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MEET
ROSA RADEMAKERS,
DIRECTOR OF VIB-UANTWERP
CENTER FOR MOLECULAR NEUROLOGY



VIB DISCOVERY SCIENCES

VIB DISCOVERY SCIENCES

At V-Bio Ventures we are constantly looking out for young, innovative companies in the life sciences area that develop solutions for high-demand unmet needs. When we find such a company, we provide support for the further expansion of the company's activities. As an early stage investor and company builder we also have the ambition to back talented scientists who seek to create exceptional companies.

Since the inception of V-Bio Ventures in 2015 we are closely working with VIB and, increasingly, also with the team of VIB Discovery Sciences. We knew from the start that VIB, with its huge pool of motivated and talented researchers, is the basis for excellent science and a great source for innovation. We now have come to realize that the team of VIB Discovery Sciences provides one of the bridges to bring that science closer to the market.

We have already worked with the VIB Discovery Sciences team in very different ways and are impressed by the flexibility and pragmatism they display, which is a necessity to collaborate successfully on such early stage projects. A key success factor for early-stage translational projects is the capacity to get the relevant industry expertise at the table sooner rather than later. VIB Discovery Sciences' ability to attract people with industry experience combined with the possibility to finance some of the early discovery work is crucial to accelerate early stage research programs.

The VIB Discovery Sciences team members are highly focused on reaching pre-set goals, such as for instance developing an HTS assay based on a novel target or find lead molecules or antibodies that modulate a novel target at predefined conditions. To find the best and fastest way to reach that goal they will either deploy their own expertise or collaborate with appropriately skilled external parties.

Enabling scientists through VIB Discovery Sciences to advance their projects beyond the stage of high-impact publications will allow more projects to be valorized. Value creation can take different forms, such as business development or new company creation. The latter option is V-Bio's core business. The creation of a company, however, is not a simple process. For the creation of a new company backed by venture capital, whether provided by V-Bio Ventures or by others, several conditions need to be fulfilled. Key among those is the availability of sufficiently compelling proof-of-concept data obtained in relevant, validated industry-standard models. This is precisely what VIB Discovery Sciences can contribute. VIB and V-Bio Ventures are natural partners in this process.

This collaboration has already yielded impressive and interesting results. A lot more is cooking and exiting news is to be expected. To be continued.

*Christina Takke and Willem Broekaert
Managing Partners, V-Bio Ventures*



Willem Broekaert en Christina Takke

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INTRODUCING VIB DISCOVERY SCIENCES: AN INTERVIEW WITH JÉRÔME VAN BIERVLIET

In 2015, VIB made a strategic investment in a team of industry-trained scientists and research infrastructure to build the 'VIB Discovery Sciences' unit. This team is embedded in VIB's Innovation & Business team and focuses on making specific expertise available to promising projects in VIB labs that are amenable to translation. In other words, the discovery unit initiates and guides the transformation of scientific insights into projects that could deliver novel therapeutics or agrochemicals. Throughout the entire process, VIB scientists remain involved to provide expertise on the basic biology of the project. The head of VIB Discovery Sciences, Jérôme Van Biervliet, elaborates on the goals and successes of the initiative so far.

Let's go back to 2015. Why was there a specific need for VIB Discovery Sciences?

"Over the years, VIB has proven to be very strong in building proof-of-concept in platforms toward new venture creation, with notable examples as Ablynx and Confo Therapeutics. In contrast, the traditional approach for single assets, for example therapeutics or agrochemicals, was historically mostly driven by industrial partnerships, rather than establishing an asset-centric spinoff. This is because it's hard to find

investors and industrial partners willing to take the mental leaps from scientific concept to development candidates. They tend to be quite risk-averse and want to see early-stage products and in vivo 'proofs-of-concept'. To bridge exactly that gap, from promising targets to the commercial development of products, we launched the VIB Discovery Sciences initiative. The team knows exactly what is needed to translate novel targets into investment-worthy assets. These assets can be intellectual property, industry-like data

packages, biological proof-of-concept data, and early-stage candidate molecules with a realistic potential for clinical application."

What type of projects does VIB Discovery Sciences typically take on? What are the criteria?

"It all starts with VIB science. The molecular research of our research groups provides VIB's Innovation & Business team with a rich source of medical, plant, industrial biotech and biomarker concepts. We pro-actively mine this basic biology work running in the institute for promising drug discovery targets. Of course, VIB scientists can also propose projects themselves. Whether a certain research project is suitable for the discovery unit is evaluated by the entire Innovation & Business team, in discussion with the PI.

All aspects for commercial opportunities are being considered, including the novelty of the project and the unmet societal need. Elementally, it should be realistic to develop the target into a medicine or agricultural product. In view of the attrition rate in such early stage projects, we only incubate a few projects with high potential at any given time. Plus, we often experience that lessons learned from one project benefit the other projects running in the team."

What is the difference with academic research and how does a project usually proceed?

"The main difference of a VIB Discovery Sciences project with academic research is the product-centric approach. We are not focused on publishing papers, but our goal is to develop a target into a product that benefits society. Basically, we start where academic research stops. We initiate the translational research needed to deliver validated candidates for small molecule or biologic therapeutics, and agro-products. Our team designs and plans early drug discovery projects, guides and executes assay development campaigns, and executes in vitro pharmacology

experiments. We also take charge of the project management, collaborate with partners with complementary capabilities (e.g. medicinal chemistry, antibody screening, etc.), and design proof-of-concept studies around novel candidate therapeutics. During the whole process, the team relies on the scientific advice and insights of the PI who initiated the project. It is the combination with top-level academic science that makes our discovery unit work. After all, the PI laboratory remains the key source of biological insights, interpretation of experimental results, research tools, scientific steering and creativity."

How would you evaluate the initiative so far? Which successes were achieved?

"To me, a successful project is one where we can make significant scientific progress and, at the same time, succeed in attracting a business partner to turn it into reality. Ever since its inception nearly four years ago, VIB Discovery Sciences is building a basis for value creation projects leading to asset-centric spin-off companies. This is elegantly exemplified by Oncurious, a spinoff founded by VIB and Oxurion in 2015 which focuses on the development of innovative oncology treatments. The portfolio of the new venture is based on the pre-clinical research conducted by the teams of Peter Carmeliet, Massimiliano Mazzone and Gabriele Bergers from the VIB-KU Leuven Center for Cancer Biology and Jo Van Ginderachter (VIB Center for Inflammation Research, VUB). By partnering early-stage innovative projects of VIB scientists we were hence able to develop the project into a new venture." (more on page 7)

"Another highlight is the drug discovery project for novel targets in Charcot-Marie-Tooth disease (CMT), based on the research of Ludo Van Den Bosch, Joris de Wit and Bart De Strooper (VIB-KU Leuven Center for Brain & Disease Research). CMT is characterized by the progressive denervation of muscles and affects touch sensation, especially in the extremities. There

DID YOU KNOW....

