Interview: RenÃ© H. Medema â?? Director of Research, Netherlands Cancer Institute (NKI)

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The Netherlands Cancer Institute (NKI) has been at the international forefront of cancer research and treatment for more than 100 years. The director of research discusses the fields and collaborations the institute is currently focusing on and why funding to (blue-sky) research should be seen as an investment.

What were the main priorities you set yourself when you became Director of Research for the Institute in 2012?

My main priority has been to ensure that we are well-positioned to make groundbreaking discoveries that have a major impact on our knowledge of cancer, and in addition to this, that we are well-equipped to translate these findings to clinical applications. This requires an excellent workforce that can generate a good pipeline of new ideas, but also requires that we focus on what we are exceptionally good at.. When I was appointed, we decided to review the instituteâ??s fields of research to identify our excellent strengths to define the areas in which we are most likely to make a unique contribution. This is something you should continuously ask yourself, and impacts the complete management of the institute, from how you do your recruitment, to how you build up your research infrastructure. Back in 2012, we were already very active in genomics, but also active in electron microscopy, for instance. Genomics, though, is taking over a very important role in cancer research, so we decided to focus on this field by expanding our infrastructure for sequencing and closed our facility for electron microscopy. Further fields we are focusing on are precision medicine and immune therapy. Thanks to the expertise we have in performing genetic screening, we believe we can make a unique contribution in this field. Immunology is high on the agenda of every cancer institute, and we are in the fortunate position that immunology has always been very active in the Netherlands, even when many thought it would never work.

The NKI has multiple divisions including medical oncology, biochemistry, molecular genetics and cell biology, among others. Could you please elaborate on some of the groundbreaking research which is being carried out here and its potential?

We have a very strong fundamental research program, especially when it comes to understanding the mechanisms that underlie cancer. In terms of mouse models for cancer, my predecessor Anton Berns made major contributions discovering the genes that contribute to the discovery of cancer. We also have a strong expertise in genetic screening, particularly in the group of Rene Bernards, with which his team has been able to uncover the sensitivity of tumor cells when, for example, a drug is expected to work in a certain way on a tumor, but does not. This has been a particularly successful exercise, where we have gone from having a drug that does not work to a combination that may work, to an on-going clinical trial to identify its potential. Over the last few years we have had at least four such examples. Last but not least, in immunology we have been working very hard on a therapy that utilizes tumor-infiltrating lymphocytes (TIL-therapy). It is something that was not discovered here at the NKI, but currently we are the main site in the Netherlands to bring this therapy to patients. We have received a preliminary financing from the Dutch Ministry of Health to look at the therapy, so it

can later be launched across the country.

The NKI had 542 publications in 2014. What is the institute doing to ensure these publications and research are being translated to real products and treatments patients can benefit from?

First of all, we have focused the activities of the institute on the fields previously mentioned, so everybody knows what they are working towards. By communicating the fields that the institute is focusing on, everybody gets more connected to the main goals of our institute, i.e. develop precision medicine, immune therapy and novel image-guided interventions. Second, we have appointed more clinician researchers to bridge the gap between basic research and clinical trial programs. Third, we twin a basic scientist with a clinician. One of the challenges in clinical research is that clinicians are usually very busy, as they are juggling their time between patient care and research. By twinning people, we ensure that clinician researchers are embedded in the labs of full-time researchers. This way, there is much more awareness about what is going on on either side, and the research group of the clinician researcher is well-embedded in an environment that can provide high-level expertise and help with daily supervision. This has been one of the most important ingredients helping us bring projects from the lab to the clinic â?? and vice versa.

The NKI was set up over a hundred years ago along with the Antoni van Leuuwanhoek Hospital. Could you please explain what is unique about this collaboration?

