ICI institute for chemical immunology

Interview

"IT SHOULD BE USEFUL AND FUN"

JANNIE BORST
Professor of Immunology
Leiden University Medical Center

Learning about what scientists in other areas are working on, is a very effective way to gain new insights and ideas. And it can bridge the gap between basic research and practical implementation. To this end, the Leiden University Medical Center (LUMC) and the Netherlands Cancer Institute-Antoni van Leeuwenhoek hospital (NKI-AvL) have started a think tank focused on immune therapy. Jannie Borst, professor of Immunology at LUMC, is heading the effort.

Why a think tank?

"In the LUMC's strategic plan, oncology has been defined as a key theme and an area for outreach. In this context, LUMC and NKI-AvL have intensified their relationship in several ways, including the appointment of a number NKI-AvL scientists and clinicians as part-time professors at LUMC. Together with John Haanen from NKI-AvL, I want to support interactions in the field of immuno-oncology, where major progress takes place and the two institutions can benefit from each other's knowledge."

What does LUMC expect from this interaction?

"NKI-AvL is very experienced in designing and running clinical trials. This is where all the new, experimental therapies are applied. Including immune therapy, which has exploded in activity and is quickly gaining ground for more and more types of cancer. Oncology is a priority area for LUMC, but we are not a specialized cancer institute, so there is a lot to learn from what is going on at NKI-AvL. Furthermore, closer ▶

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connections also offer more possibilities for oncologists here in Leiden to get their patients enrolled in trials at NKI-AvL."

NKI-AvL is a specialized cancer institute, which prompts the question what LUMC is bringing to the table.

"NKI is a relatively small research institute compared to LUMC and the additional scientific capacity of Leiden University with its basic research in biology, chemistry, pharmaceutical sciences and physics. All this is very interesting to NKI-AvL, because they are constantly looking for new insights and ways to innovate and expand their expertise. And their focus is mostly on translational research, but that requires basic science to start from. Immunology has become more important within NKI and is a strong area at LUMC. I think there is a really good match between the two centers."

Improving immune therapy is a broad ambition, but also a bit diffuse. Can you be more specific as to what exactly the think tank will be addressing?

"We want to connect key people from the two institutions and show them where the opportunities lie. It is important to realize that every breakthrough in oncology, including immune therapy, was preceded by decades of basic science and technology development in different areas that at a

"There is a good match between the two centers"

certain point came together and opened whole new world of possibilities. When the breakthrough in immune therapy took place in 2013, it was widely perceived as a huge surprise, but the science behind it had been in the making for decades. Since the early 1980s, I have been working on the interface between immunology and cancer, but it took a long time to be able to actively deploy the power of the immune system against tumors. That is a very recent development and now, the field is moving very fast ahead. My point is that it takes a lot of work in different fields to achieve real breakthroughs and the best way to stimulate that is to bring people with different expertise and perspectives together to learn from each other's insights."

Where do we stand with immune therapy?

"Right now, blocking antibody to PD1 is the mainstay of immune therapy, it has proven to be the most effective and the least toxic. It can be combined with other inhibitors, most notably anti-CTLA4, but we don't really understand the underlying mechanism of this synergy. We know that both inhibitors release the brake on the system so that the immune response is activated, but why it works the way it does is still not completely clear. One important topic is to find out which other combinations are possible with anti-PD1 to target specific types of cancer."

So, there is a lot of basic research ahead?

"Yes, we need to keep on expanding our basic knowledge of the immune system and all the players involved. Everything we learn is important and relevant to the development of new and improved therapeutic options. There is a lot of interest in enhancing the efficacy of anti-PD-1 by making combinations

"We need to be guided by mechanistic insight"

with other immunomodulatory antibodies or other therapies. But there are infinite possibilities and we cannot test them all. We need to be guided by mechanistic insight to test the most promising combinations and to find new targets."

But the think tank concentrates on improving immune therapy. That sounds like an impossibly big leap when you start from basic insights.

"That step is sometimes much smaller than you think. But it does require that the people working in basic science and those working in the clinic are aware of each other's insights, questions and problems. Cross fertilization is the key. During the first meeting we organized, clinicians from AvL presented the spectacular results of neoadjuvant immunotherapy in a diversity of cancers. Speakers from LUMC explained advanced analytical techniques that can be used for high end diagnostics. This is needed to correlate efficacy of treatment to specific biomarkers and to understand the mechanisms underlying treatment success or failure. Just showing what is possible can be very informative."

What are the next steps?

