ICI institute for chemical immunology

Interview

SCIENTIFIC CROSS-OVERS PROVIDE THE RESEARCH QUESTIONS FOR THE FUTURE

JET BUSSEMAKER
Minister for Education, Culture and Science

When it comes to research funding, everyone in the scientific community has an opinion. But looking to the government alone for solutions is too easy, according to Jet Bussemaker, Minister of Education, Culture and Science. "We all need to keep an open mind and not shy away from new approaches and experiments."

The Institute for Chemical Immunology (ICI) is one of a select group of large-scale research projects funded through the Dutch NWO Gravitation Program. The program was started in 2012 to inspire excellent Dutch research groups and bring them together in long-term collaborative research projects to be funded for a period of ten years. ICI Bulletin talks to minister Jet Bussemaker, who is responsible for the Gravitation Program, about the importance of collaboration, the future of Gravitation projects and how we can ensure development opportunities for young scientists.

The Institute for Chemical Immunology brings together two very different research fields: chemistry and immunology. Was this type of scientific cross-over a specific objective of the Gravitation Program?

"The most important scientific insights are the result of collaborations between scientists working in different areas. Furthermore, the big questions our society is facing are too complex to be addressed by a single scientific discipline. So yes, stimulating collaboration between research fields is a key element in the Gravitation Program, and the Institute for Chemical Immunology has chosen a very interesting cross-over to generate new insights and innovative solutions. What I would also like to see are collaborations across the domains. For example between science and the humanities, or between the natural and social sciences." ▶

Contents

What, in your view, constitutes a meaningful collaboration?

"A collaboration should not be driven by a practical, one-way need as in, 'I just need you to perform this experiment or answer this question'. We want to stimulate long-term partnerships that enable scientists to formulate new questions together. Such partnerships are not only needed to tackle current questions, but also to shape the relevant questions for the future. In this respect, ICI is a very good example of what we envision with the Gravitation Program."

In ICI non-academic partners like pharmaceutical companies and patient associations are also involved. Is industry involvement an opportunity or a threat to science?

"Collaborating with partners outside academia offers many opportunities to further develop scientific results into tangible applications that have a clear social benefit. This is also an important part of the Gravitation Program. At the same time, we should always safeguard the independent position of academic research. Scientists should never be pressured when it comes to the content or the timing of their, preferably open access, publications."

"Stimulating collaboration between research fields is a key element in the Gravitation Program"

The funding horizon of the Gravitation Program is ten years. What happens after that term? Can successful partnerships apply for follow-up funding?

"I don't think it would be wise to guarantee funding for an indefinite period of time. Gravitation funding is limited to ten years. We expect successful initiatives to be able to secure the necessary funding from other sources after that period. To me, it is important that initiatives fit within the long-term research lines of the Dutch National Research Agenda, because that provides the context for new research themes that should be addressed. It is quite possible that existing Gravitation projects can generate new partnerships to take on new large-scale research challenges. Such new projects could be eligible for Gravitation funding."

The Gravitation Program supports large-scale initiatives that are internationally leading in their respective fields. There is a trend to fund big initiatives in other national and European programs as well. This automatically favours established scientists with proven track records and large networks. Many scientists, including those involved in Gravitation projects, worry that this trend will lead to less and less room for young researchers to make their mark and develop their own ideas. Do you share that concern?

"There should always be ample room for young talent"

"I am well aware that a relatively small number of scientists in the Netherlands attracts a very large share of the available research budget. And for good reasons: they really are doing outstanding work. But this 'winner takes all principle' is a serious point of concern. It is essential that young research talent has the opportunity to develop into the next generation of leading scientists. On the other hand, large-scale projects offer many possibilities for young researchers to gain experience and carve out a niche of their own. The Gravitation projects have a clear responsibility when it comes to the education and training of young scientists."

Nevertheless, the overall pressure on research budgets has made the competition in the few funding programs that provide personal grants even fiercer. Scoring excellent points on your proposal is no guarantee for funding. Increasing the budgets for these funding schemes seems the most direct way of creating opportunities for young researchers.

