**MARIE SKŁODOWSKA-CURIE POSTDOCTORAL FELLOWSHIPS 2024**

***EXPRESSION OF INTEREST FOR HOSTING MARIE CURIE FELLOWS***

## HOST INSTITUTION

NOVA Medical School (NMS)

## RESEARCH GROUP AND URL

Lysosomes and Disease Group (https://www.nms.unl.pt/en-us/research/research-groups/research-group/n/lisossomas-em-patologias-cronicas-humanas )

## SUPERVISOR (NAME AND E-MAIL)

Otilia V. Vieira, otilia.vieira@nms.unl.pt

## SHORT CV OF THE SUPERVISOR

I did my PhD on the lab of Prof. R. Salvayre, Univ. Paul Sabatier, Toulouse. I did my 1st post-doc in the lab of Prof. S. Grinstein, at the Univ. of Toronto. My second post-doc was in the lab of Prof. K. Simons, at the MPI-CBG, Dresden. In 2006, I returned to Portugal to establish myself as an independent scientist at the Center for Neurosciences and Cell Biology at the Univ. 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 on the use of surfactants as topical microbicides to prevent sexually transmitted infections. In 2014, I was awarded with the prestigious iFCT award at the consolidator level and moved to NOVA MEDICAL SCHOOL (NMS), New University of Lisbon, where I am the Principal Investigator of the group -Lysosomes and Disease. In NMS taking advantage of my previous experience in atherosclerosis and membrane traffic I started a translational research project on cardiovascular diseases. 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 assistant researcher, 2 PhD students and 2 research fellows. I have published a total of 50 articles in peer-reviewed journals, 12 as first author, 24 as last author and 25 as corresponding author in high impact journals such as PNAS, Nat. Cell Biol, J. Cell Biol, EBioMedicine and Matter. Four of my publications have been highlighted in the J Cell Biol, one in PNAS, one in EBioMedicine and three have been recommended in F1000Prime. From the articles published during the last year, 2 were selected for covers of the journals (J. Lipid Res. and Traffic). According to Scopus my publications have been cited 5389 times and my h-factor is 31. 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 have raised more than TWO Million euros. I was also awarded with 2 INOVC awards. In addition to my core scientific activities, I am also an Assistant Prof. with habilitation (Tenure Track) in NOVA MEDICAL SCHOOL where I teach more than 200 h/year. 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 was member of the following H2020 consortiums: Twinning, RISE and COST Action. Presently, I am member of the Twinning on Extracellular Vesicles. I have also been involved in science dissemination events. I interrupted my career once on maternity leave in 2007.

## 5 SELECTED PUBLICATIONS


- 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
-

- Domingues N, Gaifem J, Matthiesen R, Saraiva DP, Bento L, Marques ARA, Soares MIL, Sampaio J, Klose C, Surma MA, Almeida MS, Rodrigues G, Gonçalves PA, Ferreira J, E Melo RG, Pedro LM, Simons K, Pinho E Melo TMVD, Cabral MG, Jacinto A, Silvestre R, Vaz W, **Vieira OV**. Cholesteryl hemiazelate identified in CVD patients causes in vitro and in vivo inflammation.
- J Lipid Res. 2023 Sep;64(9):100419. doi: 10.1016/j.jlr.2023.100419. Epub 2023 Jul 21.
-
- Domingues N, Estronca LMBB, Silva J, Encarnação MR, Mateus R, Silva D, Santarino IB, Saraiva M, Soares MIL, Pinho E Melo TMVD, Jacinto A, Vaz WLC, **Vieira OV**. Cholesteryl hemiesters alter lysosome structure and function and induce proinflammatory cytokine production in macrophages.
- Biochim Biophys Acta Mol Cell Biol Lipids. 2017 Feb;1862(2):210-220. doi: 10.1016/j.bbalip.2016.10.009.
-
- 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 Jul;24(7):284-307. doi: 10.1111/tra.12888. Epub 2023 May 2.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

## PROJECT TITLE AND SHORT DESCRIPTION

**ROLE OF LYSOSOME DYSFUNCTION IN THE PATHOGENESIS OF ATHEROSCLEROSIS**

Atherosclerosis is a non-resolving chronic inflammatory disease that develops in the medium to large arteries and is listed as the primary cause of cardiovascular diseases (CVD). A key event in atherogenesis is the formation of lipid-loaded macrophages, lipidotic cells, which exhibit irreversible accumulation of undigested modified low-density lipoproteins (LDL) in lysosomes causing their malfunction. This event culminates in the loss of cell homeostasis, inflammation, senescence and cell death.

Recently, we have identified, through lipidomic analyses, a family of end-products of cholesterol esters oxidation, named cholesteryl hemiesters (ChE), in the plasma of CVD patients and in human endarterectomy specimens that are responsible for lysosome dysfunction and loss of cell homeostasis. Now we are investigating the molecular and cellular mechanisms responsible for the impairment of lysosome function in plaque macrophages and its connection with cell senescence and impact on interorganelle communication. To achieve our goals, we are applying several omics technologies and modern biochemistry and cell biology techniques.

## SCIENTIFIC AREA WHERE THE PROJECT FITS BEST*

Life Sciences (LIF), *Biomedicine, molecular mechanisms of disease*