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A Fresh Wind is Blowing in from Asia Professor Michael Raghunath Arrives at ZHAW Waedenswil

Prof. Michael Raghunath interviewed by
Elsbeth Heinzelmänn

Abstract: In summer 2016, Michael Raghunath from the National University of Singapore (NUS) will take over the professorship from Ursula Graf-Hausner in cell culture technology and tissue engineering at ZHAW Life Sciences and Facility Management. What are his objectives and the corresponding strategies? What challenges will he face, what will he choose to focus on? Michael Raghunath was kind enough to let us have a look behind the scenes.



Elsbeth Heinzelmänn: “Singapore is a fine city”, so the saying goes. Singapore is a modern, multicultural society with a highly diverse ethnic mix and an international orientation, wealthy and progressive, with a Buddhist majority. What was your motivation to leave this island state of 4.8 million inhabitants after living there for 13 years and to come and settle in a country of 8 million in the heart of Europe?

Michael Raghunath: Actually, when I moved to Singapore in 2003 my family added three more people to a population of 3.8 million. Now, there are roughly 5.6 million people living in Singapore, which might give you an idea of the breakneck pace of population growth in this city state, which is predicted to reach 6.9 million by 2020. So, in the near future, Singapore will have a population not very much smaller than that of Switzerland, but compressed into an area the size of the city of Hamburg or the canton of Glarus. But both countries face similar challenges in building their knowledge-based economies, and both wish to excel in biotech industries. My motivation to leave is the same one that brought me to Singapore: an opportunity for professional and personal growth. In Singapore, I had the exciting opportunity to assemble my own research team and make a contribution to the field of regenerative medicine, and to help build a world class Biomedical Engineering Department. I taught many undergraduate and graduate students from Singapore, China, India and surrounding South East Asian countries, including a few Europeans, US Americans and Africans. I will soon have graduated 25 PhD students, and supervised a great number of bachelor theses. The international league tables document the fact that NUS has reached the top world rankings. However, the quality and recognition of the research coming out of the biomedical engineering department at NUS was always more important to me, as it shows that we have made it scientifically into the top bracket. After 13 years I am now ready to take on new tasks and responsibilities, and to experience a different type of student. My tissue engineering work is informed by my expertise as a hard-core

matrix biologist, and this is derived from fundamental research work. In Singapore, I began to move my research downstream, towards the translational end. As a trained physician you always ask yourself how a piece of knowledge can be put to good use in terms of an improved outcome for a patient. The strong industrial ties of group leaders at ZHAW resonate with me, as does the whole outlook of scientific integration of ZHAW in a Swiss landscape of big and small industrial players. My experience in industrial R&D enables me to understand the biotech business mindset. The biotech landscape in Switzerland and neighbouring countries is vibrant. Last but not least, it is also good to be closer again to family in Germany and friends in Europe. My wife and I have old friends in Zurich and surrounding regions dating back to my time as a postdoc in the University Children’s Hospital. It will be like coming home.

Elsbeth Heinzelmänn: The *Tissue Modulation Lab* you currently head at the National University of Singapore (NUS) has been spearheading *Macromolecular Crowding*, a technology to boost culture medium by polymeric additives in order to accelerate the formation and maturation of connective tissue *in vitro* and thereby generate stem cell microenvironments and enhance tissue-engineered constructs. This technology obviously constitutes the thrust of all your research. The field of *Tissue Modulating Materials* focuses on materials that can locally deliver compounds to suppress scar formation (*Scar Wars*). To be able to proceed with this work you first had to build a tissue-engineered antifibrotic drug discovery tool (*Scar in the Jar*) that has been adopted by the pharmaceutical industry. Recently, you have published work on generating blood vessel-stabilizing cells (pericytes) from blood, and you propose to conduct research on *Metabolic Tissue Engineering*. Can you enrich the range of activities at ZHAW from this pool of research lines, and what actually is *Metabolic Tissue Engineering*?

Michael Raghunath: ZHAW has an excellent reputation for 3D tissue models and bioprinting, and I will infuse this set-up with macromolecular crowding approaches to generate more coherent microtissues. Extracellular matrix is the key here; I bring knowledge to the table on how to empower cells *in vitro* to build up, analyse and stabilise this matrix. I expect this to be a valuable contribution to the range of activities at ZHAW, but I will also learn a lot from my colleagues at ZHAW. I am quite sure that the enrichment will work both ways. I coined the term *Metabolic Tissue Engineering* to describe the building of living tissue equivalents of human white fat, brown fat, and skeletal muscle, respectively. These are tissues that store or burn energy, and that fulfil important functions in energy balance. The global epidemic of obesity and diabetes has put brown fat, along with skeletal muscle and white fat, in the limelight of pharmacological and nutraceutical considerations. However, not many functional human models of brown fat exist, and this is where we will make a difference at ZHAW.

