**MARIE SKŁODOWSKA-CURIE INDIVIDUAL FELLOWSHIPS 2019**

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

## HOST INSTITUTION

NOVA School of Science and Technology | NOVA.ID.FCT - Associação para a Inovação e Desenvolvimento

## RESEARCH GROUP AND URL

Glycoimmunology Group
http://sites.fct.unl.pt/glycoimmunology/home

## SUPERVISOR (NAME AND E-MAIL)

Paula Videira
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## SHORT CV OF THE SUPERVISOR

**Paula Videira (*female*), PhD: Assistant Professor of Immunology, Leader of the Glycoimmunology Group at NOVA University and Co-director of CDG&Allies PPAIN**

Videira received a PhD. in Biotechnology at University of Lisbon (Portugal) in 2002, where she investigated enzymes involved in glycosylation biosynthesis in bacteria. During her Post-Doctoral studies, she extended these studies to *Burkholderia sp*, opportunistic pathogens in immunocompromised patients. In 2005 she was appointed by NOVA Medical School as invited assistant professor of Immunology, and in 2015 she moved to the FCT-NOVA with a permanent position. In 2008 she founded the Glycoimmunology group, whose main aim is to identify mechanisms on how glycans modulate the immune responses, focused on Congenital disorders of Glycosylation (CDG) and cancer. Her group is identifying novel therapeutic targets and developing new immunotherapies, as antibody- and dendritic cell (DC)-based strategies. In 2016, together with Vanessa Ferreira, APCDG president, she co-founded and coordinates the CDG&Allies-PPAIN (http://www.researchcdg.com/), an international volunteer network of professionals and patient associations involving **early career scientists** in awareness and research in diseases of Glycosylation.

Videira was awarded by the Portuguese Science Foundation (PhD, Master and Post-Doc), as fellow by Erasmus (1995), University of Bologna (2007), EMBO (2011) and Fulbright Commission (2013) at Harvard Institutes of Medicine and endowed with the Santander- NOVA (2013), Bluepharma-UC (2014), and Tagus Tank (2019) prizes. She developed competences in leading multidisciplinary research (national and international) consortiums as PI of several projects and as Steering committee of the GlycoCan (EU 676421) project. At EU level she participates in MetabERN, NanoCarb, EuroGlycoforum, COST Action Proteostasis and InovafunAgeing projects. She is a member of Immunology and Glycobiology international societies (AAI, SFG). She authors more than 76 international peer-review publications in high impact journals, 4 patents, 2 books, several book chapters and posters. She is frequently invited as keynote speaker and organized several international and national meetings. She participates as jury/reviewer in several scientific calls and scientific journals. She supervised 10 PhD students (plus 5 ongoing), 5 Post Docs (plus 3 ongoing) and several master and undergraduate students. **NOVA University of Lisbon** through the **School of Science and Technology (FCT NOVA)** is one of the most prestigious European engineering and public school. Videira belongs to the UCIBIO Research Unit, one of the 3 top in Portugal. It contains several facilities and belongs to **Congento** (EU Consortium for Genetically Tractable Organisms)

supporting technologies to study biological mechanisms. Videira team has extensive experience with in vitro, patient-derived ex vivo co-cultures cultures (from blood, lymph nodes or fibroblasts), immunomodulation (maturation, antigen presentation, T cell profile/activation), cytokine and, transcript assessment and lectins-based assays for assessing cell surface glycans. As well as patient centric approaches (e.g. questionnaires, PROMs).
ORCID 0000-0001-5987-2485

## 5 SELECTED PUBLICATIONS


- Pascoal C, Francisco R, Ferro T, Dos Reis Ferreira V, Jaeken J, **Videira PA**. *CDG and immune response: From bedside to bench and back* (2019) J Inherit Metab Dis. May 16. doi: 10.1002/jimd.12126.

- Altassan R, Péanne R, Jaeken J, Barone R, Bidet M, Borgel D, Brasil S, Cassiman D, Cechova A, Coman D, Corral J, Correia J, de la Morena-Barrio ME, de Lonlay P, Dos Reis V, Ferreira CR, Fiumara A, Francisco R, Freeze H, Funke S, Gardeitchik T, Gert M, Girad M, Giros M, Grünewald S, Hernández-Caselles T, Honzik T, Hutter M, Krasnewich D, Lam C, Lee J, Lefeber D, Marques-de-Silva D, Martinez AF, Moravej H, Õunap K, Pascoal C, Pascreau T, Patterson M, Quelhas D, Raymond K, Sarkhail P, Schiff M, Seroczyńska M, Serrano M, Seta N, Sykut-Cegielska J, Thiel C, Tort F, Vals MA, **Videira P**, Witters P, Zeevaert R, Morava E. *International clinical guidelines for the management of phosphomannomutase 2-congenital disorders of glycosylation: Diagnosis, treatment and follow up* (2019) J Inherit Metab Dis. Jan;42(1):5-28. doi: 10.1002/jimd.12024.

