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VIB

RESEARCH IN TIMES OF CORONA

EVERY CRISIS CREATES NEW OPPORTUNITIES

Jo Bury

Marijke Lein

Recent breaking news at VIB was the change in the general management. Johan Cardoen stepped down from his role as managing director for health reasons. Jérôme Van Biervliet will follow in the influential footsteps of Johan, who will remain active in a consulting role. Enjoy reading the double interview with Johan and Jérôme on page 23.

Jérôme didn't start up in easy times. COVID-19 has catapulted us all into a new reality. In the past months, we had to remodel both our professional and personal lives. With the lock-down, we had to strictly limit the lab activities. Now, we are starting up again with ups and downs. Other activities were re-organized and adapted to the circumstances. Training at VIB moved online for all one-to-one training sessions like career counselling. VIB conferences will follow this virtual trend.

It is great to see how fast people can adapt to new situations, no matter how difficult these might seem. Besides working from home (facilitated by the enormous support from the IT teams), we realize that virtual meetings work quite well, with effective decision-making in reasonably short time periods. Maybe we will continue doing so in the future. However, these virtual meetings can sometimes be less efficient for creative thinking and strategy.

But, every crisis creates new opportunities. For instance, VIB was requested by the federal government to provide extra capacity for COVID-19 testing. It was heartening to see over 600 volunteers register for this. A VIB-taskforce quickly mapped the available infrastructure and expertise, and assembled selected volunteer teams to contribute to COVID-testing. Together with Ghent University, Ghent University Hospital, Anacura, and Biogazelle they processed about 120,000 samples, to which the VIB volunteers contributed greatly with over 30,000 samples processed. We tested half of all residents and personnel in the residential care homes in Belgium!

A great example of the VIB slogan 'from science to value' was the work of VIB scientists quickly turning their expertise to the fight against SARS-CoV2. Read about the contributions of Bart Lambrecht and Peter Carmeliet about life saving clinical trials and the development of new treatment options. The most remarkable example was the work by the teams of Xavier Saelens and Nico Callewaert, leading to promising drug candidates to treat the disease. These efforts have already led to the development of a new start-up company, ExeVir Bio, which will develop these drugs into the clinic: read all about it on page 4.

It has been a turbulent period, that much is certain. However, we are very happy to have witnessed the resiliency of VIB and its people, and we remain convinced that together we will be able to face whatever challenges that come our way.

Jo Bury (managing director VIB)
Marijke Lein (HR director VIB)

Thanks to the efforts of its employees, VIB was able to keep going strong during the pandemic – both in and out of the lab

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At lightning speed

TOWARDS A COVID-19 TREATMENT

Fiona du Monceau (COO), Dominique Tersago (CMO) and Torsten Mummenbrauer (CEO)

VIB leverages Belgian strengths to bring SARS-CoV-2 nanobody spin-off ExeVir Bio to life

Four years ago, scientists from Xavier Saelens' lab (VIB-UGent Center for Medical Biotechnology) developed an effective antibody – with the help of Winter the llama – to fight the SARS-CoV-1 virus. When COVID-19 exploded onto the global scene in January 2020, VIB raced against the clock to set up a spin-off company with an audacious ambition: to initiate clinic tests with a novel COVID-19 treatment based on this antibody by November 2020 and to start commercial production by mid-2021.

PART 1:
building the foundations of a legendary spin-off
Before the new spin-off saw the light of day, the tireless efforts of VIB personnel and innovative partners were crucial in paving the way and setting the record-breaking pace needed to move from molecule to manufacturing in a handful of months.

Joining forces across facilities, universities and functions
The first step was an intense collaboration between the antibody engineering group of Nico Callewaert's lab (VIB-UGent Center for Medical Biotechnology) and VIB Discovery Sciences (Catelijne Stortelers and Bruno Dombrecht) to accelerate the development of a preclinical lead molecule.

With special financial support from the cabinet of Hilde Crevits, Flemish Minister for Science and Innovation, VIB successfully financed the necessary hamster efficacy studies with a contract research organization. These results provided crucial evidence that the antibody can effectively fight off COVID-19 and complemented the results of an academic collaboration with the lab of Johan Neyts at KU Leuven.

Achieving a patented world first
At the same time, colleagues from the VIB Innovation & Business team (Griet Den Herder and Jan Demolder) took the initiative to get the valorization part rolling. As a first step, the IP team filed several patents claiming the innovation in a very proactive manner – only a few weeks after the release of the first SARS-CoV-2 sequence. Thanks to their tireless dedication, VIB was likely the first institute worldwide to patent an antibody to fight SARS-CoV-2.

"VIB was likely the first institute worldwide to patent an antibody to fight SARS-CoV-2."

Jan Demolder (Head of IP)

Next, the Business Development team (Tim Van Acker and Jan Staelens) explored different routes to commercialization and formalized all the necessary underlying agreements with the different collaborating academic institutes. Third, the New Venture team (Katrien Swerts and Griet Van Poucke) started drafting the business plan for a possible spin-off company, organized the fund-raising and due diligence process with venture capital investors and negotiated all the necessary financing agreements.

Even under 'normal circumstances', these tasks are already formidable challenges. But in the case of what would become ExeVir Bio, they were successfully

Xavier Saelens

performed during the first national lockdown in Belgium and at record-breaking speed!

Boosted by proactive advice from international regulators
An important stride was taken when Jérôme Van Biervliet, Managing Director of VIB, succeeded in convincing Dhaval Patel, CSO of UCB, and his management team to start a collaboration in which UCB colleagues initiated the necessary work to help design and to produce the lead antibody using the CMC (Chemistry, Manufacturing & Controls) process for biologicals. This is a highly engineered activity that is impossible in an academic setting and that requires top-notch expertise.
UCB committed to delivering the first batch of the therapeutic antibody for the first clinical studies – a significant investment.

This collaboration was extremely productive and allowed VIB, for the first time ever, to compile a dossier aimed at receiving regulatory advice from authorities in Belgium and Germany. This advice was crucial in making decisions early on to accelerate development towards testing in patients.

Dominique Tersago

Torsten Mummenbrauer

Securing the dedicated support of specialized partners and funders
"It has been a great experience to be part of the team, along with Catelijne, Bruno, Xavier and Nico, that helped engineer, characterize and test this potential new therapy for COVID-19 as well as prepare for the journey to the regulators and then to the clinic," asserts Alistair J. Henry, Senior Vice President & Head of Discovery Science at UCB. "This was a true collaboration right from the start, with ideas and expertise being shared by scientists from both UCB and VIB, driven by a real sense of purpose and urgency and focused on a tremendous goal."

Another important milestone was when Fund+, led by Philippe Monteyne, stepped in as a lead investor to raise the funds needed to take the ongoing trial to clinical testing as quickly as possible. Soon afterward, an ambitious investment syndicate made up of UCB Ventures, Vbio-Ventures, FPIM and several Belgian family offices successfully raised 23 million euros in the first A round. This achievement was essential in recruiting a top-notch management team for the spin-off in record time.

"This was a true collaboration right from the start, with ideas and expertise being shared by scientists from both UCB and UCB and VIB, driven by a real sense of purpose and urgency and focused on a tremendous goal."

Alistair J. Henry, Senior Vice President & Head of Discovery Science at UCB

PART 2:
the leaders of the new company share their vision
Enter ExeVir Bio, led by Torsten Mummenbrauer (CEO), Dominique Tersago (CMO) and Fiona du Monceau (COO) – each with experience in critical domains for this new biotech player.

What led you to dive into a brand-new company at such short notice?
Torsten: "I was the pandemic lead at GlaxoSmithKline, and when VIB invited me to embark on another pandemic journey, I jumped at the chance to make a difference in the fight against SARS-CoV-2. But it was clear from the outset that this couldn't be a one-man show. We immediately started searching for leadership team candidates and were fortunate to bring Dominique and Fiona on board."

Fiona: "I came in from the investor side – one of the funds supporting ExeVir Bio is UCB Ventures. We were deeply passionate about this initiative to have an impact on the pandemic. I personally wanted to be more hands on involved to help build ExeVir, bringing me back to the initial reason I moved into this industry, a fascination with viruses, specifically Ebola at the time. It was a no brainer when I was approached to join."

Dominique: "While we come from different backgrounds, we are defined by the drive to act rather than to observe in the face of this pandemic."

"While we come from different backgrounds, we are all defined by the drive to act rather than to observe in the face of this pandemic."

Dominique Tersago, CMO of ExeVir Bio

Torsten, you describe ExeVir Bio as an unusual spin-off. Why?
Torsten: "It's unusual because it was set up within the context of an unfolding pandemic situation; things moved extremely quickly. A typical spin-off raises funds for six to nine months, which generally involves lots of travel and meetings with investors. Then, there's the process of finding a strong leadership team, arranging the legalities, visiting the notary and getting everything stamped, etc. In our case, the entire setup process happened almost completely virtually and in a matter of weeks."

Dominique: "Even though we met each other face to face for the first time at the beginning of July, we were already highly focused and engaged as a team. The speed at which we set up the company and established investors reflects our shared sense of responsibility: we all wanted to apply our expertise to make a real difference as quickly as possible. Anybody unsuited to this type of environment and this urgency would have dropped out early on in the process."

"Also important was the strength of the Belgian biotech and pharma sectors – as well as the research – which was all in place and ready to accelerate the process."

