BIOGRAPHICAL SKETCH

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NAME	**POSITION TITLE**
Claudia G. Almeida	Principal Investigator

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Faculty of Sciences, **University of Lisbon**, Portugal	BSc	1999	Biochemistry
Faculty of Medicine, **University of Lisbon**, Portugal	MSc	2002	Neurosciences,
Faculty of Medicine, **University of Lisbon**, Portugal	PhD	2007	Neurosciences
Weill Medical College of **Cornell University**, New York, US		2002-2007	Alzheimer's disease
Institute Curie, Paris, France		2007-2012	Cell biology Intracellular trafficking

A. Personal Statement.

My research is focused on understanding aging-related silent pathological mechanisms that will eventually trigger the onset of Alzheimer's disease. The prevalence of neurodegenerative diseases in the aging European population is increasing due to the higher life expectancy. Alzheimer's disease (AD) is the most common neurodegenerative disease and it remains without effective treatment. Cognitive decline develops with aging and often precedes AD. Unknown mechanisms drive the loss of synapses associated with aging-cognitive decline. Most neurons have our chronological age and thus face great challenges to maintain functional synapses. We hypothesize that with aging and with certain genetic risk factors neurons build up defects that will impact synapses.

I was trained as a neuroscientist for eight years and as a cell biologist for six years. During my PhD, I became an expert in AD neurobiology, acquired skills in synapse biology and intracellular trafficking in neurons. During my post-doc I expanded my skills by studying fundamental cellular mechanisms using state of the art microscopy and quantitative data analysis. I have the unique know-how to tackle the cellular mechanisms of AD.

In 2013, I joined CEDOC, a research center on chronic diseases of the NOVA Medical school to lead the neuronal trafficking in aging lab, composed by one post-doc, three PhD students and one Engineer. I will oversee and provide hands-on-assistance in all aspects of this project.

The current project counts with the help of several colleagues to setup some experimental assays in the lab: with G. Raposo (Institute Curie, Paris) expert on electron microscopy of intracellular organelles; with E. Gomes (IMM, Portugal) who has expertise in N-WASP in Bin1-dependent regulation of the actin cytoskeleton (EMBO Mol Med. 6:1455-75 [2014]); with the experience of A. Gontijo (CEDOC, Portugal), in Crispr/Cas9 technology; with N. Moreno from the Cell Imaging Unit (IGC, Portugal) an expert in super-resolution imaging that will help us to use dSTORM; with C. Brito (iNOVA4Health, IBET, Portugal), an expert in neuronal differentiation from human IPSCs cells (eg. Tissue Eng Part A. [2014]; Methods. 56:452-60 [2012].

Currently, we are studying how neuronal aging disrupts synapses. We have first hypothesized that neuronal aging

increases the production of the synaptotoxic beta-amyloid. Next, we will investigate whether the aging of lysosomes impairs synapses. Moreover, we are dissecting the mechanisms whereby genetic variants found in patients with the late-onset form of AD increase the risk of developing the disease. Rare coding mutations were found in regulators of endosomal trafficking and actin dynamics. However, the molecular mechanisms used by the identified genetic variants to disrupt synapses need to be investigated. Endosomal trafficking is responsible for maintaining synapses and for producing beta-amyloid. Neuronal actin dynamics is essential for synaptic plasticity and regulates endosomal trafficking. We aim to determine the specific molecular mechanisms of dysfunction of endosomal trafficking and actin dynamics that silently could drive synaptic decline and to determine if aging potentiates these mechanisms triggering AD. For that we use unique cellular systems in combination with single vesicle quantitative live imaging, super-resolution microscopy, biochemistry and synaptic biology assays.

Recently, we published that loss of function of two genetic risk factors polarizes beta-amyloid accumulation in neurons by differentially controlling endosomal sorting in axons and dendrites. We found that neurons lose synapses due to increased production of beta-amyloid as they age because of increased endocytosis of the amyloid precursor protein. Moreover, we found that in neurons actin dynamics is important at endosomes to control beta-amyloid production. Now, we are investigating if rare AD mutations in genes that control endosomal trafficking and actin dynamics impact synapses independently or not of beta-amyloid.
We ultimately aim at identifying molecular targets for therapeutic intervention to treat aging cognitive decline and prevent neurodegeneration.

B. Positions and Honors.

2016-current Invited Assistant Professor, Nova Medical School, Nova University of Lisbon, Lisbon, Portugal

2013-current Principal Investigator, FCT researcher, CEDOC – Chronic diseases research center – of Nova Medical School, Nova University of Lisbon, Lisbon, Portugal

2007-2012 Post-doctoral fellow in the Laboratory of “Morphogenèse et signalisation cellulaires" headed by Daniel Louvard, CNRS UMR144, Institute Curie, Paris, France, under the supervision of Dr. Evelyne Coudrier.

2002-2007 PhD student with Dr. Gunnar K. Gouras, Laboratory of Alzheimer’s Disease Neurobiology, Department of Neurology & Neuroscience, Weill Medical College of Cornell University, New York, USA.

1999-2002 MS in Neurosciences, Faculty of Medicine, University of Lisbon, Portugal. Master student with Prof. Alexandre de Mendonça, Laboratory of Neurosciences.

1994-1999 BSc in Biochemistry, Faculty of Sciences, University of Lisbon, Portugal. Undergraduate Research Assistant with Prof. Dora Brites, Faculty of Pharmacy, University of Lisbon, Portugal, 1998-1999.