- ...that the VIB Discovery Sciences team interacts with outside partners in its network, typically Contract Research Organizations (CRO's), on a project-by-project basis to find expertise that is not available within VIB?
- ...that a VIB Discovery Sciences unit is currently being set up in the Tech Lane Ghent Science Park? The team there will focus on early discovery activities for therapeutic biologics. On April 1st two new colleagues joined the team in Ghent: Jimmy Borloo and Nadja van Boxel.

currently are no specific therapeutics available for this neurological disorder. Over the last years, the VIB research groups uncovered several biological pathways in peripheral neuropathies that represent promising therapeutic targets for CMT. VIB Discovery Sciences is now taking the project further towards the preclinical development of new therapeutics based on these novel targets. Importantly, we were able to attract external financing which allows us to really accelerate the project.” (more on page 9)

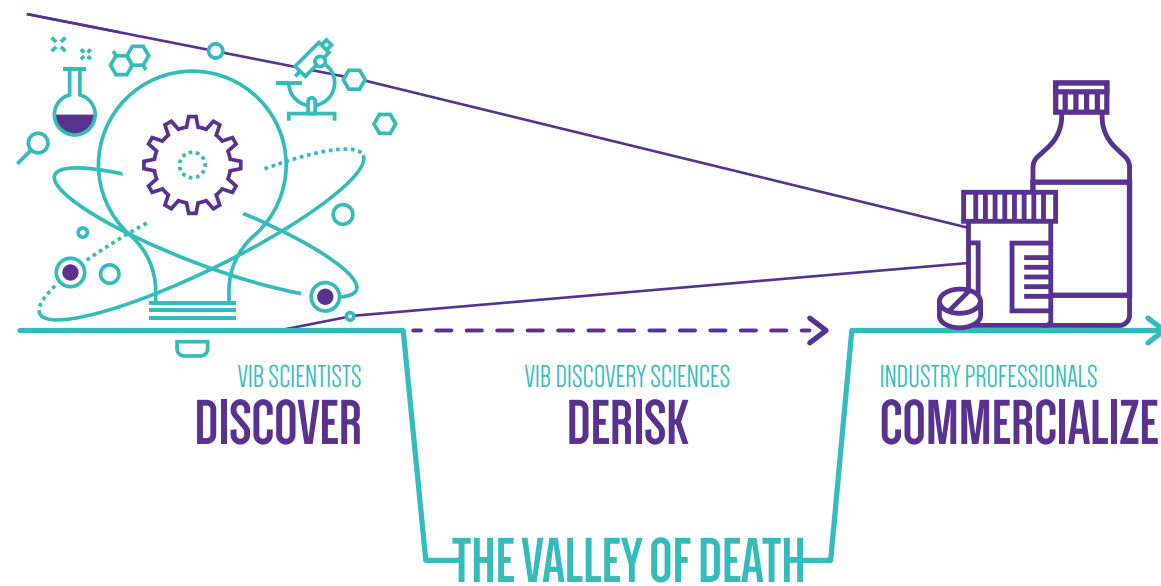
What type of scientists work in the team?

“In a couple of years’ time, the VIB Discovery Sciences team really has matured, with a team of 10 scientists and 7 technicians lead by senior scientists with strong industrial backgrounds: Bruno Dombrecht and Laurent Galibert. They each supervise a sub-team of project leaders and technicians. Many project leaders are former postdocs fresh out of VIB labs, who have a strong interest in industry. Moreover, several master students are already involved in the Leuven unit at the moment. As such, VIB Discovery Sciences doubles as a training ground for these young scientists in transition

to industry-type activities. For example, they learn what makes a good drug target and face questions like: which aspects are relevant to evaluate a novel target, what are the key uncertainties, and which experiments are needed to address these uncertainties? To extend further on this training aspect, the Innovation & Business unit has also launched an internship program. The idea is that the trainees rotate in the different units of the team, including in the Discovery Sciences team.

“You have the opportunity to work closely with very knowledgeable people having experience in the biotech industry, who introduce you to the world of antibodies, nanobodies, recombinant proteins and small molecules. They guide and stimulate you towards strategic thinking, target population and pharmacokinetics. You can take project responsibility while designing timelines, determining milestones and collaborating with CROs and partners.”

- Isabelle Cambré



ON THE IMPORTANCE OF BEING TRANSLATIONAL

The VIB Discovery Sciences team bridges the gap between academic research and product development. Translating novel targets, emerging from research of VIB research groups into promising projects of drug-development and agro-biotech innovations is its core business. And the team proves to be successful. Time to present this established track record through three novel collaboration models. The very first model in the field of immuno-oncology is clarified by Jean Feyen, chief scientific officer at Oxurion and Bruno Dombrecht, who joined the Discovery Sciences team in 2018 and specializes in therapeutic biologics.



Bruno Dombrecht and Jean Feyen

ONCOLOGY BIOTECH

A clear and confident press release on September 1st, 2017 announced the acquisition by Oncurion, a Belgium-based biotech company, of a unique portfolio of next-generation immune-oncology assets from VIB.

The exclusive licenses regarded five unique next generation immuno-oncology assets, based on seminal work originating from the labs of Massimiliano Mazzone and Gabriele Bergers (VIB-KU Leuven Center for Cancer Biology), and from the VIB-VUB lab of Jo Van Ginderachter (VIB Center for Inflammation Research).

Oncurion thus broadened its ongoing clinical development activities in orphan pediatric oncology indications with preclinical research and drug development programs, resulting in an exciting

“I believe that the possibility to launch a drug discovery program on targets that are so complementary, will give VIB and Oncurion a prominent position in the field of immune-oncology having the advantage to test novel combinations that trigger anti-cancer immunity by tackling the problem from diverse angles.”

- Massimiliano Mazzone

pipeline of next-generation immuno-oncology drugs targeting a broad spectrum of cancers.

The acquisition of this portfolio by Oncurion was the result of an intense, constructive collaboration?

