MARIE SKŁODOWSKA-CURIE POSTDOCTORAL FELLOWSHIPS 2025

EXPRESSION OF INTEREST FOR HOSTING MARIE CURIE FELLOWS

HOST INSTITUTION

iNOVA4Health, NOVA Medical School

RESEARCH GROUP AND URL

Molecular Mechanisms of Disease
https://www.nms.unl.pt/en-us/research/research-groups/research-group/n/molecular-mechanisms-of-disease

SUPERVISOR (NAME AND E-MAIL)

Miguel Seabra
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SHORT CV OF THE SUPERVISOR

Miguel C Seabra (MCS) graduated in Medicine in 1986 at Faculdade de Ciências Médicas, Universidade Nova de Lisboa, Portugal. Fascinated by a career in science, MSC enrolled in a PhD in Biochemistry and Molecular Biology at the University of Texas Southwestern Medical Center at Dallas, USA (UTSW) supervised by Nobel laureates MS Brown and JL Goldstein, with a Fulbright and Gulbenkian fellowship. Soon, after accomplished her PhD thesis in 1992, MCS started his own lab as an Assistant Professor in 1994 at UTSW. In 1997, MCS moved his lab to Imperial College London, UK where he became full Professor in 1999 and head of Section of Molecular Medicine.

In 2007, MCS moved to his hometown of Lisbon, Portugal, as Professor of Biomedicine and head of Biochemistry and Cell Biology at Nova Medical School (NMS). Since then and until 2015 MCS maintained a position as Honorary Professor at Molecular Medicine, NHLI, Faculty of Medicine, Imperial College London, UK. Since 2016 MSC is Honorary Professor at the UCL Institute of Ophthalmology, University College London, UK.

In 2012, MCS became president of Fundação para a Ciência e Tecnologia (FCT) the public grant-funding body in Portugal in all areas of science. Whilst president of FCT, MCS served one term as president of Science Europe, a Brussels-based organization combining research-funding and research-performing European organizations. In 2016, MCS returned to NMS as a group leader of the Molecular Mechanisms of disease Lab, and as Full Professor.

In 2021, MCS created a new lab at Fundação Champalimaud to implement a Global Eye Research Initiative in collaboration with the LV Prasad Institute in India with the goal of developing and implementing low-cost solutions for common eye diseases.

MCS is a holder of a patent on AAV2-Choroideremia gene therapy (UK patent application 1103062.4 and international application PCT/GB/12/050376, entitled "AAV-vectors for use in gene therapy of choroideremia", filed by the University of Oxford, jointly with R. MacLaren and Matt During)

MCS trained so far 23 postdoctoral fellows and 37 PhD students. These have become successful academic professors and research group leaders, entrepreneurs, industry workers, science communication, policy and administration experts. Overall, he has received over 13 million Euros in competitive grants as group leader in USA, UK and Portugal.

5 SELECTED PUBLICATIONS

- 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 Oct;33(19-20):528-539. https://doi.org/10.1089/scd.2024.0105

- Cardoso MH, Hall MJ, Burgoyne T, Fale P, Storm T, Escrevente C, Antas P, **Seabra MC**, Futter CE. Impaired Lysosome Reformation in Chloroquine-Treated Retinal Pigment Epithelial Cells. Invest Ophthalmol Vis Sci. 2023 Aug 1;64(11):10. https://doi.org/10.1167/iovs.64.11.10
- 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
- Flores R, Carneiro A, Serra J, Gouveia N, Pereira T, Mendes JM, Coelho PS, Tenreiro S, **Seabra MC**. Correlation study between drusen morphology and fundus autofluorescence. Retina. 2021 Mar 1;41(3):555-562. https://doi.org/10.1097/IAE.0000000000002881

PROJECT TITLE AND SHORT DESCRIPTION

TOWARD A BIOMIMETIC *IN VITRO* MODEL OF AGE-RELATED MACULAR DEGENERATION FEATURING DRUSEN FORMATION

Age-related macular degeneration (AMD) is the leading cause of blindness in the Western world and remains incurable. The primary pathological hallmark of AMD is the degeneration of the **retinal pigment epithelium (RPE)**. Miguel Seabra's laboratory has developed an **in vitro model** that recapitulates key features of AMD. In this model, RPE monolayers are fed with **photoreceptor outer segments (POS)**, leading to the accumulation of **autofluorescent granules** reminiscent of lipofuscin observed in vivo—an indicator of RPE stress and dysfunction (Escrevente et al., 2021). This model is currently being utilized to investigate **drug repurposing strategies** for the treatment of early and intermediate stages of AMD.

Another hallmark of AMD is the formation of **drusen**—extracellular deposits that accumulate between the RPE and **Bruch's membrane**. Drusen are central to both the diagnosis and progression of AMD. They are composed of lipids, proteins, and complement components, implicating mechanisms such as **inflammation**, **oxidative stress**, and **defective waste clearance** in disease pathogenesis. However, the **precise cellular and molecular mechanisms** driving drusen formation remain unclear, primarily due to the **lack of suitable in vitro models** that replicate this aspect of the disease.

We hypothesize that **lysosomal exocytosis** may play a significant role in drusen biogenesis. To test this, we aim to develop an **advanced in vitro AMD model** that mimics drusen formation. To achieve this, we are particularly interested in incorporating **3D bioprinting approaches**, an area of expertise currently lacking in our team. Expertise in this domain would be highly valuable to the success of this project.

SCIENTIFIC AREA WHERE THE PROJECT FITS BEST*

Life Sciences (LIF)