MARIE SKŁODOWSKA-CURIE INDIVIDUAL FELLOWSHIPS 2019

EXPRESSION OF INTEREST FOR HOSTING MARIE CURIE FELLOWS

HOST INSTITUTION

NOVA School of Science and Technology | UCIBIO – Applied Molecular Biosciences Unit

RESEARCH GROUP AND URL

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

SUPERVISOR (NAME AND E-MAIL)

Paula Videira
p.videira@fct.unl.pt

SHORT CV OF THE SUPERVISOR

Assistant Professor at Faculdade de Ciência e Tecnologia/ Universidade NOVA de Lisboa. Founder the Glycoimmunology Research Group and highly interested in novel immunotherapeutic approaches to treat patients with cancer and with congenital disorders of Glycosylation (CDG). Co-founder of CellmAbs, a project focused on researching and developing innovative biopharmaceuticals for the treatment of cancer.
Current goals and motivations are:
-To identify novel therapeutic targets and to develop novel antibody-based approaches to treat cancer. Expert in addressing aberrant glycosylation in different types of cancer, such as bladder, lung and breast cancer. The work is a pioneer and contributed with a solid understanding of glycans implications in tumour growth and metastasis and immune response. Development of anti-glycan antibodies (PCT 110526/ 2019000001)
-To understand the role of glycans expressed by dendritic cells (DC). Expert in exploiting DC-based immunotherapy, and fining-tune the immune response, based on specific glycan modifications. Development of innovative technology to enhance DC-based vaccines (WO 2017002045 A1).
- To improve awareness on CDG, improve patient's quality of life, and research on these rare conditions. Currently interested in mechanisms behind altered immune responses. Director and co-founder of CDG & Allies-PPAIN, an international network of professionals and patient associations dedicated to CDG and allies such as cancer (www.researchcdg.com).
Previous Fulbright fellow, presently leading both national and international research projects, with multidisciplinary consortiums. Currently supervising six PhD students and several Master students and postdocs. The author in more than 75 international peer-review publications, as first or corresponding author in 36 of these publications. National and international jury at 18 scientific project calls, reviewer at 15 scientific journals. Presently member (Portuguese representative) of COST Scientific Committee and the editorial board of international scientific journal.

5 SELECTED PUBLICATIONS

- **Videira PA**, M Silva, K C Martin, and R Sackstein. 2018. Ligation of the CD44 Glycoform HCELL on Culture-Expanded Human Monocyte-Derived Dendritic Cells Programs Transendothelial Migration. J Immunol. 201:1030-1043. doi: 10.4049/jimmunol.1800188.

- Silva M, Silva Z, Marques G, Ferro T, Gonçalves M, Monteiro M, van Vliet S, Mohr E, Lino AC, Fernandes AR, Lima FA, van Kooyk Y, Matos T, Tadokoro CE and **Videira PA**. Sialic acid removal from dendritic cells improves antigen cross-presentation and boosts anti-tumor immune responses. Oncotarget. 2016. 7:41053-41066 doi: 10.18632/oncotarget.9419.

- Bugalho A, Martins C, Silva Z, Nunes G, Mendes AS, Ferreira I, **Videira PA**. 2016. Immature Myeloid Cells and Tolerogenic Cytokine Profile in Lung Adenocarcinoma Metastatic Lymph Nodes Assessed by Endobronchial Ultrasound. Tumor Biology, 1-9. doi: 10.1007/s13277-015-3885-1

- Carrascal MA, Severino P, Cabral MG, Silva M, Ferreira JA, Quinto H, Pen C, D. Ligeiro, LL Santos, Dall'Olio F, **Videira PA**. 2014 Sialyl Tn-expressing bladder cancer cells induce a tolerogenic phenotype in innate and adaptive immune cells. *Molecular Oncology*. 8:753-65 doi.org/10.1016/j.molonc.2014.02.008.

- Cabral MG, Silva Z, Ligeiro D, Seixas E. Crespo H, Carrascal M, Silva M, Piteira AR, Paixão P, Lau JTY, **Videira PA**. 2013 The phagocytic capacity and immunological potency of human dendritic cells is improved by α2,6-sialic acid deficiency. Immunology, 138:235-45; doi: 10.1111/imm.12025.

PROJECT TITLE AND SHORT DESCRIPTION

Innovative approaches for dendritic cell-based therapy

Dendritic cells (DCs) have a pivotal role in both innate and adaptive immunity. These cells have the ability to induce long-lasting immune responses against invading pathogens and tumor cells. For this reason they have been considered as an attractive strategy to be used on anti-cancer vaccines. However, clinical trials, showed a limited success in the use of this type of immunotherapy. The major problems reported were linked with the inefficient maturation of DCs, thus compromising their antigen presentation abilities and T cell activation.

Sialylation, the presence of sialic acid sugars on glycoconjugates, is known to modulate several immune functions. However, its role in DC immunobiology is still elusive. Our group previously reported that human monocyte derived DCs (mo-DCs) have a high content of a2,6-linked sialic acids. Alteration in specific sialic acid content affected phagocytosis, maturation and ability to prime T cells.

Cancer cells usually up regulate the levels of sialic acids. Recent studies from our group and others have demonstrated that tumor-derived sialic acids have broad immunomodulatory effects, and it has also been described that cancer cells secrete higher levels of soluble sialyltransferases. However, the functional relevance of such tumor-derived sialyltransferases is unknown.

In cancer, the main pathways involved in DC responses and effector functions after maturation remains to be completely elucidated. The lack of understanding on this field is a critical step-down on generating more effective

therapies against cancer. In this project, we hypothesize that tumor cells are able to increase cell surface sialylation of DCs, presumably due to presence of extrinsic tumor-derived sialyltransferases, which most likely impairs DCs efficacy in activating T cells.

The main objective of this project is to elucidate the interplay between sialylation and immunological tolerance. In particular, to fully elucidate the molecular mechanism behind the already described effect of sialidase in the generation of DCs with increased stimulatory capacity. In this way, the efficacy of sialidase treatment to generate DCs with better capacity to stimulate, *in vitro*, more efficient anti-cancer responses will be tested.
The ultimate goal of this research is the translation of DCs with altered glycan contents into new immunotherapeutic applications.

SCIENTIFIC AREA WHERE THE PROJECT FITS BEST

Life Sciences (LIF)