Interview: Thomas WÃ¼rdinger â?? Head of Neuro-Oncology at VUMC, Galenus prize winner, VU Medical Center, The Netherlands

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Thomas WÃ¼rdinger, winner of the 2014 Galenus prize, discusses his research teamâ??s efforts to developing new treatment options and protocols for brain cancers, and the need for greater attention and investment in brain cancer treatment development, an area he identifies as the greatest unmet medical need in the field of oncology.

Thomas, to begin could you please introduce yourself to our readers around the world, with reference to your current research interests, educational responsibilities, and your involvement in the private sector?

I am professor at the cancer center of Amsterdam at the Free University (VU) and director of the neuro-oncology research group, which is an integral part of the Amsterdam brain tumor center.

Within the VU medical center (VUMC) cancer center, we have a particular focus on neurology and neuro-oncology, where we fuse a partnership together between the two campuses; there should be more input on diagnostics tests for brain cancer patients. I did my post-doc at Massachusetts general hospital medical school in the lab of Professor Blakefield, the head of neurology at that institution, and I still hold a position there so I can go back and forth between the two universities to exchange ideas. We work as an interdisciplinary team that works in all sectors that include the departments of neurology, pathology, pediatric oncology, medical oncology and radiology.

After Leukemia, brain cancer is the second most prevalent form of cancer in children and young adults, which serves as a strong motivator for departments and specialists to collaborate to fight this disease. Moreover, as cancers in the brain can drastically affect a patientâ??s cognitive functions and behaviors, it can have a particularly strong impact on family and friends. I currently lead a team of 20 researchers that include medical specialists, molecular biologists, chemists and a bioinformatics team. In order to present our ideas to patients we publish our work, but we also work on the valorization of our findings, transferring technology and intellectual property to private sector companies to bring solutions to the market. I have started two biotech companies myself, the first being ThromboDx which focuses on blood platelet based diagnostics and is moving into their third year, and towards the launch of our first product. We are collaborating with several big pharmaceutical partners that use diagnostic tests to guide their therapies and to screen patients, so we expect to have a good market for our product. Ex-Biome is another company I have recently begun and focuses on micro-RNAs for diagnostic purposes. The technology transfer from academic to startup companies here in the Netherlands is very strong, as we have a strong tech transfer offices in our universities, and quite a bit of experience in this regard, and researchers in academia are actually encouraged to and given the support to create start-up companies from their research in the universities.

How do you find the Dutch model for moving academic research into the academic center for valorization into the biotech hub in Boston?

You cannot compare the situation here to that of the one in New England. The similarities between the two regions are that we both have equal creativity and business oriented cultures, with the Dutch having a long history of international trade knowledge based industry. The main difference between the two regions is the small size and population of the Netherlands, which has led us to orient our selves towards Brussels and the EU now for funding and development.

The Dutch mind-set in early investment scene is quite different due to a much smaller pool of VC funding, and a greater aversion to financial risk; in terms of â??disruptive technologyâ??, Dutch investors want to see proof that a technology is disrupting and changing society before investing, and are less inclined to invest to help change society as Americanâ??s might. The current level of funding has created a stable environment with some success stories, but has not created a truly successful and flourishing system for investment and biotech companies.

Should the Netherlands take a more direct role in supporting life science startups, or is this something that should be dealt with in a European context?

This could definitely be done in a larger European context, and the Netherlands is simply too small to generate real growth or traction on its own, so integration with the EU is necessary for Dutch companies to grow. There are a lot of incentives at the EU level and funding in the form of Eurostar investments for public-private partnerships involving academia, but in terms of domestic grant and supports such as tax deductions for SMEs they arenâ??t precise enough on their own, and it may in fact make more sense to abandon domestic supports for life-science development in favor of strengthening EU level supports further. The room for growth can be achieved via direct partnerships

with institutions and companies across the EU, and EU level funding can be used to support growth on both sides of a partnership and target regions with high potential.

Congratulations on winning the Galenus prize last year! Could you tell us a bit about the research that earned you this recognition?

We aim to work on translational research with the aim of improving treatment efficacy for patient populations with relatively unmet needs. There is a relative shortage or lack of treatment options for brain cancers, and brain cancer patients are severely under examined. Most cancer research is oriented towards receptors and mechanisms that do not have any effect on the brain, and since brain tissue and chemistry is so vastly different from any other area of the body there is almost no transferability of drugs that can be used to combat other cancers in the brain. As such, there is a real need for an increased focus on developing brain cancer specific drugs.

