



graduating from a European PhD focusing on the humanization of the Nglycosylation of recombinant mAb produced in transgenic plants, in 2001, Dr Muriel Bardor joined Prof Ajit Varki's group at the Glycobiology Research and Training Center, University of California San USA where she Diego, demonstrated the uptake mechanism of the non-human sialic acid N-glycolylneuraminic acid. At the end of 2003, she obtained an Associate Professor position at the University of Rouen, France where she initiated and led a regarding the project characterization and of the Nengineering glycosylation processing in plant and microalgae. From 2010-2012, she has done an oversea long-period stay in Singapore as a Research Scientist, group leader of the Analytics department at Bioprocessing Technology Institute, A*STAR initiating the development of glycomic capabilities within the institute. She recently moved back to the Glyco-MEV laboratory, University of Rouen.

2 Meet the Researcher: French – Singaporean research collaboration in glycobiology

Glycosylation is the most widespread post-translational modification encountered on proteins. It is well known that specific glycosylation patterns have been associated with diseases such as cancers or rheumatoid arthritis. The glycosylation is also of particular interest for biopharmaceutical proteins since more than 70% of biopharmaceuticals are glycoproteins. The presence and/or structure of glycans are known to affect the functional properties, efficacy and stability of glycoproteins. Having the capacity of glycosylation is an advantage for any system used for biopharmaceutical production. Among the different production systems available today such as cultured mammalian cells, insect cells, yeast or plant cells, none of these are able to perform a perfect human-type glycosylation on pharmaceutical recombinant proteins. Therefore, controlling and analyzing the glycan structures associated with these proteins of interest are of major importance. The aim of the collaborative research project is to develop faster and sensitive analytical tools which will allow us to better characterize the glycosylation, such as N- and O-glycosylation, on either biopharmaceuticals or endogenous glycoproteins produced by CHO cells (used by BTI as a model host system) or plant and microalgae cells (Glyco-MEV models).

Dr Bardor and Dr Zhang, thank you for agreeing to share your research project with the readers of the EURAXESS Links ASEAN newsletter. Can you explain to our readers the scope of your research project?

ZPQ: The research scope of BTI Analytics Group covers media profiling, metabolite analysis and biopharmaceutical product characterization. In recent years, we have been focusing more on the analysis of glycans, that is, the sugar chains attached to proteins. This is very important as glycans play a pivotal role on the performance of biopharmaceutical drugs. The group is equipped with a range of analytical instruments, including liquid chromatography (LC) as well as mass spectrometry (MS) systems. We are constantly developing novel methods for the analysis of complex biomolecules as mentioned above.

MB: The research scope of the Glyco-MEV (Glycobiology and plant extracellular matrix) is dedicated to the understanding of the structures, biosynthesis and functional properties of plant glycoproteins and cell wall polysaccharides. The activities of the lab can be divided into two main topics: one focusing on the Biosynthesis and function of primary cell wall in relation to plant development and immunity whereas the second one aims to decipher the glycosylation pathways in higher plants and microalgae in order to use those organisms as alternative cell factories for the production of recombinant glycoproteins (monoclonal antibodies, EPO...) used in human therapy.



Dr Zhang Peiqing is a scientist at the research Analytics Group in Bioprocessing Technology Institute, Singapore. He received his PhD from the National University of Singapore in 2011. His previous research focused on analysis glycomic and glycoengineering of selected mammalian cell lines for research and production of recombinant glycoproteins, as well as detailed functional analysis of glycosylationrelated proteins especially the nucleotide-sugar transporters. Recently, he has been working on glycoanalytical technology development, particularly novel UPLC-based analytical workflow for automated glycan analysis, as well as MS- and LC-MS-based methods for Oglycosylation analysis. His broad research interests encompass the use of imaging, chemical biology, and analytical tools to understand involvement of the cellular glycosylation in physiology and the regulation of glycosylation at systems level.

Dr Bardor, you are based at the Glyco-MEV laboratory of the University of Rouen while your colleague Dr Zhang is a research scientist with the Analytics Group at the Bioprocessing Technology Institute in Singapore. Why is the collaboration between Singapore and France so important to your project?

