ICI institute for chemical immunology

Interview

KEY TO CANCER VACCINES LIES IN THE TUMOR MICROENVIRONMENT

JOLANDA DE VRIES
Professor of Immunology
Radboudumc Nijmegen

Today, balloons and party flags show directions to the office of Jolanda de Vries, professor in Immunology. The department is celebrating her 25th work anniversary at Radboudumc. In this quarter of a century immunotherapy gained a prominent position in cancer treatment, yet cancer vaccines remain a quest.

What's the biggest change in onco-immunology you witnessed?

"When I started in this field, there was large skepticism in the medical world about cancer immunotherapy. Many felt it would never work. Today, immunotherapy is as logic an option to consider for the treatment of cancer as surgery, drugs, or chemotherapy. Immunotherapy has even become the number one choice in some prominent types of the disease. The main question is no longer 'will it work', but why do some patients not respond to immunotherapy, or why do they no longer respond."

The main question for you, too?

"Certainly, we study the microenvironment in and around the tumor. How does a tumor try to evade the immune system? And how do these processes depend on characteristics of the patient, the tumor, or other factors? The tumor microenvironment is our main focus in research, and in particular the role of dendritic cells herein."

►

Contents

You hold a degree from Delft University of Applied Sciences. Not the most usual path towards an academic career?

"I was competing in speed skating at the international level when I finished secondary school. Sport was my number one priority in my decision in further education. A job as a technician seemed to combine well with a sport career."
"However, an injury ruined my chances of reaching the top. I think that shifted my focus and competitive drive towards science. One of the teachers complained that I would never be a good, servant technician because I was asking too many questions. During my final internship in Davos, Switzerland, I was encouraged to follow up on my own ideas and curiosity. I really enjoyed the research work."
"That internship resulted in an invitation to start PhD studies at Utrecht UMC. I had never set a foot in a university and did not have a very good idea of what a PhD position implied, apart from doing your own research project, which seemed a very nice idea. It didn't feel special at the time, but in hindsight, I'm really grateful that I was given this opportunity."

"My focus and competitive drive shifted towards science"

Does this background provide advantages?

"I was good at lab work, ha-ha. More seriously, I'm perhaps more practically oriented than someone with a Master of Science degree. You often enroll in what you like and are good at. So, it may be no coincidence that I'm in a research field that is close to the clinic, closest to actual application."

In 2018, you received the Huibregtsenprijs for developing immunotherapy with patient-own dendritic cells all the way to the clinic. How are these studies going?

"For dendritic cell vaccination, we isolate dendritic cells from patients' blood, load them with tumor antigens in the laboratory and return them to the patient. The cells can present the antigens to T-cells effectively, resulting in a strong immune response. It works, but unfortunately, not in all patients. In a study in melanoma patients some benefitted, the overall results did not warrant continuation of the study."
"However, we are continuing our research in dendritic cell therapy by looking for more relevant tumor antigens, and we have put a lot of effort in the highly precise detection of DCs in tumors. We are studying DCs loaded with tumor lysates and are using a particular subset of DCs which are particularly good in cross-presenting. Currently, we are preparing for a clinical study to deliver this particular subset of DCs to ovarian cancer patients shortly after surgery. It's known that the presence of this particular DC subset in the tumor microenvironment coincides with a favorable disease outcome."

"Today the question is: why do some patients not respond to immunotherapy"

"For a long time, immunologists – myself included – envisioned cancer vaccines as a monotherapy. However, tumors are excellent at escaping the immune system; there are too many ways they can dodge a single therapy. Therefore, vaccines must either be developed for specific receptive subgroups of patients, or as an effective additional therapy. I believe the future of cancer treatment lies foremost in combination therapy."

Is your group also working on other vaccines?

"Yes, preparing dendritic cells under strict GMP [good manufacturing practice, ed.] is quite demanding, and also very labor intensive, thus expensive. To circumvent this, we are also investigating whether tumor antigens encapsulated in nanoparticles can reach dendritic cells in patients."
"We have just included the first patients in a phase-I study with nanoparticles loaded with antigens and an adjuvant. This is work in close collaboration with the group of Carl Figdor who developed the particles. My group has the expertise and facilities to produce the vaccines under GMP in quantities for a clinical study. It's been quite a job to set up all necessary procedures, but we are very exciting to have brought this cancer vaccine to the clinic. Till now, we did not observe major side effects so we can proceed."

Any news on chemical immunology from your lab?

"Currently, there are no ICI-projects running under my supervision. I think ICI has developed a clever concept in which both fields gain from the cooperation. I'm really curious how the knowledge and experiences of this new generation of scientists will influence the output of the laboratories and companies they will work in." ■

"The future of cancer treatment lies foremost in combination therapy"

WHERE IMMUNOTHERAPY AND CHEMISTRY MEET

Simmunext develops novel immunotherapies by mimicking immune cell function through its proprietary polymer platform technology. "We aim to develop synthetic off-the-shelf solutions to directly stimulate and expand immune cells in order to fight cancer and (auto)immune diseases," explains co-founder Carl Figdor.