"We've only had this first meeting and we are still exploring how to proceed. It all sounds very fancy to have a think tank, but we need to find an effective way to operate. I think we need a small group of people with overview of what is going on within AvL and LUMC and from that, we can define more specific topics for other groups to discuss. Whatever form it takes, it is essential that people participate because it is useful and fun. Nobody wants more meetings and procedures and red tape. We just want to stimulate interaction and build a network that inspires people." ■

"We are still exploring how to proceed"

FOCUS ON CHEMICAL IMMUNOLOGY

Chemical immunology is a nascent field that is of growing interest for AbbVie, a global research-driven biopharmaceutical company. Principal Research Scientist Melanie Patterson: "The field is ripe for exploration; the tools are there. This is a most exciting time."

Eleven years ago, Melanie Patterson was pursuing a career in academia as a tenure track professor at DePaul University in Chicago when AbbVie (then Abbott) convinced her to join industry. Patterson: "It's a misconception that leaving academia always means abandoning exploratory research. I'm involved in early drug discovery where cutting edge science is required to deliver better medicines to patients."
The deciding factor for her to join AbbVie was the opportunity to do team science, explains Patterson. "In academia you are your own brand. AbbVie has over 47.000 employees across 175 countries that work together to make an impact."

New opportunities

One of her more strategic tasks today is to proactively identify new opportunities to fill AbbVie's pipeline. Currently Patterson is particularly interested in how cancer cells 'talk' to T-cells. "Tumour cells present different information to the immune system than healthy cells. If we can understand these unique signals, we can take immunotherapy a step further," she said. That notion made her reach out to ICI when building her team. "A critical focus of my research is to identify peptides presented by the MHC complex, and ICI develops tools and strategies to study this from a chemistry angle using small molecules."
Patterson started at AbbVie as a bench scientist providing her expertise in mass spectrometry to project teams. Today she co-leads a team of fourteen scientists in the Chemical Biology and Emerging Therapeutics group. "My team steps in to help solve problems, supporting any therapeutic area at AbbVie such as immunology, oncology, neuroscience, and virology, to name a few. In addition, we have an exciting opportunity to explore emerging therapeutic possibilities."
Leading the team means that Patterson keeps projects on track, discusses research results, scouts new opportunities, and prioritizes resources. She is also a mentor for two employees in different parts of the organization through AbbVie's mentoring program. "I've always enjoyed teaching, but mentoring helps me learn from others as well."

Need for chemical immunologists

What qualities does a scientist need to become successful in industry? Patterson: "The most crucial part of my work is prioritizing because all companies have limited resources and time. You need to have a keen sense of the probability of success. Will the investment outweigh the benefits? Is there a quick win? Is it too risky? Working in industry helps one develop these skills with experience over time."
What kind of chemical immunologists would AbbVie consider as future employees? "We're looking for scientists who are able to creatively solve scientific problems and push forward to find new paths. But, above all, AbbVie needs team players. There is a culture of connectivity. You are part of a team where the results are greater than the sum of our parts." ■

abbvie

Making a remarkable impact on people's lives

- Voluntary work and donations through AbbVie Foundation support underserved and marginalized communities
- There is a company-wide equality, diversity & inclusion strategy, and a commitment to diversity in clinical trials
- Partner in ACTIV: Accelerating COVID-19 Therapeutic Interventions and Vaccines
- Partner in CARE: Innovative Medicines Initiative's Corona Accelerated R&D in Europe

The double check on tolerance

PhD project: Mechanisms of self-antigen expression in tolerance inducing lymph node stromal cells

Stromal cells turn out to play a role in 'double checking' self-tolerance. However, how this additional prevention against auto-immune diseases is regulated is a big question. A question which PhD-students Janna Roet and Tom Schoufour intend to answer.

"We are working in shifts at the moment, so we can run experiments six days a week," tells fresh ICI PhD-student Janna Roet. She and her ICI duo-partner Tom Schoufour had an unusual start of their PhD-studies: reading literature at home for two months because of the pandemic. "It's good to be well read-in, but I'm very happy that we can work at Leiden University now, together." Because laboratories allow a limited number of people during the pandemic, Roet and Schoufour decided to share a work space. Schoufour: "We're working together on a genome wide activation screen. That is quite new technology for both of us. Having a sparring partner to solve small problems is actually very pleasant." Roet agrees: "Tom has a bit more experience in cloning which is a great help to me and it's quite nice when you get a text at the end of the day saying: It worked!"

