Interview: Dr. Marc Diederich – Director, Laboratoire de Biologie Moléculaire et Cellulaire du Cancer (LBMCC), Luxembourg

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Marc Diederich, Director of the LBMCC and principal investigator conducting independent research, leading and training a 25-person group including PhD and MSc students, runs us through the raison d'être of the Laboratory, how it is dedicated to the study of the cell and molecular biology of cancer and is focused on

basic and applied research linking inflammation, cancer and leukemia.

The Laboratoire de Biologie Moléculaire et Cellulaire du Cancer (LBMCC) is a non-profit research laboratory dedicated to applied research linking inflammation, cancer and leukemia; differentiation therapy and novel therapeutic approaches for cancer based on compounds of natural origin. What made you originally decide to set up the laboratory back in 2002, and how would you say its scale and offering have evolved over the past 14 years?

I came back to the University of Nancy in France in 1994, as a Lecturer, and got an offer for a position as a research scientist working for the private foundation, Fondation de Recherche Cancer et Sang. I then established a research group based at the Centre Universitaire du Luxembourg (the former building of the University of Luxembourg) and headed by a Luxembourg oncologist, Prof Mario Dicato. I started alone and, at the end of 2003, had the opportunity to move to larger

facilities. At that time, we had around eight researchers, including Master and PhD students, and moved to this space at the Kirchberg Hospital early 2004. We have therefore been based at the Kirchberg Hospital for around 12 years.

As a private foundation, we were excluded from any major funding from the National Research Fund (FNR) from 1999-2015. This however changed early 2015. We will soon be able to submit grant proposals directly to the FNR, and this is very positive. I am at last happy to see that we can now apply for grants and financial support from the authorities. Of course, this is a costly and time-consuming process, we have to undergo audits to meet all requirements and conditions, but I am confident these investments are worth it.

Just how supportive is Luxembourg as an ecosystem for establishing this kind of endeavor?

In 2007 we visited the Institute for Systems Biology directed by Leroy Hood and, from that moment on, there was a big change in the overall government mentality to supporting research in Luxemburg. The following two to three years saw the creation of the Integrated BioBank of Luxembourg (IBBL) and the Luxembourg Center for Systems Biomedicine (LCSB) at the University of Luxembourg headed by Rudi Balling. These became, to some extent, the spearhead research projects of the government.

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Research in Luxembourg is generally very well appreciated by the public who can be very impatient at the apparent slow pace of investment from the public side. People I talk to do not understand why there is not even more support for biomedical research science. The public donates a lot for research, especially in the field of cancer. In the absence of public funding, my lab therefore managed to achieve success thanks to the activity conducted by the Belgian National Research Fund in collaboration with Radio Television Luxembourg (RTL) called Télévie, a cancer and leukemia telethon. We have been organizing this event in Luxembourg since 2002 and it has so far raised about EUR 15 million (USD 16.5 million), all of which has gone into cancer research in Luxembourg. Without this funding, there would not have been any seed for the further development of this aspect of cancer research in Luxembourg.

Most of your funding comes from private individuals; looking forward, is there any potential for diversifying your sources of funding?

We have had collaborations with start-up biotech companies that fund research projects into specific compounds and we are interested in working more in this area. We are able to quickly execute research findings and update the portfolio of molecular mechanisms and biomarkers that might be required for Phase I clinical trials. For example, we were collaborating with a biotech company called CORAL BIOME based in Southern France, which has interesting molecules we investigate. Additionally, UNIBioscreen, a previous start-up from the Free University of Brussels, asked us to provide a mechanistic background for leukemia for the compound UNBS1450, which is what we did and we still work with that compound.

What we do best, for selected pharma projects and companies, is to take a compound and within six months provide the company with molecular mechanisms related to cell death, inhibition of proliferation, epigenetic mechanisms and inflammation if required, which is directly linked to anti-cancer.

