MARIE SKŁODOWSKA-CURIE POSTDOCTORAL FELLOWSHIPS 2025

EXPRESSION OF INTEREST FOR HOSTING MARIE CURIE FELLOWS

HOST INSTITUTION

NMS, iNOVA4Health

RESEARCH GROUP AND URL

Catarina Homem, Proliferation and Fate Regulation of Stem Cells, https://www.nms.unl.pt/en-us/research/research/research-groups/research-group/n/proliferation-and-fate-regulation-of-stem-cells

SUPERVISOR (NAME AND E-MAIL)

Catarina Homem, Catarina.homem@nms.unl.pt

SHORT CV OF THE SUPERVISOR

Catarina CF Homem is a Principal Investigator and Independent Group Leader in NOVA Medical School, Universidade NOVA de Lisboa since 2016. Catarina CF Homem has completed her PhD in Biology at the University of North Carolina at Chapel Hill-USA and a Postdoc in the Institute of Molecular Biotechnology of Austria. Catarina CF Homem has published over 20 articles in international peer-reviewed high impact journals, several as last author (e.g. Plos Biology, 2024; Development, 2023; Front Cell Dev Biol, 2022; Dev Biol, 2021; Front Cell Dev Biol, 2021; Embo J, 2020; Nature Reviews in Neuroscience, 2015; Cell, 2014 & Cell, 2014). Catarina CF Homem received an FCT project grant in 2025&2021, an ERC starting grant in 2017, is a Howard Hughes International Investigator and has been granted an EMBO Installation Grant. As a student and postdoc fellow has been granted a PhD fellowship and an EMBO-long term postdoctoral fellowship.

During her PhD at UNC, Catarina CF Homem explored how cell-cell adhesion and the actin cytoskeleton are dynamically regulated to allow for the changes in cell adhesion required for morphogenesis. Pursuing her interest in the dynamic regulation of developmental processes, during her postdoctoral research Catarina CF Homem studied how neural stem cells are temporally regulated during brain development. To address the unresolved question of how neural stem cell proliferation is regulated during animal development, she utilized Drosophila neural stem cells, known as neuroblasts (NB), as a model system. The outcomes of this study unveiled the crucial roles of the steroid hormone Ecdysone and the transcriptional regulator Mediator in regulating energy metabolism, subsequently impacting the growth and fate of NBs. These findings established an unexpected connection between cellular metabolism and the proliferation/fate of stem cells (Homem et al., Cell, 2014). This discovery opened up a new avenue of research that Catarina CF Homem has pursued as an independent researcher. The primary goal of her lab is to develop a pioneering research program that investigates how the interplay between temporal cues and metabolism influences the fate of stem cells and neural cells, ensuring proper animal development. In addition, their research also focuses in exploring how dysregulation of metabolism contributes to diseases such as brain tumors and neurodevelopmental disorders. Catarina CF Homem's group has large expertise in genetics, animal model *Drosophila*, Metabolomics with Untargeted or Targeted Mass-Spectrometry, Metabolic profile analysis with Seahorse, metabolic biosensors, single cell and bulk transcriptomic analysis, chromatin analysis (TADA and Chip-Seq), confocal microscopy and bioinformatics.

Catarina CF Homem is also an active member of the scientific community, having organized 2 scientific conferences, being a Scientific Editor in Plos Biology and eLife, a frequent scientific reviewer for several journals as Elife, Plos Biology, Dev Cell, Plos Genetics, Developmental Biology and served as jury in several MsC defenses, PhD defenses, academic awards and conference juries. Catarina CF Homem is a board member of the Portuguese Society of Stem Cells and Cellular Therapies. Catarina CF Homem has several

active national and international scientific collaborations (e.g. New York University, NYU-Abu Dhabi, University College London, I3S-University Porto). Catarina CF Homem has supervised to successful completion 8 Master thesis and 5 PhD students. Catarina CF Homem is currently supervising 2 PhD students (all awarded competitive PhD fellowships including a LaCaixa fellowship) and 2 Postdoctoral fellows (awarded EMBO long-term postdoctoral fellowship, FCT fellowship).

5 SELECTED PUBLICATIONS

- Marques GS, Teles-Reis J, Konstantinides N, Brito PH, Homem CCF. (2023) Asynchronous transcription and translation of neurotransmitter-related genes characterize the initial stages of neuronal maturation in Drosophila. ***PLoS Biology*** 21 (5), e3002115
- Silva EAB, Venda AM, Homem CCF. (2023) Serine hydroxymethyl transferase (Shmt) is required for optic lobe neuroepithelia development in Drosophila. ***Development*** dev. 201152
- Rebelo AR, Homem CCF. (2023) dMyc-dependent upregulation of CD98 amino acid transporters is required for Drosophila brain tumor growth. ***Cell Mol Life Sciences***, 80 (1), 30.
- Osswald M, Barros-Carvalho A, Carmo AM, Loyer N, Gracio PC, Sunkel CE, Homem CCF, Januschke J, Morais-de-Sá E. (2022) aPKC regulates apical constriction to prevent tissue rupture in the Drosophila follicular epithelium. ***Current Biology*** 32 (20), 4411-4427. e8
- Homem CCF, Steinmann V, Burkard TR, Jais A, Esterbauer H, Knoblich JA (2014) Changes in energy metabolism triggered by Ecdysone and Mediator end proliferation in *Drosophila* neural stem cells. ***Cell*** 158, 874-888

PROJECT TITLE AND SHORT DESCRIPTION

Metabolism and Fate Regulation: Uncovering New Pathways in Stem Cell Identity

Stem cells (SCs) possess self-renewal and differentiation properties, making them fundamental for development and regeneration. However, our understanding of stem cell differentiation is limited. Beyond their bioenergetic roles, metabolism is a key regulator of stem cell fate, influencing gene expression and chromatin remodeling. Additionally, the balance between aerobic glycolysis and oxidative phosphorylation (OxPhos) is crucial in regulating SC fate, with metabolic intermediates influencing gene expression and chromatin remodeling. However, the link between metabolism and these networks remains poorly understood.

Interestingly, tumor cells, like stem cells, prefer glycolysis over OxPhos, even in oxygen-rich conditions; this phenomenon is called the Warburg effect. This event suggest that tumors may exploit stem cell metabolic pathways to sustain proliferation and prevent differentiation. However, it is still unclear to what extent the metabolic control of fate decisions is conserved between stem cells and tumor cells. Understanding these parallels could provide insights into development and tumorigenesis.

This project aims to dissect the role of metabolism in controlling stem cell differentiation and tumor progression. Specifically, we will investigate how key metabolic enzymes interact with chromatin regulators and transcription factors to influence SC fate and support tumor maintenance. Using Drosophila neural stem cell lineages and brain tumor models, we will employ a multi-faceted approach—including biochemistry, fixed and live confocal imaging, genetics/CRISPR, and ChIP-seq—to identify critical metabolism-chromatin interactions and elucidate their mechanisms. In a second phase, we will assess the conservation of these mechanisms in mammalian stem cells.

By elucidating how metabolism intersects with gene regulatory networks, this project will reveal fundamental principles governing SC fate decisions and tumor development. These insights may inform new strategies to manipulate metabolism in regenerative medicine and cancer therapy.

SCIENTIFIC AREA WHERE THE PROJECT FITS BEST*

Life Sciences (LIF)