Interview: Dr. Ronald Li – Director, Ming Wai Lau Center for Reparative Medicine, Hong Kong

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The Ming Wai Lau Center for Reparative Medicine was established in October 2016 as the first international arm of Karolinska Institute (KI) in over 200 years! What is the Center's mission?

First and foremost, the Center's focus is on stem cells and regenerative medicine but we decided to use the term 'reparative medicine' to broaden our scope: we would like to not only regrow but also repair. The holy grail in regenerative medicine is to design and create transplantable grafts or organs. This is the long-term objective.

Our scientific vision for the next few years is to focus on developing 3D mini-organs for various applications like drug discovery, disease modelling and other therapeutic purposes. We would like the center to be technologically oriented. We are looking in parallel at a few technology areas like biomedical engineering, bio-informatics (single-cell transcriptomics), bio-imaging and advanced stem cell technologies. In the beginning, we nonetheless have particular interests in the heart, brain and liver. The heart happens to be my personal area of expertise, the brain and central nervous system (CNS) are areas in which our Swedish colleagues are very strong, and there are many liver experts in this part of the world, which sees a higher incidence of liver disease, with whom we have extensive collaboration. In fact, our collaborative networks in the above areas are very extensive, locally and internationally, covering some of the most renowned groups and institutions in Hong Kong, EU, Canada and the U.S..

As you mention, it is the first time KI has established an international branch in its entire history. It goes without saying that scientific and academic excellence is a fundamental objective. Above and beyond that, however, we aim to position the Center as an embassy of sorts to connect firstly, Sweden and Hong Kong (as a part of China), and then through that, to contribute to building partnerships between China, the EU and North America via our vast networks so as to facilitate R&D, commercialization and innovation, and translation for the public community to benefit.

How exactly will the Center be structured in terms of its staff and projects?

[Featured_in]

The idea is that the Center will function as one entity in two physical locations: Stockholm and Hong Kong. There is constant communication between the two.

Even though we are still very new, we have been building significant momentum rather quickly. We already have 11 principal investigators (PIs) leading their own research groups. Seven will be based in Stockholm and the remaining four are to based in Hong Kong, with the goal of having a fifth recruited by the end of the year. At steady state, we plan to have around 100 investigators and researchers in total; by the end of the summer, we expect to already have 60.

The key is quality, not quantity. We have a very focused scope of research and the idea is to deliver impact. It is important for us to work efficiently and synergistically across the 12 groups at the Center.

In terms of deliverables, it goes beyond saying that with KI’s legacy, scientific and academic excellence is at the core of our establishment. Publications are the standard measure of that but these are also just the starting point. But we also encourage our investigators to look at the ‘D’ in R&D: to develop technologies, file IPs, build inventions, set up companies, and work extensively with both academic and industry leaders. For this reason, we do not function like a traditional academic department; we intentionally free many of our investigators from formal classroom teaching duties, for instance, but we do emphasize staff training and development as that is the key for scientific success. We want our scientists and trainees to be able to decide if they want to stay in academia or move into industry as our goal is to train the next generation of scientific leaders.

In Asia, Singapore is a role model when it comes to the downstream development and commercialization of upstream research. The model is not new but it is a first for Hong Kong. We are aiming to adapt this international research institute model to the Hong Kong context and

needs.

In terms of the field of stem cell regenerative medicine, we have heard about the magic potential of stem cells for perhaps two decades now. How much has the field developed today?

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It is a tremendously exciting time for the field. Many of my colleagues and I began to work in this modern field of stem cell and reparative medicine in the late-1990s. At that time, we were still discussing the potential in human embryonic stem cells. The excitement was over the possibility that scientists could make human heart, brain and pancreatic cells – the building blocks of life. We used to describe the idea of a bio-engineered organ as a ‘fantasy’, when then became a ‘hope’ – and today, it is now a ‘goal’. Today, the excitement is about engineering these cells by design, in a systematic fashion, into highly specialized tissues and organs that otherwise cannot be regenerated. We are certainly more optimistic yet pragmatic today than two decades ago. We are starting to see a flood of new tangible applications and maturing technologies arising from the collective ground work in the past two decades or so. Such will only continue to grow in the coming few years and decades.

The reassuring fact is that we are not starting from ground zero. We are building on two decades of work so our goals are very achievable and certainly, for the Center, we want to make substantial progress in the field of 3D mini organs within the next five years.

As another example, two decades ago, we had very poor yields when it came to creating individual human heart cells. At the beginning of the millennium, only a handful of institutions would even have the technology to synthesize these cells and the yield was less than 0.5 percent. Today, we can make billions of cells as needed with yields ranging from 90 to 99 percent.