"Players from across Flanders and Belgium came together over handshake agreement to ensure not just a quick start-up, but also accelerated manufacturing and formulation. VIB played a key role here."

Fiona du Monceau, COO of ExeVir Bio

Fiona: "Absolutely, players from across Flanders and Belgium came together to ensure not just a quick start-up, but also accelerated manufacturing and formulation. VIB played a key role here, as Xavier Saelens, Nico Callewaert, Catelijne Stortelers and Bruno Dombrecht performed all of the basic science and preclinical work needed to develop the SARS-CoV-2 nanobody® in preparation for manufacturing scale-up – which is now in the hands of UCB."

How does the nanobody developed by ExeVir Bio act against the SARS-CoV-2 virus?
Torsten: "This nanobody targets larger proteins, just like antibodies do. But because of its miniscule size, it can reach into small **clefts** on the surface of the SARS-CoV-2 virus whereas human-derived antibodies cannot, blocking its ability to bind to human cells, replicate and cause the COVID-19 disease."

Fiona du Monceau

"The nanobody® that we are developing is miniscule, enabling it to reach into tiny clefts on the surface of the SARS-CoV-2 virus that normal antibodies cannot, blocking its ability to bind to human cells."

Torsten Mummenbrauer, CEO of ExeVir Bio

Dominique: "Our nanobody isn't just tiny, though. It is also extremely specific, binding to a unique contact site on the surface of the virus that appears to be conserved by many SARS-CoV-2 mutations."

Fiona: "Our lead candidate is an antiviral treatment that is administered to people who are already infected, not a traditional vaccine. A vaccine works by exposing the immune system to the virus, 'training' it to effectively fight off the virus. As a first-line treatment, the ExeVir nanobody will be instrumental in safeguarding the health of people at high professional or medical risk of severe illness."

Has the company's status as a VIB spin-off led to advantages for ExeVir Bio's growth plans?
Torsten: "The value of our collaboration with VIB cannot be overestimated. Compared with my past experience with other research institutes, I find it very unique that VIB is so involved in the funding and development of a biotech product. They were responsible for identifying a manufacturing partner, coordinating plenty of steps along the road to commercialization. The VIB scientists are still 100% supportive."

"VIB supported us on the manufacturing side – but also with trials, disease model studies, regulatory prep work – all of these aspects were coordinated by VIB scientists. They have shown exceptional dedication."

Dominique Tersago, CMO of ExeVir Bio

Dominique: "And it's not just on the manufacturing side that VIB supports us, but also on the nonclinical and clinical preparation side, the disease model studies, the regulatory prep work to ensure the quick, low-risk development of an antiviral treatment – all of these aspects have been coordinated by VIB scientists. They have shown exceptional dedication to making this a real, accessible product."

Fiona: "VIB also has strong ties with partner institutes involved in the preclinical, *in vitro* and *in vivo* studies. This strong spirit of scientific collaboration is a huge benefit for ExeVir Bio. We already have our compound and we will kick off manufacturing this summer. We're years ahead of where most biotech start-ups would be at this stage."

How close are you to having the antiviral treatment on the global market?
Fiona: "The pandemic is unfolding now. It's an unusual situation where we have to accomplish in a year and a half what, under normal circumstances, would take many years – and regulators are willing to help."

Dominique: "On the assumption that we have our clinical data ready from a Phase II study next year, we anticipate an accelerated approval process. We need to be ready to provide the treatment globally – not just to the developed world."

"We plan to start commerical production in the first half of 2021 and start shipping the antiviral treatment by the end of 2021."

Torsten Mummenbrauer, CEO of ExeVir Bio

Torsten: "This means initiating commercial manufacturing activities as soon as possible. As soon as the manufacturing is fully developed by our partner UCB, we plan to start commercial production in the first half of 2021 and start shipping the treatment by the end of 2021, with the support of international partners and funders."

What are your ambitions for ExeVir Bio beyond the COVID-19 pandemic?
Torsten: "The future of ExeVir Bio is closely linked to VIB, as we plan to establish a close R&D collaboration. In our first year, our focus will be on fighting the coronavirus, including developing a next-generation antibody that is even more specific."

Fiona: "Our long-term goal is to build these nanobody-based antiviral treatments out into a rapid-response platform – not just for COVID-19, but for other viral diseases as well. In order to move quickly, we will balance internal and external resources, with the ambition of bringing more resources and talent in house over the next few years and establish a durable company in our Belgian ecosystem."

And finally – how did you choose the name of the spin-off?
Torsten: "I'm not sure we want to get into this! (laughs) It was actually a pretty complex process. We held a vote among all scientists and personnel involved in the project based on a list of options that came up during a brainstorming session. This list was thinned out quite a bit by the trademark guys, though."

Dominique: "The 'Ex' is for 'excel', 'execute', 'exterminate' – and the 'Vir' is pretty clear."

Fiona: "We wanted something short, catchy, energetic, with a connection to what we do: excel at what we do and destroy viruses. Mission accomplished."

"For the name of our company, we wanted something short, catchy, energetic, with a connection to what we do: excell at what we do and destroy viruses. Mission accomplished."

Fiona du Monceau, COO of ExeVir Bio

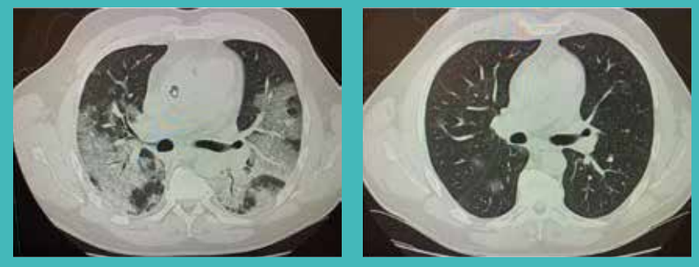
We wish the team every success in their virus-exterminating ambitions and look forward to future collaborations. Interested in the latest news on ExeVir Bio? Follow them on **linkedin.com/company/exevir** and visit their website at **exevir.com**.

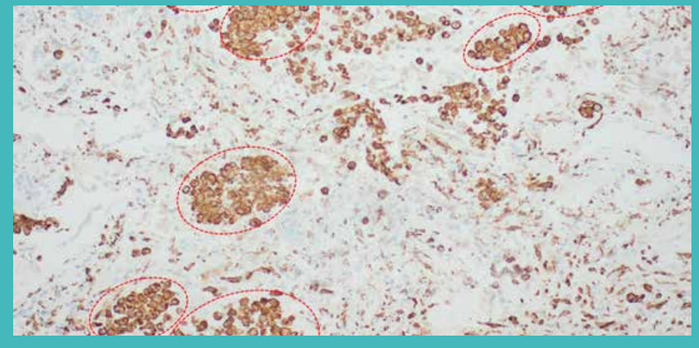
Responding to

A CRISIS SITUATION

Diether Lambrechts

Jeroen Raes





VIB and COVID-19

VIB wouldn't do itself justice if it would not show resilience and flexibility in times of crisis. The current COVID-19 pandemic creates many challenges with regards to both mitigation and treatment. VIB aims to contribute to contain COVID-19 and is currently assessing all the ways in which the institute can provide solutions concerning diagnostics and research towards treatments. Many of VIB's research groups have been actively working towards designing and performing studies to gain insight into the immune response to COVID-19 and how this could be improved, specifically in the most severely affected patients.

On the one hand, there is the research of the Xavier Saelens lab on antibodies that tackle the SARS-CoV-2 virus which is described further in this issue of VIBtimes. On the other hand, we have been able to use some funds still available in the Grand Challenges Program to finance three projects.

VIB's Grand Challenges Program tackles COVID-19 from several angles

Specifically, three approaches will be pioneered through the rapid development within the purview of VIB's Grand Challenges Program. These projects were implemented in close collaboration with hospitals and hospital laboratories. These partners take the lead in the clinical trials and have placed priority on the regulatory evaluation and approval of these projects, which means that these three proposed studies were initiated quickly.

The three projects are:

CONTAGIOUS TRIAL

Led by Joost Wauters (University Hospital Leuven)

A prospective observational clinical study by University Hospital Leuven, VIB, and KU Leuven to gain more insight into the immune response during the different stages of COVID-19 infection, allowing identification of host factors that contribute to (hyper) susceptibility of patients. The study includes specific patient groups and collects an extensive database of bodily tissues for downstream analysis, for example single-cell immunophenotyping by Diether Lambrechts (VIB-KU Leuven Center for Cancer Biology) and microbiome analysis by Jeroen Raes (VIB-KU Leuven Center for Microbiology).

The partners in this project are:

- KU Leuven/University Hospital Leuven: Joost Wauters, Els Wauters, Christophe Dooms, Jonas Yserbut, Rik Schrijvers, Greet Hermans, Philippe Meersseman, Dieter Dauwe, Michael Casaer, Jan Gunst, Walter De Wever, Natalie Lorent, Dries Testelmans, Robin Vos, Alexander Wilmer, Steffen Rex, Stephanie Humblet-Baron, Sabine Tejpar, Frederik De Smet, Johan Neyts, Abhishek Garg, Patrick Matthys, Carine Wouters, Paul Proost, Francesca Maria Bosisio, Kim Martinod, Isabelle Meyts, Katrien Lagrou, Birgit Weynand and Karin Thevissen
- VIB: Diether Lambrechts and Jeroen Raes

SARPAC TRIAL

Led by Bart Lambrecht
(VIB – UGent – University Hospital Ghent)

An academic intervention study performed by University Hospital Ghent, VIB, UGent, AZ Sint-Jan Brugge and San Matteo Hospital, Pavia (Italy). In 80 confirmed COVID-19 patients with acute shortness of breath a treatment with Leukine®, made available freely by Partner Therapeutics, was initiated. Leukine® is a known, well-tested immunomodulator which might support the immune system and lung function. Furthermore, a Biobank of tissues is being developed, and the associated clinical data was used for analysis, such as single-cell immunophenotyping by Martin Guilliams, Yvan Saeys and Niels Van Damme (VIB-UGent Center for Inflammation Research).

