MARIE SKŁODOWSKA-CURIE POSTDOCTORAL FELLOWSHIPS 2023

EXPRESSION OF INTEREST FOR HOSTING MARIE CURIE FELLOWS

HOST INSTITUTION

NOVA MEDICAL SCHOOL (iNOVA4Health, research unit)

RESEARCH GROUP AND URL

LYSOSOMES AND DISEASE
https://www.nms.unl.pt/en-us/research/research-groups/research-group/n/lisossomas-em-patologias-cronicas-humanas

SUPERVISOR (NAME AND E-MAIL)

Otília V. Vieira otilia.vieira@nms.unl.pt

SHORT CV OF THE SUPERVISOR

I did my PhD on the -Effect of oxidized-LDL on endothelial-cell apoptosis and the protective effects of phenolic compounds-, (Robert Salvayre Lab, Toulouse and Leonor Almeida Lab, Coimbra). During my 1st post-doc, I worked on -Host-pathogen interactions-, (Sergio Grinstein Lab, Toronto). On my 2nd post-doc I worked on -TGN sorting of newly synthesized cargo in polarized cells- (Kai Simons Lab, MPI-CBG, Dresden). In 2006, I returned to Portugal to establish myself as an independent scientist at the CNC, University of Coimbra. My group worked mainly on the mechanistic understanding of the process of plasma membrane resealing by lysosomes and its regulation during M. tuberculosis infection and also on the use of surfactants as topical microbicides to tackle sexually transmitted infections. In 2014, I was awarded with the prestigious iFCT award at the consolidator level and moved to NOVA MEDICAL SCHOOL, New University of Lisbon, where I am the PI of the group -Lysosomes and Disease (https://www.nms.unl.pt/en-us/Research/Research-Groups/Details/investigationgroupid/2219) - and Assistant Professor with Habilitation (Agregação). In NOVA MEDICAL SCHOOL RESEARCH, devoted to Chronic Diseases and Translational Medicine, I started a translational research project on cardiovascular diseases taking advantage of my previous experience in atherosclerosis and membrane traffic. The main objectives of my research are to identify the biochemical and cell biological etiology of atherosclerosis at the bench and to carry this knowledge through modern analytical chemical techniques to a clinical prediction of CVD risk. The team involved in my research includes cardiologists, molecular cell biologists and biophysical chemists. My group is composed of 1 senior scientist (that is in the World's Top 2% of the highly cited researchers worldwide), 1 junior scientist, 2 PhD students and 1 research fellow. In total I published 46 articles, 12 as first author, 20 as last author and 21 as corresponding author in high impact journals such as PNAS, Nat. Cell Biology, J Cell Biology and EBioMedicine. Four of my publications have been highlighted in the Journal of Cell Biology, one in PNAS, one in EBioMedicine and three have been recommended in F1000Prime. Excluding the-Guidelines for the use and interpretation of assays for monitoring autophagy- citations, my publications have been cited more than 5000 times and my h-factor is 31 (Google Scholar). In the last five years, I published 15 articles, 10 as last author and 5 as co-author. Our J. Cell Biol. (2016) has 73 citations and was highlighted in J. Cell Biol. and recommended twice in F1000. Our recent publication on the journal EBioMedicine was also subject to a commentary by this journal and our Journal Cell Science publication was selected to be published in a special issue of Cell Biology of Lipids. Currently, we are revising one manuscript on Lysosome Dysfunction in Atherosclerosis. Additionally, we have two other manuscripts submitted for publication. Since 2006, I completed the supervision of 9 post-

doctoral fellows, 7 PhD students and 3 MSc students. In competitive calls for funding, which included the creation of an international consortium with Harvard Medical School, USA, of which I was the coordinator, I raised around TWO Million euros. I was also awarded with 2 INOVC awards. In addition to my core scientific activities, I am also an Assistant Professor (Tenure Track) in NOVA MEDICAL SCHOOL. I am an Editor for Scientific Reports (Nature Publishing Group) and an Associate Editor for the Frontiers in Cell and Developmental Biology. I also act as examiner in MSc/PhD theses; and participate in peer- and grant proposal reviewing. I am also member of the following H2020 consortiums: Twinning, RISE and COST Action.