Jean: “Yes, indeed. Oxurion, formerly Thrombogenics, with its expertise in drug development teamed up with VIB. They both are the founding partners of Oncurion, in what basically can be described as an innovative model of company co-creation. With Oncurion we created a strong and solid research and development team with an extensive track record in drug discovery and development.”

Bruno: "In essence it is a dedicated trust-built partnership and we are primarily capitalizing on synergies by combining the strengths of VIB research groups, VIB Discovery Sciences and Oxurion. It definitely all starts with the science. But the excellence in oncology and immunology of the VIB research groups joins forces with the expertise in multi-specific biologic drug discovery and immuno-oncology of the VIB Discovery Sciences team. At that team we also have easy access to VIB Core Facilities and other in-house technological expertise. At Oxurion on the other hand, we can rely on trusted experience in preclinical and clinical development and on bringing a product from the research bench to the market. It all adds up."

What is the current status of the immuno-oncology drug discovery pipeline?

Jean: "We are currently in a phase 1/2a clinical trial evaluating TB-403 (against placental growth factor) for relapsed medulloblastoma with the support of the US Consortium Beat Childhood Cancer. Initial data of this trial are anticipated towards the end of 2019. The orphan designation in the EU is approved, in the US the application is pending. And obviously we are developing the pipeline of 5 next-generation immuno-oncology compounds targeting a broad spectrum of cancers."

"The partnership of Oncurion and VIB to solidify several novel and innovative targets in the competitive immune-oncology arena is unique as it enables a valuable flexibility to complement and combine strategies ancillary to generate potent next-generation drugs in immuno-oncology."

- Gabriele Bergers

Bruno: "From a statistical perspective, the success rate of new medicines is extremely low. But at the Discovery Sciences team we help reduce the scientific and financial risks that usually come with drug

development funding. As a matter of fact, we can stay under the radar and that provides us with extra advantages versus the more conventional models in biotech collaboration. We collaborate in a lean and integrated manner with a light and flexible governance, we have early access to breakthrough science, we rely on the VIB network of technology and expertise and our company partners have lower upfront investments in infrastructure and know-how than other industry start-ups. In other words, we are extremely focused on protecting and maturing innovative drug concepts."

"The decision of Oncurion to engage in drug discovery against targets that are still relatively early in the validation process, is rather exceptional. It can bring both Oncurion and VIB in pole position to deliver the next generation immuno-oncology drugs that may be complementary to the well-known immune checkpoint blockers."

- Jo Bury

What are the ambitions of Oncurion for further growth?

Jean: "We hope to bring Oncurion to the point of being a solid stand-alone biotech company in Flanders thanks to our novel collaboration model. At the moment, we are co-creating and developing Oncurion's preclinical drug discovery pipeline. Oncurion will leverage the expected in vivo proof-of-concepts from this collaboration to attract additional funding, either by out-licensing or round A investments. Over time, Oncurion will take on full responsibility for these assets as a fully-funded stand-alone biotech company."

Bruno: "Creating Flanders-anchored biotech companies certainly is one of our targets. But being close to the source of scientific breakthroughs and immediately translating these into drug candidates creates a high societal impact as well and that is of course equally rewarding."

PATIENT-DRIVEN THERAPEUTICS

Our second example of the intense exchange of our basic science researchers with the Discovery Sciences team leads us into the field of neurology and peripheral neuropathies. More specifically to Charcot-Marie-Tooth disease (CMT), an incurable progressive weakening and atrophy of distal limb muscles. Patients develop foot deformities and gait difficulties, and also experience sensory abnormalities. CMT has a severe impact on the quality of life of its patients. Ludo Van Den Bosch, who is specialized in CMT, is professor neurobiology at the VIB-KU Leuven Center for Brain & Disease Research. His ultimate goal is to contribute to the development of new therapeutic strategies for neurodegenerative disorders. He partnered with Laurent Galibert of the Discovery Sciences team, who has over 20 years of experience in drug discovery and therapeutic modalities. They are both at the very core of a new ambitious project with the mission to develop innovative therapies for patients suffering from CMT. The project is currently in a proof-of-concept phase and recently external funding was obtained to finance the feasibility study.



Ludo Van Den Bosch



Laurent Galibert

What was the basic scientific breakthrough, the spark that set off the collaboration between the VIB-KU Leuven Center for Brain & Disease Research and the VIB Discovery Sciences team?

Ludo: "Our research group focuses on the mechanisms of neuronal degeneration and regeneration. Axonal degeneration of the motor and sensory axons is the main characteristic of CMT. We focus on the pathogenic mechanisms underlying this degeneration, with a particular focus on CMT induced by mutations in HSPB1 and GARS. Our research concentrates on the involvement of cytoskeletal modifications and the role

of axonal transport defects in the pathogenesis. Histone deacetylase 6 (HDAC6) modifies the components of the tracks needed for axonal transport and selective inhibition of HDAC6 reverses the axonal transport defects, as well as the phenotypes observed in our different disease models."

"Moreover, our team discovered that HDAC6 inhibition has a broad therapeutic potential both for inherited peripheral neuropathies, such as CMT, as well as for acquired chemotherapy-induced neuropathies. Thanks to the Discovery Sciences team, we can further develop this potential."

Laurent: "The main question for the VIB Discovery Sciences team is how one can take the scientific breakthroughs of Ludo's team and translate them into a viable drug discovery project with a competitive edge. We are there to define all parameters for this endeavor, constitute a project team, define the characteristics of the products that will result from this effort and the ways to fund such an endeavor."

The academia-industry cultural divide is often perceived as being huge. How does the VIB Discovery Sciences team bridge that gap?

Laurent: "Basic science aims at advancing knowledge and is discovery driven. Its final goal is an understanding of the world. The basic rules are those of competition via intellectual insight. The world of the biotech companies on the other hand is application driven and product-centric. In the biotech sector competition is based on innovation. Translational science, the playing field of the Discovery Sciences team, tends to imagine, develop and optimize a product. We have to spot business and valorization potential, take the lead in pre-clinical research, develop drugs and agro-biotech innovations and attract investors. We are walking the bridge both with the academics and the industry to meet in the middle."

Does a scientist feel more confident when approaching the industry if he or she is assisted in that process?

Ludo: "A researcher is likely to pay more attention to the translation of his fundamental research into products if he is backed by a team offering industrial know-how and business expertise. But the key starting point is always high-quality research and let's not forget the patients. It is for the benefit of the patients that we want to translate our scientific discoveries into drug candidates. That's our most powerful motive."