Stromal cells

The PhD-students study stromal cells from lymph nodes. The well-known role of these cells is providing structural integrity to tissue, but recently it was shown that some stromal cells also express self-antigens to filter away autoreactive T-cells that have slipped through the main control system in the thymus. Roet: "In the thymus self-tolerance is mostly under the control of auto-immune regulatory gene (AIRE), but it's clear that that's not the case in lymph node stromal cells. We want to discover what molecular mechanism lies behind this double check."
Using genome wide activation screening with CRISPR/Cas9 the PhD-duo wants to identify the regulatory genes and proteins responsible. These may be possible targets in controlling auto-immune diseases in the future. Roet: "Finding a gene that stimulates self-antigen expression first of all makes the study of these stromal cells a lot easier. They are actually kind of needles in a haystack." The final goal is to unravel the complete control mechanism in stromal tissue. A feasible target for their PhD? Schoufour: "We will at least identify some important genes and proteins involved. If we can figure out the whole system, I will be more than satisfied."

"We're working together on a genome wide activation screen"

Cloning work

When the screening results provide first clues, Roet will move to VUMC in Amsterdam. "My main focus is on studying the exact function of the genes we identify in the screens using cell cultures and animal models." Schoufour will complete the screening work and handle the accessory bioinformatics. "We're now doing a lot of cloning work, but when the actual screening starts it will provide a load of data. It's up to me to separate real hits from noise." Quite a different expertise? "I have some experience and I like programming. I think analysing your own data is much better."
Both Roet and Schoufour have a master in Biomedical sciences from Amsterdam University, but never met before they both got this job offer from ICI. Schoufour: "I was immediately enthusiastic about the idea of a duo-project, but also realized that the success depends upon a good match. Those worries didn't last long, Janna is very clever, we get along really well." ■

Janna Roet
Molecular cell biology and immunology, VUMC
Reina Mebius group

Tom Schoufour
Chemical Immunology, LUMC
Sjaak Neefjes group

Insights in autoantigen-expressing B-cells

PhD project: Targeting inhibitory checkpoints on autoreactive B-cells to silence autoimmunity

In autoimmune diseases B-cells respond to self-antigens. What role do v-glycans play in this process? And how can you inhibit or 'fish out' the derailed B-cells? ICI's PhD-duo Miles Holborough-Kerkvliet and Margot van Weijsten plan to unravel some B-cell mysteries.

"Perhaps Margot is a bit more into chemistry than me," tells life scientist Miles Holborough-Kerkvliet. "However, it is not like she is going to synthesize compounds which I'm going to test. We are both focusing on autoantigen-expressing B-cells. The idea is that we exchange knowledge and experiences and come up with a common project which we both can attribute to."
His ICI-partner, Margot van Weijsten, holds a master in Chemistry for life. "I found all life sciences very interesting, but after my first course in immunology, I knew exactly what I wanted. The immune system fascinates me because of its incredible complexity, and relevance."
Holborough-Kerkvliet 'tasted' both business and science during his master Life science & technology and Science based business. "I definitely liked the research part at the laboratory most." Why? "The feeling when you have everything set for an experiment and can start. It's a bit of a high to me, I guess."
He found a PhD-position at the rheumatology laboratory at LUMC. That immunology is 'hot' was not decisive in his choice. "I think oncology is also highly interesting and important."

Main question

The studies of the PhD-duo focus on ACPA-expressing B-cells. ACPA stands for anti-citrullinated protein antibodies and they are the most prominent autoantibodies found in patients with rheumatoid arthritis. The ACPA's are remarkably glycated at the v-domain. These glycans are not involved in binding autoantigens, instead there are indications that they play a role in breach of tolerance and thus may be a target for future therapy.
Holborough-Kerkvliet focuses on the v-glycans: "They are abundant in sialic acid. I'm using synthetic analogues to identify to what proteins they bind, in order to find out more about their role in breaking self-tolerance. 'What does sialic acid do on ACPA's is essentially my main question." Will it lead to a cure for rheumatics? "Judging from genetic risk factors B-cells are important, but probably not a central cause. B-cells are a bit of an unexplored territory. Just before the Covid19-pandemic I was at a large rheumatics conference where I was one of the few studying B-cells."
Van Weijsten's main goal is specific inhibition of ACPA-expressing B-cells. "Removal of B-cells is a common therapy in autoimmune diseases, but that compromises the whole immune response." Targeting the one percent that is involved in autoimmune diseases is thus a goal at the horizon in immunotherapy. Van Weijsten has started constructing various peptide-fluorophore conjugates targeting ACPA-expressing B-cells. "I'm going to study their binding and whether they enter the cells. Later I will use this knowledge to design peptide-toxin combinations that inhibit the cells or lead to apoptosis."