Simmunext is a company name made of three words; a mix of 'simulation' (referring to simulating the immune system), 'immune' (referencing the immune system) and 'next' (indicating a next-generation approach). "This describes our innovative approach," says Carl Figdor, professor in Tumor Immunology at Radboud UMC and scientist at Oncode Institute. His research group has developed a method to use polymers as artificial antigen-presenting cells that stimulate the immune system to obtain a therapeutic response.

Mimic the immune system

Carl Figdor's Tumor Immunology group has been working with dendritic cells for a long time. These immune cells present antigens to T-cells, which then target cancer cells expressing the antigen they are activated against. "I always found that because you are getting these cells from patients, the procedure can be very difficult." Therefore, his team started looking for a method to avoid this problem and, surprisingly, they found the solution at the chemistry department.

The immunologists got interested in the polymers this department made, especially the so called polyisocyanopeptide. The chemists had shown this polymer to be very suitable for culturing human cells outside the body. "We asked ourselves: 'could we make artificial antigen-presenting cells by using this polymer for mimicking the immune system?' Of course, polymers are not cells, but we could equip them with molecules that can also be found on immune cells." Ultimately, the chemists and immunologists jointly succeeded in developing unique semi-flexible polymers decorated with a variety of immunomodulating molecules to mimic natural antigen presenting cells. "These 'immunofilaments' are designed to specifically activate and expand immune cells such as antigen specific cytotoxic T cells, CAR-T cells, or NK cells," Figdor says.

From science to business

This innovative approach to create polymers which can act as artificial antigen-presenting cells laid the foundation for Simmunext Biotherapeutics, a spinoff of Radboud UMC, Radboud University and Oncode Institute. "It means bringing a decade of work to the next level and taking steps towards the clinic," explains Figdor.

Simmunext was founded last March. The company first focus now on preparing artificial dendritic cells under strict GMP conditions and looks for industrial partners specialized in upscaling such production processes. Furthermore, the entrepreneurs need to find investors for their company. "These tasks are new and quite unusual for an academic as me. Fortunately, we are supported in this by Oncode's valorization team," Figdor concludes. With a strong IP position and management team in place, the company is now ready for its journey to leverage this platform technology to bring novel cancer therapies to the clinic. ■

simmunext BIOTHERAPEUTICS

E info@simmunext.com
W www.simmunext.com

Unknown features of ubiquitous membrane proteins

PhD project: The chemistry of complement-tetraspanin interactions

A superfamily of four transmembrane proteins called tetraspanins are organizers of the membranes of immune cells. Although ubiquitous, understanding the precise role of some of these tetraspanins in the complement system is the challenge in this ICI PhD project.

"Personally, what I like most about this project is the communication and interaction between the researchers, the different views on the same topic," says Fabian Schwerdtfeger, PhD student at Radboudumc, Nijmegen. Schwerdtfeger studied biochemistry and biophysics in Germany, but this was 'too chemical' for him. He found a PhD position at the Department of Tumor Immunology at Radboudumc, in a group with a lot of expertise in microscopy. "My PhD project combines cell biology with immunology and advanced microscopy which I find quite nice."
His research partner Elisa Lamottke, working at Structural Biochemistry section at Utrecht University, finished a Master's in biochemistry in Germany. She was interested in a PhD abroad using the microscopic technique cryo-EM. "With cryo-EM you can create a 3D model of proteins without having to crystallize them first, which is tricky."

Each its own strategy

This is exactly what Lamottke does now to elucidate the structure and function of tetraspanins. Tetraspanins are transmembrane proteins folded four times through the cellular membrane. They are key players in organizing the membrane and in immune cell function such as fighting tumors. But how tetraspanins do that remains an important question. Both PhD students follow their own strategy towards answers.
Lamottke explains: "I developed a protocol to purify tetraspanins inside a membrane environment and then prepare them for cryo-EM analysis. The standard protocol replaces the membrane with a bilayer, but this is not a relevant biological environment. I am proud of this success, and I'm working to improve the protocol."
Schwerdtfeger's research has two distinct parts. One part focuses on understanding the function of two new tetraspanins (Tspan3 and Tspan13) in immune cells. The antibodies against these tetraspanins that he needed for the study were not readily available. "Elisa produced the essential proteins for our project in a great cooperation."

