



Preface

Post-translational modifications in brain health and disease[☆]

Post-translational modifications (PTMs) such as phosphorylation, glycosylation, methylation, acetylation, ubiquitination, nitrosylation, SUMOylation and many other types, are crucial regulators of protein properties and functions [1]. PTMs can modulate the turnover, localization, activity, and interaction of proteins thus, playing a crucial role in the regulation of multiple cellular pathways [2]. Among other functions, PTMs of proteins play a key role in neurodevelopment and in the adult brain by modulating activity-dependent processes for complex brain functions such as learning and memory [3,4]. So, it is not surprising that altered PTMs play a role in several brain disorders as discussed in the special issue “*Post-translational modifications in brain health and disease*”. In this special issue Picón-Pagès and colleagues [5] discuss the role of nitric oxide-dependent PTMs in brain function and dysfunction. Then, Singh and colleagues [6] scrutinize the role of histone PTMs in the sexual differentiation of the brain under normal conditions and how sex-specific modulation of histone PTMs may be involved in several psychiatric conditions. The role of histone PTMs in several neurodegenerative diseases is also debated by Cobos and colleagues [7]. In the context of Parkinson's disease (PD), Pajarillo and colleagues [8] highlight the role of PTMs of α -synuclein and LRRK2 in the pathogenesis of PD and discuss the impact of environmental risk factors on abnormal PTMs. In addition, Junqueira and collaborators [9] review findings on the PTMs phosphorylation, SUMOylation and ubiquitination that have been shown to affect PD-related proteins putting the focus on mitochondria. The study by Esteves and colleagues [10] demonstrate that acetylation of α -synuclein and tau protein affects microtubule-dependent autophagy in PD and Alzheimer's disease (AD) context, respectively. Concerning tau protein, Hernández and colleagues [11] found that human and murine tau proteins present differences in structure and function. The authors report that the N-terminal of human tau protein binds the mitochondrial creatine kinase B, a situation that is not observed in AD possibly due to the modification of creatine kinase B by oxidation. The review by Butterfield [12] discusses the involvement of protein phosphorylation in neuronal degeneration and death, which contribute to cognitive decline in preclinical AD and mild cognitive impairment (MCI). In the same line, Kelley and colleagues [13] highlight the importance of mass spectrometry in the study of PTMs in various stages of AD. The study by Pinho and collaborators [14] demonstrates that decreased levels of O-linked N-acetyl-glucosamine glycosylation in AD is associated with mitochondrial anomalies. In turn, Klimova and collaborators [15] debate ischemia/reperfusion-induced changes in the metabolic intermediates nicotinamide adenine dinucleotide (NAD⁺) and acetyl coenzyme A, how these affect relevant

PTMs, and therapeutic approaches that restore the physiological levels of these metabolites leading to neuroprotection. Finally, Ke and colleagues [16] debate PTMs in methylmercury (MeHg)-induced neurotoxicity, including the most commonly PTMs, as well as PTMs induced by oxidative stress and PTMs of antioxidant proteins.

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In 2007, Sónia C. Correia obtained her degree in Biology from the Faculty of Sciences and Technology, University of Coimbra, Portugal. Then, Sónia C. Correia received her PhD in Cell Biology from University of Coimbra, Portugal, in 2012. Currently, she is a postdoctoral researcher at Center for Neuroscience and Cell Biology (CNC) with a fellowship from the Portuguese Foundation for Science and Technology. Sónia C. Correia's research is mainly focused on deciphering the molecular mechanisms underlying Alzheimer's disease in order to uncover novel therapeutic targets to prevent or halt the progression of this devastating neurodegenerative disease. Despite her young age, Sónia C. Correia has already an impressive number of publications, as evidenced in her Curriculum Vitae that includes > 50

scientific peer-reviewed and an h-index = 27 and > 2370 citations, according to Google Scholar. In 2010, Sónia C. Correia won the ASN Neuro Poster Prize sponsored by the American Society of Neurochemistry.