> *"We haven't had a live meeting yet"*

Apart together

The PhDs had just started experiments when their laboratories closed down because of the pandemic. Van Weijsten: "I'm very well read-in now, but also really happy that I could start experiments again." The duo has not had a live meeting yet. "We were about to meet last March at the ICI-conference, but the meeting was cancelled." Holborough-Kerkvliet: "We have both been very busy starting-up our own research projects. Once we're fully running, we will start meeting and discuss a common project." ■

Margot van Weijsten (right)
Synthetic organic chemistry, RU Nijmegen
Kim Bonger group

Miles Holborough-Kerkvliet
Rheumatology, LUMC
Rene Toes group

“It is a moral obligation to produce this compound”

Sjaak Neefjes didn’t need long to figure out what to do with his €2,5 million Spinoza prize. The money came at exactly the right moment in his efforts to manufacture a variant of the anticancer drug doxorubicin. “Companies are not interested, so we decided to do it ourselves.”

“Doxorubicin is widely used, but among clinicians it has become known as ‘toxorubicin’ because of its serious side-effects, including cardiac damage. The cytotoxic effect of doxorubicin lies in its ability to cause DNA breaks in the tumor cells and unfortunately, in healthy cells as well. However, we discovered that there is an additional mode of action in which doxorubicin forces nucleosomes out the cell’s chromatin. As a result, the DNA can no longer be neatly packed and loses its structure, leading to cell death.”

Better

“Within an ICI project together with the group of Hermen Overkleeft, we created doxorubicin variants that apply either one of the two mechanisms, to find out which mode of action is the most effective. It turns out that the nucleosome-removal variant exhibits higher activity against tumor cells and is less toxic. So, this is clearly the better compound, but the problem is that this variant, as many other doxorubicin variants, have been prepared before. They lack novelty, which makes it impossible to file for a patent on these compounds and without a patent, pharmaceutical companies are not interested in pursuing further clinical development.”

▼ *Sjaak Neefjes wants to spend the accompanying cash prize to manufacture a variant of the well-known anticancer drug doxorubicin without the unwanted side effects.*

Opportunity

“Of course, you could say: ‘what a pity, but we are academics so we can’t do anything about that’, but that doesn’t suit me. If you come across a compound that offers better performance than what we have now and that might improve the well-being of patients, you just cannot ignore that opportunity. That is why we decided to take further development into our own hands.”

Protocols

“However, producing a compound for a clinical trial comes with a host of regulatory requirements, such as compliance with GMP protocols, that is beyond our capabilities. We teamed up with the specialists at Mercachem-Syncom, to design the necessary manufacturing protocols and then we need to find a manufacturing company to take care of the actual production. Just when I was getting worried where we could get the money to finance that step, which will probably take around one million euro, I got the news about the Spinoza Prize. Perfect timing.”

Obligation

“How far we can take this? I don’t know, we must first pass the clinical trials and then get regulatory approval. I know that the market is interested, because of the better toxicity profile. But we, as academics, cannot run a full-scale pharmaceutical production and formulation enterprise. At some point, a commercial party needs to get involved. We’ll see but whatever happens, I strongly feel that we have a moral obligation to produce and test this compound as it may provide better prospects for cancer patients.” ■

Spinoza prize

The NWO Spinoza prize is, together with the Stevin prize, the most prestigious personal scientific recognition in the Netherlands. It is awarded yearly to a maximum of four scientists who have demonstrated scientific excellence and are internationally recognized as leaders in their field. The prize is named after scientist and philosopher Baruch Spinoza (1632-1677) who dared to think radically and cherished the power of reason.

“We aim to be as smart as a T-cell”

Using his €2,5 million Stevin prize, Ton Schumacher wants to design an algorithm that can predict which epitopes a T-cell can and cannot recognize. “If we can make this work, we create a host of new opportunities for diagnosis, monitoring and therapy.”

“Suddenly, you get this huge amount of money thrown at you. That is a surreal experience. Normally, the development of new research lines is a gradual process. You spend a lot of time thinking about what you would like to do and why, you write a proposal and hope for the best. But now, I didn’t have a well worked out plan. I know from other people who have had this experience before that you should look for those dreams that have been lingering in the back of your mind, ‘wouldn’t it be great if we could….’, and that brought me to the idea of a predictive algorithm for T-cell recognition.”