"It is interesting to get a different view on the same subject"

Joint discussions

Schwerdtfeger found that both tetraspanins are highly expressed by human B cells, as compared to T cells. These two immune cell types resemble each other, so the difference must have a reason, he explains. "We investigated this by immunoprecipitation, where we isolate a protein complex by binding it to a bead covered in antibodies for this particular protein. From this we found previously unknown interactions for both tetraspanins."
In addition, Schwerdtfeger uses a super resolution microscope to image proteins with a resolution of 20 nm. He can observe clusters of the tetraspanins of interest and draw conclusions about the interactions the protein has with other molecules. The results are promising but it is still early days, he says. "The idea is, if we can see how the protein is organized, we may be able to predict how, for example, antibodies can be used to treat cancer."
The teams meet regularly to present their results and to discuss where they can help each other out. A great advantage, say both young researchers. "It is interesting to get a different view on the same subject," says Lamottke. "They work with entire cells; I work with isolated proteins. Fabian can use our results to see if they are relevant in cells, which will be very interesting." ■

Elisa Lamottke (left)
Structural Biochemistry, Utrecht University
Piet Gros group

Fabian Schwerdtfeger
Tumor Immunology, Radboudumc Nijmegen
Annemiek van Spriel group

Regulating T cell activity as cancer therapy

PhD project: Exploiting metabolism for therapeutic intervention in regulatory T cells

An imbalance between two types of T cells causes problems in autoimmune diseases and cancer. A selective intervention in the activity of these cells could be a therapeutic strategy, but the question is: how? Two ICI PhDs are finding unique metabolic features that discriminate between the two types.

"I'm interested in the lifestyle of T cells: which signals are important and how do they process these? It would be brilliant if we can find a vulnerability that has a relevance for treating cancer," says Mark Mensink, a PhD student at the Tumor Biology and Immunology group at the LUMC.
The desire to contribute to fighting cancer drives both PhD students cooperating in this project. Originally from Vietnam, collaborating researcher Thi Tran Ngoc Minh came to Utrecht for a Master's in cancer biology. "I wanted to do a PhD in cancer research where the immune response and metabolite interaction is gaining importance. This project in the Metabolomics group in Utrecht combines it all."

Joint search

Conventional T cells act to clean up pathogens and tumor cells. Regulatory T cells counteract this, thereby preventing excessive inflammation and autoimmunity. An imbalance in this system contributes to disease. Therapeutic strategies involve restoring the balance by stimulating or inhibiting the activity of one of the cells. The question is: how? Conventional and regulatory T cells have similar expression of cell surface receptors, but previous results show that they do have different regulation of intracellular metabolic pathways. Tran and Mensink set out to identify key differences, potentially allowing for selective drug targeting.

"It would be brilliant if we can find a vulnerability that has a relevance for treating cancer"

The cooperation between the two researchers and their colleagues is very clear-cut. The Leiden group is specialized in immune cell biology. Mensink and colleagues grow the T cells and activate them using costimulation by various receptors and feeding them different nutrients. At a predetermined stage in this biological process the cells are lysed and handed over to Tran and colleagues for metabolomics analysis.
Tran is a mass spectrometry specialist, using this method to identify the metabolites secreted by the cells. "Our group employs a method to label them with a heavy isotope. To annotate metabolites correctly we use a large set of standards."

Only advantages

One of the results so far is that both types of T cells appear to be activated by different signals. Regulatory T cells are greatly activated by a receptor called TNFR2, while conventional T cells mainly rely on other receptors for their activation. TNFR2 also influences the processing of the nutrients glucose and glutamine in a different way in the two cell types.
In addition, Tran uses a statistics method called sparse PLS-DA for mining the large amount of data collected by not only metabolomics but also proteomics and transcriptomics methods. "We can learn for example which genes correlate with the response of conventional and regulatory T cells upon specific costimulation."
Mensink sees only advantages in the cooperation: "It is fascinating that they can follow how atoms travel through cells. We both have our own expertise. It's great to meet live, but the video meetings are fine too because they save time."
Tran has over three years of her PhD study to go, but is already interested in a postdoc position, preferably in bioinformatics. "I like the big data side of science," she says.
Mensink wants to complete his research by the end of this year. "After my PhD I'm staying as a researcher in this group to finish some projects. I've already worked here since 2016." ■

Thi Tran Ngoc Minh (left)
Metabolomics, Utrecht University
Celia Berkers group

Mark Mensink
Tumor Biology and Immunology, LUMC
Jannie Borst Group

Teaching immunology with humor

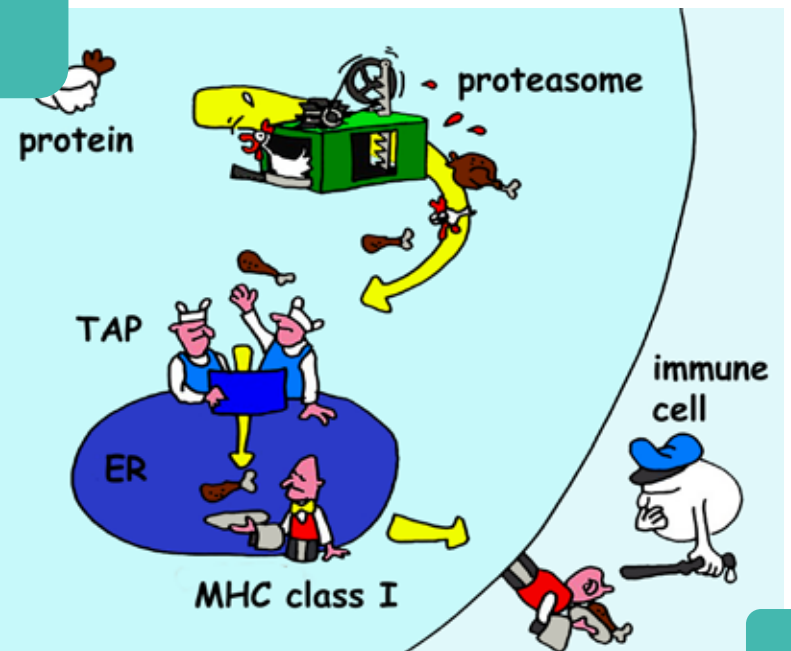
Donor and recipient need to match for organ donation. But what needs to match? And why are still immunosuppressive drugs necessary in case of a good match? Eric Reits and Jacques Neefjes explain it for a broad audience in a 'Comic book adventure'. Everyone is invited to steal and use the cartoons.