"It goes without saying that investing in young researchers is the key to the future of science. But we should stop looking immediately to the government to provide a solution. I think the universities could play a more active role here as well. It is also up to them to ensure career opportunities for upcoming researchers. We all need to keep an open mind and not shy away from new approaches and experiments. That is why I am very pleased that a number of universities are starting to offer scholarships to graduate students. I know this is controversial, and we will of course closely monitor and evaluate the consequences. However, scholarships offer graduate students a more independent position, allowing them to focus more on their own ideas. Whatever the outcome, I am convinced that we should not be afraid to try something new. If we don't dare to experiment, we will keep on facing the same problems."

If you had to choose between funding large programs led by established scientists or young researchers with far-reaching, groundbreaking ideas?

"That is a choice that I don't want to make and I'm not going to make. The reason is simple: we need both. In my view, funding should first and foremost be based on the scientific content of a proposal and that content should align with the Dutch National Research Agenda. But whatever the organisational form of the research project, there should always be ample room for young talent." ■

MERUS EXPLOITS THE POWER OF BISPECIFIC ANTIBODIES

Merus is a clinical-stage immuno-oncology company developing innovative cancer therapeutics that combine the benefits of monoclonal antibodies with the ability to simultaneously bind to multiple targets. "Our bispecific antibodies provide a new generation of cancer medications that activate the natural immune system of the human being," says CSO Mark Throsby.

Merus' product programs are based on the Biclonics® format. The strength of this technology platform is its ability to generate thousands of full-length, bispecific human IgG antibodies addressing combinations of targets expressed by tumour cells. Administration of specific antibodies has proven to be a successful therapy in cancer treatment. "The technique that we develop, however, goes a step further," explains Throsby. "Biclonics® are capable of attacking tumours simultaneously at two recognition domains which not only leads to killing tumour cells but also to recruiting the immune system for prolonged survival."

MeMo®transgenic mouse

Merus NV, listed on the American Stock Exchange Nasdaq since May 2016, was founded in 2003 by Ton Logtenberg, an entrepreneur *pur sang*. As a professor of immunology at Utrecht University, he founded his first company (UBiSys) in1996, which in 2000 merged into Crucell where Logtenberg became CSO. In 2003 he left this rapidly growing and successful pharmaceutical company – by now Crucell has joined Janssen Pharmaceutical Companies of Johnson & Johnson – and he started Merus (Greek for 'zuiver') based on his new ideas in the field of therapeutic antibodies. This initial research ended up with starting Merus' bispecific antibodies program in 2006.

Merus' current technologies encompass the proprietary MeMo® transgenic mouse for the production of its full-length IgG Biclonics®. These bispecific antibodies are robustly produced from a single clonal manufacturing cell line using an industry-standard system. Throsby: "Our Biclonics® are designed to bind to multiple disease-associated targets, thereby eliminating tumour cells more efficiently and preventing tumours from growing."

Merus

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Promising therapy

Merus' lead bispecific antibody candidate, MCLA-128, is being evaluated in a Phase 1/2 clinical trial as a potential treatment for HER2-expressing solid tumours in breast, colorectal or ovarian cancers. "Targeting HER2 and HER3, MCLA-128 acts in two ways," Throsby explains. "First, tumour expansion is stopped by blocking growth and survival pathways and, in addition, tumour cells are directly killed by recruiting and enhancing immune effector cells. Based on the current trials, we may choose to evaluate the use of MCLA-128 for the treatment of additional solid tumours, gastric cancer and non-small cell lung cancer."

Merus' second bispecific antibody candidate, MCLA-117, is being developed as a potential treatment for acute myeloid leukemia (AML). It binds to CD3 expressed by T-cells and CLEC12A expressed by AML tumour cells and stem cells. "In preclinical studies, MCLA-117 has been shown to recruit and activate the immune system's own T-cells to kill AML tumour cells and stem cells."

Life-saving

Besides the above discussed successful progressions, Merus has a pipeline of candidates in preclinical development, including MCLA-158, which is designed to bind to cancer stem cells and is being developed as a potential treatment for colorectal cancer and other solid tumours, and Biclonics® designed to bind to various combinations of immunomodulatory molecules, including PD-1 and PD-L1.