5 SELECTED PUBLICATIONS

Domingues N, Marques ARA, Calado RDA, Ferreira IS, Ramos C, Ramalho J, Soares MIL, Pereira T, Oliveira L, Vicente JR, Wong LH, Simões ICM, Pinho E Melo TMVD, Peden A, Almeida CG, Futter CE, Puertollano R, Vaz WLC, Vieira OV. Oxidized cholesteryl ester induces exocytosis of dysfunctional lysosomes in lipidotic macrophages. **Traffic**. **2023** May 2. doi: 10.1111/tra.12888. Online ahead of print.PMID: 37129279

Alves LS, Marques ARA, Padrão N, Carvalho FA, Ramalho J, Lopes CS, Soares MIL, Futter CE, Pinho E Melo TMVD, Santos NC, Vieira OV. Cholesteryl hemiazelate causes lysosome dysfunction impacting vascular smooth muscle cell homeostasis. **J Cell Sci. 2022** Mar 1;135(5):jcs254631. doi: 10.1242/jcs.254631. Epub 2021 Oct 22.PMID: 34528688

Matthiesen R, Lauber C, Sampaio JL, Domingues N, Alves L, Gerl MJ, Almeida MS, Rodrigues G, Araújo Gonçalves P, Ferreira J, Borbinha C, Pedro Marto J, Neves M, Batista F, Viana-Baptista M, Alves J, Simons K, Vaz WLC, Vieira OV.Shotgun mass spectrometry-based lipid profiling identifies and distinguishes between chronic inflammatory diseases. **EBioMedicine**. **2021** Aug;70:103504. doi: 10.1016/j.ebiom.2021.103504. Epub 2021 Jul 24.PMID: 34311325

Santarino IB, Viegas MS, Domingues NS, Ribeiro AM, Soares MP, Vieira OV. Involvement of the p62/NRF2 signal transduction pathway on erythrophagocytosis. **Sci Rep. 2017** Jul 19;7(1):5812. doi: 10.1038/s41598-017-05687-1.PMID: 28724916.

Encarnação M, Espada L, Escrevente C, Mateus D, Ramalho J, Michelet X, Santarino I, Hsu VW, Brenner MB, Barral DC, Vieira OV. A Rab3a-dependent complex essential for lysosome positioning and plasma membrane repair. **J Cell Biol. 2016** Jun 20;213(6):631-40. doi: 10.1083/jcb.201511093.PMID: 27325790

PROJECT TITLE AND SHORT DESCRIPTION

Title: Lysosome Dysfunction and cellular Senescence in atherogenesis: is there a link?

Atherosclerosis is a progressive insidious chronic disease that underlies most of the cardiovascular diseases (CVD), the main cause of death and disability in the world. The exact molecular and cellular factors that influence the initiation and progression of atherosclerotic lesions are extremely complex and poorly understood.

One of the early characteristics of atherogenesis, observed in lesions of different origins, is the sequestration of lipids in lysosomes of vascular smooth muscle cells (VSMC). With time, accumulation of undigested lipids in these organelles, leads to disruption of lysosome function. VSMC also undergo premature senescence, promoting atherosclerosis and plaque instability. Therefore, we aim to unveil if and how lysosome dysfunction induces VSMC premature senescence. Our research will unveil the molecular mechanisms involved in lysosome dysfunction and premature VSMC senescence. It will also contribute to assess the value of a novel family of oxidized lipids identified by us as marker of lysosome dysfunction and cell senescence in atherosclerosis and hopefully will open new avenues to therapeutic interventions to improve the treatment of atherosclerotic diseases.

SCIENTIFIC AREA WHERE THE PROJECT FITS BEST*

Life Sciences (LIF)