Laurent Galibert: "We at VIB Discovery Science like to think we are 'bilingual', speaking both the academic and industrial language. We have also already walked the path from scientific discovery to industrial innovation several times. This, we hope, provides reassurance to researchers venturing into drug discovery. In addition, we certainly tend to operate in fields with high societal impact that would have little chance of success without our involvement."

A QUEST FOR NEW PRODUCTS

The portfolio of the VIB Discovery Sciences team does also include agro-applications. Anne Helfer was a senior scientist at BASF Plant Science Crop design before joining the VIB Discovery Sciences team. She has rich experience in crop protection and plant growth regulation. She collaborates with Lieven De Veylder, group leader at the VIB-UGent Center for Plant Systems Biology. In his research, Lieven aims at identifying mechanisms that link cell division with environmental stimuli. Both Anne Helfer and Lieven De Veylder are engaged in a quest for new products.

What major challenges does agriculture nowadays face?

Anne: "The challenges are threefold. The agricultural industry desperately needs new products, farmers face low income and consumers want healthy foods at low cost. Innovation in support of sustainable agriculture is an important societal challenge. New 'perfect' products need to be safe and user friendly, economically viable with a good cost/benefit ratio for the farmer, biologically efficient with a fast impact and of course environmentally sound with no toxicity. Knowing that worldwide some 30.000 weeds compete with crops for space, nutrients, water and light, it is clear that the search for weed management strategies is on."

Were you specifically searching for an effective herbicide?

Lieven: "No, my job as a scientist is to unravel the chemical biology of plants. We basically address the question: how do plant cells know when to proliferate and when to stop dividing? In doing so we screen for compounds inducing polyploidy in plants. Polyploidy increases crop yield and we found that one specific new compound C17 induces polyploidy and possesses strong herbicidal properties. In short, it can be the



Anne Helfer and Lieven De Veylder

starting point for a program to develop a spray herbicide."

Anne: "That's when we at the VIB Discovery Sciences team come forth, we spotted the potential of C17 in its use in combination with other existing herbicides and we started the activities to discover additional novel compounds."

Does this mean that the process towards a new agro-biotech innovation smoothly unfolds according to plan?

Lieven: "Optimization of the compound is still crucial. C17 needs to get a higher potency, its eco/toxicity profile needs tailoring and we need to enhance its

formulation. But that is exactly why the VIB Discovery Sciences team is assisting us."

Anne: "It's like an intricate puzzle. The research grant of FWO as a funding agency allows the scientists to develop novel biology, we have a hit compound discovery thanks to the activities of the VIB Discovery Sciences team and the VIB Screening Core. The current activities are aimed at optimizing the compound together with a chemistry partner, the KRICT. For the actual development we will set up a search for an external partner. Every little piece of the puzzle needs to fit flawlessly before we can partner around this project to further develop an innovative agro-product and thereby achieve impact for farmers."

ANTIBODIES YOU CAN EAT

A THERAPEUTIC REVOLUTION FROM THE CALLEWAERT LAB AND COLLABORATORS

Therapeutic antibodies are being used increasingly in the clinic for the treatment of various diseases. Yet, oral to gut targeting of antibodies remains a challenge due to their incapability to survive digestion and reach gastrointestinal tissues. Now, the labs of Nico Callewaert (VIB-UGent Center for Medical Biotechnology), Ann Depicker (VIB-UGent Center for Plant Systems Biology), Henri De Greve (VIB-VUB Center for Structural Biology) and Eric Cox (UGent Faculty of Veterinary Medicine) have developed a new antibody technology that combines the advantages of antibody-based therapies with the convenience of oral drug administration. Importantly, these antibodies are manufactured using yeast or soybean in a process as straightforward as food manufacturing. This work, led by Vikram Virdi, was published in *Nature Biotechnology*. This technology may have potential uses in various areas, from fighting veterinary and human gut infections, treating inflammatory and metabolic disorders, to the development of microbiome altering food supplements.

Did you grow up wanting to be a scientist?

Vikram: "Well, as a curious child I wanted to be a scientist in a white coat, but it was much later, around 16 or 17 years of age, while watching a TV program on plant-made insulin, that I was captured by a fascination for molecular farming. This led me to pursue a PhD making VHH based antibodies in plants which, during my postdoc time, got refined and developed to the current innovation together with the guidance of my mentors and advisors."

Was there a specific 'Aha-moment' during this research journey?

Vikram: "Discovering that monomeric-IgA-like bivalent VHH-IgA works in the gut lumen just as well as the secretory VHH-IgA

version was a pleasant surprise. We couldn't have predicted this, as it's the secretory version that is found in our gut. This discovery was significant as it presented the possibility to produce the single-gene-requiring VHH-IgA antibodies in a variety of platforms. As we demonstrated, we could produce these VHH-IgAs in soybean seeds and yeast cells of *Pichia pastoris*. A second serendipitous discovery was that the yeast-secreted VHH-IgAs can be freeze-dried or spray-dried, just as milk powder is manufactured. This preparation is stable for up to 2 years at room temperature and requires no encapsulation for oral delivery. These features are significant as they will ease manufacturing and further broaden the scope of applications."

There were a lot of collaborators from different fields involved. How did this improve the scientific research?

Ann: "Producing antibodies in plants started quite naively. We had no idea how complicated it is to bring a pharmaceutical product, such as an antibody, to the market. It's not so much the production, but the subsequent purification and quality control that gobbles up most of the budget. On top of that there are the clinical trials to test the safety and efficacy of the antibody. So, it was really stimulating, inspiring and eye-opening to have groups with complementary knowhow and facilities contributing to this project: plant, industrial and biomedical biotech, food and feed processing, animal husbandry, and control of infectious diseases.

In fact, it was amazing to realize how incompetent we are as scientists from the moment we step out of our own expertise and comfort zone."

What's next? Are you going to follow up this groundbreaking research?

Vikram: "We are currently exploring the application of this technology to target human ailments such as inflammatory bowel disease, *Clostridium difficile*, and others. We would like to explore the potential for preventing enteric infections in resource-poor and/or post-disaster settings to prevent humanitarian crises like the cholera epidemic in Haiti following the 2010 the earthquake. Being cold-chain-free, we envisage convenient deployment of the edible VHH-IgA

together with the relief force. We would like to work towards realizing this dream."

What do you see on the horizon, based on this work?

Vikram: "We hope our work gives impetus to monomeric IgA-based passive mucosal immunization efforts, inspiring other non-invasive needle-free ways of antibody mediated protection."

