Interview: Rudi Balling – Director, Luxembourg Centre for Systems Biomedicine (LCSB)

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Rudi Balling discusses his distinguished career in the life sciences, the LCSB's mission, and Luxembourg's burgeoning reputation as a biomedicine, interdisciplinary research, and scientific innovation hub.

Earlier this year you were awarded the 'Ordre de Mérite' for your longstanding contribution to science by the Luxembourg government following a distinguished career that most recently has seen you establish the Luxembourg Centre for Systems Biomedicine (LCSB) at the University of Luxembourg. Please start by introducing yourself and how you came to accept the invitation to assist the Luxembourg state in developing its life sciences research ecosystem?

My initial background was actually as a human and animal nutritionist, but over the years I have taken it upon myself to embrace a wide range of scientific and medical fields encompassing genetics, reproductive biology, bone health, infectious disease and much more. Aware that the learning curve generally starts to flatten after 5 to 7 years, and always motivated by a strong quest for knowledge, I have made it a habit to regularly expose myself to new areas of science.

After attaining a Diploma in Human Nutrition from the University of Bonn, Germany, a Masters degree in Animal Nutrition from Washington State University, USA, and a PhD at the University of Aachen in Reproductive Biology, I completed a stint in embryology in Canada, before transferring

to the Max Planck Institute of Biophysical Chemistry in Göttingen and the Max Planck Institute for Immunobiology in Freiburg, so as to gain greater understanding of the molecular biological basis for disease. In 1993 I was nominated Director of the Institute for Mammalian Genetics at the GSF-Research Centre for Health and Environment in Munich and in 2001 I became Scientific Director of the Helmholtz Centre for Infection Research (HZI) in Braunschweig, Germany.

It was at the HZI that I perceived the radical transformations underway within the disciplines of biology and medicine and how the advent of big data is necessitating the integration of additional capabilities and skill-sets such as mathematics and systems analytics and modeling. When the Luxembourg authorities came calling, I was actually away on sabbatical at Harvard and MIT-backed Broad Institute studying mathematics. Essentially the government wanted to enlist my support in diversifying the national economy towards life sciences and in this context establish a new Centre for Systems Biology. My suggestion that they place emphasis on systems biomedicine and especially the study of neurodegenerative diseases was warmly received hence the inception of the Luxembourg Centre for Systems Biomedicine (LCSB), which I was tasked with establishing and directing at the University of Luxembourg.

Can you please elaborate upon the rationale behind the establishment of the LCSB?

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To make the most of the huge quantities of data that we are now able to collect, the scientific community needs to bring in engineers and mathematicians able to design, assemble and interpret models and computer simulations that can predict health outcomes under a given set of variables. Most biologists and physicians are missing this kind of engineering language and training and as a community we are late to the game compared to other industries such as finance and banking. This is precisely why, at the age of 55, I considered it so important to take time out to study these critical technological tools and the mechanisms behind them.

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We set up the LSCB back in 2009 with the specific aim of accelerating biomedical research and bridging the gap between biology and medicine through deploying a systems approach to disease networks that involves uniting an interdisciplinary team composed of computer scientists, biologists, physicists, mathematicians and engineers all under the same roof. This differs markedly

from the traditional academic model of individual laboratories working within their specific disciplines and which I consider to be ill suited to handling the emerging challenges of biomedicine.

As an institution, the LSCB seeks to fill a gap in scientific advancement, while simultaneously positioning Luxembourg at the vanguard of breakthroughs in biomedicine. It was clear to me that a new type of formal organization was required: one that was collaborative, interdisciplinary, and technological and mathematically astute if we are to be able to gain a clear understanding of the genetic basis of disease, and how to translate that awareness into more effective prevention, diagnosis, and treatment.

The LSCB has made it its mission to focus in on neurodegenerative disease and in particular Parkinson’s disease. Why is that?

We were aware of the risk of spreading ourselves too thinly so were very attentive to defining the limits of our scope of action. We resolved that it was important to focus on a single therapeutic area that we could deal with in depth so as to be able to establish mastery and become genuine thought leaders for that particular specialism. The idea was to build flagships that would bring us international visibility and recognition. We were also keen to choose an area where we could have maximal impact and get the biggest bang for our buck.