ZPQ: Glycomics is an emerging field involving multi-disciplinary approaches, such as organic chemistry, analytical chemistry, biology, etc. Obviously, no one can conquer the field single-handedly. In order to advance glycomics, collaboration between researchers with complementary backgrounds is the key. Fortunately, we identified such research complementarity: here at BTI in Singapore, our lab works on glycosylation analysis of mammalian-derived biologics, while Muriel's lab in France focuses on glycosylation in plant and microalgae. Despite the difference in the model of study, we both use similar approaches to analyze sugar structures. In this context, this collaboration is very important to us as it allows intimate exchange of ideas and data and this will translate into accelerated development of analytical methods and breakthroughs in glycobiology.

MB: Our respective research projects request fine and detailed characterization of glycans, oligo- and polysaccharides which can only be achieve by the

development of powerful, robust and sensitive analytical methodologies. By joining forces, we hope to develop advanced analytical methods that will help us to position our institutions in the forefront of the international picture.

Can you tell us a little bit about the anticipated outcome of this research project? How will the general public benefit from it?



ZPQ: We anticipate a wide range of outcomes, in terms of joint publications, coorganized workshops, and scientific visits. In addition, we aim to bring in more Singapore- and France-based researchers together through this collaboration. Glycomics and glycobiology are fundamental to human health. Through this collaboration, we hope to reward the general public through detailed pharmaceutical glycomic characterization for consistent drug performance, and novel discovery in glycobiology which may translate into new drugs or drug targets.

MB: By this project, we are also expecting to extend the glycosylation analytical capabilities of the French and Singaporean partners. At the same time, we know that these novel methodologies would be helpful for the scientific community since glycan analysis is increasingly applied nowadays in biological and clinical research as well as pharmaceutical biotechnological production. A first important outcome which has already been achieved and celebrated last month is the signature of a tripartite MOU between BTI, the Glyco-MEV laboratory and Agilent Technologies. This research initiative will enable us to optimize new glycan analytical workflows on the Agilent HPLC-Chip/MS system.

MERLION

The project received funding through the <u>Merlion Programme</u>, a joint Franco-Singaporean collaboration aimed at creating and strengthening scientific co-operation between the two countries. This strategic partnership strengthens the collaboration between BTI and Glyco-MEV laboratory with Agilent's technological expertise on board. In addition, the Glyco-MEV laboratory becomes Agilent's Glycomics Reference Site in Europe and BTI, A*STAR its Glycomics Reference Site for South-East Asia, positions which enhance Singapore's and France's international reputations. Through this collaboration, we are also expected to nurture young scientists into the glycobiology field; some of them are currently running a PhD project with one supervisor from France and one from Singapore.

Given the geographical distance between France and Singapore how did you meet and how did your collaboration start?

MB: I moved to Singapore in 2010 to follow my husband who was working there. At that time, I was hired as a research scientist at BTI where I met Dr Zhang Peiqing and his collaborators. I successfully obtained a Merlion Grant together with my former colleagues from the University of Rouen in France. After my 2-year contract in Singapore ended last August, I returned to France to resume the position of Associate Professor at the University of Rouen. Concurrently, I have agreed to become a Visiting Scientist at BTI to facilitate our nice and efficient collaboration.

You received funding through the Merlion project of the French embassy in Singapore. Which impact has this grant had on your collaboration?

ZPQ: The most prominent impact of this grant is on scientific exchange with our French collaborators. Indeed, we have made three trips so far to Glyco-MEV Lab in Rouen. This has given us the opportunity to talk face-to-face to not only our collaborators, but also their colleagues at the University. From there, new opportunities have arisen to establish more collaborative projects.

MB: This Merlion grant allows us to exchange staff and students between France and Singapore which was helpful in the first place to understand better each work environment and evaluate the potential for each partner. As

mentioned by Peiging, these exchange trips also allowed us to meet scientists from other institutions and laboratories working in different fields such as immunology, cancers for e.g., which hopefully in a near future will lead to the establishment of new collaborations between France and Singapore.

You both had the opportunity to spend some time in each other's countries. How did you experience each other's research communities? "The most prominent impact of this grant [Merlion] is on scientific exchange with our French collaborators. Indeed, we have made three trips so far to Glyco-MEV Lab in Rouen. This has given us the opportunity to talk face-toface to not only our collaborators, but also their colleagues in the University. From there, new opportunities have arisen to establish more collaborative projects."