Elsbeth Heinzelmänn: Doubtless you will exploit the synergies with the Singapore-MIT Alliance for Research & Technology (SMART) and the Institute of Medical Biology (A*STAR). The advisory panels of these institutions are studded with eminent

scholars, while the scientists in SMART and IMB hail from renowned universities worldwide. Do these scientists belong to your network, thereby enabling ZHAW to benefit from these relationships in future?

Michael Raghunath: I will certainly leverage the contacts and successful collaborations with colleagues in the MIT, and the IMB in Singapore. I am sure this will help raise the international profile of the tissue engineering efforts at ZHAW, resulting in collaborative scientific projects and student exchanges. However, I also enjoy good contacts with Canada, Australia and Japan. My excellent network in Europe will fit very well with ZHAW's future strategies. But you're right – when you are in Singapore you will see eminent scientists passing through on a daily basis, and that also holds true for members of advisory panels. Therefore, site visits give you a great opportunity not only to introduce your work to these scientists, but also to get to know them on a personal level. My personal criteria for choosing collaborators are primarily the quality of their work, regardless of their location and position, and the existence of good chemistry between us. The idea is to go the full distance together and enjoy getting results and solutions.

Elsbeth Heinzelmann: I assume that you have had a closer look at the activities at ZHAW. How do you assess the scientific state of the art at ZHAW compared to the international research scene?

Michael Raghunath: I find ZHAW an amazing place, and the infrastructure in Waedenswil for example is outstanding. Normally, when I show visitors around our tissue engineering set-up at NUS, their eyes widen when they see our equipment and facilities. However, I could have flown in my whole group from Singapore and continued almost seamlessly at ZHAW. Traditionally, universities of applied sciences concentrate on the downstream end of research, where an application in the market and industry is just around the corner, or where an immediate solution to an industrial problem is sought. In this regard, I believe that the 3D tissue work at TEDD is cutting edge; Ursula Graf-Hausner has indeed built up a tremendous tissue engineering programme at ZHAW that is well known in international industry circles and applied research groups in universities, and some excellent publications have come out of TEDD. Incidentally, when I told international colleagues in the field in Singapore that I was joining ZHAW, it turned out that some of them knew about TEDD already. I think that says it all.

Elsbeth Heinzelmann: Do you already have an idea about the key research areas that you want to establish?

Michael Raghunath: Absolutely. I believe that we can boost 3D tissue engineering with my core technology of macromolecular crowding and spur on the development of bioink for bioprinting. I will introduce Metabolic Tissue Engineering as a research theme in Switzerland with the aim of making an impact at national and international levels. The beauty of our technology is that it

will allow a two-pronged approach. We will build a nutraceutical platform for screening compounds that will either activate brown fat cells to become fuel (*i.e.* glucose and fatty acid) guzzlers, or prompt white fat cells to become brown fat cells, or support the differentiation of stem cells located in bone marrow and subcutaneous fat all the way to brown fat cells. We will be able to offer this to food and pharmaceutical companies and will pitch this to market leaders. Again, I would like to stress that this will involve human, rather than mouse, cell systems. On the other hand, I am keen to encourage academic colleagues to leverage our platform to solve basic science questions. I can foresee exciting research collaborations, co-supervisions and student exchanges resulting from this. Finally, developing a commercial cell culture product would be of great interest to me, but first let's see what evolves.

Elsbeth Heinzelmann: Thank you for your comments. We wish you all the best and every success for the future!

Goodbye ...

Microbiology and cell biology were still in their infancy when *Ursula Graf-Hausner* joined ZHAW in 1990. As Head of Research and Development in chemistry and biotechnology she worked with heart and soul on dental regeneration with adult stem cells, headed R&D projects on biomolecule production, the development and application of biomaterials, the characterization of cells and tissues, the development and application of cultivation systems and automation. Sabbaticals in USA allowed her to expand her professional knowledge, especially in tissue engineering. This provided the basis for the TEDD Competence Centre, a collaborative innovation platform dedicated to 3D cell culture technology and organ-like tissue models for drug development, substance testing, personalized and regenerative medicine.

... and welcome!

Michael Raghunath holds a medical degree from the University of Mainz, and a habilitation in Physiological Chemistry and Pathobiochemistry from the University of Muenster. Having worked at the University Hospital there as a resident in dermatology, in 2000 he joined Dr Suwelack Skin & Healthcare as Director of R&D. In 2003 he moved to the National University of Singapore where he will continue until summer 2016 as an Associate Professor for Bioengineering, after holding the posts of Deputy Head Research & Enterprises and Director of the Graduate Programme in Bioengineering (GPBE).

His work in the *Tissue Modulation Laboratory* focuses mainly on influencing the development and composition of tissue in wound healing and repair by modulating the behaviour and the phenotype of cells building or remodelling their micro-environment. He employs synthetic compounds, small chemicals or large sugar polymers that have already been approved for a different clinical indication. Using this approach he hopes to shorten the bench-to-bedside time and ease regulatory pathways.