The partners in this project are:

- University Hospital Ghent: Bart Lambrecht, Eva Van Braeckel, Pieter Depuydt
- AZ Sint-Jan Brugge: Stefaan Vandecasteele
- VIB: Bart Lambrecht, Martin Guilliams, Yvan Saeys, Niels Van Damme

You can read more about this project in this issue.

IL6/ILI STUDY

Led by Bart Lambrecht
(VIB – UGent – University Hospital Ghent)

An academic joined study by University Hospital Ghent, VIB, and UGent that compares known interleukin inhibitors (IL6/IL6R/IL1) for their effectiveness in suppressing the cytokine storm that characterizes severe deterioration in patients with viral infections, especially COVID-19. The resulting insights will be used to guide treatment strategies in the most critical phases of the infection. An extensive databank of tissues and associated clinical data is being collected for further analyses, such as single cell immunophenotyping aimed at characterizing the immune response in proposed combination therapies. This is done by Martin Guilliams, Yvan Saeys and Niels Van Damme (VIB-UGent Center for Inflammation Research).

The partners in this project are:

- University Hospital Ghent: Bart Lambrecht, Eva Van Braeckel, Pieter Depuydt
- VIB: Bart Lambrecht, Martin Guilliams, Yvan Saeys, Niels Van Damme

Old drugs and

NEW TREATMENTS

Bart Lambrecht

Bart Lambrecht (VIB-UGent Center for Inflammation research) has taken the lead in several clinical trials that are running under the promotorship of University Hospital Ghent across Belgium, in partnership with VIB. Some trials repurpose existing drugs to treat patients infected with COVID-19. A first trial is evaluating the effect of inhaled Leukine® on lung function and patient outcomes. A second approach focuses on several existing rheumatism medications to alleviate the excessive inflammatory reaction in severely affected COVID-19 patients. Two other trials employ new drugs to target the pro-inflammatory and pro-coagulant complement system.

Leukine® against COVID-19

Alveolar macrophages, a cell type in the lungs, depend on the growth factor GM-CSF for differentiation and normal functioning. GM-CSF plays a critical role in the defense against viruses and maintaining proper function of the immune system and gas exchange of the lungs.

The growth factor provides resistance to influenza and, in animal studies, GM-CSF reduced mortality due to viral pneumonia. Recent data highlight the importance of understanding the immune status of patients and the activation of the immune system to help clear viruses and reduce the risk of secondary infections.

Leukine® is a yeast-derived version of GM-CSF, developed by Partner Therapeutics. It was initially approved in the United States in 1991 and has been approved for use in five clinical indications. Its safety and tolerability profile are well understood.

“Patients with COVID-19 who progress to acute hypoxic respiratory failure due to COVID-19 have very limited treatment options and a high mortality rate,” says Bart Lambrecht. “We rapidly initiated this study with Leukine® because GM-CSF has profound effects on antiviral immunity, can provide the stimulus to restore immune homeostasis in the lung, and can promote lung repair mechanisms.”

For the treatment of COVID-19 associated acute hypoxic respiratory failure, Leukine® is used as a nebulized form for direct inhalation. Nebulized Leukine® has previously been studied in phase 2 and phase 3 randomized trials in lung conditions that affect alveolar macrophages. IV administration of Leukine® has been investigated extensively in other conditions, including sepsis, and was found to be safe. Currently, more than 60 patients are enrolled in this Leukine® trial in Belgium.

Rheumatism medication against COVID-19

University Hospital Ghent, VIB and the Belgian Heath Care Knowledge Centre (KCE) are testing existing biologicals normally used to treat rheumatic diseases for their potential to also mitigate the excessive inflammatory reaction in COVID-19 infections. In doing so, they could prevent or limit lung damage.

In about 20% of hospitalized COVID-19 patients the infection leads to severe lung damage. The patient cannot take up sufficient oxygen into the blood due to the excessive inflammation in the lung alveoli, which leads to shortness of breath and confusion. This type of severe lung inflammation is initiated by cytokines (inflammatory molecules that also play an important role in rheumatism and gout).

“Research from China and Italy shows that more cytokines are present in patients that are being ventilated on intensive care,” says Bart Lambrecht (VIB-UGent Center for Inflammation Research) who coordinates the study. “Sometimes these cytokines are present in such great numbers that we call it a ‘cytokine storm’.”

The new treatment aims to use medication for rheumatism to mitigate the excessive inflammatory reaction and resulting lung damage. In the study, 342 patients with severe COVID-19 infection and early signs of a cytokine storm will be treated with the medication anakinra (Kineret®, an inhibitor of interleukine-1), tocilizumab (Roactemra®, an inhibitor of the interleukin-6 receptor) or siltuximab (Sylvant®, an inhibitor of interleukin-6).

A group of control patients (1 in 5 of the study’s participants) only receive the current standard treatment, which can even include dexamethasone, a proven anti-inflammatory agent. “The studies from abroad show that up to 75% of the patients with this severe form of COVID-19 experience a favorable effect when given medication against rheumatism, but this was not compared to the standard treatment. We have to find out which of the rheumatism medications works best and whether combination therapy might work even better. At the moment, there is too much experimentation with these treatments. We hope our study brings clarity about the mechanisms and possible side effects,” says Bart Lambrecht.

The study was financed by the KCE, which co-designed the study. “Our clinical research teams have worked day and night to get this on the rails as quickly as possible. Everyone felt the urgency. Procedures that normally take weeks, were now completed within 48 hours. We currently have more than 90 patients enrolled in the trial,” says Bart Lambrecht.

Complement system as a new target

The complement system is a complicated cascade of proteins that gets activated in response to infection and tissue damage. Autopsy studies from severe COVID-19 patients have revealed that the complement system is activated early in disease and could be responsible for causing coagulation problems in the lungs and recruitment of the inflammatory cells that are responsible for the cytokine storm, late in the disease.

Studies from the Lambrecht preclinical lab have shown that blocking complement can stop some of the most severe lung damage caused by lung viruses and improve survival. Two clinical trials launched by the Lambrecht team tap into the complement system. In a first study, 81 patients will be treated with Zilucoplan, a small molecule C5 complement inhibitor from UCB Pharma. Another study will check the safety and feasibility of targeting C2 complement with monoclonal antibody Argx117 from Biotech company argenx. “The complement is such an upstream regulator of lung inflammation during COVID-19, that we believe that blocking it early could have a profound impact on disease progression in patients with moderate disease”.

Finally, Bart Lambrecht stresses that VIB has been instrumental in setting up these trials in the hospital setting. The VIB-UGent Center for Inflammation Research, within the framework of the Grand Challenges Program, is doing molecular research to see who will most benefit from these new and existing treatments, so that the cytokine storm can be better prevented in future infections.

“There is extensive collaboration between all the basic science labs and VIB Core facilities. With the Singularity platform, we are doing scRNA sequencing, CITESeq analysis and 30 color flow panels. “This is VIB at its best,” says Bart Lambrecht. “All the MDs that work in our center as basic scientists in the MD/PhD track, have volunteered to become the clinical trial doctors, returning to their posts in the hospital. They are the real heroes who made these clinical studies possible.”

Peter Carmeliet

COVID-19

the vasculature unleashed

A recent paper by the team of Peter Carmeliet (VIB-KU Leuven Center for Cancer Biology) postulates that endothelial cells are essential – yet overlooked – contributors to severe cases of COVID-19. Their innovative hypothesis, published in *Nature Reviews Immunology*, has garnered a lot of attention and has already proven to be a pioneering paper in the fight against COVID-19.

Changing barrier integrity

The severity of COVID-19 infection differs among patients, but in the worst cases, the virus can be lethal. The leading cause of death in patients with COVID-19 is hypoxic respiratory failure from acute respiratory distress syndrome (ARDS). PhD student Laure-Anne Teuwen and colleagues from the Carmeliet lab suggest that lung endothelial cells play a crucial role in this process.

Normally, endothelial cells maintain vascular integrity and barrier function. They also prevent inflammation and there are strong indications that – in the lungs – a subtype of endothelial cells also fulfils a function in the protection against respiratory pathogens.

But, in patients with a severe COVID-19 infection, endothelial cells may play a crucial role in the development of ARDS. Proposed mechanisms include vascular leakage, the promotion of inflammation, and the initiation of coagulation. Another interesting observation that supports a key role for endothelial cells, is that known risk factors for severe COVID-19 (old age, diabetes, obesity, and high blood pressure) are all characterized by changes in the endothelial cell metabolism.

When an essential role for endothelial cells in COVID-19 is uncovered by further research, these findings may open up the way to new treatment options aimed at normalizing the vasculature.