Receptor sequence

“We know that the specificity of T-cells is determined by the T-cell receptor sequence. Over the years, we have developed a variety of tools and techniques to measure what a T-cell receptor can recognize, but it would be even better if we could move towards prediction. What I envision is that, in the future, we will only need a read-out of the receptor sequence, for example isolated from peripheral blood or the tumor site, and that information will allow us to deduce which epitopes will be recognized and lead to activation of the T-cell response.”

Targeted stimulus

“If we can make this work, we can monitor immune responses of patients and determine the nature of those responses in a much more efficient way. Are we dealing with an auto-immune disease or is it a response to a pathogen? There are also therapeutic opportunities. Take a tumor sample, analyze what those T-cells can recognize and develop a targeted stimulus to boost that response. I am certain we will reach a point someday, in which we look back and say to each other: do you remember the old days, when we could only measure what a T-cell recognizes, whereas now, we know right away.”

Huge datasets

“To get there, we first need to build huge datasets that contain sequences of T-cell receptors combined with data on epitopes that are recognized and those that are not. It may seem strange to also include the latter, but we know that T-cell receptors are not as specific as we usually describe them. Including epitopes that will certainly not be recognized simply adds an additional layer of information and creates a ‘richer’ dataset. Once these datasets are compiled, we will design and develop an algorithm that will learn to predict which epitopes a T-cell will recognize and which ones will not. Our ultimate goal is actually a humble one: to be as smart as a T-cell.” ■

▼ *Ton Schumacher wants to spend the accompanying cash prize to develop a predictive algorithm for T-cell recognition.*

Stevin prize

The NWO Stevin prize is, together with the Spinoza prize, the most prestigious scientific recognition in the Netherlands. It is awarded yearly to one or two scientists for exceptional achievements in creating impact for society. The prize is named after engineering pioneer Simon Stevin (1548 - 1620) who applied his knowledge of mathematics and physics to establish new fields of applied research, including water infrastructure, geodesy and construction.

Edinburgh and Nijmegen scientists are joining forces

Seeing immune cells in a new light

Understanding what goes on at the cellular level requires advanced imaging techniques. Especially when you not only want a static, but also a dynamic view of whatever is happening. A new collaboration between Edinburgh and Nijmegen promises a detailed view of the actual behavior of immune cells.

"I am a chemist by training and when I started out in this field, I only had a very basic understanding of the immune system," says Marc Vendrell, professor of Translational Chemistry and Biomedical Imaging at the Centre for Inflammation Research (CIR), which is part of the University of Edinburgh's Medical School. The CIR studies the role of immune cells in various diseases, including cancer, inflammation and infections. Vendrell has been with CIR for eight years now, and the immune system has completely captured his attention. "Over the years, when I learned more about its intricacies, I realized that the immune system is a fascinating world in itself that offers many opportunities for chemists to work on interesting problems."

Fluorophores

One of those interesting problems is to catch a glimpse of immune cells in action. "In my group, we develop dynamic activatable fluorophores, which are chemical probes that allow visualization of immune cells in a new way; you only see them when they are actually performing a specific activity. It is not just about measuring their presence and location; it is about finding out whether they are active or not. We are interested in the dynamics and the function of immune cells."

Intriguing questions from an immunological and biological perspective, but what makes it worthwhile for a chemist? "Immune cells don't operate autonomously; their activity is coupled to that of others. The function of one immune cell is directly implicated in the functioning of another and so on. The orchestration of all those different cells is fascinating, also from the perspective of a chemist. Everything is related and to understand that, you need to image the functioning of all these cells as a whole. That is a major chemical challenge, because it comes down to the question of which molecules enable you to see what you want to see." Vendrell emphasizes that his approach is not a replacement of other imaging techniques, but offers a complementary platform.

Teaming up

Earlier this year, Vendrell teamed up with the group of Martijn Verdoes at Radboud UMC in Nijmegen. What was the driver behind this new collaboration? "It's quite a funny anecdote how we met a few years ago at the conference in Heidelberg, simply because of our names. Vendrell and Verdoes were next to each other in the alphabetically ordered list of posters and that is how we got talking. I knew his work from Stanford and at that time, Martijn was just back in the Netherlands and we talked about what his plans were. Because of our shared expertise in activity-based probes, we kept contact and he invited me over for an ICI meeting. When we first met, we were both still starting up, but by now our labs are more established and our platforms are ready to enter into a collaboration."