- Pascoal C, Brasil S, Francisco R, Marques-da-Silva D, Rafalko A, Jaeken J, **Videira PA**, Barros L, Dos Reis Ferreira V. *Patient and observer reported outcome measures to evaluate health-related quality of life in inherited metabolic diseases: a scoping review* (2018) Orphanet J Rare Dis. Nov 28;13(1):215. doi: 10.1186/s13023-018-0953-9.

- Marques-da-Silva D, Francisco R, Dos Reis Ferreira V, Forbat L, Lagoa R, **Videira PA**, Witters P, Jaeken J, Cassiman D. *An Electronic Questionnaire for Liver Assessment in Congenital Disorders of Glycosylation (LeQCDG): A Patient-Centered Study* (2019) JIMD Rep. 44:55-64. doi: 10.1007/8904_2018_121.

- Brasil S, Pascoal C, Francisco R, Marques-da-Silva D, Andreotti G, **Videira PA**, Morava E, Jaeken J, Dos Reis Ferreira V. *CDG Therapies: From Bench to Bedside* (2018) Int J Mol Sci. Apr 27;19(5). pii: E1304. doi: 10.3390/ijms19051304.


## PROJECT TITLE AND SHORT DESCRIPTION

***Drug repositioning: Accelerating novel therapies for Congenital Disorders of Glycosylation (CDG)***

Congenital disorders of glycosylation (CDG) are a group of inherited metabolic disorders (IMDs) with impaired synthesis and attachment of glycans to glycoproteins and glycolipids. The some 130 known CDG can be divided into: a) protein N- and O-glycosylation disorders, b) glycolipid and glycophosphatidylinositol anchor defects. Glycosylation is essential for a variety of biological processes, thus CDG patients present heterogeneous clinical phenotypes ranging from mild to severe and involving single or multiple organs. Clinical signs/symptoms reported include neurological, skeletal, cardiac, hepatic, hematological and endocrinological impairment.

Until now, there are few treatment options for CDG patients. Dietary supplementation with sugars (e.g. mannose), nucleotides (e.g. uridine) and trace elements (e.g. $Mn^{2+}$) has been used with positive outcomes for some types. However, some of the patients' signs/symptoms, such as heart and liver manifestations still persist and organ transplantation has been used for patients with severe presentation or with rapid disease progression. The development of personalized molecular medicine has led to other approaches, such as pharmacological chaperones or gene therapy. Despite all of these advances, curative treatments are still not available, due to the difficulties in clinical trials development. The high costs allied to a reduced number of subjects and ethical issues are some of the central pitfalls encountered.

Drug repositioning, which consists in the use of approved drugs as therapeutic agents for other disorders, presents as a possible solution. The main advantage of this approach is the availability of information regarding compound safety and pharmacokinetics in humans, reducing time and costs in research and development and speeding marketing approval. The use of literature mining allied to drug reposition has also been used as a robust approach to identify new drug candidates.

Drug repositioning has been successfully used for a number of IMDs such as CDKL5 syndrome, Friedreich's ataxia and Wolfram syndrome (http://www.findacure.org.uk/drug-repurposing-case-studies/). A clinical trial has also been registered to assess the effect of acetazolamide, a carbonic anhydrase inhibitor used for different disorders on cerebellar involvement in PMM2-CDG patients (Clinical trial identifier 2017-000810-44).

Drug reposition represents a novel and promising avenue for the discovery of new curative treatments for CDG patients. By combining data mining and machine learning in the computational drug repositioning research we will develop an integrative approach in which we will combine information from the elevated number of metabolic routes involved in CDG, the underlying disease pathophysiological mechanisms and drug composition. The knowledge generated using this multi-faced approach will allow further identification of new therapeutic targets amenable to existing, marketed medicines.

## SCIENTIFIC AREA WHERE THE PROJECT FITS BEST

Life Sciences (LIF)