Fundamental research is difficult, but clinical research is even more so. This is because clinicians do not have a lot of time and are usually not trained in the fundamentals of research. A lot of what is done in clinical research is â??me-too researchâ??. The real challenge is to do clinical research that has a big impact, and to do so you need to have a certain rigor in the choices you make. The temptation to say â??I think this might be helpful to the patientâ?• without thinking â??What is the best thing I can do now to make a difference to the patientâ?• is huge, especially when you do not have a lot of time. Youâ??ll quickly do the things you *can* do rather than the things you *want* to do. In research, every good project starts with the question â??What do I want to do?â?• and not â??What can I do?â?• This has implications in the way we do fundamental science. At the NKI we ask ourselves: â??What problems do we want to solve and how can we solve them?â?• Thatâ??s why in our fundamental research program we put a lot of emphasis on technological innovation, which allows you to answer questions nobody was able to answer before. That should be the most important ingredient in a fundamental research program.

Could you please run through some of the other key collaborations the NKI is involved in?

Kite Pharma is a very important collaboration: we very much believe in immune therapy and they are using our technology to gain foothold in Europe. We are very much looking forward to what they are developing. Another collaboration we are excited about is with a new start-up that is trying to use drugs that are currently on the shelf because they do not have any anti-cancer activity when given as a single agent. This company can quickly determine if there are combinations of drugs possible that do have anti-cancer activity, so that these drugs may eventually be of benefit to the patient. In my own research line, I am very excited about testing tumors on their genetical instability and use that as their weak spot. We are working with the Netherlands Translational Research Center (NTRC) to develop inhibitors of the kinase TTK to make the cancer cells even more unstable, with the aim to kill them.

The NKI boasts truly state-of-the-art equipment such as the most modern high throughput sequencing machines. What is the impact technology is having on the way research is carried out and the potential outcomes of that research?

Itâ??s massive. Our innovation is driven by technological innovation, and we have allocated the limited in-house start-up funding we have to technological innovation. The main problem for technological innovation is that itâ??s very difficult to get funding to develop a new technology. There is no proof-of-principle that it will work, so obtaining extramural funding the early stage development is close to impossible. In the past, we have decided to finance such out-of-the-box high-risk projects for technological innovation. Today, thanks to these projects we can suddenly ask ourselves questions we could not have answered before. Also, in our recruitment, we have a keen eye for people that can bring new technologies to our institute because thatâ??s what makes the difference. And one of the reasons for our success it that we have a very open research structure, meaning that if someone brings in technology everybody has access to it. We are a very small institute, but we definitely want our science to be up there with the best.

What are the current challenges in terms of funding to research in the Netherlands?

Overall funding has gone down. I think globally there has been a big shift: people want results and are often not aware that results require years and years of hard work. The appreciation for true blue-sky research has dropped over the past years and, in order to survive, researchers have started shifting away from blue-sky towards applied research. That is not all bad, but insufficient funding for fundamental science implies a big risk that in a few years time we wonâ??t have necessary new insights that can catalyze the development of new therapies in the future. Also in the Netherlands funding to research has decreased, particularly for fundamental research. Fortunately not as much from institutes such as the Cancer Society â??that actually funds research quite generouslyâ??, but definitely from the government. In the past, revenues from natural gas were destined to R&D, but since the crisis hit in 2008 this money has been diverted to minimize our national deficit. As a consequence, there are very limited options available to researchers in the Netherlands to apply for funding for blue-sky research. The limited options are largely restricted to personal grants, which are great, but limited to a certain age group, and limited in numbers. Thatâ??s a major challenge, and research in the Netherlands would greatly benefit if more funding opportunities would be available for blue-sky research. The European Research Council (ERC) is one of the institutions supporting individual researchers of any nationality and age to pursue their frontier research, but this funding is accessible from all countries within Europe. As a consequence, the overall opportunities for funding are often better in other countries in Europe. In Germany, for instance, government funding to the German Research Society (DFG) is around 40 percent, in the Netherlands itâ??s below 15 percent. Hence, I think talent is likely to move outside of our country.

Where would you like to see the NKI in five years from now?

Iâ??d like the NKI to play a leading role in the development of new therapies, especially in the fields of precision medicine and immune therapy; be among the leading cancer institutes in Europe; and be the number one translational research center in Europe. This will only be possible if we manage to maintain a solid basis of hard-core fundamental research. I believe cancer research has to change in Europe: if we want to develop new therapies, we need to work together, combine our insights and our science to really make a difference for patients.

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