"Part of it is fun of course, but it's useful fun," emphasizes Eric Reits, professor of Medical Biology and Neuroscience at Amsterdam UMC. "A message often sinks in better when you bring it with some humor. I often use cartoons in my lectures for professionals, for students and patient foundations."
Reits has drawn as long as he can remember. In his teens he drew over a hundred comic books just for himself. As a student, he made cartoons of events in the classroom and internships, but also of main scientific principles he needed to memorize, and as a PhD student he published the compulsory Dutch summary of his thesis in the form of a comic book. "The doctorate board at Leiden University held a special assemble to discuss if such a summary was acceptable, but after some debate it was accepted," he laughs.
When his former promotor, Jacques (Sjaak) Neefjes, professor of Chemical immunology at Leiden UMC, asked him to illustrate an educational article explaining the crucial role of HLA molecules in our immune system, he said yes. "About half of the cartoons are new, the other half I made before or are updates of previous work."

Characters

Reits uses a number of returning characters in his scientific cartoons. Most prominent is the chicken which represents proteins. In immunology cartoons, the chickens are sawn in pieces by a magician (the proteosome) and parts such as chicken legs are subsequently shown by a waiter (the class I MHC system) to a police officer (cytotoxic T-cell). The officer carries a large baseball bat too fight of intruders. The chickens also pop up in cartoons on Reits' current research field: Huntington's disease. Here, chickens with deformed feet (wrongly folded proteins) get tangled up.

▼ *Upon degradation, protein fragments are shuttled into the endoplasmic reticulum (ER) where they bind MHC class I molecules for subsequent presentation to the immune system.*



"I'm only happy when somebody copies my cartoons"

Pondering on how to translate a particular concept into characters and scenes consumes most of the time he needs, tells Reits. Making a final sketch with pencil takes about twenty minutes, which is colored using photoshop. Reits: "I never add my name or initials. All cartoons are free to use by anyone. I'm only happy when somebody want to use or copy them." With perhaps one little exception. "It hurts a little when cartoons are altered by others. I often think I would have done it a bit differently myself."

Comic book

The educational Comic book adventure on transplantation, autoimmunity and infection control has been published in the journal *HLA: Immune Response Genetics*. The text was written by Neefjes, and each paragraph is illustrated by Reits. Why not telling the complete story in pictures? Reits: "I'd like to do that. Actually, I already started twice to make such a comic book, but I just cannot find the time to finish it."
The Comic book adventure can be downloaded freely at the website of the Leiden Department Cell and Chemical Biology, in over twenty-five different languages including Hebrew, Hindi, Hague (Haags) and Ukrainian (*https://ccb.lumc.nl/comic-book-273*). Neefjes is the driving force between the many translations. "I want to make the information available to all teachers in biology and immunology, therefore I asked colleagues around the world whether they wanted to assist. Everyone can participate. A translation into Arabic is, for example, very welcome," he explains. ■

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The immunology behind Long COVID

Infection with SARS-CoV-2 can result in months, even years, of extreme fatigue, 'brain fog', breathing and other physical and mental problems: Long COVID. Immunologists are discovering remarkable changes in the immune system in patients with this syndrome which provides first clues to possible therapies.

About half of the patients who suffered so severely in the acute phase of SARS-CoV-2 that intensive care was needed, report long term symptoms. Additionally, 5-30 percent of people who had only mild symptoms are diagnosed with Long COVID (also named post-acute sequelae of SARS-Cov-2, PASC). The symptoms span from very mild to severely debilitating and often follow a relapsing–remitting pattern, for example recurrent spikes of fever.
Most Long COVID patients are middle-aged or older, and women are more likely to develop persistent symptoms than men. High body mass index, diabetes II and having autoantibodies at the onset of the acute infection are known risk factors.
Depending on a smaller or broader definition, 20-37 percent of the Dutch population suffers from Long COVID three months after the initial infection. After five months still one in eight reports problems. In time the percentage decreases, however, after two years still some keep (severe) complains.