Ann: "An even greater social impact of this work is that these experiments in piglets can be used as model and proof of concept for preventing human gastrointestinal infections, such as traveler's diarrhea, which is caused by a gut-colonizing bacterium. Our results suggest that ingesting specific antibodies with one's meals could prevent a variety of viral and

bacterial gut infections in humans."

Any reflections now that the work has culminated in a major publication?

Ann: "Looking back, I can say that I'm truly happy that I was able to contribute to societal progress through a combination of fundamental and applied research. Research that, I might add, was conceived to inch towards the realization of the United Nation's Sustainable Development Goals. Not only gaining knowledge and understanding has given me a lot of satisfaction, but also collaborating on the development of products flowing from our fundamental research."

Virdi *et al.*,
Nature Biotechnology 2019



Vikram Virdi, Ann Depicker and Nico Callewaert

FROM SPINAL CORD INJURY TO RECOVERY

Spinal cord injury disconnects communication between the brain and the spinal cord, disrupting control over part of the body. Studying the mechanisms of recovery, Leuven researcher Aya Takeoka (NERF - empowered by imec, KU Leuven and VIB) found that a specific type of neuronal feedback from sites below the injury plays a crucial role during early recovery and for maintaining regained motor functions. These new basic research findings implicate the importance of continued use of affected body parts for rehabilitative success in spinal cord injury patients.

"Following spinal cord injury, disrupted neuronal pathways can no longer provide sufficiently strong signals to the spinal networks below the injury, often leading to permanent and devastating motor impairment," explains Aya Takeoka from NERF (NeuroElectronics Research Flanders), an interdisciplinary research center empowered by VIB, KU Leuven and imec. Her lab studies the mechanisms of motor learning and control, including how motor functions recover after injury.

"Incomplete injuries, where only parts of the neuronal connections are damaged, frequently recover spontaneously," adds Aya. "We know that activating a very specific type of sensory feedback pathway plays a crucial role during rehabilitative training, promoting the formation of detour circuits. Understanding this process in more detail can help us design rehabilitation strategies with maximal benefit for spinal cord injury patients."

Early and maintained feedback for maximal success

One type of so-called somatosensory feedback is proprioception, which entails the unconscious perception of self-movement and body position through nerve cells that are in close proximity of the spinal cord and can detect muscle stretch.

To learn more about where and when proprioceptive feedback affects locomotor recovery after injury, Aya devised a conditional genetic approach to eliminate this type of feedback at different locations and time points in mice. Using these models, she showed that proprioceptive feedback below but not above the site of injury is critical for naturally occurring circuit rearrangement and locomotor recovery.

"We found a central role for so-called proprioceptive

afferents, nerve fibers which signal proprioceptive information back to the spinal cord," says Aya. "Afferents below the lesion undergo specific rearrangements soon after injury, and without them regained motor function cannot be maintained, even if detour circuits have formed."

In short, proprioceptive feedback is not only essential to initiate locomotor recovery but it is also permanently required to maintain any regained motor function. According to Aya, these findings can inform rehabilitation practices for patients as well:

"The fact that proprioceptive feedback, specifically from below the site of injury, is so important, suggests that task-specific rehabilitative training that emphasizes such feedback is likely to maximize functional outcomes in rehabilitation clinics."

Takeoka & Arber, Cell Reports 2019



Aya Takeoka

MAPPING CELLULAR DIVERSITY

A Belgian team of computational biologists led by Stein Aerts (VIB-KU Leuven Center for Brain & Disease Research) has developed a new bioinformatics method called cisTopic. Inspired by text-mining methods, cisTopic helps scientists to gain insight into the mechanisms underlying the differences in gene regulation across and within the cells in our body by looking for common topics.

"All the cells in our body essentially contain the same DNA," explains Stein Aerts, who heads the lab for computational biology at VIB and KU Leuven. "What makes every cell type unique is which genes are active at any given time."

Recent advances in single-cell technology have enabled scientists like Stein to look at gene activity and the accessibility of regulatory DNA regions for thousands of individual cells. But this information has not yet solved the challenge of reverse engineering the genomic regulatory code.

Clustering cells

Carmen Bravo González-Blas and Liesbeth Minnoye, two young researchers in Stein Aerts' lab, set out to tackle this problem. "The data we can obtain from a single cell, regarding accessibility of specific regulatory regions in its DNA, is very sparse. Yet, we wanted to group individual cells into clusters based on similarities of these accessible regions."

To tackle this problem, Carmen borrowed a computational technique from the text-mining field, called 'topic modelling'. She explains: "In text mining, computers can discover 'topics' from large collections of text, as well as terms that are important for each topic. When applied to our problem of gene control, the computer discovers topics that are important for each cell type in our body. It also allowed us to identify regulatory regions for each topic."

"We evaluated our new method on a variety of data sets and found that it allows us to accurately recover both expected and new cell types," adds Liesbeth. "Particularly on very sparse data, our method is more robust than previously developed approaches."