Parkinson’s disease happens to be Europe’s second most common neurodegenerative disease today after Alzheimer’s. In line with demographic changes in which people are living longer, incidence of these sorts of neurodegenerative disease is very much on the rise. As a result, they are becoming an ever-greater burden for state finances and the public purse. Despite this, our understanding of the mechanics of these diseases is still very incomplete. So far our knowledge of the disease mechanisms is limited to being able to diagnose them and temporarily alleviate some of the symptoms. In Parkinson’s, although we can reduce some symptomatic elements such as the tremor, once the cells degenerate, there is virtually nothing we can do to get them back. In short, there is no cure.

We have therefore chosen to scope in upon a therapeutic area, which is both economically significant, and at the same time scientifically exciting. The learning curve is steep, but we do feel we are on the cusp of breakthroughs. This is, of course, the ‘decade of the brain.’ There have been a lot of incremental improvements in areas such diagnosis and understanding of dementia over the past five or so years and it is very much our intention to build upon that momentum. We are convinced that placing emphasis on quantitative systems and on understanding disease pathways will allow us to make a great deal of headway. Already we are beginning gain much greater

familiarity with the way that different organs interact with one another during the onset of maladies like Parkinson’s and the nexus between other co-morbidities such as diabetes or changes in metabolism.

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Comparatively, how well does Luxembourg perform in terms of promoting biomedicine, interdisciplinary research and scientific innovation? And what advantages are accrued from being based out of this country?

Luxembourg as a state has been an incredible promoter of my proposal to establish the LSCB right from the very start. Not only did the Junker government commit an initial EUR 140 million for financing the project, but it felt like the entire state apparatus was mobilized behind us with no less than four ministries giving us their direct assistance and support – namely Jeannot Krecké’s Economy Ministry, Mars Di Bartolomeo’s Health Ministry, François Biltgen’s Ministry for Research and Higher Education and Claude Wiseler´s Ministry for Public Works.

We have been able to leverage this very supportive enabling ecosystem to propel ourselves forwards. To give you a sense of the pace of our development, within only five years we’d recruited a multi-functional staff of around 120 professionals, which we then doubled in 2014. We have also managed to diversify our funding sources to include both competitive grants and EU research money.

The beauty of being based out of Luxembourg is actually the simplicity and streamlined nature of the national health apparatus. Back in 2008 there were only 5 hospitals and that figure has actually fallen to 4 after the merger of two of them. Moreover, there is only one healthcare insurance institution, the CNS. This makes it very easy to compile standardized health data for the entire country and to gain the cooperation of all the relevant stakeholders. If we were trying to achieve the same thing in Germany, by contrast, we would find ourselves running into all sorts of complexities with different insurance systems, reimbursement mechanisms, data compilation techniques and so on for each of the 26 federal states. Just trying to gather reliable and standardized data sets for the nation would be incredibly difficult.

We consider it far better to be conducting a finely targeted initiative in a small country that can then be used as a showcase and beacon project before being replicated elsewhere and scaled up in other countries. Estonia and Cataluña are great example of countries and regions that have been used as a test-bed and laboratory for medical innovation and public health policy breakthroughs. The fact that we have been starting virtually from scratch in Luxembourg where there was

previously very little research base for biomedicine further confers upon us advantages. We can build up an entirely fresh ecosystem that is tailor made for the task at hand rather than having to grapple with changing the old outmoded, but deeply ingrained methodologies of previous generations.

What other aspects mark Luxembourg out as distinctive and exceptional as an environment for carrying out leading edge innovation in biomedicine?

From a managerial perspective, Luxembourg does throw up a few novel challenges. It entails a whole new level of flexibility to be able to efficiently manage the cultural potpourri that you encounter. We're talking about a small multilingual, hybrid country of some 500 000 people that straddles the cultures of Belgium, Germany and France. This sense of cultural collision and a melting pot is perhaps no more pronounced that in Luxembourg City where foreign bankers, eurocrats and lawyers brush shoulders with a strong public sector. Whereas the more francophone members of your workforce may expect a lot of top-down direction and guidance, the Germanic staff members will tend to seek greater delegation of responsibility. Properly navigating this cultural mosaic thus requires some deft footwork.

On the other hand, cultural diversity is also one of the great gifts of Luxembourg in the sense that the make-up of the talent pool lends itself to fresh thinking and new ideas. This is especially useful when we are endeavoring to foster an outward-looking, interdisciplinary and collaborative approach to the critical medical issues of our time.