Brain mass reduction

Although post-acute infection syndromes have been described for more than a century, the causes have remained unclear. Four leading hypotheses in Long COVID include the presence of persistent virus or viral antigens in tissues that drive a chronic inflammation, the triggering of autoimmunity by the acute infection, a disruption of microbiome or virome, and unrepaired tissue damage. A remarkable physiological discovery, made by MRI at King's Colle Hospital (UK), is that brain mass is reduced in Long COVID patients.
Professor of Immunobiology Akiko Iwasaki and co-workers from Yale University published the most in-depth study thus far of Long COVID immunology. Her research group compared the immunological status of a hundred Long COVID patients (>400 days after initial infection) with a similarly large group of people who did not catch the virus or did, but without persistent symptoms. The Long COVID group reported fatigue (87 %), brain fog (78 %), memory difficulty (62 %), and confusion (55 %). Half of them reported negative effects on their employment status.

Exhausted T cells

The most striking result is a roughly halved level in cortisol plasma in the Long COVID group. Cortisol is an immunosuppressant and reductions of this stress hormone have also been reported in chronic fatigue and in traumatic brain injury. Furthermore, there were significant changes in circulating leukocytes. More precisely, increases in levels of non-classical monocytes, activated B cells, double-negative B cells, exhausted T cells, and IL-4/IL-6CD4 T cells, and decreases in conventional DC1 and central memory CD4 T cells. Antibody levels against SARS-CoV-2 antigens were raised, and also against herpesvirus antigens. However, no significant changes were found in autoantibodies.
In interviews Iwasaki emphasizes that Long COVID is not just one illness, but a syndrome with subtypes caused by different underlying biological mechanisms. For effective treatment, it will be necessary to separate patients in subgroups. At the moment, however, subtyping is difficult because of lack of data. Iwasaki is confident, however, that this 'pandemic after the pandemic' will finally provide fundamental insight into the causes of post-acute infection syndromes, and possible therapies. ■

"A roughly halved cortisol plasma level is most striking"

References

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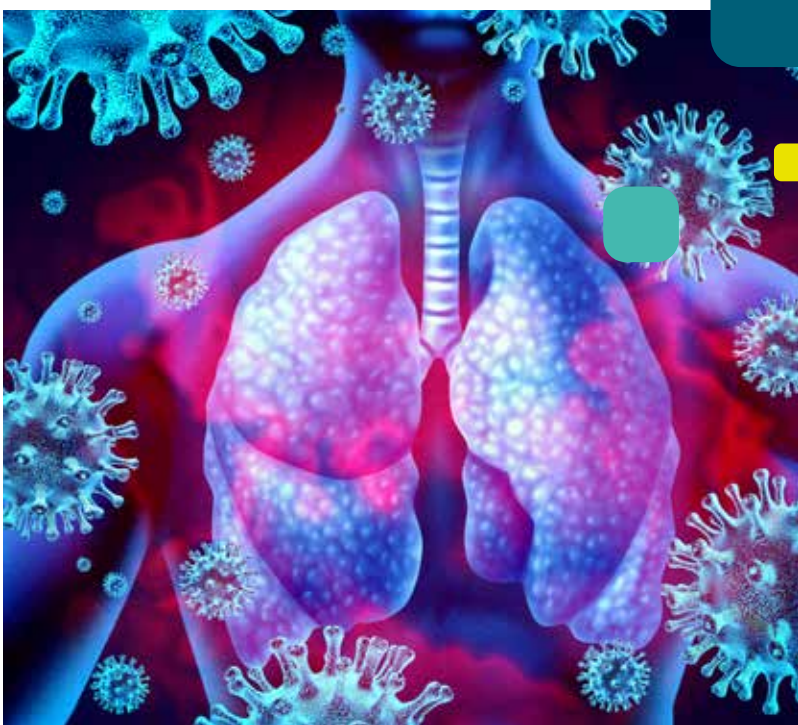
Akiko Iwasaki et al. **Distinguishing features of Long COVID identified through immune profiling** medRxiv 2022.08.09.22278592; doi.org/10.1101/2022.08.09.22278592 (preprint August 10, 2022)

▼ *Long COVID is a syndrome with subtypes caused by different biological mechanisms including notable changes in the immune system.*



Oncode-PACT
Together towards better drug candidates

The just established consortium Oncode-PACT brings together Dutch knowledge in the drug discovery process to improve the success rate in oncology.

In 2017, the Dutch Oncode Institute was established to 'outsmart cancer'. Within the institute 61 research groups from different universities and research institutes work together to study cancer biology at the molecular level. The Oncode-PACT consortium was initiated last April. Within this consortium newly discovered candidate drugs -from Oncode Institute, but also from others- are studied to evaluate and accelerate their chances on the market. "Every good proposal is highly welcome," says Mario van der Stelt. His group contributes probe-technology to study on- and off-target interactions of small molecules with all kinds of human proteins.