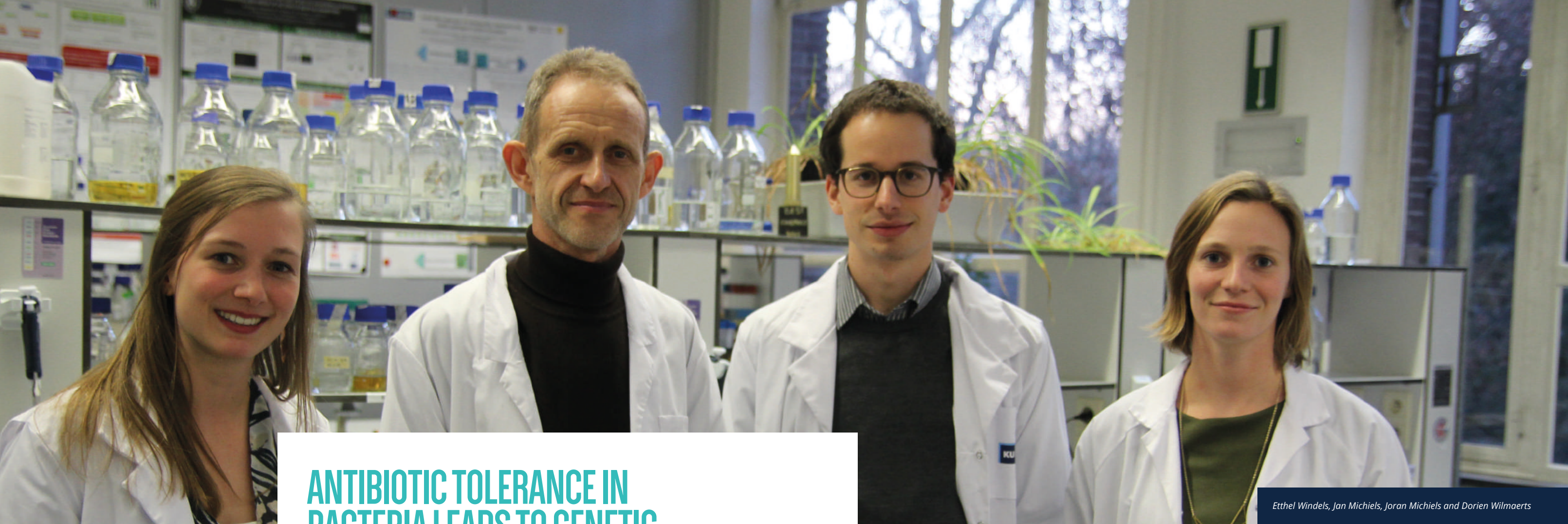
Learning more about complex tissues

The researchers applied cisTopic to cell populations that are biologically complex, such as the cells present in the mammalian brain. Not only did cisTopic allow them to recover the major cell types in the brain, but the team was also able to identify new subpopulations and master regulators of neuronal cell types.

"In addition to the brain, we also used cisTopic to investigate dynamic changes in gene accessibility in melanoma cell cultures from patients," adds Stein. "When we modulated one of the known important modulators in these cancer cells, we could - for the first time - track changes in the accessibility of different DNA regions over time. Such approaches will finally allow us to better understand what these master regulators actually do in cancer cells, and which genes they control."

These different applications illustrate the value of the team's new method for studying the players and mechanism that orchestrate gene regulation in our cells. According to computational biologists like Stein, this is an important step towards real-time and personalized monitoring of cell states in health and disease.

Bravo Gonzalez-Blas *et al.*, Nat Methods 2019



Ethel Windels, Jan Michiels, Joran Michiels and Dorien Wilmaerts

ANTIBIOTIC TOLERANCE IN BACTERIA LEADS TO GENETIC RESISTANCE

A study conducted at the VIB-KU Leuven Center for Microbiology supports the theory that in bacteria, the strategy of generating 'sleeping' persister cells to survive antibiotic treatment drives the evolution of highly resistant strains. The findings indicate that therapeutic strategies combatting the emergence of persister cells are crucial to fighting antibiotic treatment failure, which claims 50,000 lives every year in the US and Europe.

Bacteria use two different strategies to survive antibiotic treatment: resistance, or a general ability to grow in the presence of antibiotics, and tolerance, the formation of small numbers of antibiotic-tolerant

'persister' cells. These persister cells serve as a reservoir that can continue to cause disease. Research has shown that the type and schedule of treatment determines which strategy bacteria use to combat the effects of an antibiotic drug. Continuous low doses of antibiotics tend to incite general resistance, while intermittent high-dose treatment causes increased tolerance and persistence.

Two different survival strategies

Ethel Windels and colleagues in the group of Jan Michiels found that when bacteria create tolerant persister cells to survive intermittent high doses of

antibiotic drugs, these persisters are more likely to generate genetic mutants that are even more antibiotic resistant than the original bacterial population.

Ethel Windels (VIB-KU Leuven Center for Microbiology): "This increased tolerance and persistence strategy was demonstrated by earlier experiments to act as a stepping stone towards the evolution of genetic resistance. This is because persister cells can produce new cells that are all genetically drug resistant. As a result, tolerance is the culprit behind many chronic and recurring infections. Our observations highlight the fact that tolerance is an important

target for therapeutic strategies, as its genetic consequences are far-reaching."

Linking drug resistance in bacteria and cancer cells

Despite recent research underlining the relevance of tolerance, doctors rarely take it into account when prescribing antibiotic regimens. Because the tolerance and persistence strategy has been documented in all major bacterial pathogens, discounting tolerance could potentially lead to the emergence of deadly genetically resistant strains. Jan Michiels (VIB-KU Leuven Center for Microbiology): "Our study suggests that the link between tolerance and the

emergence of resistance is widespread. Even more, there are marked similarities between this strategy in bacteria and drug resistance in cancer cell populations. As a result, new insights in these two fields may be complementary."

Preventing cells from 'falling asleep'

Earlier work by Dorien Wilmaerts, also from the Jan Michiels Lab, published in mBio, revealed important insights into the mechanisms driving resistance and persistence in bacteria.

Dorien Wilmaerts (VIB-KU Leuven Center for Microbiology): "Our research also focused on bacterial

persister cells, which go into a sort of protected hibernation mode in order to survive antibiotic drugs. We investigated the mechanisms behind how these cells fall into this deep sleep and thus avoid being killed, potentially leading to new ways of preventing the formation of persister cells."

Wilmaerts *et al.*, mBio, 2018
Windels, Michiels *et al.*, The ISME Journal, 2019

MOLECULAR MACHINES AND EVOLUTIONARY RIDDLES: THE SAVVIDES GROUP ELUCIDATES BOTH

A research team from Savvas Savvides' lab in the VIB-UGent Center for Inflammation Research, led by Kenneth Verstraete, has unraveled the three-dimensional structure and molecular mechanism of ATP citrate lyase (ACLY). This is a central metabolic enzyme needed to produce acetyl-CoA which fuels essential biochemical processes in cells, such as the production of fatty acids and cholesterol. Their findings could help with targeting ACLY in cancer and metabolic diseases such as atherosclerosis. The structure of ACLY also unmasked a crucial evolutionary relationship that radically changes our understanding of the origins of cellular respiration.



Koen Verschueren, Ann Dansercoer, Savvas Savvides and Kenneth Verstraete

Where did the idea for this research come from?

Kenneth: "I joined the lab in 2004 as a master thesis student to work on the ACLY project aiming to optimize the production and purification of human ACLY for structural studies by X-ray crystallography. However, the size and modular nature of ACLY made structural studies challenging, and admittedly a bit to my disappointment, at the end of my master thesis, the elucidation of the ACLY structure was not in sight. I was so much triggered by the field of structural biology that I started a PhD project with Savvas. After that, during my FWO-funded postdoctoral research, I remained fascinated by the still enigmatic structure of ACLY and the intriguing evolutionary link with other central metabolic enzymes. Near the end of 2016 and building on the experience I had gained in structural biology, I took the initiative to revisit the ACLY project. Important factors that then contributed to an increased feasibility were the availability of affordable custom gene synthesis and the introduction of high-throughput screening."