"The immune system offers interesting problems for chemists"

The partnership is still in the early stages, but some outlines of the intended research can be sketched. Macrophages will definitely be involved. "Martijn concentrates on macrophages and studies them from different angles. Macrophages are very versatile and can change their phenotype over time. Our probes can be used in macrophages to image their functioning in different environments, we are now more confident about what we can see and I think the time is right to combine our approaches to target specific subsets of macrophages and study their function. We can apply the probes in animal models and in human samples that we have available here and that should give us insight into what macrophages are doing in different environments and diseases, which is very relevant to the development of targeted systems for drug delivery that can operate in a specific microenvironment."

Combining expertise

According to Vendrell, combining the expertise of the two groups will allow a more detailed view of macrophages in action. "Different techniques enable different things to be seen and by joining our platforms I think we will gain specificity for subgroups of cells that each individual technique does not allow. If we combine our activatable probes with those of Martijn, we can track disease-causing cells in a whole new way. Taken together, I think we will be able to create new tools that tell us on the spot which macrophages are doing what in different diseases."

"We don't develop technology for the sake of it"

That knowledge is useful to all kinds of clinical application. For example, in identifying patients that are likely to respond to a certain therapy or to determine their risk of disease progression. For Vendrell, the step to the clinic is an integral part of the work. "We don't develop technology for the sake of it, but strongly focus on translating new tools and techniques to the clinical practice, because in the end, that is where they are needed." ■

Complementary technologies

"By bringing our approaches together, we can create an additional layer of information," argues Martijn Verdoes, assistant professor at the Nijmegen department Tumor Immunology of Radboud UMC.

"Our technologies are really complementary, both for imaging purposes and for developing new drug delivery strategies," explains Verdoes about his new collaboration with the group of Marc Vendrell. "Our lab is very strong in designing and creating specific fluorogenic probes for sampling the chemical microenvironment. That is very interesting, because when we combine our reporter probes with his fluorogenic dyes, we can not only image active proteases, but also explore and visualize their direct environment. Think about pH, oxidation state, enzymatic composition."

Crucial information

More insight into the different chemical environments within a cell is essential to the development of vaccines or drug delivery systems, says Verdoes. "Immune cells have different receptors that are coupled to different pathways, which lead to different biological outcomes. We want to know the chemical differences between those pathways so we can connect those differences to specific outcomes. When you're developing a vaccine or a drug delivery vehicle, you need to know what your cargo will encounter when it enters the cell via a specific receptor. That is crucial information for your chemical design, to ensure that the cargo remains intact until the right moment and the right location for release and action."

And then there are the new possibilities for studying macrophages, specifically TAMs, tumor associated macrophages. "When we combine our cathepsin platform with Marc's technology using cytokines, we can create even more selective methods to target specific subsets of macrophages. When you know which chemical and biological properties allow you to target cells very specifically, you can use that same chemistry to deliver drugs that can eliminate cells or change their phenotype. That is very interesting, if we can use that information to change the TAM phenotype. There are studies that indicate a correlation between the presence of certain TAMs and certain clinical outcomes. A better understanding of those relationships can lead to therapeutic, but also diagnostic applications, such as patient stratification based on TAM profiles. Our combined approaches allow us to more selectively visualize what we know is there and at the same time, we can start to discover what else is present. This research in this project is both very targeted and very explorative in nature." ■

A smooth and a surprising job transition

In her new job at spin-off DC4U Technologies, former ICI PhD-student Eveline Li is pursuing some of the most promising ideas from her PhD-studies. PhD-partner Tim Hogervorst said goodbye to hands-on research. He now advises companies on innovation at scale-up Findest.

Together Eveline Li and Tim Hogervorst synthesized and studied the immune stimulating effect of antigen-adjuvant conjugates carrying well-defined mannoses during their PhD-studies at ICI. Pharmaceutical scientist Li is now continuing the research as a project manager at DC4U Technologies, a spin-off from the same laboratory where she did her PhD-studies. "It's a unique chance to bring the research I worked on towards the clinic. We're working in the field of oncology, allergies and autoimmune diseases."
Her project-partner at ICI, organic chemist Tim Hogervorst, decided to leave academia. "I enjoy research and lab work, but also wanted to explore other opportunities." He came across an intriguing vacancy on LinkedIn from a start/scale-up

"It would be very cool if our work is developed into a real therapy"

from VU Amsterdam: Findest. He now advises companies on technological innovations using Findest's self-developed software tool. "It's a kind of Google+ or Elsevier+ that searches and selects information on new technologies from highly diverse sources and from often surprising disciplines."
The atmosphere at Findest is comparable to the university, finds Hogervorst: "Many young people and no nine-to-five mentality". A large difference however is the highly goal-oriented way of working. Hogervorst: "During a PhD you dig into every interesting or surprising detail. At Findest, I work no more than a few days to complete a request. Then I move on to a new client and often a very different technology question."