Honors:

2015 NOVA/Santander-Totta award for collaborative project in life sciences, Portugal

2013-2018 “Investigador FCT”, Foundation for Science and Technology, Portugal

2011-2012 Institute Curie fellowship for foreign post-docs, Paris, France

2010 2010 WICB Childcare Grant for ASCB 2010, Washington DC, USA
2009-2011 Marie Curie Actions, Intra-European Fellowship, Paris, France

2007-2009 European Molecular Biology Organization, EMBO long-term fellowship, Paris, France

2002-2006 Foundation for Science and Technology, Portugal - PhD. Fellowship

2004 Travel Fellowship for the 9th International Conference on Alzheimer's Disease and Related Disorders in Philadelphia, Pennsylvania, USA, July 17-22, 2004.

2001-2002 Foundation for Science and Technology, Portugal - MS fellowship.

C. Selected peer-reviewed publications (in chronological order).

1. **Guimas Almeida C**, Sadat Mirfakhar F, Perdigão C, Burrinha T. Impact of late-onset Alzheimer's genetic risk factors on beta-amyloid endocytic production. **Cell Mol Life Sci.** 2018 Jul;75(14):2577-2589. doi: 10.1007/s00018-018-2825-9. Epub 2018 Apr 27. Review.
2. Ubelmann F, Burrinha T and **Guimas Almeida C**. A Novel Protocol to Quantitatively Measure the Endocytic Trafficking of Amyloid Precursor Protein (APP) in Polarized Primary Neurons with Sub-cellular Resolution. **Bio-protocol.** 2017 7(23): e2629. DOI: 10.21769/BioProtoc.2629.
3. Ubelmann F, Burrinha T and **Guimas Almeida C**. Measuring the Endocytic Recycling of Amyloid Precursor Protein (APP) in Neuro2a Cells. **Bio-protocol.** 2017 7(23): e2635. DOI: 10.21769/BioProtoc.2635.
4. Ubelmann F, Burrinha T, Gomes R, Salavessa L, Ferreira C, Moreno N., **Almeida CG.** Bin1 and CD2AP polarize beta-amyloid endocytic generation. **EMBO Rep.** 2017 Jan; 18(1):102-122. doi: 10.15252/embr.201642738.
5. **Almeida CG**, Yamada A, Tenza D, Louvard D, Raposo G, Coudrier E. Myosin 1b promotes the formation of post-Golgi carriers by regulating actin assembly and membrane remodelling at the trans-Golgi network. **Nature Cell Biology**. 2011, Jun 12;13(7):779-89.
6. Tampellini D, Magrane J, Takahashi RH, Li F, Lin MT, **Almeida CG**, Gouras GK. Internalized Antibodies to the Abeta Domain of APP Reduce Neuronal Abeta and Protect against Synaptic Alterations. **J Biological Chemistry**. 2007 Jun 29;282(26):18895-906.
7. **Almeida CG**, Takahashi RH, Gouras GK. Aβ42 accumulation impairs multivesicular body sorting by inhibiting the ubiquitin-proteasome system. **J Neuroscience**. 2006 Apr 19;26(16):4277-88.
8. **Almeida CG**, Tampellini D, Takahashi RH, Greengard P, Lin MT, Snyder EM, Gouras GK. Beta-amyloid accumulation in APP mutant neurons reduces PSD-95 and GluR1 in synapses. **Neurobiol Dis**. 2005 Nov;20(2):187-98.
9. Snyder EM, Nong Y, **Almeida CG**, Paul S, Moran T, Choi EY, Nairn AC, Salter MW, Lombroso PJ, Gouras GK, Greengard P. Regulation of NMDA receptor trafficking by amyloid-beta. **Nature Neuroscience**. 2005 Aug;8(8):1051-8.
10. Gouras GK, **Almeida CG**, Takahashi RH. Intraneuronal Abeta accumulation and origin of plaques in Alzheimer's disease. **Neurobiology of Aging**. 2005, 26:1235-44.

Takahashi RH, **Almeida CG**, Kearney PF, Yu F, Lin MT, Milner TA, Gouras GK. Oligomerization of Alzheimer's beta-amyloid within processes and synapses of cultured neurons and brain. **J Neuroscience**. 2004 Apr 7;24(14):3592-9.

D. Research Support.

2018 Impact of the genetic risk factor CD2AP on the development of Alzheimer's disease, 10.000€ (Total 40.000€) INOVA4Health (CO-PI: Cláudia G. Almeida)

2017 Impact of the genetic risk factor CD2AP on the development of Alzheimer's disease, 25.000€ Award Maratona da Saúde (PI: Cláudia G. Almeida)

2016-2019 NAB3, 150.000€, cofund JPND/H2020, (Partner: Cláudia G. Almeida)

2015 Recapitulating late-onset Alzheimer's disease in a three dimensional human neural cell model, 25.000€ Award Santander/Totta and Universidade NOVA de Lisboa (PI: Cláudia G. Almeida)

1/4/2013-31/3/2017 Marie Curie Integration grant (334366, TrafficInAD), Marie Curie Actions, EC (PI: Cláudia G. Almeida)

15/5/2013-14/5/2018 Investigador FCT exploratory project, 50.000€, Foundation for Science and Technology, Portugal (PI: Cláudia G. Almeida)

1/7/2013 - 31/12/2016 Imaging the structure and dynamics of molecules and complexes in living organisms (RECI/BEX-BCM/0083/2012), Foundation for Science and Technology, Portugal (PI: Nuno Moreno, Partner: Cláudia G. Almeida)

E. Bibliometric.

1. Total number of citations (google scholar): 3403
2. hfactor (google scholar): 13
3. Accumulated impact factor 79.269+5.788+8.568=93.625
4. Number of papers with impact factor over 7 during the last 5 years: 1
5. Number and impact of papers as corresponding or last author during the last 5 year: 2 (Total Impact factor 14.356)