Cimarosti's lab.



Camila A. Zanella: In the first semester of my PhD (Jun – Dec 2015), I implemented the methodology for primary astrocyte cultures (Image 2), and already conduct my first experiments successfully. Furthermore, I am in the process of adapting several techniques to our laboratory needs, *e.g.* protein assay, SDS-PAGE, Western blotting, cell viability assays, etc. I am also starting the *in vitro* models of Alzheimer's disease in the lab. Initially I used cultures treated with beta-amyloid. However, I am currently in Prof. Henley's lab in the UK learning how to use cultures overexpressing APP as an alternative model. In June 2015 I presented my project at the Pharmacology Winter Course at UFSC, which is aimed

at undergraduate students from all over Brazil. This talk attracted the attention of several students' to our lab. This year I presented my work at several conferences, such as the Brazilian Purines Meeting, NTS & INA Meeting, as well as being selected to participate in the FAMELab.



Stella Junqueira: In order to carry out my PhD project, which is related to the understanding of the role of SUMOylation in Parkinson's disease, I received training in cell cultures procedures and other essential techniques in Cimarosti's lab. During this period we have managed to establish two *in vitro* models of Parkinson's disease using a neuroblastoma cell line, SH-SY5Y cells, and rat neurons exposed to MPP⁺. These models will complement my *in vivo* work looking at SUMOylation in mice treated with intranasal MPTP. In July 2015 I also attended the 9th World Congress of IBRO in Rio de Janeiro, Brazil. I am also visiting Prof. Henley's lab in the UK (Feb – Oct 2017) to carry out some core experiments related to my PhD thesis.

Image 1: Researcher Links Workshop group photograph taken at the Maria Do Mar Hotel on 21st September 2015.



Left to right: Melissa Andrews, Massimiliano Stagi, Sovan Sarkar, Simone Molz, Helena Cimarosti, Andrea Serio, Angela Bithell, Francesco Tamagnini, Patrick Lewis, Evan Delivopoulos, Lenir Pereira, Mariza Bortolanza, Fernando Vasconcellos, Wajeeha Aziz, Francisco Dubiel, Terence Duarte, Mar Canadell, Anupam Hazra, Tatiana Rosenstock, Patricia Brocardo, Roger Walz, Darius Widera, Cleide Souza, Robert Deller, Cristiano Jesse, Juliana Ben, Juliana Cortines, Ben Whalley, Camille Soubrane, Charlie Arber, Juliana Redondo, Sebastien Gillotin, Marcio Dutra, Tetsade Pierpertiri, Ana Cristina de Souza, Rui Prediger, Selina Wray

Image 2: First astrocyte primary cell culture produced by Camila A. Zanella at Cimarosti's lab, UFSC, Brazil.

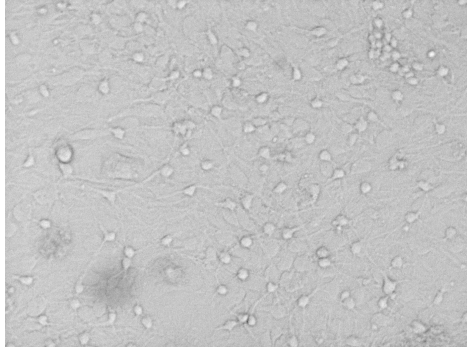


Image 3: Some members of the LINQ Group. From left to right: Camila A. Zanella (PhD student), Helena Cimarosti (Principal Investigator), Izi I. Floriano (Pharmacy undergraduate student) and Leticia C. Silva (MSc student).



List of Publications during the Award period

1. Silva, L.C., Stephens, G.J., Cimarosti, H. (2017) SUMOylation and calcium signalling: Potential roles in the brain and beyond. *Neuronal Signaling in press*, DOI: 10.1042/NS20160010.
2. Anderson, D.B., Zanella, C.A., Henley, J.M., Cimarosti, H. (2017) Sumoylation: Implications for neurodegenerative diseases. *Advances in Experimental Medicine and Biology* 963, 261-281.
3. Guerra de Souza, A.C., Prediger, R.D., Cimarosti, H. (2016) Mitochondrial dysfunction and SUMOylation targets in Parkinson's disease. *Journal of Neurochemistry* 137, 673-686.
4. Martins, W.C., Tasca, C.I., Cimarosti, H. (2016) Battling Alzheimer's disease: Targeting SUMOylation-mediated pathways. *Neurochemical Research* 41, 568-578.
5. Hoppe, J.B., Salbego, C.G., Cimarosti, H. (2015) SUMOylation: Novel neuroprotective approach for Alzheimer's disease? *Aging and Disease* 6, 322-330.
6. Tasca, C.I., Dal-Cim, T., Cimarosti, H. (2015) In vitro oxygen-glucose deprivation to study ischemic cell death. *Methods Molecular Biology* 1254, 197-210.