Making waves

Even though the hypothetical role of endothelial cells in COVID-19 needs to be confirmed, the article has already attracted immense interest. The work has been featured in editorials in Science, Sciences et Avenir, The New Scientist, Knack, and more. Only one month after publication, the paper has been accessed over 38,000 times, reached an Altmetric score of 695, has already been cited, and has been retweeted over 1,000 times.

Peter Carmeliet says: “Our Nature Reviews Immunology paper has been accessed in a record time since publication. I never experienced such immense impact before. It is a very good sign, since we wrote this article to raise a red flag, which apparently has been recognized globally.”

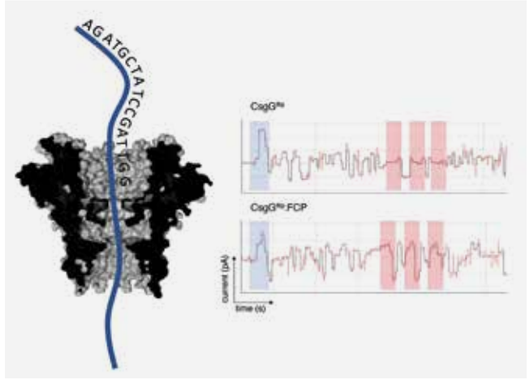
Teuwen *et al*. Nature Reviews Immunology 2020

Han Remaut

ENGINEERING PROTEIN NANOPORES

to improve DNA sequencing

DNA sequencing provides insight into the blueprint of living cells and individuals and is used in many aspects of biology, medicine, biotechnology, and forensic sciences. An ultrafast way to sequence DNA is to read the nucleotide letters of single DNA strands as they pass through a protein nanopore. A new study by the team of Han Remaut (VIB-VUB Center for Structural Biology) and Oxford Nanopore Technologies presents a nanopore with two constrictions or ‘reader heads’.



The sequence of our DNA holds a treasure of information. Sequencing parts or the entirety of our DNA (our genome) can inform us about the risk for inherited diseases, or the presence and progression of cancer, for example. Also, sequencing the DNA or RNA can identify the presence of pathogens such as bacteria and viruses, and predict how these will respond to antibiotic therapy.

In 2014, the UK company Oxford Nanopore Technologies (ONT) developed a powerful new way to sequence DNA: nanopore sequencing. In this technique DNA strands are passed through a protein nanopore that resides in an electrical field. The passage of the different nucleotides (DNA ‘letters’) alters the electrical current that is generated by ions flowing through the nanopore.

In a joint effort with Oxford Nanopore Technologies, the team of Han Remaut (VIB-VUB Center for Structural Biology) developed prototype dual constriction nanopores to sequence DNA, finding that two reader heads made it easier to decipher the DNA letters in homopolymer regions. With conventional nanopores DNA needs to be reread multiple times to reach high accuracy in these regions. The dual constriction nanopore was 20-70% more likely to get it right the first time. These results open the road to further engineer this pore complex into a tool to read DNA with the highest possible accuracy, using minimal amounts of material and time.

Han Remaut: “At VIB, we’re constantly on the lookout to see how studying fundamental biological processes can inspire new ways to build powerful technological tools and help solve medical and societal needs.”

Van der verren *et al.* Nature Biotechnology 2020

MICROBIOME BREAKTHROUGHS

Jeroen Raes

The team of Jeroen Raes (VIB-KU Leuven Center for Microbiology) has published two papers that represent advances in our understanding of how our gut flora affects several traits. A first paper, published in *Nature*, identified the common cholesterol-lowering drug statins as a potential microbiota-modulating therapeutic. The second study, which appeared in *Nature Microbiology*, described genetic associations that involve several microbial traits.

Large scale collaboration

In 2012, the European Union MetaCardis consortium (www.MetaCardis.net), comprising 14 research groups from six European countries with multidisciplinary expertise set out to investigate a potential role of the gut microbiota in the development of cardiometabolic diseases. This project, coordinated by Prof Karine Clément at INSERM (France) studies more than 2,000 deeply phenotyped European participants in health and at different stages of cardiometabolic disease (obesity, diabetes and cardiovascular diseases).

Jeroen Raes (VIB-KU Leuven Center for Microbiology) and colleagues explored gut bacteria in a Metacardis cohort subset comprising nearly 900 individuals from 3 different countries (France, Denmark and Germany) with BMI ranging between 18 and 73 $kg.m^{-2}$.

Prof. Jeroen Raes says: “Recently, our lab identified a single gut microbiota configuration or enterotype with increased prevalence among patients suffering from intestinal inflammation, multiple sclerosis, and depression. We observed this disturbed enterotype to be characterized by low bacterial abundances and biodiversity, notably deficient in some anti-inflammatory bacteria. In fact, even among healthy individuals, we detected slightly higher inflammation levels in carriers of Bact2 enterotype. As obesity is known to result in increased systemic inflammation levels, we hypothesized that Bact2 would also be more prevalent among obese study participants.”

The statin effect

Exploring gut microbiota configurations of lean and obese volunteers, the researchers observed that Bact2 prevalence increased with BMI. Only 4% of lean and overweight subjects were characterized as Bact2 carriers, but this rose to 19% among obese volunteers. The same trend was observed among 2,350 participants of the VIB-KU Leuven Flemish Gut Flora Project population cohort.

Sara Vieira-Silva (VIB-KU Leuven Center for Microbiology): “We found systemic inflammation in participants carrying the Bact2 enterotype to be higher than expected based on their BMI. Even though this study design does not allow inferring causality, our analyses do suggest that gut bacteria play a role in the process of developing obesity-associated comorbidities by sustaining inflammation. While these key findings confirmed our study hypothesis, the results we obtained when comparing statin-treated and -untreated participants came as a total surprise.”

Statins are commonly prescribed to reduce risk of developing cardio-metabolic diseases. Besides their target cholesterol-lowering effects, statins also tend to appease patients’ systemic inflammation levels. Now, Vieira-Silva and colleagues have identified an additional potential beneficial effect of statin therapy on the gut microbiota. In obese individuals, the prevalence of the dysbiotic Bact2 enterotype was significantly lower in those taking statins than in their non-treated counterparts.

For many years, microbiota modulation strategies have been revolving around dietary interventions, pro- and prebiotics, introducing or promoting growth of beneficial bacteria. Only recently, a revived interest in the effect of small molecules and drugs on the colon ecosystem appeared. This study will further fuel that momentum.

Untangling associations

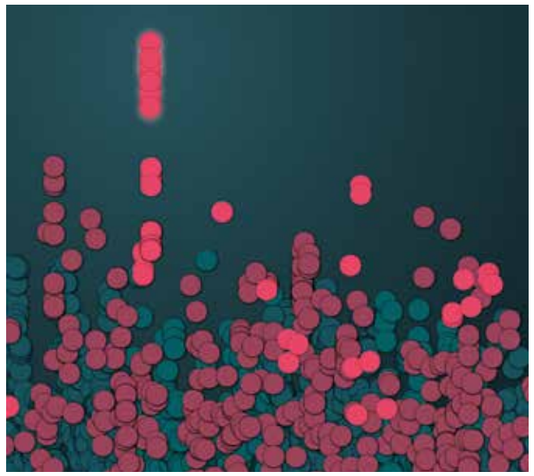
As more and more studies begin to investigate our gut flora, more and more possible factors are being proposed that can affect the variation of the gut microbiome. However, there is a poor overlap in genetic association across human studies that look at genetic factors associated with gut microbiome variation. With data from the Flemish Gut Flora Project and two German analogues, the team of Jeroen Raes and international collaborators identified genetic associations that involve several microbial traits.

Analyzing the data from the Flemish Gut Flora Project and two German cohorts through refined analysis pipelines allowed the team to detect evidence for host genetic associations with the gut microbiome. The researchers also estimated the proportion of gut microbiome variation explained by genetic variation between individuals, a measure of heritability. In total, they identified 13 genera of gut bacteria that were heritable.

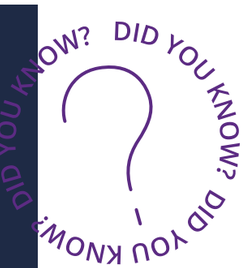
Rodrigo Bacigalupe (VIB-KULeuven Center for Microbiology) says: “As a microbiologist, working in collaboration with experts in human genetics was an exciting opportunity to integrate knowledge from two fields that traditionally have stayed apart. This was a successful collaboration, as we identified novel signals of human genetic variation that affect the gut microbiota composition. Remarkably, our findings were supported by three independent cohorts, which highlights the robustness of our results. This study represents a step for helping us to understand the link between human genetics, our gut bacteria and whether these are a cause or a consequence of human disease.”

Further analysis enabled them to estimate the association between microbial traits and disease. While care needs to be taken in interpreting genome-microbiome associations, this study is an important step in collating a catalogue of such information, with a strong relevance for diseases influenced by microbiome alterations.

