CDG One-to-One Interviews, a series of interviews with some of the brightest and most influential minds that have been introducing breakthroughs in the field of CDG, thus reshaping the present and future of the CDG community. **This is an initiative led by the** Portuguese Association for CDG (www.apcdg.com) and coordinated by **Vanessa Ferreira**.

Paula Videira: a woman of science dedicated to unravelling the sweetest aspects of immunology

Serious diseases like Congenital Disorders of Glycosylation (CDG) and cancer are Videira's main research focus

6th **of September 2016, By Rita Francisco (**CDG community social manager. Email: sindromecdg@gmail.com).

Introduction

My name is Rita Francisco, from the Portuguese Association for CDG (APCDG, www.apcdg.com). Today, I have the pleasure to talk to Pf Paula Videira, Researcher and Director of the CDG & Allies - Professionals and Patient Associations International Network, whose dedication to the CDG community has been tremendous and of the utmost importance. Welcome Professor—it is very gratifying for us to have you at CDG One-to-One!

Unlocking a sweet subject: Glycoimmunology

Rita Francisco: Immunology is a very broad and interesting subject, which I know has been very close to your heart for several years now. But, along the way a subarea of this complex and large subject has become your main focus – Glycoimmunology. What first interested you in this specific immunology-related field? And, could you please explain to us what it is and how important it is.

Prf Paula Videira: Thank you very much Rita for this nice introduction and it is a pleasure to talk with you one to one.

Well, Glycoimmunology is a term that we and others adapted to refer to all immunological mechanisms that involve glycans, i.e. sugars. All this is important, first because our immune cells have a tremendous and complex task of surveying our body and protect us from pathogenic microorganisms that cause diseases. At the same time, our immune system has to distinguish between what is self and non –self. It has to distinguish microorganisms that are not harmful and populate, for instance, our mucosas, from the pathogenic microorganisms. Basically, the immune system needs to distinguish the good guys from the bad guys and to initiate an efficient response to eliminate the bad ones (the pathogens), sparing the good ones and our cells. This is very complex, and very well-orchestrated. On the other hand, glycans are all over. They cover all our cells and decorate all our membrane proteins. So that means that any immunological mechanisms, which involve many cell-cell interactions, proteins-protein interaction, will have glycans around. Nowadays we have been discovering exactly how these mechanisms work, but we are still far from knowing them all. We believe that this knowledge will be helpful to design novel and better therapies for a number of diseases.

Rita Francisco: In general, science is still mostly populated by men. Glycobiology is a field where that imbalance is particularly visible. Do you think there are any specific reasons for that? If so, what needs to be done in order to overcome these issues?

Prf Paula Videira: I believe there is a general imbalance in science. I could point two main reasons that frequently come to my mind. One is time, dedication. Science needs dedicated and enthusiastic people, which usually work more than the standard 7-8 hours' work/day. Women are highly motivated, but often have more difficulties to get the enough time, because they need to split time with family and they will always put family in front of any situation. The other reason, is funding for science, which is really needed, otherwise no science can be done. It is more difficult for women to get assess to funding, because they have less access to positions where information and even lobby can be obtained. So this is all related with professional positions (i.e. career) and the typical stereotype that hinders women from having higher positions that we see in other professions. People in higher positions tend to be better informed or be included in systems that help them get funding and even influence the funding agencies.

That said, the only solution would be to empower women and give them equal opportunities. I believe things are now much better now than a couple of years ago.

Rita Francisco: In spite of all these hurdles, how would you encourage more women to get involved in glycoimmunology? Are there any specific measures or actions that would affectively help women participation in this field?

Prf Paula Videira: The best way is to divulge this field and to show what are the exciting things we know now and the mysteries in glycoimmunology that we still need to unveil. Also, in general, both the Glycobiology and the Immunology communities are very collaborative, which turns study very stimulating.

Rita Francisco: Gender issues aside, what advice would you have for a college student who is interested in pursuing a PhD in glycoimmunology?

Prf Paula Videira: I think that a PhD in Glycoimmunology makes all sense. I would recommend to take a look at the most recent literature. We have exciting examples of basic studies which are now paving the way for novel therapies, for instance glycan-based vaccines for infectious diseases and cancer. If students have the chance, I also recommend to visit different labs, and most important to keep on networking.

Rita Francisco: Professor, in your research work you have been particularly focused on establishing the role of aberrant glycosylation in cancer and Congenital Disorders of Glycosylation (CDG). If you had to point out the greatest lessons you have learned from your research what would those be, both professional and personally?

Prf Paula Videira: One of the lessons myself and my group learnt is that little details in science, curiosities, can gives us hints for bigger solutions. When we started studying the role of sialic acids in immune cells and in cancer cells it was curiosity and little was known at the time. Just recently we suggested manipulating sialic acid content to improve immune function against cancer. Anything that we studied, always brought us novel questions and unveiled more exciting

"unknowns" that we want to address. Even though with what we have achieved so far, we were able to suggest therapeutic solutions, such as novel vaccines based on dendritic cells and novel therapeutic antibodies.