"It is our strategy to use the power of bispecific antibody engineering for developing differentiating therapeutics aimed at substantially prolonging the lives of cancer patients," concludes Throsby. ■

Catching dendritic cells' full attention

PhD project: Exploring crosstalk between CLRs and TLRs using single molecule vaccines

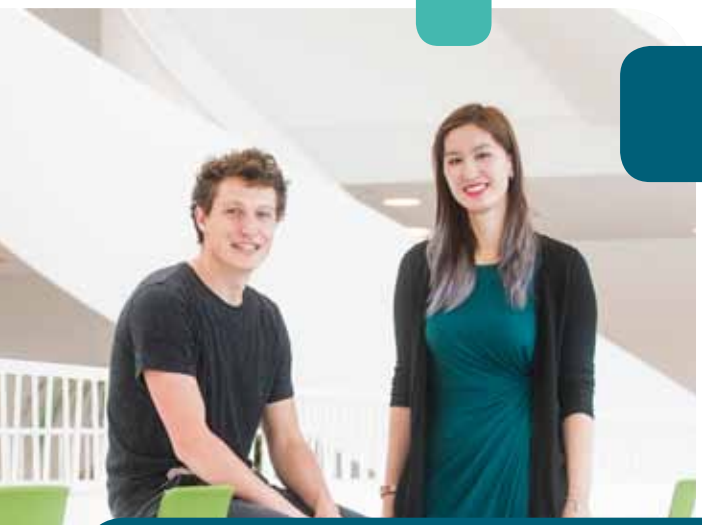
The immune system can recognise and kill cancer cells, but the immune response is often not strong enough to cure. Therapeutic cancer vaccines aim to boost the system. PhD students Eveline Li and Tim Hogervorst search for the minimum requirements for a full response using a single molecule.

"Dendritic cells have always been my favourites," affirms Eveline Li, who holds a master's degree in pharmaceutical sciences. "That's because they are the true conductors of the immune system. It's the dendritic cells that discern danger from innocence at the molecular level."
Unfortunately, these dendritic cells often do not recognise derailed, harmful cells in cancer tumours as evil. Consequently, the immune response is too weak or becomes suppressed. That allows tumours to keep growing and spread. Boosting the immune system from the outside with a cancer antigen may cure cancer as pioneering science has proven. "We are now searching for the minimum requirements to boost the immune system with a therapeutic vaccine," relates Tim Hogervorst, Li's PhD partner. "What is the simplest construct that induces a complete response against a cancer antigen?"

Endless combinations

Hogervorst couples a known antigen to an adjuvant, a substance that stimulates the innate immune system. Such a conjugate must both stimulate the production of specific antibodies and elicit a strong general immune response. The first structures Hogervorst made were small test-peptides containing various mannoses which stimulate the uptake of an antigen. Hogervorst, who holds a master's degree in organic chemistry, prepares these compounds at the bio-organic synthesis laboratory at Leiden University.
"In principle there are endless combinations of antigen and mannoses," Hogervorst explains. "But in daily practice, the limited solubility and reactivity of the compounds restrict the possibilities considerably. It takes about a month to synthesise a complete conjugate."
Li studies the effect of test-compounds and conjugates on dendritic cells at the immunology lab in Amsterdam. At the moment the main question she is addressing runs: does the construct activate dendritic cells or not? Li: "We're in the middle of the design phase. A simple yes or no provides Tim with plenty information for new variants. But we've already noticed large differences in activating power between the various mannoses."

> *"I couldn't do without my chemistry book anymore"*



Tim Hogervorst, MSc
Leiden University, LIC/Bio-organic Synthesis
Gijs van der Marel-group

Eveline Li, MSc
VUmc, Molecular Cell Biology and Immunology
Yvette van Kooyk/ Sandra van Vliet/Juan García-Vallejo- group

Speak, mail, app

The PhD partners speak, mail or app each other every week. Li: "We work with highly defined mannoses. From my talks with Tim, I gain a great deal of insight into the chemistry too. I really couldn't do without my chemistry book anymore. And I've learned that what might seem irrelevant in chemistry, can be relevant in biology, and the other way round." Hogervorst: "We really like to explain things to each other. It's fun, and it turns out to be very useful. And I learn a lot just by peering over Eveline's shoulder in the immunology lab."
Studying the effect of the melanoma antigen gp100 linked to mannoses and another compound that triggers the innate immune system is the next ambition. The project may also be broadened to other antigens.
The most promising antigen-adjuvant combinations will have a fluorophore to trace them in an *in vivo* murine melanoma model or in *in vitro* and *ex vivo* (skin) arrays. Hogervorst: "It's all in the plan, but testing the conjugates in cell assays is already a huge achievement to me. I focus on proof of principles. The patient in the clinic is very relevant, absolutely, but a result may still be twenty years away." ■

