MARIE SKŁODOWSKA-CURIE POSTDOCTORAL FELLOWSHIPS 2025

EXPRESSION OF INTEREST FOR HOSTING MARIE CURIE FELLOWS

HOST INSTITUTION

iNOVA4Health, NOVA Medical School

RESEARCH GROUP AND URL

Degeneration and Ageing Group
https://nms.unl.pt/en-us/research/research/research-groups/research-group/n/sandra-tenreiro-lab

SUPERVISOR (NAME AND E-MAIL)

Sandra Tenreiro
stenreiro@nms.unl.pt

SHORT CV OF THE SUPERVISOR

Sandra Tenreiro (ST) is the Group Leader of the Degeneration and Ageing Lab at NMS-UNL. Her research is focused on clarifying the molecular mechanisms of neurodegeneration in the context of ageing diseases, such as retinal degeneration, using *in vitro* models such as retinal organoids. She is also collaborating with ophthalmologists and actively involved in clinical studies (ClinicalTrials.gov database identifier: NCT06355830).

ST is the NMS-UNL Coordinator of the MPS_NOVA Twinning project, aiming to improve NMS expertise in the Microphysiological Systems (MPS) field, in partnership with ITQB NOVA, supported by leading European institutions in MPS and stem cell research, including Universitätsklinikum Jena UKJ (Germany), Max Delbrück Center MDC (Germany) and Fondazione Human Technopole FHT (Italy).

ST is also the chair of the Retina & Vision Research area at NMS-UNL and Co-Coordinator of the Ageing Strategic Area from NOVAhealth-UNL. ST is a member of the Management Committee (MC) of COST ActionBenBedPhar, "Bench to bedside transition for pharmacological regulation of NRF2 in non-communicable diseases" (CA20121, 2021-2025).

S Tenreiro has served as the Principal Investigator (PI) and Co-PI in several research projects and has been extensively involved in advanced training, overseeing post-docs (7), PhD students (7), MSc students (21), scientific traineeships (19), and managed 7 research assistants. Additionally, she collaborates with various PhD and MSc programs at both UNL and Coimbra University.

Overall, her scientific career is exemplified by 61 peer-reviewed publications, with an H-index of 33 and ~4000 citations, as reported by Scopus. Moreover, S Tenreiro ST has one patent under review (pending patent PCT/IB2023/062075).

5 SELECTED PUBLICATIONS

- de Lemos L, Antas P, Ferreira IS, Santos IP, Felgueiras B, Gomes CM, Brito C, Seabra MC, **Tenreiro S**. Modelling neurodegeneration and inflammation in early diabetic retinopathy using 3D human retinal organoids. In vitro models. 2024 3, 33–48 https://doi.org/10.1007/s44164-024-00068-1
- Dias SB, de Lemos L, Sousa L, Bitoque DB, Silva GA, Seabra MC, **Tenreiro S**. Age-Related Changes of the Synucleins Profile in the Mouse Retina. Biomolecules. 2023 Jan 15;13(1):180. doi: https://doi.org/10.3390/biom13010180
- Fonseca AF, Coelho R, da-Silva ML, Lemos L, Hall MJ, Oliveira D, Falcão AS, **Tenreiro S**, Seabra MC, Antas P. Modeling Choroideremia Disease with Isogenic Induced Pluripotent Stem Cells. Stem Cells Dev. 2024 33,528-539. https://doi.org/10.1089/scd.2024.0105
- Flores R, Fradinho AC, Pereira RS, Mendes JM, Seabra MC, **Tenreiro S**, Carneiro Â. Identifying Imaging Predictors of Intermediate Age-Related Macular Degeneration Progression. Transl Vis Sci Technol. 2023 Jul 3;12(7):22. https://doi.org/10.1167/tvst.12.7.22

- Escrevente C, Falcão AS, Hall MJ, Lopes-da-Silva M, Antas P, Mesquita MM, Ferreira IS, Cardoso MH, Oliveira D, Fradinho AC, Ciossek T, Nicklin P, Futter CE, **Tenreiro S**, Seabra MC. Formation of Lipofuscin-Like Autofluorescent Granules in the Retinal Pigment Epithelium Requires Lysosome Dysfunction. Invest Ophthalmol Vis Sci. 2021 Jul 1;62(9):39. https://doi.org/10.1167/iovs.62.9.39

PROJECT TITLE AND SHORT DESCRIPTION

Innovating diabetic retinopathy disease models: dissecting pathophysiology and pioneering therapeutic strategies

Diabetic retinopathy (DR), a common complication of diabetes, is a primary cause of vision impairment on a global scale, affecting ~30% of patients within five years of their diabetes diagnosis. Presently, there are no definitive treatments for DR; existing interventions primarily target advanced stages of the disease, often after significant vision loss has occurred. There is an urgent need for innovative therapeutic approaches addressing early-stage DR to impede its progression to severe forms that compromise vision integrity. The current disease models employed for studying DR and conducting pre-clinical trials possess notable limitations.

Recently, the research group led by Sandra Tenreiro, generated a model of early DR, using retinal organoids derived from Human-Induced Pluripotent Stem Cells (hiPSCs), where the early events reported in DR patients are reproduced (Pending Patent Application PCT/IB2023/062075) (De Lemos et al, 2024), However, the current model can be improved to reproduce also the intermediate and late stages of DR.

Our goal is to engineer a robust 3D system that integrates vascularized retinal organoids with microglial cells and to characterize its cellular composition using single-cell RNA sequencing (scRNA-seq). This advanced model will serve as a foundation for future studies aimed at improving our understanding DR. Ultimately, we seek to develop stage-specific models of DR to de-risk drug discovery and enhance the reliability of preclinical testing for novel anti-DR therapies.

In parallel, we aim to refine protocols for generating retinal organoids that recapitulate key features of ageing, including the exploration of transdifferentiation approaches.

We are particularly interested in strengthening our team with expertise in single-cell RNA sequencing, to complement our knowhow in retinal organoids and retinal disease research.

SCIENTIFIC AREA WHERE THE PROJECT FITS BEST*

Life Sciences (LIF)