As a child, could you have imagined doing something like this?

Kenneth: "My fascination with research in the biological sciences was ignited in high school when I was first exposed to the *central dogma of molecular biology*. I still

vividly remember my amazement about the intricate organization of life at the molecular level."

At which moment did you realize that this work was going to be so significant?

Kenneth: "Since ACLY is an enzyme of central carbon metabolism found in all domains of life, we anticipated that elucidating the structure and mechanism for ACLY would be highly significant. Moreover, in recent years, human ACLY gained much interest as a therapeutic target in metabolic diseases and cancer. Finally, our structure-driven hypothesis that the oxidative Krebs for cellular respiration emerged from the reverse Krebs cycle added a most fascinating insight about the evolution of metabolism on earth."

How did the collaboration with others (both within and outside of VIB) improve the scientific research?

Savvas: "This work is the result of great collaborative efforts in the spirit of integrative structural biology and has relied on state-of-the-art approaches and access to European synchrotron radiation facilities. Our research benefitted from fruitful collaborations with teams from the EMBL (Hamburg, Germany) and ISB-CNRS (Grenoble, France) that allowed us to obtain valuable insights about the structural plasticity of ACLY that could not be attained by crystallographic studies alone."

But also the result of great team work within your lab?

Kenneth: "Indeed! Ann Dansercoer and Koen Verschueren were key to the success of this story. Ann performed recombinant production of ACLY enzymes, and Koen and I conducted crystallographic studies. The study is really the result of a close and intense collaboration. I will always look back with a happy feeling to the period between February and December 2017, when Koen and I travelled about a dozen of times to different European synchrotrons located in Switzerland, France and Germany. Most importantly, in that period, we were able to determine different high-resolution structures of ACLY in quick succession, with the structure of human ACLY in December 2017 providing the icing on the cake."

In a hypothetical world where funding and time are not an issue, how would you like to follow up this work?

Kenneth: "I have applied for an ERC 2018 starting grant with a research proposal on ACLY and I'm currently on the reserve list. We aim to unravel the regulatory protein interaction network of ACLY by biophysical and

structural studies. Moreover, our recent results form a molecular framework to develop or optimize ACLY inhibitors in cancer and metabolic disorders. In the future I very much hope we can contribute in this field. In this regard, I'm very keen to develop collaborations with academic groups or pharmaceutical companies that have running programs on ACLY inhibitors."

What was the most pleasant aspect of the entire process from study design to publication?

Kenneth: "Solving the structure of the first ACLY enzyme, from the green sulphur bacterium, *Chlorobium limicola*, in February 2017 was an important boost for the project. It demonstrated that structural studies on ACLY were indeed possible."

What is the main lesson you learned during the years you dedicated yourself to this research?

Kenneth: "I think my 15-year long journey in this project taught me to not give up easily. In addition, I think it is important to always be critical about, and if necessary rethink, your research strategy."

Verschueren, Verstraete *et al.*, Nature 2019

WHAT MAKES MEMORIES STRONGER?



Fabian Kloosterman

A team of scientists at NeuroElectronics Research Flanders (NERF - empowered by imec, KU Leuven and VIB) found that highly demanding and rewarding experiences result in stronger memories. By studying navigation in rats, the researchers traced back the mechanism behind this selective memory enhancement to so-called replay processes in the hippocampus, the memory-processing center of the brain. These important findings provide new insights into one of the most enigmatic brain features: memory consolidation.

When we experience something important, we usually remember it better over time. This enhanced memory can be the result of stronger memory encoding during the experience, or because of memory consolidation that takes place after the experience. For example, experiences that turn out to be very rewarding have been found to lead to stronger and longer-lasting memories.

“One of the ways in which our brains consolidate memories is by mentally reliving the experience,” explains Fabian Kloosterman, whose research is aimed at unravelling memory processing in the brain. “In biological terms, this boils down to the reactivation or replay of the neuronal activity patterns associated with a certain experience. This replay occurs in hippocampal-cortical brain networks during rest or sleep.”

The question Kloosterman and his team at NERF (empowered by imec, KU Leuven and VIB) set out to answer was whether the positive effect of rewards on hippocampal replay extend beyond the time of the experience itself and thus could further support enhanced memory consolidation.

Rewards and challenges

To find answers, the researchers trained rats to learn two goal locations in a familiar setting. One of the goals was a large reward—nine food pellets—while the other goal location only had a single food pellet on offer as a small reward.

“Perhaps unsurprisingly, we found that rats remembered better the location where they found the large reward,” says Frédéric Michon from the Kloosterman lab, who conducted the experiments. “But we also observed that this reward-related effect on memory was strongest when the food pellets were located in places that required more complex memory formation.”

Replay for better memory

To assess the contribution of replay brain activity after the actual experience, the researchers disrupted this particular signaling network, but only after the rats got a chance to discover the reward locations. Michon: “Mirroring our earlier findings, we observed that memory was impaired only for the highly rewarded locations, and in particular, when the rewards were at challenging locations.”

In sum, the researchers could demonstrate that hippocampal replay, occurring after initial learning, contributes to the consolidation of highly rewarded experiences, and that this effect depends on the difficulty of a task. “A relatively simple experimental setting with rats and food pellets can teach us a lot about memory,” says Kloosterman. “Our results demonstrate that replay contributes to the finely tuned selective consolidation of memories. Such insights could open future opportunities for treatments that help to strengthen memories and could also help us understand memory decline in diseases such as dementia.”

Michon *et al.*, Current Biology 2019

MEET ROSA RADEMAKERS

NEW DIRECTOR OF THE VIB-UANTWERP
CENTER FOR MOLECULAR NEUROLOGY

Since Christine Van Broeckhoven will be retiring as director of the VIB-UAntwerp Center for Molecular Neurology, we needed someone to replace her. Hers, however, are big shoes to fill. Fortunately, VIB managed to attract Rosa Rademakers, an alumna of the center and former student of Christine. Rosa has made a name for herself on the international dementia research stage as professor at the renowned Mayo Clinic (Jacksonville, Florida, US). Now, she returns home, backed by more than a decade of experience and a portfolio of the highest quality research.

We were pleased to talk to her about the next step in her already great career, and her move back to Belgium, VIB and the University of Antwerp.

