Interview: Christine Mummery – Professor of Developmental Biology and Chair of the Department of Anatomy and Embryology, Leiden University Medical Center, The Netherlands

13.11.2015

Tags: Pharma, Pharmaceuticals, The Netherlands, Netherlands, Holland, Leiden, Christine Mummery, Stem Cell, Research, Research and Development, R&D, PPP, Public Private Partnership

Stem cell therapy holds the promise to treat diseases for which there are currently no or only limited therapeutic options. Christine Mummery, Professor of Developmental Biology and Chair of the Department of Anatomy and Embryology at the Leiden University Medical Center, discusses how academia and industry can work together to develop or repurpose drugs and the need for investment in basic research, as well as the current environment to undertake research in the Netherlands.

Could you please introduce yourself to our international readers?

I'm the head of the department of anatomy and embryology at the Leiden University Medical Center (LUMC), and, until recently, I was on the board of the Royal Netherlands Academy of Sciences. Before I joined the LUMC, I spent most of my career at the Hubrecht Institute. I am also on the board of the Netherlands Medical Research Council (ZonMW) and have several responsibilities in scientific advisory boards. I have worked for many years on stem cell research —initially in human embryonic stem cells— and have always been interested in how to work with

heart cells. In 2007, I was a joint Harvard Stem Cell Institute/Radcliffe fellow. At the time, the institute was working on induced pluripotent stem cells, so I took the technology home and have worked on stem cells deriving from patients to make heart and blood vessel cells. I'm interested in figuring out how to make these cells efficiently from stem cells and measure changes that occur due to a disease.

I recently received a second chair at the University of Twente, which is very interested in developing disease models-on-a-chip as a screening process for the pharmaceutical industry. For that purpose the hDMT institute (Institute for human Organ and Disease Model technologies) was created. It is a public-private consortium bringing together technologies, facilities and expertise from different disciplines and nine different institutions, including three universities of technology (Twente, Eindhoven, Delft), the Leiden University and University Medical Centre, Erasmus Medical Centre, the Hubrecht Institute, and two companies, Genmab and Galapagos. We try to incorporate all institutes interested in disease modeling in one virtual institute. It's meant to be a portal for the industry to 'organ on chip' technology in the Netherlands, whether to identify technology to license or partners who can help them in product development.

What is your assessment of the collaboration between industry and academia in the Netherlands at the moment?

I think at the moment it's developing really well. It has created opportunities, which would have not arisen if we had not been forced to think about it. Many of us realize that using stem cells directly as therapy is quite challenging, as you need huge resources and the Netherlands is not a great investor in science. However, we are good at basic science, and the quickest way to the clinic is by identifying new drugs or repurposing existing ones. I happened to help a physician with a study on patients who had chronic nose bleeds. We have been able to get stem cells from these patients, and we discovered that a specific drug was beneficial and reduced the bleeding. It's interesting to see what motivates the pharma industry to look into a new drug. A few years ago they were only looking for blockbusters, so if you had a therapy for a rare disease there was no interest. Now such treatments receive a lot of attention, because if you can impact the underlying mechanism of the disease you can have a broader application or you may go to precision medicine.

In one long-term research project you are using stem cells as the "patient" rather than the "drug." Can you please explain more about this project and how can your lab-grown cardiomyocytes help with drug development?

We derive stem cells from patients, but some tissues hardly have any stem cell population, such as the brain or the heart. However, we can make heart cells from the stem cells we create from patients. In essence, we can take a biopsy from the skin, or even collect kidney cells from urine, and reprogram them into stem cells which we then turn into blood vessel and heart cells. The heart cell has the same genetic baggage as the patient, meaning the heart cell *is* the patient. If we can cure the symptoms in the heart cell, we can do so in the patient. In this way, for example, we can do preclinical trials to identify risks in patients and reactions to specific drugs. The more you understand about the disease and measure it, the greater the chances of finding an effective drug.

What was your particular motivation to work with heart cells?

The heart is among the most important organs in the human body, and heart risks and diseases can affect every age group. I'm a physicist by origin, and I have always enjoyed measuring cells' activity. I always found the heart fascinating and, by chance, it was the first very successful experiment I did. I first got human embryonic stem cells from Australia and had a hypothesis about how to turn them into heart cells, and it worked. That's why I continued working on it and later focused on the area to become an expert. It's very tempting to move into other fields, but you can end up wasting time and being a jack of all trades, master of none.

Given the work being done at the Hubrecht Institute and by researchers such as yourself, where do you and your colleagues here in the Netherlands fit the European map for stem cell research?

I think several of us are leaders in the field. We have colleagues in different countries and closely collaborate, and I have actually trained many of them. They go out in the world and do their thing, but we keep in touch. For instance, we work at a project for GSK with a colleague I trained in the past and we exchange students. AstraZeneca is also very keen to interact with us. Among our main objectives is training people and supplying cells to academics and companies to do their screening. We believe in dissemination of knowledge.

Given your experience in the UK, the US and Netherlands, how would you compare and contrast the research and innovation environments? What are the strengths and weaknesses of the country?

The strength and weakness of the Netherlands is its size: on the one hand it's not greater than the greater Boston area so excellent for collaboration, on the other in some areas there is lot of competition, not because people are naturally competitive, but because the cake is very small. It's a disappointment that we failed in convincing the government to increase investment in basic

research. The emphasis – overall in Europe – has shifted towards translation, but we won't translate anything if we do not do basic research. I would not have heart cells if I had not worked for ten years as a developmental biologist, which is a field that currently receives almost no funding. The perception is that we are doing so well that we should not bother in investing in basic science, but the truth is that we are doing so well because we have invested in basic science in the past. As many governments only stay for four years, they do not realize the importance of research. The Netherlands invests a smaller percentage of GNP in basic research than a country such as Portugal. We are quite successful in in getting European funds, but Europe is trimming grants trying to force national governments to increase their funding. Also, since Organon is gone, we do not have any major pharmaceutical companies here. There is little solid interest in bioscience and biomedical research. What we do have are very good students, who are valued everywhere. We have them, but we need to keep them.

Do you have any suggestions about how to retain them in the country?

We need to have a much better structure for tenure track for junior researchers. I think no Dutch medical center has tenure track options today. The institutes do: after five years if you do well they give you a position, otherwise they ask you to leave. But we do not have this system properly implemented in universities.

You were the first to derive iPSC lines from patients in the Netherlands. What other milestones would you like to achieve in your research space in the coming years?

If I could repurpose a drug and cure patients, I would be extremely satisfied. If it could be a new drug, I would be happier and even much happier if a pharma company could sponsor it. I think there will soon be a stem cell cure for Parkinson's disease and for diabetes, and there is one on its way for blindness. I'd like to help introduce these therapies in the Netherlands, and I'm encouraging to create infrastructure to do so.

What is keeping you motivated every day?

I love science, and I find it fascinating, I like the excitement of learning new things, meeting new people and ideas and getting feedback all the time. I like the field, and I would not do anything else. And I'm proud that my older daughter is following my steps. Making people enthusiastic is a great personal motivation.

Given your success in your career, as a female researcher is there a personal recommendation you would like to give to other female researchers such as you?

I have never felt a glass ceiling: the only glass ceiling I have faced was the one I put when I doubted myself and had problems of self-confidence. Focus is the most important thing, and I always ask my students: “What’s the label on your forehead?” If you do not have a label people won’t know who you are. I have stem and heart cells on mine. If young people have not decided what label they want to have it, nobody will do it for them.

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