"Only one in twenty candidate drugs entering clinical trials in oncology reaches the finish line", tells Mario van der Stelt, professor of Molecular Physiology at Leiden University, principal investigator at the Dutch Oncode Institute, and participant in ICI. In other disease areas, the success rate is higher: one in eight to one in ten. "That's because cancer is actually a collection of diseases manifesting itself differently per individual and because animal models are hardly predictive."
The new Oncode-PACT consortium aims to improve the drug discovery process with advanced methods to study toxicology and efficacy in the preclinical phase. For example, new human organoids are created to study the effects of drug candidates more precise, and artificial intelligence is used to optimize the molecular structure of possible drug candidates. Another aim is to select subgroups of patients who are more likely to benefit from a drug candidate. All efforts must guarantee that the drug candidates entering clinical trials are safer and more resulting in a higher success rate and savings in precious time and costs. Van der Stelt: "Drug discovery research in oncology was quite fragmented in The Netherlands, the consortium stimulates cooperation and bundles expertise."

"The consortium stimulates cooperation and bundles expertise"

Platform technology

An important asset that the group of Van der Stelt contributes to Oncode-PACT is Activity Based Protein Profiling (ABPP), a platform technology to analyze which enzymes are targeted by a drug candidate in the human body, on- and off-target. Van der Stelt: "ABPP allows you to monitor the activities of multiple enzymes simultaneously, using fluorescent or biotinylated probes. It provides information about the selectivity of a drug candidate and therefore of possible toxicology and unwanted side effects."
The technology was invented by Ben Cravatt of the Scripps

Research Institute. Van der Stelt: "When I learned about this methodology, I was immediately interested to use it to learn more about the endocannabinoid system which has been a main line of research in my career. Marc Baggelaar, my very first PhD student, went to Cravatt's laboratory to gain expertise and set up the technology at his return in my lab in Leiden."
Just in time, to start an investigation into the tragic death of a volunteer in a French first-into-human study at the start of 2016. Van der Stelt and colleagues revealed that the drug in question inhibited several off-target lipases, which was overseen in the preclinical phase. The resulting Science paper on the off-targets led to the recognition of the value of the ABPP technology in drug discovery. Van der Stelt: "It is now a standard procedure in most pharmaceutical companies, and we have a lot of cooperations in this field." Within ICI the methodology is used to study which enzymes are involved in multiple sclerosis.

Artificial Intelligence

Van der Stelts research group consists of a mix of chemists and biological chemists who design and synthesize probes to use in 'profiling' proteins, mostly enzyme families. In oncology, the focus is on detecting and following the activity of kinases, which is a large (>500 different types) and often targeted family of enzymes in cancer therapy. However, also probes to study lipases and other hydrolases have been developed. Next to the experimental work, artificial intelligence (AI) is increasingly used to predict activity and selectivity. Van der Stelt: "AI is clearly the future to select the best compounds to be tested in animal models and clinical trials, and to make the drug discovery process mor efficient."
The Dutch National Growth Fund invests in facilities for the Oncode-PACT consortium, for example in equipment for protein production, in tools for screening libraries and in proteomics techniques. Van der Stelt: "Thanks to Oncode-PACT, our platform technology will be upgraded with new mass spectrometers, new microscopes, and synthetic robots. They make it possible to analyze enzyme activity at single cell levels and proteome wide." ■

Oncode Institute

Preclinical cancer drug development facilities above all

It's been called a catch-22. Academic researchers often lack the expertise or financial means to set up the trajectory necessary to turn their discovery into a medicine. Whereas pharmaceutical companies are hesitant to invest in a discovery until it has advanced to a stage in which it is likely to reach the clinic. As a result, many discoveries never get a chance to prove their potential.
The new Dutch public-private partnership Oncode-PACT wants to bridge the gap by accelerating and optimizing the preclinical drug development phase. PACT stand for Preclinical Accelerator for Cancer Treatments. Tale Sliedrecht, co-executive director: "Oncode-PACT brings together experts and infrastructure. Its unique selling point is in novel elements such as organoid models, artificial intelligence, and early access to well-defined patient cohorts, ultimately leading to more effective and saver medicines."
The consortium has received a grant of 325 million euros by the National Growth Fund (NGF) for eight years to set up a national infrastructure for advanced preclinical drug development. NGF supports innovations that drive structural and sustainable economic growth and Oncode-PACT-facilities will be 'open' to all Dutch scientists. The NGF funding is matched, in cash or kind, by the more than 40 participating organizations and companies. The companies, small and large, are actively involved in technology development within Oncode-PACT, e.g., Philips, Immunoprecise, and Mimetas.
Furthermore, any scientist from academia and industry may nominate a particular target for a 'PACT demonstration project'. Sliedrecht: "When you have convincing scientific arguments that targeting protein X with for instance a small molecule or gene therapy will result in a good drug candidate in oncology you can apply for a demonstration project. PACTs independent investment committee will select the most promising projects."
The PACT-consortium intends to create revenues with 'on demand' services in drug discovery, and through returns on PACT-discoveries that successfully reach the clinic. Revenues will be invested in the development of new drug discovery technologies and keeping the PACT-facilities upgraded to the highest level. Sliedrecht: "After eight years, PACT is expected to continue its activities based on this business model."