Vieira-Silva, Falony, Belda, *et al*. Nature 2020
Hughes, Bacigalupe, *et al*. Nature Microbiology 2020



- **... that Chan Zuckerberg co-invested in a machine-readable feed of COVID-19 papers on their META repository, which is open to everybody?**
- **... that VIB has a new international celebrity mascot? Llama Winter was mentioned in the Joe Rogan podcast and on Trevor Noah’s Daily Show.**
- **... that the same llama Winter was adopted by artist Koen Vanmechelen and will join his ‘evolving’ art site LABIOMISTA?**



Bart Lambrecht

NEWLY DISCOVERED CELL TYPE PLAYS A CRUCIAL ROLE

in the immune response to respiratory infections

With a discovery that could rewrite the immunology textbooks, an international group of scientists, including the teams of Bart Lambrecht, Martin Guilliams, Hamida Hammad, and Charlotte Scott (all from the VIB-UGent Center for Inflammation Research) identified a new type of antigen-presenting immune cell. These cells, part of an expanding family of dendritic cells, play a crucial role presenting antigens to other immune cells during respiratory virus infections.

When our body faces an infection, it responds with inflammation and fever. This is a sign that the immune system does its work, and leads to the activation of many cells, like soldiers in an army. Dendritic cells (DCs) are the generals of that army. They can activate and instruct the soldiers to kill infected cells by presenting antigens derived from the 'invaders' to cells of the immune system.

There are several types of DCs that perform antigen-presenting functions in the body. Monocyte-derived DCs are easily prepared in vitro from monocytes isolated form human blood, and it was always assumed these cells were very important antigen-presenting cells. Clinical trials using monocyte-derived DCs in cancer therapy have however been disappointing.

A study by the teams of Bart Lambrecht, Martin Guilliams, Hamida Hammad, and Charlotte Scott (all from the VIB-UGent Center for Inflammation Research), shows that monocyte-derived DCs are poor antigen-presenting cells, but have wrongly been assumed to have these functions because of a case of mistaken identity.

Hamida Hammad

The reason for all the confusion is that a look-alike new DC emerges –inflammatory type 2 conventional DC, or inf-cDC2 – that combines some of the characteristics of monocytes, macrophages, and conventional DCs, to induce the best form of immunity.

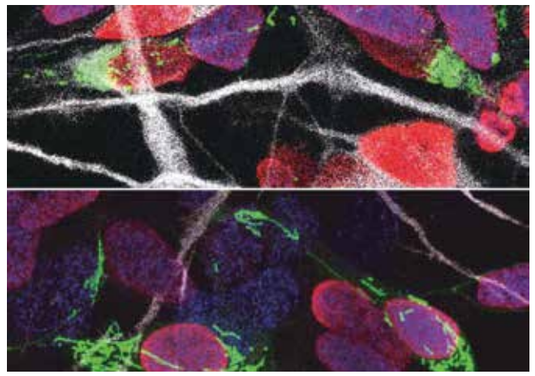
Bart Lambrecht: "This was a big surprise for us. We've all been taught that monocyte-derived cells are excellent antigen presenting cells, certainly when there's inflammation. Now, we show that it's actually a new hybrid DC type that's doing all the work. This really changes what we know about the immune system and is very important knowledge for understanding respiratory viral infections and

Cedric Bosteels, lead author of the paper: "One of the unique features of the new DCs is that they express functional Fc receptors for antibodies that are found in the plasma of patients who have recovered from COVID-19."

Since boosted DCs induce a much stronger immune response, this study reveals a new target for therapeutic intervention for viral infections and other inflammatory diseases.

Bosteels, Neyt *et al*. Immunity 2020

Charlotte Scott and Martin Guilliams



BECOMING A NERVE CELL

timing is of the essence

Mitochondria are small organelles that provide the energy critical for each cell in our body, in particular in the high fuel-consuming brain. A Belgian team of researchers led by Pierre Vanderhaeghen (VIB-KU Leuven Center for Brian & Disease Research) finds that mitochondria also regulate a key event during brain development: how neural stem cells become nerve cells. The findings highlight an unexpected function for mitochondria that may explain how humans developed a bigger brain during evolution, and how mitochondrial defects lead to neurodevelopmental diseases.

Our brains are made up of billions of diverse neurons. They first arise in the developing brain when stem cells stop self-renewing and differentiate into a particular type of neuron. This process, called neurogenesis, is precisely regulated to give rise to the enormous complex structure that is our brain. To gain insight in this process, Pierre Vanderhaeghen (VIB-KU Leuven Center for Brian & Disease Research) and his colleagues examined the mitochondria in the developing brain.

"Diseases caused by defects in mitochondria lead to developmental problems in many organs, in particular the brain," explains Vanderhaeghen. "We used to think that this was related to the crucial function of mitochondria to provide energy to the cells, but this is only part of the story: recent work in stem cells suggests that mitochondria have a direct influence on organ development."

Ryohei Iwata, a postdoctoral researcher in the Vanderhaeghen lab, developed a new method to watch mitochondria in detail as the neural stem cells are 'caught in the act' of becoming neurons. "Shortly after stem cells divide, the mitochondria in daughter cells destined to self-renew will fuse, while those in daughter cells that become neurons show high levels of fission instead," says Ryohei Iwata. So mitochondrial dynamics are important to become a neuron—but there is more. "We found that the influence of mitochondrial dynamics on cell fate choice is limited to a very specific time window, right after cell division," says Pierre Casimir, a PhD student in Vanderhaeghen's lab.

"Previous findings were primarily focused on fate decision of neural stem cells before they divide, but our data reveal that cell fate can be influenced for a much longer period, even after neural stem cell division," says Vanderhaeghen. This may have interesting implications in the field of cell reprogramming, where non-neuronal cells are converted in neuronal cells, for example for therapeutic purposes.

Iwata *et al*. Science 2020

Pierre Vanderhaeghen

THE PAST, PRESENT, AND FUTURE OF DNA SYNTHESIS TECHNOLOGIES

A Tech Watch technology highlight by Michiel Bontinck, Aline Van Acker & Toon Swings

Synthetic DNA is one of the most used products in molecular biology labs across the globe. Many researchers use synthetic DNA from companies like IDT or Twist Biosciences on a daily basis for experiments ranging from (q)PCR, cloning and Next-Generation Sequencing, to more complex applications such as (CRISPR) gene editing, protein and metabolic pathway engineering or even generating entire synthetic chromosomes.

The ever-increasing demand for longer synthetic DNA fragments and bigger, more complex oligo pools and variant libraries is confronting today's providers with the limitations of current DNA synthesis processes. This has spurred the development of several ground-breaking innovations which are reshaping the field of DNA synthesis as we know it. Here, we discuss the limitations of current DNA synthesis chemistry and provide an overview of the companies ready to revolutionize the DNA synthesis field.

Solid phase phosphoramidite chemistry

Solid phase phosphoramidite chemistry (Fig.1) has been the gold-standard for DNA synthesis for almost four decades. This chemistry is typically performed using either flow-through columns, which synthesize a single oligo sequence per column and excel in flexibility, yield and accuracy, or array-based platforms which synthesize massive amounts of oligos on the same chip, delivering high-throughput and low-cost synthetic DNA. For example, the latest innovation in array-based synthesizers developed by Twist Bioscience can synthesize over 1 million oligonucleotides in parallel on a single silicon wafer.

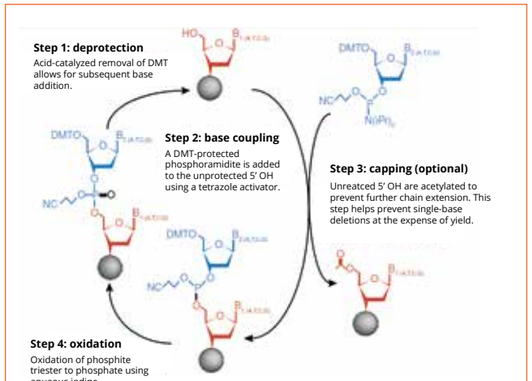


Fig. 1 DNA synthesis using phosphoramidite chemistry *Adapted from Kosuri and Church, Nature Methods 11: 499-507 (2014).*

Still, due to a limited base coupling efficiency, oligonucleotides exceeding 150-200 bp in size cannot be synthesized at a yield or cost that is commercially/economically viable. To generate longer DNA fragments, a wide variety of oligo assembly and error removal methods have been developed, which are now routinely being offered as a commercial service. Other companies have developed benchtop devices for in-house assembly. Custom, non-commercial gene assembly set-ups such as DropSynth have also been developed for specific use cases. However, assembling sequence verified DNA fragments from pools of overlapping oligos remains a time-consuming and expensive process which currently seems to be limited to a few thousand base pairs in length with turnaround times of typically a week or more from commercial service providers.

One company which seems to be particularly close to launching a new way of assembling DNA fragments is Evonetix, which has developed a new silicon chip enabling precise temperature control at thousands of independent reaction sites. After temperature-controlled oligo synthesis, a binary assembly process prevents incorrect oligos from being incorporated based on the specific annealing temperature of the growing DNA fragment. Evonetix recently announced a partnership with imec to scale up their chip production, suggesting an upcoming commercial launch of this technology. Other companies, such as Ribbon Biolabs and Camena Biosciences propose to use enzymes to stitch together custom fragments from large libraries of small, accurately pre-synthesized oligos rather than pools of overlapping oligos.

Enzymatic de novo synthesis

Rather than innovating fragment assembly, certain companies are aiming to revolutionize the basic concept of DNA synthesis. Phosphoramidite chemistry relies on harsh chemicals and solvents which damage the growing oligos with increasing cycles and produce flammable and hazardous waste products. However, de novo synthesis using enzymes can be performed in an aqueous medium, reducing the environmental impact, and promises the synthesis of longer oligonucleotide sequences at a faster writing speed with a lower error rate and production cost. Several companies have been developing enzymatic DNA synthesis methods based on engineered terminal deoxynucleotidyl transferase (TdT) enzymes, which catalyse the template-independent addition of a nucleotide to an oligo (Fig. 2).