Nor should we underestimate the exceptional ICT infrastructure in Luxembourg. In our line of business of developing computational models to mathematically describe diseases through simulations it is essential to have a high performance ICT infrastructure at your disposal. As a result of the country's longstanding prowess as a financial center, Luxembourg performs very highly in terms of connection speed, data storage, and sequencing centers. To power stock markets it is essential to have fast reliable communications systems and secure data storage mechanisms. We are able to piggyback on all of these fine assets. One of the big topicalities at the moment is also the issue of privacy and the security of data. We feel that the country can quickly become a leader in this aspect given that it is an issue our banking community has been dealing with for a long time.

In July, it was announced that Luxembourg via the LSCB is to become a European Data Hub in biomedicine. Just how significant is this development?

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This is great news and will serve to place Luxembourg on the map as a biomedicine IT and data hub for Europe. Right now, biology and biomedicine are generating gigantic amounts of research data from the analysis of genomes and gene products. Often, however, this data is only kept in one place, making comparisons between different studies difficult and the legalities regarding their use unclear so the EU has come up with ELIXIR – the European life sciences Infrastructure for biological Information – to remedy this situation.

Through ELIXIR, 18 European countries are providing the ICT infrastructure for making data from biological and medical studies permanently accessible, to enhance their analysis and to support scientists´ research. As an ELIXIR node for translational biomedicine we will serve both the national and the European research community hosting data from our own research as well as from our partners in Luxembourg and from other European institutions and consortia. Additionally, the LCSB will be tasked with developing innovative methods of bioinformatics to analyze such immense amounts of biomedical data.

With ELIXIR, Luxembourg aims to connect the national digitalization strategy with the fast growing sector of biomedicine. Establishing the associated infrastructure here represents a great opportunity for the LCSB and the whole of biomedical research in Luxembourg and means we can keep sight of current and future developments in research as well as even actively shaping them.

Is there anything where you feel Luxembourg could still be better?

I am a very strong proponent of the proposal to construct a national medical school. Personally I feel this is exactly what is needed to make our local ecosystem complete. I do understand the reticence of some politicians towards the idea because these do tend to be expensive projects with high upfront costs. Your typical model for a fully-fledged medical school entails employing between 70 and 100 professors and departments covering all the main therapeutic areas from rheumatology and cardiology to endocrinology and anatomy. That can, of course, result in running costs of EUR 100 million each year and understandably some politicians worry that this would be a vanity project that would not represent value for money. My suggestion is to press ahead with the idea but to control costs by having the proposed school on focus on a limited number of therapeutic bases.

We really have to be more attentive to educating the new generation of chemists, biologists and physicians in recognition of the fact that medicine is becoming increasingly IT driven. Medical informatics is increasingly the name of the game. In this era of electronic medical records, mobile health and remote monitoring, modern physicians need to be IT-competent in handling heterogeneous data and be able to relate to machinery that is highly supported by smart technology. Even the relationship with the patient is undergoing transformation with normal people increasingly informed about their ailments and able to easily access health information through open Internet sources. The doctor thus no longer plays the role of god, but instead has become a partner or mentor to the patient by moderating that information and exercising a degree of quality control. All of this needs to be reflected in the medical curriculum so that the new cohort of physicians is trained in these additional skill sets. In my view, Luxembourg really needs to possess its own national medical academy if we are to ensure that we are always at the head of the technological curve.

Where do you aspire to take the LSCB next?

> “You don’t get quality healthcare without top quality life sciences research to back it up.”

The first 5 years of the LSCB’s existence have been all about building up our reputation for producing internationally competitive and relevant research. This had to be the priority because we can never be attractive to industry if our research findings are not considered to be of the very highest quality. Putting that quality research to industrial use will be the next phase. We want, of course, to continue with the excellent science and continue to feed our research pipeline, but the time has now come to start working more closely with industry, payers, policy makers and clinicians to apply this knowledge in reforming healthcare provision and the whole discipline of population health in general.

The sort of biotech industry that our research will hope to attract into Luxembourg is rarely a big job creation machine in itself. The real job creation happens around healthcare, not life sciences. However, it must be recognized that you don’t get quality healthcare without top quality life sciences research to back it up. The two are intrinsically linked and this is a message that I am very keen to get across. In this next phase of our existence I will be keen to highlight the very tangible contribution that we are making both to Luxembourg and Europe wide.

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