Eradicating a false memory from the immune system

PhD project: Trojan horses for antigen-specific B cell targeting in rheumatoid arthritis

In rheumatoid arthritis the immune system mistakes the body's own compounds for foreign material. PhD students Lianne Lelieveldt and Hendy Kristyanto are striving to fix that error. Their tool is a kind of Trojan horse slipping a prodrug into the B memory cells that orchestrate the auto-immune attacks.

Rheumatoid arthritis is a well-known example of an unintended immune response. The error behind this and other auto-immune diseases is 'stored' in B memory cells. These cells produce specific antibodies against the body's own material and direct other immune cells towards it. Depletion or killing of the memory cells would eradicate the problem. However, that is a far from easy task. The harmful B cells can only be discerned from other profitable B memory cell by their affinity for a body's own compound. Targeting a toxic drug towards it would unavoidably affect the body itself. Lelieveldt and Kristyanto explore a new strategy to circumvent the problem by administering two substances. One targets B cells; the other is a protected prodrug containing a peptide that resembles an antigen involved in rheumatoid arthritis. When the two meet, the first removes the protective group that shields the antigen. This will only happen near B cells, guaranteeing that a prodrug will be taken up by the target cells. Once incorporated the prodrug causes cell death, as it releases a cytotoxic drug inside.

Teamwork

"It's a true puzzle," according to Lianne Lelieveldt, PhD student at Radboud University Nijmegen. She has a background in molecular sciences with a specialisation in organic synthesis. Lelieveldt has been working on the prodrug conjugate over the past year and a half, synthesising various peptides with a citrulline-group. Lelieveldt: "I'm searching for the ideal spot to block the recognition of the antigen. It's complex chemistry, as the protecting group must be easily removable by a reactive group attached to the antibody. And deprotection must of course occur without harming the prodrug. This complexity, however, is also what makes it such an interesting and challenging puzzle."
Once Lelieveldt has synthesised a promising conjugate, it is tested at the immunology laboratories at Leiden UMC, where her PhD partner Hendy Kristyanto is located. He holds two master's degrees, in cancer genomics and immunology. "I take the lead, especially when the experiments require a lot of experience. But we try to do as much together as possible." Lelieveldt feels that they are slowly growing together. "Hendy is starting to recognise chemical structures. I'm quickly learning principals in immunology."
While Lelieveldt is synthesising in Nijmegen, Kristyanto is busy with the further characterisation of their target cells, the B memory cells involved in rheumatoid arthritis. "I study what kinds of proteins they express and the ways they trigger other types of immune cells. It's great to work on a project that might actually help many people. And for me the chemistry is cool. I have decided to follow an organic chemistry course too."

"It's a complex but challenging puzzle"

Next step

The cell-depleting capacity of the protected antigen-prodrug conjugate and deprotecting-antibody will first be tested in *in vitro* B cell culture assays. When a successful combination has been found, the next step will be to transfer the successful chemistry to another auto-antigen in rheumatoid arthritis: carbamylated peptides. In contrast to citrulline containing peptides, there is a mouse model available for testing *in vivo* efficacy. However, that's the future; in the coming months or years the two students will be puzzling out how to find the correct chemistry for directing their Trojan horse to the target cells. ■

Lianne Lelieveldt, MSc
Radboud University, Biomolecular Chemistry
Kimberly Bonger/Ger Pruijn-group

Hendy Kristyanto, MSc
Leiden UMC, Rheumatology
René Toes/Hans Ulrich Scherer-group

What 5.2 million cells tell us about our gut

Using a blood sample as a proxy to study what is going on elsewhere in the body is established clinical routine. But it is not without risk. A system-wide mass cytometry study of the intestinal immune system clearly shows that the immune cells in blood are highly distinct from those in the intestinal tract.