Something different

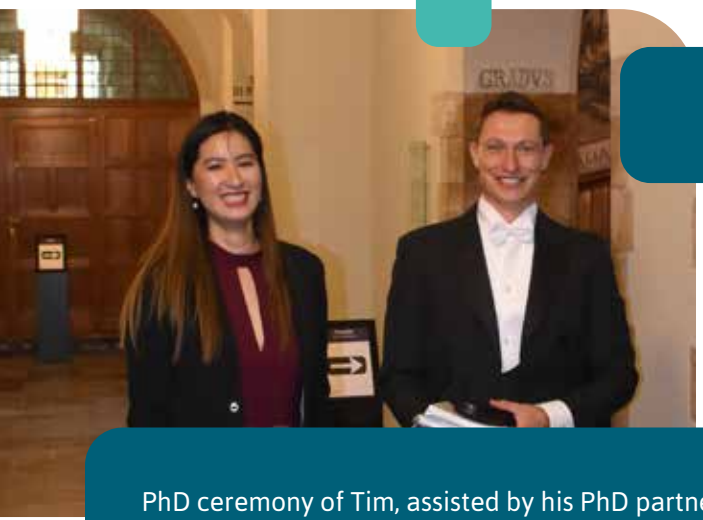
Hogervorst is happy that Li continues to work on some of the ideas they developed together. "I think her new job fits Eveline perfectly. She has thorough knowledge of the field, and she is good at organising and communication. And it would be very cool if our work is developed into a real therapy." Li couldn't agree more. "I was considering a post-doc or a job in industry to be more involved in bringing products to the market. This job has it all, and I remain in chemical immunology which I think is a fascinating field and booming at the moment."
Li was a bit surprised by Hogervorst career choice. "I guess I envisioned him in a more traditional research function, but Tim wanted to try something different." Hogervorst sometimes finds it a pity that he is not involved in the follow-up of his advices, the technology implementation. "Perhaps, that is something for the future," he ponders. His new job gives him a good overview of future options. "I get in contact with a lot of different companies. Before the pandemic we also used to visit every new client which also gives a good impression of the corporate culture."

Friends

Li and Hogervorst were the very first PhD-duo within ICI. How do they look back at their project? Li: "I was really lucky to be coupled with Tim. His enthusiasm and interest in my work were really encouraging. We really made some cool compounds and became good friends, too." Hogervorst: "It took some time to start up, but it resulted in a few really nice papers. I think I was lucky to be coupled with Eveline." Is there a secret behind their successful cooperation? Hogervorst: "Ask your duo-partner to send you reviews that fascinate her or him and discuss them together. It opens up your world and provides new ideas and opportunities." ■

Reference

PhD project Tim Hogervorst and Eveline Li: Exploring crosstalk between CLRs and TLRs using single molecule vaccines (see ICI Bulletin November 2016, Issue 3, P 4)



PhD ceremony of Tim, assisted by his PhD partner Eveline as a paranymph

Post PhD

ICI PhD projects from the first phase of the Chemical Immunology Institute are gradually being finished. Some PhD students have already defended their thesis and earned their PhD degree. In this section, Career, we follow the young scientists' first steps on their career ladder.

News

ICI Project Manager

As of September 2020, Daphne van Elsland is the ICI's project manager. She manages the organizational infrastructure of the ICI and provides support to the ICI community. Daphne combines the project management position with her work as a post-doc researcher in the lab of Sjaak Neefjes. Pauline Hoftijzer will continue to be part of the project office and will remain to be active as project assistant.

Alternative ICI Conference 2021

After the forced cancellation of the ICI Conference 2020 due to COVID-19, we are working on a corona proof concept for 2021. March 19th, we hope to offer a hybrid format conference that will allow us to meet at one or more (international) locations. By reaching a wider audience of like-minded scientists worldwide we try to turn a disadvantage into an advantage. More information will follow soon.

Smart chemistry

During their joint ICI PhD-project, Dennis Wander and Sabina van der Zanden have made an important discovery regarding the widely used anticancer drug doxorubicin. They have found a smart chemical pathway to reduce its unwanted side effects without sacrificing its effectiveness. This is encouraging because the serious side effects are often a reason to discontinue treatment. Initially there was a lot of skepsis, but recently their 'discovery' has been recognized with a PNAS article.