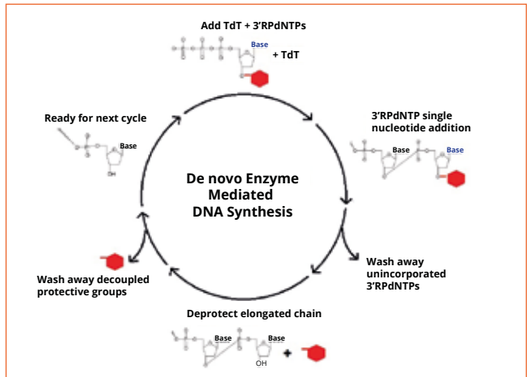


Fig. 2 Enzyme-mediated oligonucleotide synthesis. *Adapted from iGEM 2014 (2014.igem.org).*

The methods under development by companies such as DNA Script, Nuclera Nucleics, Molecular Assemblies, Ansa Biotechnologies, and Kern systems differ from one another primarily in the type of engineered TdT enzyme used, the chosen base incorporation strategy, the elected nucleotide blocking group, and the blocking group cleavage mechanism.

Benchtop DNA printers

Looking at these companies and others, however, the most interesting observation is perhaps the re-emergence of benchtop DNA printers. Despite their initial popularity upon release in the early 80s, benchtop DNA printers were quickly replaced by large service providers who leveraged production scale to outperform benchtop printers in price and speed. These advances in scale and cost have enabled applications which require synthetic DNA at scale, such as NGS or more recently single-cell sequencing. However, advances in obtaining large, custom DNA fragments from service providers have been lagging, with cost, turnaround time and success rate still being major obstacles for many synthetic biology projects. With commercialisation of the Codex BioXP and the Kilobaser, and development of novel DNA printers by Evonetix, DNA Script and Nuclera Nucleics, there is hope that this bottleneck will soon be resolved. In theory it makes sense - you wouldn't print a book on your home printer, but you also wouldn't go to the copy center to quickly print a single page. Maybe this time the market is ready for benchtop DNA printers?

The Tech Watch team at VIB is in touch with many DNA synthesis companies and will evaluate a first prototype benchtop DNA printer from DNA Script soon. If you would like to learn more or get involved in one of the projects, feel free to contact Aline (aline.vanacker@vib.be), Michiel (michiel.bontinck@vib.be) or Toon (toon.swings@vib.be).

DID YOU KNOW? DID YOU KNOW? DID YOU KNOW?

- … that the EM expertise unit at the VIB-KU Leuven Center for Brain & Disease Research received a large FWO infrastructure grant? The funds will be invested in a brand new 200kV cryo-transmission electron microscope (TEM).
- … that Frederic Rousseau (VIB-KU Leuven Center for Brain & Disease Research) received a Hercules grant to acquire an atomic force microscope with spectroscopic capabilities?
- … that the Metabolomics Core Facility in Leuven has obtained a large research infrastructure grant of the FWO? With this funding, an extreme high-resolution magnetic resonance mass spectrometer will be purchased to deploy in the field of metabolomics and lipidomics.
- … that the Flow Core received an FWO infrastructure grant to support the BD FACS Symphony FACS cell sorter? This is the most advanced multiparameter fluorescence-activated cell sorter that allows the identification and purification of rare cells for functional characterization.
- … that Gert Van Isterdael, manager of the Flow Core, has received the Royal Microscopical Society Flow Cytometry Medal, in recognition for his interdisciplinary work in flow and image cytometry, as well as his engagement in the international microscopy community.

A LOOK AT THE PAST AND THE FUTURE

A conversation with the departing and new co-managing director of VIB

Jérôme Van Biervliet and Johan Cardoen

This spring, Johan Cardoen was succeeded by Jérôme Van Biervliet as co-managing director of VIB. Jérôme has 20 years of experience in various environments, from research to business consulting to business development. Jérôme is no stranger to VIB. Since 2009, he has led the Business Development activities within VIB. In 2015 he took on an extra assignment as head of VIB Discovery Sciences.

Like his predecessor, Jérôme becomes head of Innovation & Business at VIB and is responsible for the general management together with Jo Bury. Jérôme did not get the new position on a silver platter. In an intense, international selection procedure, he had to compete against 30 pre-selected candidates. In VIBtimes we look both to the past and to the future with Johan and Jérôme: how have VIB and the Flemish biotech ecosystem evolved over the past decade and what does the future hold?

Johan, you made the switch to VIB in 2012 after a management career of almost 25 years in the agrobiotech industry. At first sight this does not seem to be an obvious decision.
Johan: I indeed doubted whether I would take on the role of VIB's co-managing director in 2012. I didn't see myself leaving the industry that quickly. Going to a research institution did not immediately feel like an option to me. But exciting conversations with Jo Bury and Rudy Dekeyser, my predecessor, convinced me. VIB had a very good reputation in the biotech and pharma industry. VIB was known as a flexible, solution-oriented and entrepreneurial organization with exceptional biotech expertise and top science. At the same time, I had the impression that VIB was struggling with its own evolutionary process from a pioneer organization to a mature institution.

The challenge was clear to me: to further professionalize VIB, to work more proactively on the business side, and to further expand the investor network, while at the same time retaining the pioneering mentality, dynamic character and existing competences. Don't forget that VIB was the first in Belgium to set up bio-incubators, that it was the cradle for companies such as Devgen, Ablynx and many other start-ups... VIB had to maintain this innovative role.

With my experience in industry and my network in investment circles, I saw opportunities to take VIB to the next level. And I must admit, already in the first month after taking up the position of co-managing director, I felt like a fish in the water at VIB. Not in the least due to the very competent, driven and dedicated colleagues who surrounded me. Professionals who all knew what they were doing. One of those people was Jérôme.

How have you seen VIB change in the past eight years?
Johan: The first project I focused on was the establishment of V-Bio Ventures, a venture capital fund affiliated with VIB. In the first years following the financial crisis, there really was insufficient capital for start-up financing. Thanks in part to V-Bio Ventures, we were able to broaden and internationalize the capital base of our start-ups.

Jérôme: A lot has also changed in the research field in those years. An example is the establishment of VIB Discovery Sciences. With this team of industry-trained employees, VIB has taken an important step towards translational research. The team initiates and guides the transformation of new scientific insights into innovative therapies or solutions in agrobiotech. VIB Discovery Sciences begins where traditional academic research often ends. Throughout the process, however, the team continues to draw on the expertise and knowledge of the group leader who initiated the project.

In addition, a thematic reorganization of the research groups was carried out. The various VIB research centers now have a more defined focus. We can say that this reorganization was successful, although there was some skepticism in the beginning. Today, nobody is questioning the reorganization. At the same time as the reorganization, a new generation of talented research directors has also taken office. They are an important foundation for the future.

VIB is said to be an important 'enabler' in the Flemish biotech ecosystem. How has VIB fulfilled that role in recent years?
Johan: I think you cannot underestimate that role. There has been an acceleration in the number of start-ups that have emerged from VIB. No fewer than 13 new start-ups have been established since 2012 and several more are in the pipeline. This is due to an improved investment climate, but VIB's extra internal efforts have also played an important role in this.

Jérôme: We also led the initiative to bring companies to Flanders or to anchor them. Think of Biocartis, argenx, Inari Agriculture and others. VIB researchers have greatly strengthened their collaboration with industry. Every year we now have 130 to 140 partnerships with small and large companies in the agrotech, biotech and pharma sector. We have become an anchor point for up-to-date know-how and technology that companies are looking for. That may be less sexy than start-ups, but it ensures that existing companies continue to invest in R&D capacity in Flanders.

Recently, an independent international consultancy firm completed an economic impact study on VIB. This shows that every 1 € invested in VIB generates a multiplication factor of 11, in other words 11 € flows back to the Flemish region. This result underpins the central role of VIB in the Flemish biotech ecosystem.

Johan: Moreover, much of VIB's impact is difficult to measure in euros. We are not only an important source of innovation and economic return, but also of talent. Because of our link with universities, we are closely involved in training researchers and professionals in the life sciences. Almost all companies in the Flemish biotech ecosystem are knowledge- and R&D-driven. VIB, Flemish universities and colleges provide them with highly trained employees. Not only in research positions but also in support and management jobs. VIB stands for a quality label in the field of knowledge and training. Anyone who has worked at VIB carries that quality label. That is why VIB's real foundation is the quality of its people and the quality of its research. That was the case in the past, it is now, and it will remain so in the future.

Speaking of that future, what are the challenges for the coming years? Where will that famous Flemish biotech cluster be in about 10 years' time?
Johan: In the aftermath of the financial crisis, start-up financing was the bottleneck. Today, late-stage funding has become the Achilles heel. To finance companies in their early phase, people are standing at our front door today. But in the scale-up phase, towards phase 2 or 3 clinical studies, there's the rub. Then it is almost impossible to anchor companies financially in Flanders. Unless the opportunity arises for an IPO (Initial Public Offering). Otherwise we still miss local growth equity funds with a long-term vision that can support a company during the scale-up phase with large budgets. This problem does not only occur in Flanders but is a European phenomenon.