How to make the perfect scientific poster

The more effective the poster, the greater the interest. But how do you create an appealing poster. That is what ICI PhD students learned during a special workshop supervised by Joost Bakker and Esther Thole, both scientist themselves and specialized in science communication.

For generating interest, the poster must be attractive and informative. “Unfortunately, too often we see hanging long rows of posters all looking the same,” Joost Bakker says. “Usually composed according to the rigid structure: title, abstract, introduction, materials and methods, results, discussion, references.” Therefore, ICI PhD students were trained to create an appealing poster characterized by a concise message, clear explanations using few words, informative images, and an eye-catching design. “A poster is more than a summary of your research. You should envision it as the marketing message, the advertisement of your work,” Bakker explains.

The full-day course took place last May and was very appreciated. One of the students summarizes the workshop as: ‘really eye opening to think about your poster before starting to make it’ and another participant puts in the evaluation: ‘I learned very tiny points and details where previously I did not pay any attention’

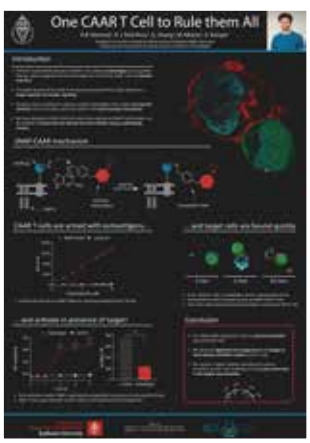
Compete for first place

One month after the course, the students could put their skills into practice by presenting a poster during the yearly ICI Conference. It resulted in an exciting match of which Kevin Venrooij became the winner. He is PhD student at Radboud University Nijmegen and was awarded the 2022 poster prize. On the phone he confirms that the course actually contributed to his honorable first place. “We were put on edge and learned to ‘think first, then act’. Formulate beforehand ‘what do you want to show on your poster’. For me, this meant that during the workshop I came up with my core message and outlined the contours of the poster.” Furthermore, but that is completely outside the context of the course, he enjoyed spending a full day with his fellow PhD students. “A unique opportunity to get to know each other and each other’s work better.”

Why his poster won? It was mainly the eye-catching design, he says. “The black background and bright colors stood out from a great distance. With that, my poster attracted attention!” The black background was actually prompted by the black background of the microscope images he wanted to show. “It prevented the images from having to be placed in separate frames.” An additional advantage turned out to be that the black background automatically led to use short text blocks that could be displayed in striking colors. ■

▼ *Poster winner Kevin Venrooij (r) receives a first edition of ImmunoWars from Dennis de Beeld, one of the developers of the game.*

▼ *The ICI PhD students learn the secrets behind a good poster.*



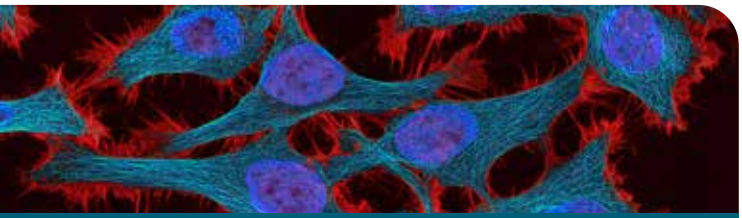
◄ *The winning poster: sleek, beautiful, bright, appealing, attractive, eye-catching...*

ICI Conference 2023: June 9

Safe the date! Following the successful ICI conference 2022 at Naturalis Biodiversity Center in Leiden, ICI will host a conference in 2023 as well. The 2023 edition will take place June 9th, and again at Leiden Naturalis Biodiversity Center. More information about the program and invited speakers will follow soon.

ICI Project Manager

As of November 2022, Sabina van der Zanden succeeded Daphne van Elsland to manage ICI's organizational infrastructure and to provide support to the ICI community. She combines the project management position with her work as a post-doc researcher in the lab of Sjaak Neefjes. Her research is aimed at unravelling working mechanisms of the anthracycline anticancer drugs, in particular on creating chemically modified analogues to reduce the often-serious side effects of these drugs. Together with Pauline Hoftijzer and Jeannette Wolf she is part of ICI's back-office team. Contact: ICI@lumc.nl



Molecule prevents cancer metastasis

An international team of scientists, led by Professor Hermen Overkleeft, has discovered a small molecule that maintains the integrity of tissue around a tumor during cancer. It concerns a sugar-like molecule that reacts with the enzyme heparanase. Once attached, the heparanase enzyme is unable to bind or cut heparin sulfate sugar chains around. In this way, the molecule prevents tumor cells from spreading from the primary cancer site to colonise other sites in the body. The research was published in Proceedings of the National Academy of Sciences (PNAS, 26 July 2022).

Recent publications

Barth ND et al.

Enzyme-Activatable Chemokine Conjugates for In Vivo Targeting of Tumor-Associated Macrophages

Angew Chem Int Ed Engl. 2022 Oct 10;61(41):e202207508. doi: 10.1002/anie.202207508. Epub 2022 Sep 5. PMID: 35993914

Wauters AC et al.