The complexity of the immune system never ceases to amaze. "We know that it consists of millions of cells, which we can classify into large groups such as CD4 T cells, M1 and M2 macrophages, B cells and so on," says Frits Koning, professor of immunology at the Leiden University Medical Centre (LUMC). "We also know that there is a large degree of heterogeneity within these major groups. There are, for example, multiple subsets of CD4 T cells that each has its own characteristics. The same goes for the other major groups." Koning and his team are interested in learning which subsets there are within each major group and whether there are associations between subsets of immune cells and auto-immune diseases.

Mass cytometry

Koning's research group focuses on the basic mechanisms underlying immune mediated diseases of the gastrointestinal tract, with a particular interest in celiac disease ('gluten intolerance') and Crohn's disease. "We already know a lot about the major groups of immune cells that are involved in celiac disease, Crohn's and their respective complications, but so far we do not have a way to study what is going on in all the major groups simultaneously. Mass cytometry allows for an unbiased, system-wide view of the immune system on a single cell level. In essence, a mass cytometer is a flow cytometer coupled to a mass spectrometer."

Mass cytometry allows for an unbiased, system-wide view of the immune system

"What makes mass cytometry so powerful is that you can measure for each single cell not only which antibodies are bound, but also how many of each," Koning explains. The team used their selected antibody panel on single cell suspensions derived from blood samples and intestinal biopsies of controls and of patients suffering from either celiac disease or Crohn's or a complication thereof. They were able to collect 102 samples for the mass cytometry measurements, resulting in a set of data points of 5.2 million individual immune cells. Advanced data analysis generated 142 distinct subsets of immune cells. Koning: "This shows that the immune system is far more complex and more heterogeneous than we previously thought."

Blood vs. tissue

Once all the data was analysed, a few things stuck out immediately. "One of the most striking results to me is the sharp distinction between blood and intestinal tissue. This is a clear indication that the immune cells in blood are hardly representative of those in the intestine." Another main outcome is the very clear clustering of patients based on their tissue samples. For example, the celiac disease patients are all neatly grouped together, but are very distinct from the patients with RCDII, the severe and persistent form of celiac disease. "We hope that this type of study will increase our understanding of the clinical differences in patients diagnosed with the same disease," Koning concludes. "If we manage to grasp these differences, I think we can really improve the way we treat patients." ■

The research has been published in Cell (17 May 2016) and previously discussed in NPC Highlights (July 2016).

◄ *Frits Koning presented this research at the ICI Annual Conference (April, 2016), where he got a lot of attention from the public.*

New scientific insights arise at the interface of disciplines

Originally he is a chemist, but over the course of his career he focused more and more on biology. Today he combines the two disciplines. "Cross-border curiosity is absolutely necessary to obtain real scientific progress," explains Jan van Hest, professor of bio-organic chemistry.

Van Hest started exploring and pushing boundaries during his doctoral research on supramolecular chemistry and dendrimers in the Bert Meijer group. Later, as a postdoc at the University of Massachusetts in Amherst (USA), he familiarised himself with protein engineering. Then at the end of the nineteen nineties, he joined DSM to work on the development of innovative material concepts. "At that time the importance of 'nature as a source of inspiration' was fast winning ground, and for me it was the basis for my further scientific work: combining chemistry and biology."
In 2000 he became professor of bio-organic chemistry at Radboud University Nijmegen.

Polymersomes

Van Hest aims to create bio-inspired materials and processes in order to combine the functionality of biological systems with the flexibility and robustness of synthetic structures. The hybrid structures are applied as artificial organelles and carrier systems in drug delivery. "In the past years we have successfully developed polymer vesicles, so-called polymersomes, into highly functional nanocapsules for biomedical applications."
These polymersomes have been modified with a range of different biomolecules, such as cell-penetrating peptides, peptides that allow crossing the blood-brain barrier and nanobodies. "Our control over their size, shape and surface functionality allows us to apply these polymersomes as scaffolds in immunotherapy." Actually, they combine chemistry and immunology aimed at designing artificial dendritic cells. "In that way, we worked on chemical immunology *avant la lettre*," laughs Van Hest.

