**MARIE SKŁODOWSKA-CURIE POSTDOCTORAL FELLOWSHIPS 2024**

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

## HOST INSTITUTION

NOVA School of Science and Technology (NOVA FCT); NOVA University of Lisbon

## RESEARCH GROUP AND URL

(Bio)molecular Structure and Interactions by NMR
https://www.ucibio.pt/research-groups/lab/biomolecular-structure-and-interactions-nmr

## SUPERVISOR (NAME AND E-MAIL)

Filipa Marcelo (filipa.marcelo@fct.unl.pt)

## SHORT CV OF THE SUPERVISOR

Filipa Marcelo is an Assistant Researcher at the Applied Molecular Biosciences Unit (UCIBIO), Department of Chemistry of NOVA School of Science and Technology (FCT/NOVA) and leader of the BioNMR Lab.
She graduated in Chemistry from Faculdade de Ciências da Universidade de Lisboa in 2003 and she received a PhD in Organic Chemistry in 2009 doing a joint PhD at the Universidade de Lisboa and Université Pierre et Marie Currie Paris VI in the field of carbohydrate chemistry under the supervision of Dr. A. P. Rauter and Dr. P. Sinaÿ. After her PhD and to diversify her background, she moved to Dr. J. Jiménez-Barbero's group at Centro Investigaciones Biológicas (CSIC/Madrid) for a post-doctoral experience (2009-2011). During that period, she became fascinated with NMR and how to exploit this technique to unveil molecular recognition events in distinct biological contexts, including in Glycoscience field. In 2012, she returned to Portugal with a FCT Post-doctoral grant to initiate a new research line in the field of Chemical Glycobiology in the BioNMR lab. In January 2017, she established an independent line of research in Chemical Glycobiology, where she synergistically combines high-resolution NMR-based approaches with molecular modelling protocols, sustained by molecular biology and carbohydrate/chemoenzymatic synthesis to uncover key molecular mechanisms of glycan recognition and protein glycosylation with the major goal to rationally design innovative glycan-based cancer therapies. Aiming to consolidate her research career, last March 2023 she initiated a permanent research contract as Assistant Researcher at FCT/NOVA from the Institutional Scientific Employment Stimulus Competition (CEEC) program. Over the last years, she was able to attract national funding as main PI and as CO-PI. At international level she is the scientific representative of Grant Holder of the COST research network CA18132-GlycoNanoProbes. Furthermore, together with, Dr. P. Videira and Dr. A. Palma, she co-coordinates a Collaborative Twinning project focused on Building Networks to Excel Glycoscience (GlycoTwinning - HORIZON-WIDERA-2021 - 101079417). She is currently supervising, 1 CEEC Junior Research, 4 PhD students (3 as main supervisor), 1 Research Fellow and 3 Senior Technicians (1 as main supervisor), and she has completed the supervision of 1 Post Doc, 2 PhD (1 Best thesis Award 2020), 7 MSc students, 6 Research Fellow (under the scope of national projects) and 8 BSc. She has also been engaged in distinct commissions of trust, namely in the Individual Fellowships, Marie Sklodowska-Curie actions (MSCA) and R&I Projects from ANR France. She has published 60 original research articles, reviews, and book chapters (11 as corresponding author) with a total of more than 1623 citations (h-index 22, scopus), besides several invited lectures and oral communications in international conferences.

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## 5 SELECTED PUBLICATIONS


5) MP Lenza, …, **F. Marcelo**, J Jiménez-Barbero, A Palazon, J Ereño-Orbea "Structural insights into Siglec-15 reveal glycosylation dependency for its interaction with T cells through integrin CD11b." Nat Commun. 14 1 (2023) 3496. Senior author

4) H. Coelho, …, Hurtado-Guerrero, **F. Marcelo** "Atomic and Specificity Details of Mucin 1 O-Glycosylation Process by Multiple Polypeptide GalNAc-Transferase Isoforms Unveiled by NMR and Molecular Modeling". J. Am. Chem. Soc. Au 2 3 (2022): 631-645. Corresponding author

3) A. M. González-Ramírez, …, **F. Marcelo**, F. Corzana, R. Hurtado-Guerrero, "Structural Basis for the synthesis of the core 1 structure by C1Gal-T1". Nat. Comm. 13 1 (2022): 2398. Senior author

2) C. D. L. Lima, …, **F. Marcelo** "Structural Insights into the Molecular Recognition Mechanism of the Cancer and Pathogenic Epitope, LacdiNAc by Immune-Related Lectins". Chem. Eur. J. 27 29 (2021): 7951-7958. Corresponding author

1) A. Diniz, …, **F. Marcelo** "The Plasticity of the Carbohydrate Recognition Domain Dictates the Exquisite Mechanism of Binding of Human Macrophage Galactose-Type Lectin". Chem. Eur. J. 25 61 (2019): 13945-13955. Corresponding author


## PROJECT TITLE AND SHORT DESCRIPTION

### Harnessing Human Macrophage Galactose C-Type Lectin for Innovative Cancer Therapies

Cancer remains a significant cause of death, particularly in cases of metastasis or advanced stages. Despite recent advancements in diagnosis and treatment, its prevalence continues to rise due to aging populations. Consequently, there is an urgent need for novel therapies. Abnormal glycan signatures found in mucin-like glycoproteins are a hallmark of cancer. These tumor-associated glycans, including sialylated and non-sialylated Tn-antigens (GalNAcα1-O-Ser/Thr), are exclusively expressed on cancer cells and strongly linked to tumor progression and immune evasion. Moreover, these antigens are shared across various tumor types, especially in metastatic cancer. The human macrophage galactose lectin (MGL) is the sole C-type lectin on antigen-presenting cells (APCs) with a marked specificity for N-acetylgalactosamine (α- or β-GalNAc), commonly present in tumor-associated glycan antigens. Studies indicate that MGL's immune responses vary based on the structure of the interacting ligand, striking a balance between tolerance and immunity. Recently, we discovered that the carbohydrate recognition domain (CRD) of MGL is highly dynamic and dependent on the structure and presentation of GalNAc-containing antigens. This flexibility allows MGL to accommodate different ligands, potentially explaining its ability to elicit distinct immune responses (tolerance vs. immunity) based on the specific GalNAc-containing structure. This evidence opens new avenues for designing rational glyco-immunomodulators and specific antibodies to modulate MGL-mediated immune responses in cancer. By targeting MGL, our innovative approach aims to address aberrant glycan signatures common to several tumors, including gastrointestinal tumors, and those associated with metastatic cancer. Ultimately, this project promises alternative or complementary strategies to existing cancer therapies, positively impacting patient treatment, survival, and overall well-being.

## SCIENTIFIC AREA WHERE THE PROJECT FITS BEST*

Chemistry (CHE)

Life Sciences (LIF)