Jérôme: What you do see is that CEOs of Flemish life science companies want to remain independent for much longer. It used to be the ambition to be taken over at the right time by a large pharmaceutical or agrotech company. Today, a number of business leaders have the clear ambition to grow sustainably into a medium-size biopharma or agrotech company. This not only creates role models for a new generation of entrepreneurs, it would be a good thing for Flanders - and Belgium - if in the long term argenx, Galapagos or others can place their foot next to Janssen, UCB or GSK.

Where do VIB's ambitions and challenges lie in the coming years?
Jérôme: We must continue to work on VIB's visibility. That remains a challenge for VIB, both in Flanders and internationally, and in investment environments. In addition, we must strengthen our social impact. Being excellent in basic sciences will always be a must for VIB. That is why we ensure that our researchers have access to the best infrastructure, state-of-the-art supporting core facilities and disruptive technologies.

Translating that excellence in basic research into tangible added value for society remains the second most important objective after generating the science. This also means maximally using new opportunities that present themselves. Take, for example, the area of 'reverse translational research', from the patient back to basic research. With our highly developed technology platforms, VIB researchers can phenotype patients' tissues extremely deeply, down to the single cell level, and even beyond. This provides new possibilities for personalized medicine. Because VIB has chosen to be an early technology adopter in the past, we will reap the benefits in the future.

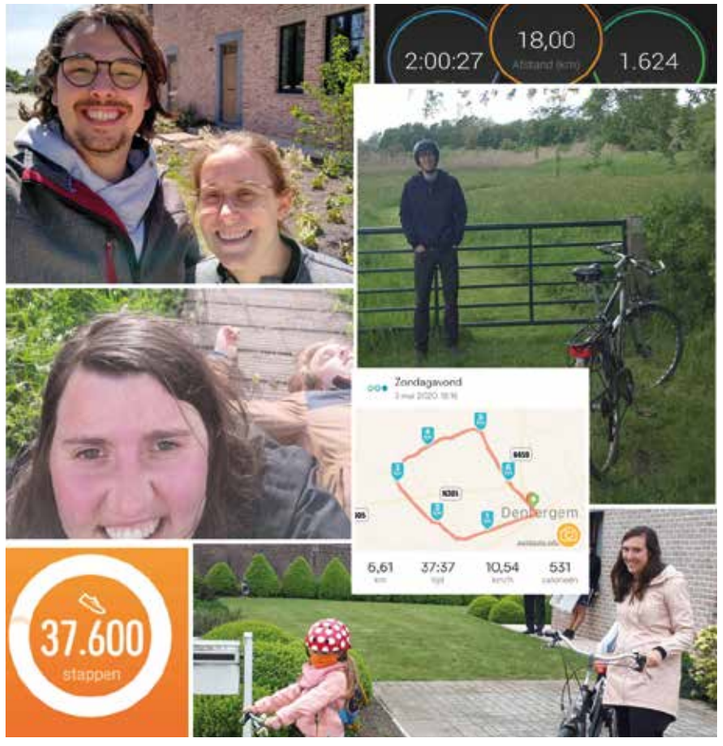
In addition to this societal impact, we must also continue to focus on our economic impact. Should it not be our long-term ambition to develop an innovation cluster in Flanders that can stand the comparison with the Boston area? A region in which a combination of infrastructure, capital, excellent science, top medicine and entrepreneurship leads to innovation and economic development that the whole world looks up to. What is holding us back from making Flanders the 'Boston on the North Sea'?

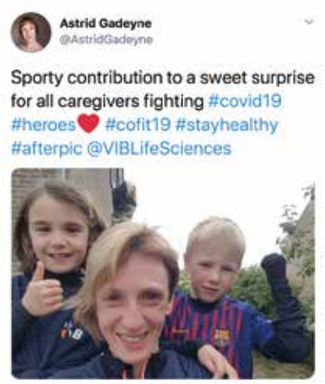
#COFIT19 CHALLENGE

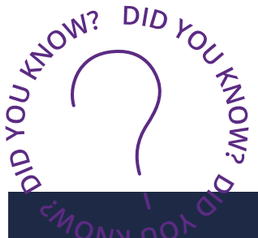
Stay fit and contribute

VIB has a longstanding reputation of participating in sporting events to raise money for scientific research. COVID-19, however, decided to interfere and unfortunately all these events have been cancelled or postponed. Hence, we invited all VIB colleagues to walk, run or bike for charity during the long weekend of May 1st.

The response was overwhelming, and the good weather inspired many VIB colleagues to take on the #Cofit19 challenge, raising money to support nursing homes to thank them for their COVID-19 efforts. We are pleased to say that we raised 2,248.80 euros in total. Thanks to everyone who contributed!







- … that VIB science has made a couple of covers? Annerieke Sierksma's research (VIB-KU Leuven Center for Brain & Disease Research) was featured on the cover of *EMBO Molecular Medicine*. The work of Cedric Bosteels (VIB-UGent Center for Inflammation Research) graced the cover of *Immunity*. David Nittner (VIB-KULeuven Center for Cancer Biology) made the cover of *Nature Cancer*. Finally, Wei-Ting Chen and Ashley Lu's study provided the cover for *Cell*.
- … that Wim Declerq (VIB-UGent Center for Inflammation Research) received a Marie Curie (training site) grant?
- … that Alejandro Cuadros (VIB-KU Leuven Center for Cancer Biology) received the prestigious Boehringer Ingelheim Fonds PhD fellowship?
- … that Diana Piol (VIB-KU Leuven Center for Brain & Disease Research) was awarded a special FWO grant to study ALS?
- … that Antonalla Fioravanti and Son Nguyen (VIB-VUB Center for Structural Biology) have received an FWO senior postdoc fellowship?
- … that you can now get 'the coronavirus in children's language' as free e-book (https://issuu.com/babraham.editions)? Available in different languages.
- … that Prof. Christine Van Broeckhoven (VIB-UAntwerp Center for Molecular Neurology) is in the running for 'Grootste Antwerpenaar'?
- … that the PhD Association at the VIB-KU Leuven Centers for Brain & Disease Research and Cancer Biology organized a virtual PhD quiz night?

SCIENTISTS ON STAGE

virtual edition

Presenting is an important skill for scientists, whether it is during a scientific conference or an outreach event. Being able to talk about your research in a way that is tailored to your audience is a skill that proves very useful throughout a scientific career. As such, VIB offers young scientists the opportunity to showcase their research during 'Scientists on stage' at its annual seminar. However, this year, COVID-19 interfered.

So we decided to give the participants a virtual stage, and asked them to briefly explain their scientific work and what it might lead to in the future.

Ania Lukasiewicz
VIB-UGent Center for Plant Systems Biology
I use genetic engineering (CRISPR/Cas) to make potatoes resistant to Late Blight disease *(Phytophthora infestans)*, the same disease that caused the great famine in Ireland which started in 1845 when the potato crops failed in successive years. I do this by introducing genes to make potato more resistant or by removing genes that make it susceptible to the disease.

Phytophthora infestans is still a major threat to crop production worldwide and the costs of controlling the disease and crop losses exceed 1 B€ in Europe. Classical breeding techniques take a long time and are inefficient, and other genetic manipulation methods like transgenesis have not led to durable resistance. I am using the new gene-editing method CRISPR to insert multiple genes at once into the potato genome and to screen for putative 'susceptibility' genes. Both approaches will ideally identify gene targets that can be used to improve potato production and provide insights in how CRISPR can contribute to creating resistant crops.

Fifty years from now, my research will be one of the pioneering projects on genetic engineering for disease resistance in potato and will lead to the development of multiple commercial resistant potato cultivars.

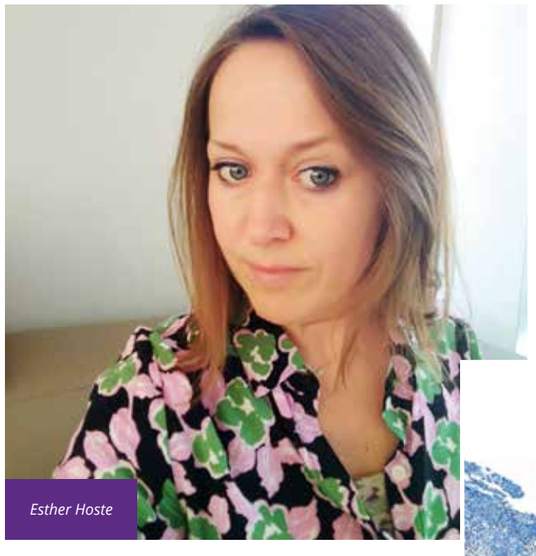

Ania Lukasiewicz

Charysse Vandendriessche
VIB-UGent Center for Inflammation Research
Despite years of research, the mechanisms behind disease progression of neurological disorders such as Alzheimer's and Parkinson's disease are not well understood.

I'm investigating the role of nanosized membrane vesicles called extracellular vesicles as facilitators to spread disease-related molecules throughout the brain and to modulate inflammatory responses in their target cells. By studying these processes, we aim to improve our understanding of the underlying disease mechanisms.

Fifty years from now, my research will hopefully have contributed to the development of novel treatment strategies and/or diagnostic tools for these devastating diseases.