Fight against cancer

"Dendritic cells are known to be key players in mediating the immune response. Applying these cells for boosting the immune system comprises a relatively new therapy in the fight against cancer," says Van Hest. "Usually the patient's own dendritic cells are used. They are activated outside of the body and then reintroduced into the bloodstream. But this method is very complex, sensitive, and it takes weeks to grow these cell lines outside of the body."
To make this approach quicker, which is a condition for large-scale clinical application, Van Hest and his colleagues Carl Figdor and Alan Rowan make tiny, synthetic molecular scaffolds that carry a small peptide fragment. These scaffolds

▼ *Jan van Hest is closely involved in both the Research Centre for Functional Molecular Systems (FMS) and Institute of Chemical Immunology (ICI).*

"One plus one equals much more than two"

are used to present the peptide fragments as a signal to the body's T-cells. "We now have the technology to determine the 3D shape of polymer particles and to control the coupling of peptides. Ideally this will be a peptide that is characteristic of the patient's tumour cells," explains Van Hest. Although the first generation has been tested successfully in cell and animal studies, he notes that clinical application is still some time away. Tests in humans usually take years. "But if these are successful, we could use this technology to 'vaccinate' people against cancer."

Change-over to Eindhoven

Last September Van Hest joined the Technical University of Eindhoven, where he starts the new Bio-Organic Chemistry group. He continues close cooperation with Nijmegen colleagues, especially with the medical specialisations at the Radboud UMC. "The change-over means an intensification of the collaboration between the two universities," he states.
At Eindhoven his work will focus on the cutting edge of (polymer) chemistry and biomedicine. "Again, challenging research at the interface, and I'm absolutely convinced that it will lead to new molecules, materials and techniques which in turn may provide promising applications in biomedical sciences." ■

Chemical immunology network in the UK

The time just seems right for chemists and immunologists to meet

You are an ambitious PhD student, but unlike many a colleague you don't have the opportunity to present your results to the right audience. What to do? Leanne Minall of Oxford University UK decided to organise the ideal meeting herself. It resulted in one of the first conferences in chemical immunology and in a national network: Mol.i.G.

Leanne Minall currently works as a postdoc at Oxford University after having finished her PhD in chemical immunology. "I choose my PhD project because I wanted to follow the sugars I synthesised all the way: from my bench to the cell. So I needed to jump the barrier with biology."
Together with two other young PhD students in the field, Kim Wals and Thomas Wright, Minall started organising a meeting for chemists *and* immunologists.
The positive, enthusiastic replies from the invited speakers kept coming in, with suggestions for even more speakers. The small meeting quickly grew into an international two-day conference with over a hundred participants: the Oxford Chemical Immunology Conference, which took place 4-5th April 2016.
Does Minall have an explanation for the overwhelming interest? "Immunology has reached a point where molecular precision is necessary to gain further knowledge. You may be able to create a fantastic immune response, but why does that happen? The exact characterisation of the structures involved is often lacking."
However, the interest certainly also came from the chemists, emphasises Minall, who holds a master's degree in chemistry herself. Chemists have created a range of tools and tricks. Complex problems in immunology are interesting and highly relevant applications for their toolboxes.
Minall: "The time just seemed right for chemists and immunologists to meet. We are probably witnessing the dawn of a new discipline."

> ***"The meeting became the kick-off of a new network organisation"***

Mol.i.G.

The initiative received immediate support from Minall's PhD supervisor, chemistry professor Ben Davis. When the plans expanded, the Royal Society of Chemistry and the British Society for Immunology also got involved. The meeting even became the kick-off of a new network organisation: Mol.i.G., or 'Molecular Immunology Affinity Group'. Why not *Chemical* Immunology Affinity Group? It was a strategic choice, Minall explains: "To me they are synonyms. However, some immunologists might be scared away by the word chemistry. The gap is real."
She is referring to the different journals immunologists and chemists read, the different meetings they attend, and the different scientists they follow and meet. "At the conference

an editor of immunology journals concluded that they had already published research on chemical immunology but didn't realise it. It's more or less a labelling problem."
Organising the conference and starting Mol.i.G. was a huge task in addition to writing up her thesis, admits Minall, but certainly worthwhile. She's heard of several new collaborations. "And I got to see the full scope of the field myself. That certainly has expanded my own research as well, and it is really wonderful to see your chemistry coming to application."