This situation may change to some extent with the recently developed immunotherapies, which have the potential to be efficacious and safe in the brain; we have initiated a new trial focusing on this subject. The Galenus prize has created more opportunity for me to create incentives and provide information to the public regarding these difficult tumors, for which there are currently very few treatment options.

Compared to other cancers do you see this as a severe unmet medical need?

Yes. This is the largest surviving unmet medical need in the field of oncology overall, as brain cancers can affect patients of all ages, and the standard of care relies on only one drug at present; temozolomide. In the Netherlands, brain cancer is the second most prevalent form of cancer among children and young adults, and is an extremely painful and cruel disease; depending on where the tumor grows, it can affect how a patient, a young child, breathes and thinks, and in extreme cases can press on parts of the brain stem, causing the sensation of choking or drowning, a fate worse than waterboarding. It is symptoms like these that can make these cancers difficult to even manage palliatively.

For doctors trying to treat these patients now, they simply lack treatment options, weapons, to even try to mount an effective fight in many circumstance. The standard of care relies on radiation therapy and temozolomide, an alkalizing agent, and they do not work particularly well. My teamâ??s goal has been to develop more options, weapons, for combating these cancers to have some ability to adapt to the specificities of the patientâ??s condition, and it was these efforts that the Galenus prize recognized. So far we have designed two therapies that can prolong life significantly when combined; we have a whole pipeline of products, some still in mice models, others already in phase I clinical trials. The therapies that we have designed are based on WEE1 inhibitors (Mir et al. Cancer Cell 2010, De Witthamer et al. Clin Cancer Res 2011, Caretti et al. Mol Cancer Ther 2013) and Notch inhibitors (Hiddingh et al. Oncotarget 2014). Both are now in clinical trial in glioblastoma patients in the US.

Our cross-discipline team works to be able to move these candidates from the lab to the clinic as fast as possible, and to do this we need the support of pharmaceutical companies. So far weâ??ve been able to implement two trials based on the support of US pharmaceutical players, but we are hoping that we are able to attract more trials and support from big pharma so that we are able to bring some new treatment options to neuro-oncologists and patients as soon as possible.

What effect do you foresee the Prinses Maxima Childrenâ??s facility in Utrecht having on your ability personally to push forward your research?

Our group currently consists of a pediatric brain cancer group which will benefit substantially from interaction with other teams studying pediatric brain cancers. Our pediatric team will be going to the Prinses Maxima Center as will other pediatric oncology teams, so there is definitely positive potential for â??collisionsâ?? in that sense.

As for our initiatives, many of the children being treated at Prinses Maxima will be treated here at the VUMC due to our advanced imaging technology, so we will be involved with them on this end as well.

Here at the VUMC we also have an autopsy protocol for pediatric brain cancers, which offers an opportunity to research how to better combat these cancers after a patient passes on. We are implanting these tissues directly into mice and in this way the tumor can live on, and we have been able to develop a living library of different types of brain cancers; this is a very unique system at the global level. This library may also have the opportunity to grow further via our involvement with the Prinses Maxima facility.

Youâ??re working on many fronts to develop new treatment options; what is the gap or hurdle that you need to overcome to be successful?

Treating cancer is like chess, for every patient and tumor you need to have a specific adaptation and positioning. Given our shortage of treatment options, at this point the cancer is able to take many more forms strategies than we are; so first of all, we need some more compounds and hopefully some of the new immunotherapies will be effective in this sense. At this point in time, there are many patients who we are not able to even try to treat.

We also need to be able to improve our intelligence through diagnostic technologies, and this technology exists but arenâ??t yet part of developed, proven treatments, so we need to bring these diagnostic technologies to the market and into hospitals. Similarly, we need better longitudinal imaging and genetic testing, both of which exist but are expensive and somewhat inaccessible; this challenge can only be solved through substantial investment, as this type of imaging center can cost EUR 100 million.

Finally, the information we have must be fully utilized, leveraged to the greatest extent possible. As such, data collection and patient registries must be improved, and we need data from pathologists, radiologists, and oncologists from all of the advanced medical centers to create a relatively comprehensive data set, and then we need to invest in teams that can effectively data-mine and perform meta-analysis. We have a lot of information already, but the oncology research community as a whole needs to be smarter about how we use it and how research is conducted so that time and resources are not used inefficiently, and if we improve our approach then we can present a more enticing investment opportunity to the pharmaceutical industry, helping to bring treatments to the market faster. The European set up for Horizon 2020 and collaborative effort needs a lot of attention, because an effective fight against brain cancer needs to be a multinational effort, because any one European country is too small to be effective.

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