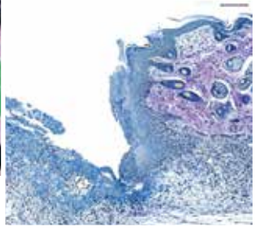

Charysse Vandendriessche


Esther Hoste

Esther Hoste
VIB-UGent Center for Inflammation Research
Chronic wounds represent a huge problem in diabetic and elderly patients.

Therefore, we generated a hydrogel based on glycyrrhizin, the active compound present in liquorice, that is able to accelerate healing of skin wounds in mice and pigs.

Fifty years from now my research could result in improved wound care in diabetic patients and patients suffering from chronic wounds.


Herovici staining of a healing wound, staining mature collagen in pink and newly deposited collagen in blue.

Frone Vandewiele
VIB-KU Leuven Center for Brain & Disease Research
I'm studying the role of ion channel TRPM4 in cardiac arrhythmias, as well as the therapeutic potential of targeting TRPM4.

Anti-arrhythmic drugs that are now available to patients have limited efficacy and high risks to adverse effects. This is mainly because the fundamental mechanisms behind cardiac arrhythmias are poorly understood. With my research, I'm contributing to the complex puzzle of the arrhythmia mechanisms.

Fifty years from now, my research will win the Nobel prize! (A girl can dream right?)


Frone Vandewiele


Pierre Van Mol

Pierre Van Mol
VIB-KU Leuven Center for Cancer Biology
Single-cell multi-omic sequencing technologies are helping us to elucidate the immunological mechanisms underlying response, (acquired) resistance and adverse events of cancer immunotherapy, opening the path to reliable biomarkers for tailored therapy and novel combination treatments.

What makes this project stand out in the field of biomarker research, is the emphasis we place on understanding and preventing adverse events of immunotherapy as opposed to solely focusing on predicting response. Indeed, preventing these immune-related adverse events is just as crucial for survival and quality of life of cancer patients. However, this aspect is often overlooked in industry-driven research. This illustrates an important role for academic biomedical research centers, like VIB-CCB, that work in close collaboration with academic hospitals; to find solutions for research questions that arise at the patient's bedside.

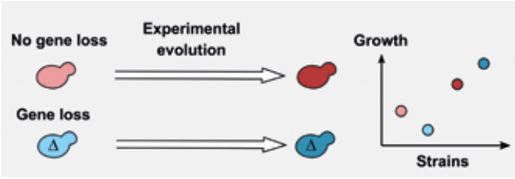
Fifty years from now, the work we do at the VIB-CCB Laboratory for Translational Genetics will have given hope and valuable life years to countless cancer patients, by contributing to the worldwide research effort that is improving efficacy while reducing toxicity of cancer (immuno)therapy.


Jana Helsen

Jana Helsen
VIB-KU Leuven Center for Microbiology
There is a phenomenon that occurs across the entire tree of life that is especially counterintuitive: loss of gene function. We observe that genes are lost frequently throughout evolution, but we do not know why this happens since losing the function of a gene can have catastrophic consequences for the organism's fitness. This poses the question: does losing a gene influence the evolutionary process in any way?

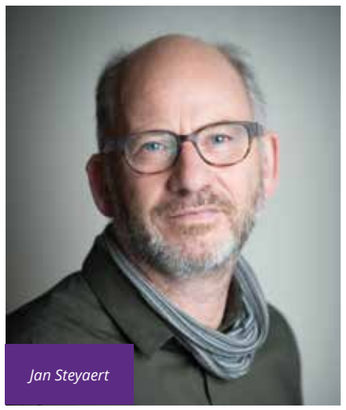
To figure this out in a controlled and systematic manner, I used hundreds of yeast strains, each of which has lost one specific gene that is important for growth, and evolved these strains for more than hundred generations. Surprisingly, it turns out that losing a gene can speed up evolution. Cells from which the growth was initially severely crippled by gene loss both evolved faster and eventually even grew faster than cells that did not lose a gene. On top of this, the way in which the strains adapted (i.e. which mutations they acquired during evolution) was clearly linked to the function of the gene that was lost and reflects the place of this gene in the overall genetic network.

In addition to showing how gene loss can positively influence evolution, my work allows us to predict how cells will evolve based on their genetic information. This is relevant for all disciplines dealing with evolutionary processes. As such, in the coming years, these results will be a first step towards better predicting how antibiotic resistance will evolve depending on the genotype of the strain and towards better understanding the evolutionary trajectories of cancer cells.



AWARDS & RECOGNITION

Jean-Christophe Marine



Jan Steyaert

Alain Goossens

Jean-Christophe Marine (VIB-KU Leuven Center for Cancer Biology), Jan Steyaert (VIB-VUB Center for Structural Biology), and Alain Goossens (VIB-UGent Center for Plant Systems Biology) have been elected as new EMBO members. Outstanding!

In recognition of his outstanding work in rheumatology, Dirk Elewaut (VIB-UGent Center for Inflammation Research and Ghent University Hospital) is the first Belgian scientist to receive the Carol Nachman prize. This award is considered as the world's highest honor awarded to a rheumatologist. Glückwunsch!

Dirk Elewaut

Sarah-Maria Fendt

Sarah-Maria Fendt (VIB-KULeuven Center for Cancer Biology) received the Fonds Baillet Latour Grant for Medical Research 2020 for her work on cancer metastasis.

Bart Lambrecht (VIB-UGent Center for Inflammation Research) and Wout Boerjan (VIB-UGent Center for Plant Systems Biology) each received an FWO Excellence Prize for their distinguished scientific career. Excellent!

Bart Lambrecht

Wout Boerjan

Christine Van Broeckhoven

In recognition of a distinguished career in Alzheimer's disease research, Christine Van Broeckhoven (VIB-UAntwerp Center for Molecular Neurology has been awarded the Khalid Iqbal Lifetime Achievement Award in Alzheimer's Disease Research from the Alzheimer Association USA. Congratulations!

Martijn Schuijs, who did his PhD in the group of Bart Lambrecht and Hamida Hammad (VIB-UGent Center for Inflammation Research) and is now a postdoc at the University of Cambridge (VK), has been awarded the prestigious 2020 ACTERIA Doctoral Prize in Allergology. The award includes a cash prize and funds for a three-year research project for which Martijn will return to VIB. Congratulations, Martijn!

Martijn Schuijs

Antonella Fioravanti

Antonella Fioravanti is on a hot streak. She has won the EOS Pipet 2020, as well as the presentation award at Subtillery2020, a virtual conference on Bacillus subtilis and microbial colleagues. She was also selected as one Fortune's of the '40 under 40' Italian talents who are making waves in their field of expertise. Congratulazioni, Antonella!

Three VIB PIs have received an ERC PoC grant: Kevin Verstrepen (VIB-KU Leuven Center for Microbiology), Patrik Verstreken and Stein Aerts (both from the VIB-KU Leuven Center for Brain and Disease Research). Exceptional!

Kevin Verstrepen

Patrik Verstreken

Stein Aerts

Dirk Inzé

Dirk Inzé (VIB-UGent Center for Plant Systems Biology) has been elected as member of the prestigious Academia Europeae.

LAB CLEANING

Ayla

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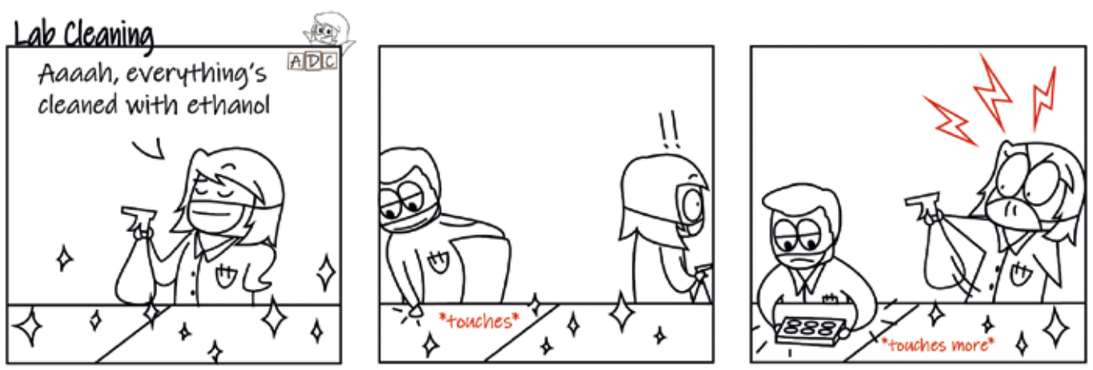

EMERGING TECHNOLOGIES IN SINGLE CELL RESEARCH

VIB's first virtual conference

On March 13th, the VIB Conference Series program was interrupted abruptly because of the rapidly evolving Covid-19 pandemic. Affected events have been postponed and the program will restart on November 19-20 with the first edition of Emerging technologies in Single Cell research, or SingleCell20 in short.

Single cell technologies provide extraordinary opportunities to address today's medical challenges. They will give us major insights into when, how, and why diseases of all kinds arise. This conference is organized by VIB and LifeTime, a pan-European research initiative. It will be VIB's first virtual conference.

If the virtual format is evaluated well, the VIB Conferences team might consider organizing hybrid conferences in future. This should make the VIB conferences accessible to scientists that cannot travel because of budget restrictions or personal reasons.

Secure your online ticket now!
https://bit.ly/SingleCell20

MARK YOUR CALENDAR

Emerging technologies in Single Cell research
November 19-20, 2020, online

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