Teaming-up

During the preparations, Minall discovered that their conference would not be the first specifically devoted to chemical immunology, as they had announced. That absolute first was the annual conference organised by ICI just a few days earlier in Amsterdam. Minall attended that too. "ICI is a great initiative. The idea of teaming up a chemist and immunologist in a PhD project is just brilliant. I love it." But the Dutch and British national initiatives have different funding. "We'd certainly love to have a research budget like ICI. But for now, we are just a network organisation."
Anyone in the UK can become a member of Mol.i.G. The counter is almost on 200. Members receive a regular newsletter with information on upcoming activities. Mol.i.G. has also started to build a worldwide directory on the internet of groups working in chemical immunology. Minall: "Anyone can send us an email with a brief description of the research group. A complete overview of the field is very valuable to everyone."
Mol.i.G. is also involved in chairing the session of chemical immunology along with Carl Figdor at the up and coming UK/NL immunology summit next December (joint BSI&NVVI Congress, see pg 11). A further Mol.i.G. initiative concerns lectures in chemical immunology. Minall: "We are preparing a series of tutorials: relevant chemistry for immunologists, and vice versa." A second international conference is also in the pipeline, perhaps in the USA. "Some conference participants from the USA launched the idea. It would be very nice to cooperate," says Minall. "When even more countries start a network group in chemical immunology, we could work together to stimulate knowledge transfer and cooperation worldwide." ■

> *"We are probably witnessing the dawn of a new discipline"*

An inspiring experience

Sander van Kasteren (group leader in Bio-organic Synthesis at Leiden University and ICI participant). He was an invited speaker at the Mol.i.G. kick-off conference in Oxford. He reports.

"I'm British educated. I studied and worked in the UK from 1996 until 2010. Therefore, the lines between my group, Oxford University and several other UK groups in chemical immunology are short. So I wasn't that surprised by Leanne Minall's invitation, but I certainly was a little daunted looking at the program. She managed to gather some pretty renowned names in immunology, which is a bit intimidating for a chemist. Especially as my talk was on signal bias resulting from widely used approaches in antigen processing research. The tools currently available to immunologists for imaging proteolysis in the immune system can give only partial answers to the immunologists' questions. Perhaps that's quite a bold statement coming from an 'outsider.' But people were very interested and asked many questions."

Exchange of ideas

"All through the conference, the atmosphere was very open and stimulating. People were really anxious to meet each other and exchange ideas. Several beginning group leaders (like myself) got the opportunity to speak, and a lot of the research they presented was still unpublished, which led to much discussion and interaction, almost like in a workshop. The three young students choose a truly bottom-up approach which worked out well. Very refreshing. For many participants the conference was also a first meeting with 'the other side.' That means you need to adjust your regular presentation. Your introduction needs to be longer for a mixed audience. You have to explain the problem you want to solve thoroughly before you start elaborating on the details. But then you need to go in full depth, even when the immunologists start shifting uneasily on their chairs, looking at your total synthesis."

Unique field

"It is a good thing that the UK scientists involved in chemical immunology also started to organise themselves, and I see signals that the USA is following. At the most recent meeting of the American Chemical Society, an inaugural section 'Chemical Immunology' was created. Chemical immunology will always be a part of chemical biology. The coming years will reveal if it remains a side-branch or develops into a unique field of research with its own networks, meetings and journals." ■

FameLab 2017

Increasingly, researchers are asked to explain their research in a (very) short timeframe and to an audience of laymen. Quite a challenge to explain something you are unravelling for four years in just a few minutes! But mastering the skill of pitching is very useful for obtaining personal grants and, of course, to get attention on your next birthday party!

Science communication competition

Together with the Cheltenham Science Festival, the British Council organises a contest for researchers: FameLab. FameLab is one of the biggest international science communication competitions in the world, designed to engage and entertain by breaking down science, technology and engineering concepts into three minute presentations. Contestants from around the world take part armed only with their wits and a few props – the result is an unpredictable, enlightening and exciting way to encourage your curiosity and find out about the latest research. They will be judged by leading researchers, media personalities and science policy makers on the content, clarity and charisma of their presentation.