Cristina Carvalho graduated in Biology from the University of Coimbra (UC) in 2007 and in the same year she was qualified to attend the specialized master program in Cellular and Molecular Biology at the Faculty of Science and Technology of UC (FCTUC), program that she finished in 2008 with a score of 18 in 20 values. She applied to a PhD scholarship from the Portuguese Science Foundation (FCT), that she started in the beginning of 2009. From 2009 to 2013 she worked under the supervision of Dr. Paula Moreira at Center for Neuroscience and Cell Biology/Life Sciences Department of PCTUC in the field of neurodegeneration with special focus in T2D-associated complications as risk factors for neurodegenerative events that could compromise brain homeostasis. Her Ph. D. project was

performed in collaboration with Prof. David Busija from Tulane University, New Orleans where she performed a scientific internship for almost seven months. Cristina completed her PhD in 2013 and from that date she developed several different works under the scope of annual fellowships from international projects, namely an international project financed by Alzheimer's Association under the supervision of Dra Paula Moreira and a Science management fellowship from Faculty of Medicine, University of Coimbra under the supervision of Dr. Raquel Seica, proving her ability to adapt and willingness to deepen conceptual and procedural knowledge in different areas. In 2015/2016 she was awarded a post-doc grant from FCT, and is presently working in explore deeper the association between type 2 diabetes and neurodegenerative diseases, such as Alzheimer's disease, unraveling the molecular mechanisms underlying the relationship among those pathologies, in order to achieve knowledge of possible therapeutic targets that could be used as preventive strategies against type 2 diabetes-induced neurodegeneration. In her curriculum it can be found 9 book chapters, an online protocol at Bioprotocol journal and > 47 papers in international peer-reviewed journals with over 2680 citations and a h-index of 25.



Susana Cardoso graduated in Biology in 2008 at the Faculty of Sciences and Technology of University of Coimbra, and in the same year got a FCT PhD fellowship with the project entitled "Deciphering the role of mitochondria and uncoupling proteins in hypoglycemia- and/or hyperglycemia-induced brain injury". Her PhD project was developed in the Department of Life Sciences of Faculty of Sciences and Technology of University of Coimbra and in the Center for Neurosciences and Cell Biology, University of Coimbra, and included a 6 months stay at the Yale University School of Medicine, department of Neurobiology and Comparative Medicine, USA. In 2013, Susana Cardoso received the PhD degree in Cellular Biology at the Faculty of Sciences and Technology of University of Coimbra.

Meanwhile, Susana Cardoso continued to work at the Center for Neurosciences and Cell

Biology with an investigation fellowship and in 2014 she was awarded with a FCT Post-doc fellowship with the project entitled "Mild mitochondrial uncoupling: exploring its protective effects against brain damage associated to insulin-induced hypoglycemic events in type 1 diabetes" that was developed during 3 years. In 2017, she received another FCT Post-doc fellowship to develop the project "2,4 Dinitrophenol: From Weight Loss To Alzheimer's Disease". During her research path she has been enrolled in the supervision and tutoring of several students, from lab rotations and investigation chairs to master students, and published several original and review papers and book chapters as first author in international peer-reviewed journals and also co-authored several others. Presently, she has an h-index of 23 and her work has been cited 1855 times (<https://scholar.google.pt/citations?user=8AEoxjwAAAAJ&hl=pt-PT>). Her scientific outcomes have been presented in > 25 scientific meetings with oral and poster presentations. She was awarded with 2 travel grants to attend at FENS (Forum of European Neuroscience; in 2010 and 2012) and with a travel grant to attend at the 51st Annual Scientific Meeting of the European Society for Clinical Investigation (2017). Presently, she is an ad-hoc reviewer in several international peer-reviewed journals.



Paula I. Moreira received her PhD in Biomedical Sciences from University of Coimbra, Portugal, in 2007. She is Assistant Professor at Faculty of Medicine, University of Coimbra and Principal Investigator at the Center for Neuroscience and Cell Biology, University of Coimbra, Portugal. Moreira's group is interested in elucidating the role of energy metabolism, with an emphasis on mitochondria (energy, homeostasis and signals) and metabolic hormones-mediated signaling pathways in brain changes occurring in metabolic disorders, such as diabetes and/or obesity and neurodegenerative diseases, particularly Alzheimer's disease. Overall, Moreira's group aims to identify novel biomarkers and therapeutic targets. Moreira has published > 180 scientific peer-reviewed articles. She is

deputy editor of *Journal of Alzheimer's Disease*, associate editor of *Journal of Alzheimer's Disease Reports* and *Frontiers of Aging Neuroscience*, section editor of *BBA-Molecular Basis of Disease* and belongs to the editorial board of *Current Alzheimer's Research*, *Rejuvenation Research* and *British Journal of Pharmacology*. Paula Moreira won the Stimulus to Research prize, in 2003, supported by the Calouste Gulbenkian Foundation and, in 2008, the L'Oréal for Women in Science Award supported by L'Oréal Portugal/UNESCO/FCT.

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