Artificial Antigen-Presenting Cell Topology Dictates T Cell Activation

ACS Nano. 2022 Sep 27;16(9):15072-15085. doi: 10.1021/acsnano.2c06211. Epub 2022 Aug 15. PMID: 35969506 Free PMC article

van Dalen FJ, Verdoes M.

Inhibitory prodrug mechanism for cysteine cathepsin-targeted self-controlled drug release

J Enzyme Inhib Med Chem. 2022 Dec;37(1):2566-2573. doi: 10.1080/14756366.2022.2122961. PMID: 36120947 Free PMC article.

van Elsas MJ et al.

Regulatory T Cell Depletion Using a CRISPR Fc-Optimized CD25 Antibody

Int J Mol Sci. 2022 Aug 5;23(15):8707. doi: 10.3390/ijms23158707. PMID: 35955841 Free PMC article

Ottria A et al.

Hypoxia and TLR9 activation drive CXCL4 production in systemic sclerosis plasmacytoid dendritic cells via mtROS and HIF-2α

Rheumatology (Oxford). 2022 May 30;61(6):2682-2693. doi: 10.1093/rheumatology/keab532. PMID: 34559222

Hagemans IM et al.

Correction to: Multiscale imaging of therapeutic anti-PD-L1 antibody localization using molecularly defined imaging agents Iris

J Nanobiotechnology. 2022 May 14;20(1):229. doi: 10.1186/s12951-022-01306-y. PMID: 35568872

Wörner TP, Aizikov K, Snijder J, Fort KL, Makarov AA, Heck AJR.

Frequency chasing of individual megadalton ions in an Orbitrap analyser improves precision of analysis in single-molecule mass spectrometry

Nat Chem. 2022 May;14(5):515-522. doi: 10.1038/s41557-022-00897-1. Epub 2022 Mar 10. PMID: 35273389 Free PMC article.

Kroos S, Kampstra ASB, Toes REM, Slot LM, Scherer HU.

Absence of Epstein-Barr virus DNA in anti-citrullinated protein antibody-expressing B cells of patients with rheumatoid arthritis

Arthritis Res Ther. 2022 Oct 13;24(1):230. doi: 10.1186/s13075-022-02919-2. PMID: 36229887 Free PMC article.

Column

DOING SCIENCE TOGETHER IS JUST SO MUCH MORE FUN

CELIA BERKERS
ICI EXECUTIVE ADVISORY BOARD

Celia Berkers is professor of metabolomics at Utrecht University

Chemical Immunology is taking center stage these past months. With Carolyn Bertozzi winning the Nobel Prize in Chemistry for 'taking click chemistry to a new dimension and starting to utilize it in living organisms'. Work that inspired many, if not all, ICI researchers. I remember how much I was in awe of her work when I heard Carolyn speak online at last year's ICI conference. And then, just one week before the announcement of her Nobel Prize, Carolyn was touring the Netherlands as part of the Heineken Prize lectures. Hearing her inspiring lecture indeed brought on a whole new dimension. She effortlessly connected chemistry to glycan biology and cancer therapeutics. And somehow managed to make that all sound rather easy. But above all, for me, her lecture showcased the strength and necessity of her interdisciplinary approach.

It is no secret that I am a big fan of interdisciplinary science. Because I am convinced that the best science often emerges at the interface of separate disciplines. Because our own mass spec data become so much more meaningful when we can put them in context together with immunologists or cancer biologists. And most of all, because doing science together is just so much more fun. Within ICI, it has been fantastic to experience first-hand how chemistry is inspired by immunology and at the same time enables the immunology field to tackle truly new questions.

This is all the more true in my own research. The realization that metabolism plays a key role in the functioning of immune cells provides 'my' metabolomics field with many exciting opportunities. Because chemistry - and mass spectrometry in particular - is rapidly becoming the favorite technology to map all these metabolic changes in immune cells. And vice versa, the fact that immunology is all about interactions between cells inspires my team to develop tools to map metabolic traffic between cells. It is funny to see how much a Nobel Prize on click chemistry and glycans triggers in this field. Instead of energy metabolism, glycan biosynthesis now seems to be everyone's favorite metabolic pathway. As Carolyn herself already predicted in a previous edition of this ICI magazine: 'glyco is the next wave'. Now that is one wave I would love to surf - metabolically speaking that is. ■

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 email to info@chemicalimmunology.nl.

Editorial Board	Martijn Verdoes, Sander van Kasteren, Sabina van der Zanden
Text and interviews	Marian van Opstal, Marga van Zundert, Bastienne Wentzel
Coordination and editing	Bèta Communicaties
Lay-out	SPRANQ, Alexander Kraaij
Photography	Erik van 't Hullenaar, Thijs Rooimans, iStock image bank
Printing	Bestenzet BV, Zoetermeer

Contact

LUMC
Einthovenweg 20
2333 ZC Leiden
Tel: +31 71 5268727
ici@lumc.nl

ICI institute for chemical immunology