74 percent of all cancer-fighting substances come from nature and, in the LBMCC, you examine plants for substances that can potentially contain and prevent cancer. What progress have you been making on this front?

The most promising compounds are from nature but have some fine tuning from the chemist; these are what we call semi-synthetic. The framework comes from nature but modifications increase the specificity towards cancer cells and decrease toxicity so that the healthy cells are not harmed and the cancer cells are more specifically attacked. Our belief is that nature provides frameworks of molecules that have intrinsic bioactivity and as such it might also have some bioactivity in the cancer cell, for example in the sense of interfering with mechanisms and blocking mechanisms.

We for example recently found a compound from a Mediterranean marine sponge that blocks the growth of cancer cells. This molecule Isofistularin-3 even enhances the effect of a cancer-fighting agent already in clinical trials, but to which many cancers are resistant. In that sense, we are very happy to have a portfolio of chemists and chemistry groups all over the world that regularly provide us with their novel molecules, whether newly extracted or newly synthesized or modified.

Including both our research teams in South Korea and in Luxembourg, we currently work with about 20 compounds which all eventually kill the cancer cells so we can use the same mechanisms, same technological approaches, and same animal models over there which we don’t have the possibility to further develop here. A simple model we developed last year zebrafish xenografts, which means the injection of fluorescent human cancer cells in zebrafish, which works very efficiently so the tumors develop similarly to the human body and can be, or not, affected by novel

compounds. This is a interesting extension of our more cell-based research in Luxembourg.

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What is the role of this South Korean lab within LBMCC's operations?

Around 2010, I got an offer from Seoul National University, which was helpful in terms of being able to attach our research to a full academic institution. This university is the number one university in South Korea, ranks 36 globally and its pharmacy department is number 21 globally. This therefore represented a good opportunity to valorize our mechanistic research by extending towards animal models, and patient samples, and overall extending our research into a more academic field. This came into force in September 2012 and since then, this collaboration has been undertaken very actively and basically all of our publications over the last two years are joint publications. It is also an interesting opportunity for our scientists to teach, which was not possible here in Luxembourg.

Financial possibilities are improving, which will be very helpful for the research side, and we are now more regularly being published in higher-impact factor journals.

You were personally involved in the rollout of Luxembourg's first ever National Cancer Plan. Where are we standing with it today?

The National Cancer Plan was a good opportunity to bring together the stakeholders in Luxembourg and get a precise overview of what is going on in cancer research; for example, we have been compiling all cancer publications since 2010 and are now in a good position to show the Ministry of Health and the Ministry of Research how much has been done in cancer research over the last five years. Within this Plan, a couple of topics emerged as projects that would be preferentially financed in the future. This is very interesting in terms of generating synergies, focusing on specific topics, and publishing in that direction. It is very important to orient the research and in that sense, I believe that it was helpful.

Where do you intend to take the LBMCC next?

Our interactions with biotech and start-up companies have been the most beneficial aspect so far. We want to considerably extend this aspect and attract more interesting anti-cancer compounds from, and in collaboration with, these companies to bring them to trial here in Luxembourg. That would be a very big step indeed. From the basic pre-clinical research, I think we have the capacities to do that, and this would be a five-year objective to really get a very clear translational application of the research, whether alone or in collaboration with research labs in Luxembourg. We want to continue with experimental compounds, from natural origin of course, and select one

or two of those compounds and really bring them into the bed of the patient.

Is Luxembourg ready for this? Is the clinical environment prepared? This project is less than a decade old…

Let’s be ambitious! With previous compounds we conducted Phase I clinical trials in two different hospitals in order to recruit the 20 patients needed. In the future, patients in Luxembourg hospitals could be one part, and patients in hospitals abroad could be another. I have no specific target country but this could be very helpful in order to see which improvements are required in Luxembourg.

What would be your final message for our international audience?

It is important that readers understand that Luxembourg has an excellent and competent research background, even though it is small, and is waiting to extend and collaborate with good partners worldwide.

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