MARIE SKŁODOWSKA-CURIE POSTDOCTORAL FELLOWSHIPS 2024

EXPRESSION OF INTEREST FOR HOSTING MARIE CURIE FELLOWS

HOST INSTITUTION

NOVA Medical School

RESEARCH GROUP AND URL

Membrane Traffic in Disease

SUPERVISOR (NAME AND E-MAIL)

Duarte Barral (duarte.barral@nms.unl.pt)

SHORT CV OF THE SUPERVISOR

Duarte Barral (DB; ORCID: 0000-0001-8867-2407; Ciência ID: 8810-DEBC-025E) is a tenured Associate Professor with Habilitation at NMS-UNL, with over two decades of expertise in investigating the mechanisms underlying membrane trafficking in both health and disease contexts.

DB earned his Degree in Microbiology and Genetics from the Faculty of Sciences of the University of Lisbon in 1997, followed by a PhD in Cell Biology from Imperial College London in 2003. He then ventured into the field of immunology, undertaking a Post-Doctoral Fellow position (2003) at Brigham and Women's Hospital, Harvard Medical School. In 2009, DB became a Principal Investigator (PI) at NMS-UNL, where he established the Membrane Traffic in Disease group, which has made significant contributions to the fields of molecular cell biology, skin pigmentation, and oncobiology. Before attaining his current position, through an international competitive selection process, DB secured his own salary through several competitive calls: undergraduate, PhD and Post-Doctoral fellowships, as well as Principal Investigator contracts (Ciência 2008 and FCT Investigator, both funded by Fundação para a Ciência e a Tecnologia – FCT). Such achievements underscore his exceptional academic profile.

DB's research aims to unravel the regulatory roles of GTPases belonging to the Rab and Arf families in the trafficking of lysosomes and lysosome-related organelles such as melanosomes, and elucidating how dysregulation of these processes contributes to human diseases, most notably cancer. Indeed, DB has helped uncover the previously unknown role of several of these proteins, namely Rab27a (Stinchcombe et al., J Cell Biol., 2001; Hume et al., Traffic, 2002; Barral et al., J Clin. Invest., 2002), Rab35 (Kuhns et al., EMBO Rep., 2019), Arl8b (Garg et al, Immunity, 2011), and Arl13b (Barral et al., PNAS, 2012; Casalou et al., J. Cell Sci., 2014; Casalou et al., Cancers, 2019).

DB has demonstrated a remarkable ability to secure competitive funding, amassing over 2.75 million € for research projects as PI/Coordinator, and in successfully overseeing the completion of 10 funded projects. These projects received national funding, including from FCT and Liga Portuguesa Contra o Cancro – LPCC, as well as from international sources, namely the European Commission. He also has a solid and consistent track record of publishing impactful studies, with 52 publications in peer-reviewed international journals and over 3000 citations (h-index 31 - Scopus).

Since 2009, DB has mentored 12 post-docs, 19 PhD students and 12 MSc students. Of these, 5 are pursuing an academic career in international research institutions, in Europe and the USA, and 7 have successfully transitioned to industry. Moreover, his group has attracted 2 foreign post-docs and 1 foreign PhD student, further enhancing the global impact of his research efforts. In total, he was involved in training almost 70 researchers (including co-supervisions), demonstrating his commitment to nurturing talent and fostering both academic and professional excellence.

DB is currently committed on exploring the complex membrane trafficking pathways governing skin pigmentation and how these are exploited by cutaneous melanoma cells. With a unique set of skills and expertise spanning both fields, he aims to leverage the fundamental knowledge acquired to develop innovative therapeutic strategies for pigmentary disorders and cutaneous melanoma. Additionally, his efforts encompass exploring cosmetic applications aimed to modulate skin pigmentation. Thus, through a comprehensive approach, DB will keep striving to make significant contributions to both cancer research and derma-cosmetic fields.

5 SELECTED PUBLICATIONS

- Neto MV, Hall MJ, Charneca J, Escrevente C, Seabra MC, Barral DC. Photoprotective melanin is maintained within keratinocytes in a storage lysosome. bioRxiv 2024.02.05.578910. doi: https://doi.org/10.1101/2024.02.05.578910.
- Cabaço LC, Bento-Lopes L, Neto MV, Ferreira A, Staubli WBL, Ramalho JS, Seabra MC, Barral DC. RAB3A Regulates Melanin Exocytosis and Transfer Induced by Keratinocyte-Conditioned Medium. JID Innov. 2022 Jun 21;2(5):100139. doi: 10.1016/j.xjidi.2022.100139.
- Moreiras H, Bento-Lopes L, Neto MV, Escrevente C, Cabaço LC, Hall MJ, Ramalho JS, Seabra MC, Barral DC. Melanocore uptake by keratinocytes occurs through phagocytosis and involves protease-activated receptor-2 internalization. Traffic. 2022 Jun;23(6):331-345. doi: 10.1111/tra.12843.
- Moreiras H, Pereira FJC, Neto MV, Bento-Lopes L, Festas TC, Seabra MC, Barral DC. The exocyst is required for melanin exocytosis from melanocytes and transfer to keratinocytes. Pigment Cell Melanoma Res. 2020 Mar;33(2):366-371. doi: 10.1111/pcmr.12840.
- Correia MS, Moreiras H, Pereira FJC, Neto MV, Festas TC, Tarafder AK, Ramalho JS, Seabra MC, Barral DC. Melanin Transferred to Keratinocytes Resides in Nondegradative Endocytic Compartments. J Invest Dermatol. 2018 Mar;138(3):637-646. doi: 10.1016/j.jid.2017.09.042.

PROJECT TITLE AND SHORT DESCRIPTION

The skin is the largest organ of the human body and provides protection against external aggressions. Its outmost layer, the epidermis, is composed mainly by two cell types: melanocytes and keratinocytes. Melanocytes localize to the basal layer and synthesize the pigment melanin. Keratinocytes are the final recipients of the pigment and differentiate from the basal to the apical layers. Melanin synthesis and transfer ensure protection of skin cells against ultraviolet radiation (UVr)-induced damage, which can lead to the onset of skin cancers. Melanin synthesis occurs in specialized membrane-bound organelles called melanosomes. Once fully mature and located at the tips of melanocyte dendrites, melanosomes are transferred to keratinocytes. Our group found evidence that the predominant mode of melanin transfer is via coupled melanin exo/phagocytosis. However, several key questions remain to be elucidated, namely the nature of the crosstalk between melanocytes and keratinocytes at the yet uncharacterized pigmentary synapse; the phagocytic receptor involved in melanin phagocytosis by keratinocytes; the role of autophagy in melanin processing within keratinocytes; and the polarization of melanin within keratinocytes to form supra-nuclear caps. The answers to these questions will shed light on fundamental membrane trafficking processes that remain elusive. Since the function of melanin is to protect skin cells from the genotoxic effects of UVr, the elucidation of these processes is essential to understand the mechanisms of protection against skin cancer, and allow their manipulation for health and cosmetic purposes.

SCIENTIFIC AREA WHERE THE PROJECT FITS BEST*

Life Sciences (LIF)

***Scientific Area where the project fits best** – Please select/indicate the scientific area according to the panel evaluation areas: Chemistry (CHE) • Social Sciences and Humanities (SOC) • Economic Sciences (ECO) • Information Science and Engineering (ENG) • Environment and Geosciences (ENV) • Life Sciences (LIF) • Mathematics (MAT) • Physics (PHY)