The idea of creating human bio-organs is still technically challenging but not farfetched at all. As we speak, we have a few mini-hearts sitting in incubators here in our center at the Hong Kong Science and Technology Park (HKSTP) and brain organoids in Stockholm. This is no longer just a theoretical concept. But I like to use the analogy of smartphones. The technology grows more sophisticated each year – and there is no final product per se. In science, there is no finishing line. Today, many of the hurdles we face are in fact engineering problems – and optimistically, these can be resolved through engineering solutions.

What interests does the industry have when it comes to collaborating with academics and research institutes in this field?

Many pharmaceutical companies are already involved but to varying extents depending on their own strategic priorities. Furthermore, with any new technology, it can take a while for the market to absorb it entirely. For instance, film photography was replaced quite quickly by digital photography, but it will still take a while for gasoline-powered cars to be replaced by electric cars. The same principle applies to this area. But we have noticed interest surging this year. Many international regulatory bodies are also watching developments very closely.

As researchers, many of us believe that, even before we see cell-based regenerative therapies as routine clinical procedures in hospitals, we are first going to see new drugs and therapeutics because of 3D human organ technologies. The traditional paradigm as it stands now is to test initially in animals, mice and so on, and then to make a huge leap to human volunteers. The fact remains that, no matter how similar animal genomes are to humans, statistically you can only make predictions about human response based on animal data with an accuracy of around 3 percent or so. Using human mini organs to discover drugs for humans would make much more sense and help tremendously.

Industry involvement is critical. AstraZeneca, for instance, is investing USD 100 million over five years in the Integrated Cardio Metabolic Center (ICMC) in conjunction with KI. We know that many conventional therapies today have been researched and designed based on Caucasian patient populations. Considering the importance of genetic diversity, there are many diseases and conditions that are more localized to Asia that have been rather overlooked. This is a very interesting opportunity from both the scientific and commercial perspectives, so the Center can use this as a starting point to raise the overall profile of the Asia region. What we can bring is the development of ethnicity-specific organs for use in drug discovery, which would be useful in tailoring drugs and therapies for diseases that are more common in this part of the world.

How well-suited is Hong Kong as a base to support the advancement of this field?

I fundamentally believe that to succeed and find solutions to problems in this field, collaboration with different institutions and countries is necessary – and Hong Kong is well-positioned. Furthermore, the indisputable truth is that the train has left the station and is moving forward. Other countries are investing in the regenerative medicine field, so if Hong Kong chooses not to engage, the world will move on without us.

Fortunately, I do believe that all the ingredients for success are present in Hong Kong. The first thing that comes to mind when we talk about science and technology is the importance of systems and process infrastructure like the rule of law, IP protection and legal infrastructure. All successful technology hubs also have a transparent financial structure and a vibrant economy that supports the commercialization of new technology. It goes without saying that Hong Kong meets this criterion.

You also need an excellent education system because the universities are where research and much of development are conducted, IPs are generated, and the next generations of talent are taught and trained. Our education system may be a little overlooked sometimes. We have eight universities in Hong Kong, with five focusing on R&D – and of those five, three are consistently ranked in the top 10 in Asia: the University of Hong Kong, the Hong Kong University of Science and Technology, and the Chinese University of Hong Kong.

Finally, Hong Kong's world-class medical infrastructure contributes to our appeal as a biotech R&D and innovation hub. Thus far, it has tended to focus more on the provision of medical services but I think there are huge opportunities along the entire biomedical spectrum that we can exploit.

Hong Kong has been a trading port for centuries, and this is something Hong Kong can continue to leverage in the science and technology fields. Everyone recognizes the firepower of mainland China but Hong Kong is also part of that, so investments in mainland China and investments in Hong Kong are not mutually exclusive. We see investing in Hong Kong as a starting point – because we have the international standards and systems that the international community is more familiar with. This is exactly how we would like to position the Center as an embassy, to link Hong Kong, China and Asia to the rest of the world.

On a more personal note, having built a successful career in the US, what motivated you to return to Hong Kong to head this center?

Stem cell research is a very "personal" business. My personal role model, Professor Douglas A. Melton from the Harvard Stem Cell Institute (HSCI), a pioneer in pancreatic regeneration, entered this area because his own children suffered from severe type I diabetes. Both my wife and I have believed in the potential of stem cell biology, and it is also a deeply personal business for us, because around ten years ago, we lost our second child in our arms. Back then, stem cells research was still not advanced enough to help him, even though there were trials at Harvard and UCSF. Both my wife and I were born in Hong Kong but moved to North America for further education and subsequently our careers. We then felt a strong calling to return to Hong Kong to contribute to the

establishment of this field in Hong Kong.

From my experience in the US, I believe it is imperative to bring academia, government and industry together in order to make impactful progress in this field. It is critical to adopt this concept of development and commercialization of new technology to this part of the world. The Hong Kong system is still young and insufficient on its own, which is why Hong Kong needs to integrate into the larger international community or ecosystem. We hope that the Center will be a critical contributor to both the establishment of this stem cell regenerative medicine ecosystem in Hong Kong as well as its integration into global partnerships.

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