Recent publications

Demmers LC, *et al.*

Single-cell derived tumor organoids display diversity in HLA class I peptide presentation

Nat Commun. 2020 Oct 21;11(1):5338. doi: 10.1038/s41467-020-19142-9.

de Kivit S, Mensink M, Hoekstra AT, Berlin I, Derks RJE, Both D, Aslam MA, Amsen D, Berkers CR, Borst J.

Stable human regulatory T cells switch to glycolysis following TNF receptor 2 costimulation

Nat Metab. 2020 Sep 21. doi: 10.1038/s42255-020-00271-w

Hurdiss DL, Drulyte I, Lang Y, Shamorkina TM, Pronker MF, van Kuppeveld FJM, Snijder J, de Groot RJ.

Cryo-EM structure of coronavirus-HKU1 haemagglutinin esterase reveals architectural changes arising from prolonged circulation in humans

Nat Commun. 2020; Sep 16;11(1):4646. doi: 10.1038/s41467-020-18440-6

Stok JE, Vega Quiroz ME, van der Veen AG.

Self RNA Sensing by RIG-I-like Receptors in Viral Infection and Sterile Inflammation

J Immunol. 2020 Aug 15;205(4):883-891. doi: 10.4049/jimmunol.2000488

Caval T, Heck AJR, Reiding KR.

Meta-heterogeneity: evaluating and describing the diversity in glycosylation between sites on the same glycoprotein

Mol Cell Proteomics. 2020 Jul 31:mcp.R120.002093. doi: 10.1074/mcp.R120.002093

Di Blasio S, et al.

The tumour microenvironment shapes dendritic cell plasticity in a human organotypic melanoma culture

Nat Commun. 2020 Jun 2;11(1):2749. doi: 10.1038/s41467-020-16583-0

Qiao X, van der Zanden SY, Wander DPA, *et al.*

Uncoupling DNA damage from chromatin damage to detoxify doxorubicin

Proc Natl Acad Sci U S A. 2020 Jun 30;117(26):15182-15192. doi: 10.1073/pnas.1922072117. Epub 2020 Jun 17

Column

ICI IN THE NEW CONFERENCE LANDSCAPE

MARTIJN VERDOES (LEFT) AND SANDER VAN KASTEREN

ICI EXECUTIVE ADVISORY BOARD

Sander van Kasteren is associate professor at the Leiden Institute of Chemistry and Martijn Verdoes is assistant professor at the Radboud Institute for Molecular Sciences.

It has been a strange year, to say the least. For the ICI, COVID-19 hit home with the cancellation of the 2020 edition of the Chemical Immunology conference due to the virus. A big loss, because our conference annually brings together the entire ICI community to socialize, connect, and garner new scientific ideas. As impactful as this decision was, it was the only right one to make. This raises the question, how does the ICI community stay connected while social distancing during COVID-19?

At the time of this writing, the virus shows no sign of abating, nor is any vaccine likely to appear in the near future. This has made our preparations for the coming conference extra challenging. However, such a challenge can also present new opportunity. We have therefore thought hard about alternative arrangements for the conference that keep the spirit of the ICI much alive. Questions such as 'how can we still network' and 'how can we provide the students access to all that the ICI has to offer' without being able to physically meet (at full capacity), have been the topic of much discussion. On top of that, how do we reduce one-directional 'screen time' in a virtual conference era and could we tackle the typical attention-span restrictions with a refreshing and timely program?

With the help of Daphne van Elsland, the new ICI project manager, we think we have cracked this nut. March 19th, 2021, we hope to offer a hybrid format conference that will allow us to meet at one or more locations. Concomitantly, we will broadcast virtually, which will allow us to showcase the ICI to a wider audience and to connect with likeminded scientists in The Netherlands, Europe and beyond. With this we hope to spark incentives for new national and international Chemical Immunology collaborations and funding opportunities to make our ICI community even stronger. We are currently inviting inspiring speakers and for the ICI PhD students we have created an abstract writing workshop. From these abstracts, we will select short talks to also keep the focus on the future generations.
As exciting this new format is for us, we do hope we can all regain our social life and science without restrictions as soon as possible and finally meet the new crop of students properly. ■

About ICI

The Institute for Chemical Immunology (ICI) is a Gravitation project, made possible by the Ministry of Education, Culture and Science, in collaboration with the Netherlands Organization for Scientific Research (NWO). ICI will define and exploit a new field termed chemical immunology and train a novel generation of interdisciplinary scientists. It aims to promote academic excellence. The ICI publishes twice-yearly the 'ICI Bulletin' featuring ICI research, education and other relevant developments. To (un)subscribe please send an mail to info@chemicalimmunology.nl.

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