Dr Zhang Peiqing

ZPQ: I am very impressed by the

people and the work they have done in Glyco-MEV. It is a small lab, not really



boasting world-class facilities. However, over the years, they have made many important discoveries and established themselves as a leading group in plant and microalgae glycobiology in Europe and the world. I think this is because of their interactive research environment, hardworking people and a strong training system that focuses on nurturing the young talents. I'm sure with the strong leadership, a highly focused approach and dedicated scientists like Muriel, the Glyco-MEV Lab will achieve more success in the near future.

MB: The first time I visited BTI, I was very impressed by the top level equipment and infrastructures positioning BTI as a world-class institute in the field of bioprocess science and engineering leading to technologies which will impact biomedical sciences and bio manufacturing. For example, specific innovative research projects that BTI is developing which attracted my interest focused on the engineering of CHO cell lines for production of biopharmaceutical proteins, generation and characterization of glycosylation mutants, characterization of mammalian glycoenzymes as well as characterization of recombinant proteins produced by mammalian host cells. It is very nice to work and exchange with their young scientists such as Peiqing since there are highly motivated to develop and build new areas such as glycoanalytics to fulfill their actual need but also build some new opportunity to position Singapore in a strategic scientific field.

In your opinion, what could be done to further enhance the mobility of international researchers?

ZPQ: I personally feel that continuity is the key to further the mobility of international researchers. It is important to find a group doing similar kind of work in a place that is out of your "comfort zone". The ability to continue what you have being interested in will give you a sense of belonging even in a totally new environment. Maybe in this regard, what could be done is to form more international research clusters in order to encourage scientific exchanges.

MB: I completely agree with Peiqing: continuity is the key to further enhance the mobility of international researchers and international collaborations. This makes me feel a little bit worried already about the way we will manage to continue the established collaboration if we don't benefit from any specific funds after the Merlion grant. There are usually some possibilities of getting grants like the Merlion's one to kick off new international collaborations but at the end of them how do you make your existing and powerful international collaboration continue in the future?

Can you share any tips with our readers for a successful application to the next round of applications for a Merlion grant?

ZPQ: My humble advice is: be complementary, be specific.

MB: The advice would be to think about complementarity and fair contribution between the two partners since you want to generate a win-win situation to come out with a fruitful collaboration.



As scientists which goals are you still hoping to achieve?

ZPQ: As a glycobiologist with first degree training in engineering, my long-term aspiration is to elucidate the complex glycobiology phenomena in simple, mechanistic models and the ability to control glycan structures in living systems with ease, at will.

MB: As a scientist, specialised in glycobiology, my long-term goal is to understand the physiological roles of glycans in plant and microalgae for which we have no clue at the moment even if it is quite clear that such oligosaccharide structures are essential in mammals for their development, their cell-cell interactions, viruses' infections.

Thank you very much!

The **MERLION PROGRAMME** is a joint Franco-Singaporean collaboration aimed at creating and strengthening scientific co-operation between the two countries.

Launched in 2006 by the Science Section (now part of the re-branded Institut Français de Singapour) of the French Embassy in Singapore, Merlion has seven Singaporean partners on board - A*STAR, NTU, NUS, SERI, SMU, SUTD and TLL. These longstanding Singaporean institutions together with their French partners connect many researchers from almost every scientific field.

Merlion presents an excellent opportunity for French and Singaporean scientists to work alongside one another; it facilitates the collaborations needed to discover new and innovative approaches or set up joint laboratories or organise pertinent workshops.

The Merlion programme is based on a system of co-financing between the Singaporean and French partners of a selected project. Funds allocated through the programme will be used for the travel costs incurred between Singapore and France to encourage exchanges between partner researchers in both countries; the funds are therefore not meant for the research work itself.

There are three funding schemes under the Merlion programme:

- Merlion Project: As each project is a joint collaboration between a Singaporean and a French partner institute, each side co-finances the travel between Singapore and France of the researchers involved in the bilateral research project. This funding is for two years.
- **Merlion Workshop:** Funding is given towards the organisation of a joint workshop involving researchers from both countries. These workshops can take place in either Singapore or France.
- **Merlion PhD**: Students who are involved in a Franco-Singaporean research project will receive financial support for a stay in France of up to six months per year over three years.

Projects are selected every year following a call for projects. In 2012, 75 projects were submitted of which 11 were chosen. **The 2013 Merlion call is open from 1 June to 30 September.** Further information may be found <u>here</u>.