CDG: When complex, metabolic diseases became Paula's sweetheart

Rita Francisco: Professor, you know that by now all our readers are wondering: how did you discover CDG and what made you dive into this field?

Prf Paula Videira: Probably the main moment was when I got in contact with the CDG community and met the families. It impressed me their motivation, and it really reinforced to me that CDG is an unmet need. We still don't know why some patients are more prone to certain infections and how to deal with that. On the other hand, our studies suggested that glycan deficiency could lead to an exacerbation of immune response, probably explaining some of the symptoms. That is what made us dive into the field.

You work with two different disease models: Cancer and CDG. Cancer is a major health problem, recognized and well-known by the scientific and medical communities as well as by society in general.

Rita Francisco: Is it easier, in technical and practical terms, to carry out research work in cancer in comparison to doing so for a rare disease? And, in your opinion, how could common diseases, such as cancer, benefit from a deeper understanding of rare disorders?

Prf Paula Videira: The major hurdle when studying rare diseases is to obtain interest from the funding agencies and pharmaceuticals to support research. General funding agencies tend to prefer projects involving more common diseases. Even within the rare diseases field, there are diseases that are less rare than others. CDG is considered really rare, and many people usually never heard about it.

When we study rare diseases we are entering a very specific and detailed pathologic mechanism which can be shared by more common diseases, or give us hints about similar mechanisms. For instance, both CDG and cancer have aberrant expression of glycans. In cancer those glycans tend to suppress immune response. In CDG, the altered glycans can exacerbate the immune response. So maybe we can learn something from this in the future.

Rita Francisco: Concerning CDG, tell us about your most recent advances? How do you see these studies being applied in the near future for CDG children and adults?

Prf Paula Videira: As I was mentioning, glycans affect immune response in several ways. We reconfirmed this in our recent revision about immune response in CDG patients. It revealed that a minority of CDG types have severe immunological dysfunction, such as infections during childhood. This is dramatic because for instance in PMM2-CDG, these infections can be lethal in 25% of the cases.

When we analyze patient samples we can observe a number of parameters, such as the number of cells that are slightly altered, but we don't know yet why. If we understand the immunological aspects of CDG we may contribute to a better management/treatment of these pathologies and even of more common diseases, such as inflammatory diseases.

Rita Francisco: CDG patients are quite dispersed and few have been diagnosed, although it is imperative to have contact with them to gain insight into these diseases pathological mechanisms. What is the role of patient groups within your research projects?

Prf Paula Videira: We are witnessing an increasing number of cases and diagnostics is slowly being improved. This is definitely because patient's groups like APCDG are working hard in awareness. The APCDG was extremely important in my case, because it oriented our research, highlighting the most relevant aspects to be studied in CDG.

Rita Francisco: Recently, you have embraced another challenge and you have been appointed Director of CDG & Allies - Professionals and Patient Associations International Network . What made you accept the offer and what is the relevance of this international project for the CDG community?

Prf Paula Videira: It actually felt like a duty to society and the CDG society in particular. It is that sense of duty that pushes me forward and I believe all leaders of patients' associations. The CDG & allies -PPAIN makes all sense! It combines patients' associations, families and professionals to create awareness among the same community, and in the larger community. Awareness will improve diagnostics and management of the patients; and also increase interest by other professionals, including funding agencies. This is a loop of profitable activities, with the final aim of improving patients' lives.

Work and personal live

Rita Francisco: Professor, your work life is very full and absorbing. How do you maintain a healthy balance between your personal and professional life?

Prf Paula Videira: I have a very understanding family, which helps me a lot. Also, my team is my other family. They have a very relevant sense of team work and work hard in leveraging ours standards with publications and funding.

Rita Francisco: Would you mind sharing with us some of your main hobbies?

Prf Paula Videira: Science is great hobby ... I love cooking and biking, especially in family.

Rita Francisco: Professor, with your work you try to touch and improve various and distinct aspects in society. Thus, I have to ask what is the next dream that you wish to accomplish?

Prf Paula Videira: My dream is to contribute to what I call "Clinically applied Glycobiology". That means to contribute to the development of relevant immunotherapies to be used to treat cancer and CDG patients.

Who is Paula Videira?

Paula Videira received her Ph.D. in Instituto Superior Técnico, Universidade Técnica in 2002. After a post-Doctoral position in the same institution, in 2005 she was invited as assistant professor in the Department of Immunology at Faculdade de Ciências Médicas, Universidade NOVA de Lisboa. She founded the Glycoimmunology research group in 2007, which she leads until today.

Her main interests are to conduct research in Glycobiology and Immunology, with the goal of identifying novel therapeutic targets. Paula is presently leading both national and international research projects. She is an author in more than 50 international peer-review publications. Moreover, Paula was appointed director of the CDG & Allies - Professionals and Patient Associations International Network. Thus, Paula's work in the field of CDG is also focused on fomenting awareness and collaborations between professionals and patients advocates.