Local competition

FameLab was started in 2005 in the UK by Cheltenham Science Festival and has quickly become established as a diamond model for successfully identifying, training and mentoring scientists and engineers to share their enthusiasm for their subjects with the public. Working in partnership with the British Council this global competition has already seen more than 5000 young scientists participating in over 25 different countries. Together Cheltenham Festivals and the British Council co-produce the FameLab International Grand Final. Each national winner goes on to compete against other contestants from around the world at The Times Cheltenham Science Festival in June. In the Netherlands several Universities take part in FameLab, amongst others Erasmus University Rotterdam, University of Amsterdam, Utrecht University and Leiden University.

FameLab is calling all scientist with a passion for public engagement to participate in FameLab 2017! If you would like to take part in the competition in the Netherlands, you can visit the British Council's website for more information or have a look at the website of your own University. ■

News

Prestigious award for NKI researcher Ton Schumacher

Ton Schumacher (NKI and ICI executive board member) has been named recipient of the 2016 William B. Coley Award. This prize is awarded yearly by the American Cancer Research Institute (CRI). It was instigated to honor scientists who have made highly important contributions to the field of cancer immunology. Schumacher receives the award for his outstanding work on the question how immune cells are able to identify and subsequently attack cancer cells.

Joint BSI & NVVI Congress 2016

On 6–9 December 2016 the BSI/NVVI Congress takes place at the Arena Conference Centre in Liverpool, UK. This is a joint event between the British Society for Immunology and the Dutch Society for Immunology, bringing together two of Europe's most established immunology organisations. BSI/NVVI expect to welcome over 1,000 delegates from the UK, the Netherlands and across the globe.

Neefjes and Ovaa move from NKI to LUMC

After a very successful career at the NKI, Jacques Neefjes and Huib Ovaa decided to continue their research at the LUMC. On September 9th, the NKI honored Jacques Neefjes and Huib Ovaa with a Farewell Symposium. Neefjes joined the NKI in 1991 as postdoctoral fellow and in 1993 he started his own research group. Ovaa joined the NKI in 2004 as junior group leader.

Recent publications

Linnemann C, van Buuren MM, Bies L, Verdegaal EM, Schotte R, Calis JJ, Behjati S, Velds A, Hilkmann H, El Atmioui D, Visser M, Stratton MR, Haanen JB, Spits H, van der Burg SH, Schumacher TN.

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Column

WHERE IMMUNOLOGY AND CHEMISTRY SHOW THEIR SYNERGY

I have always regretted not packing more chemistry into my own training. Although my bachelor's degree (in 1975) lists biology and chemistry as its two main components, I would not be able today to perform a retrosynthetic analysis or comment in a meaningful manner on a clever new synthetic strategy. My biggest accomplishment at the bench has been the completion of the first 12 steps in the synthesis of 1-deoxymannojirimycin, an iminosugar, when this was still a challenge (certainly for me). This deficiency in my own scientific upbringing notwithstanding, it makes me proud that over the years I have managed to attract a cohort of talented chemists sufficiently adventurous to throw their lot in with mine. In a desire to apply their chemical skills to biological problems, some of the founders of the ICI have worked with me and developed into the only type of prescient scientists that could have gotten this exciting endeavour off the ground.

Why is the ICI important? First of all, the chemistry-immunology interface provides immunologists with much needed precise molecular tools. Emphatically, the goal need not be the design and synthesis of a small molecule with drug-like properties. The generation of tool compounds with which to probe biological pathways is just as important, so that we better understand how cells work. There is no better area to apply this to than immunology with its ready access to the molecular and cellular players, and of course its clinical relevance. Immunologists must be educated on basic principles of chemistry so that a dialogue can start with the synthetic chemists and they not be led astray by the biologist's faulty understanding of what is possible at the bench and in the fume hood. On the other hand – and without deprecating the beauty of pure chemistry for chemistry's sake – there is satisfaction to be derived from seeing one's work find a meaningful application in everyday life.

HIDDE PLOEGH

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Let's take the example of adjuvants or our understanding of innate immunity more generally: the synthesis of imidazoquinolines and derivatives such as TLR7 agonists and the identification and synthesis of cyclic dinucleotides such as STING activators. These are but two examples where immunology and chemistry show their synergy. The clinical application of boronic acid esters and new generations of proteasome inhibitors are true therapeutic breakthroughs, but: proteasome inhibitors were research tools first and drugs second. I am convinced that the ICI will make a meaningful contribution to the future of both chemistry and immunology, in the Netherlands and beyond.

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 Organisation 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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