You return to your alma mater, after almost 14 years in the department of Neuroscience of Mayo Clinic. And you return to the research center where you did your PhD. How do you feel about this?

“I am very excited to return home. Christine’s retirement provided an incredible opportunity to take the next step in my career and to be closer to my family. It is a double-edged sword, though. It takes time to build a lab with great people. It’s sad to leave that behind and start over.”

But you will keep interacting with your current lab? Perhaps even bring some people with you?

“There are a few people who will come with me. But

it’s hard to convince Americans. Fortunately, Cristina Vicente and Cyril Pottier, a postdoc and a senior staff scientist with European roots, will join me to help with setting up the lab. We have also worked out a scenario where I remain affiliated with Mayo Clinic. This means that the patient samples, the network of clinicians and researchers, will all still be available to me. This allows me to start a new adventure and at the same time continue the work I’ve set up in the US.”

How has the research/scientific world changed in these 14 years? In the US? In Flanders?

“It has progressed tremendously, in both places. The focus of my research is neurogenetics. When I did my PhD with Christine in Antwerp, we looked at two affected families to try and find involved genes, or even the chromosome where these were located. This took me my entire PhD and we didn’t even find it. Now, we sequence a whole genome in a day. Bioinformatics and statistics have also become much more relevant. We build large consortia that study vast numbers of patients with new methods and statistical approaches.”

You talk about consortia and the relevance of bioinformatics. Does it still matter where you do your research?

“That’s something I asked myself as well. And the answer is I’m not sure. Basically, everyone is working together now. I personally think that it doesn’t matter that much anymore where you are. Of course, there are more local interactions, which is an exciting opportunity for me to get involved in European studies. The funding



Cristina Vicente, Cyril Pottier and Rosa Rademakers

is different though. I'll have to learn how to write an ERC grant. In general, you can do the research in Belgium just as I would do it in the US, especially at VIB, which is really at the forefront of the research."

Moving from group leader to science director is a big step. How do you see this? How will you deal with this challenge?

"That's the part I'm most excited about. This is the next big step in my career, to build on the work already done in Antwerp. In addition to Albena Jordanova and myself, we will recruit three new group leaders and reshape the center. It's a great opportunity to build a team filled with people who are passionate and work well together."

"The VIB-UAntwerp Center focuses on team-science and integrates innovative clinical, genetic, computational and functional biology approaches to define the molecular causes of neurodegenerative diseases and its key disease-modifying pathways to create a world where individuals at risk for neurodegenerative diseases can be identified before the onset of clinical symptoms, where disease progression can be halted and individualized treatments are available to delay, reverse or prevent neurodegeneration."

Mission statement VIB-UAntwerp Center for Molecular Neurology

- Rosa Rademakers

Looking at your mission statement we have a few questions about it: you stress the integration of technologies. How important were the technology-related programs at VIB (Cores, Tech Watch, Innovation Lab) in your decision?

"Truthfully, I only learned about these things during the interview process, so it wasn't the primary factor in my decision. But after I found out, I was very happy to see that VIB invests in new technologies. It is great to know that when new technologies are developed, we'll be among the first to be able to use them, which is very important in neurogenetics to get the maximum out of your samples. It opens opportunities and can be important to recruit top people, to make it attractive for new PI's to join us. I did know about Mojca Strazisar, the expert technologist in the VIB-UAntwerp Center, who is certainly an asset. The challenge is to keep up since these technologies change so rapidly."

You consider technologies important, but also team science. How do you see this?

"Team science occurs at multiple levels. On the one hand, I want people to work together in a collaborative environment. Ideally in an interdisciplinary way, for example computational biologists working with geneticists, structural biologists, and clinicians. This doesn't have to be all in our center. We could collaborate, for example with the Center in Leuven."

These interdisciplinary collaborations are often more than the sum of their parts."

How do you think the collaboration between the different VIB neurological research centers in Antwerp and Leuven should evolve?

"It's incredibly important to create strong ties with Leuven. We've already been in contact and they will certainly be involved with the recruitment of new people in Antwerp. But we will also retain our own identity. In Antwerp I would like to focus on computational biology. It's all big data now. We have data from hundreds, thousands of patients. And not only on the genetics, but also on the epigenetics, transcriptomics, proteomics... If you can apply novel computational methods on this data, it will be possible to do incredibly exciting research. But to get a complete picture we need functional validation and we need to understand what happens in the brain. That's where we could use partners, including the experts in Leuven."

This brings us to your ambition to define the molecular causes of neurodegenerative diseases. How much of the iceberg do we still have to uncover?

"We've certainly made good progress. There are of course differences for the various types of dementia. Through the study of families with autosomal dominant inheritance we've explained the tip of the iceberg, the major causal mutations; whereas genome-wide association studies in larger patient populations have identified the first risk factors. But there are still a lot of patients we can't explain yet. We also need to focus more on complex mutations including copy-number variation and repeat expansions."

It is not easy to translate this into therapies and diagnostics, I suppose?

"The hope is that when you see certain shared pathways, you can identify therapeutic targets. The starting point is highly complex, the statistics and computational models and so on, but eventually it might give us a clear idea about a downstream target that affects a large group of patients. The challenge is the step in between, the development of screening assays or tests to narrow the list of therapeutic targets. This step is also where different disciplines meet, again stressing the importance of teamwork and interdisciplinarity."

What are you looking forward to the most coming back to Belgium/VIB/Antwerp University?

"On the professional side: the fresh start. The chance to build something and recruit the right people. But

personally, just moving back to Europe. European food! Also, the ability to take vacations in Europe. When you live abroad, vacation is always coming back to Belgium for visits. I am looking forward to making Belgium our base to explore the rest of Europe, to expose our kids to different cultures. And to being closer to our families, of course."

Are there (not science-related) aspects of working in the US that you would like to introduce here?

"What I want to take with me is having confidence in your work. This relates to the idea of the American dream, aiming high. People, scientists, in Europe tend to be more modest. I want to bring that to the center, the pride in their/our work, the conviction that they/we are among the top, not to be intimidated. That's something I learned. I went to the US with an FWO-fellowship and in the lab of Mike Hutton I was part of the team that found the gene progranulin I'd been looking for during my PhD. Then Mike left, and I had the opportunity to lead the lab. This simply illustrates the American way of 'just doing it.' I remember talking to my colleagues in Belgium then, and their amazement."

WHO IS ROSA RADEMAKERS?

Rosa Rademakers started her academic journey at the University of Antwerp, where she got a BA in Biology and an MA in biochemistry. She stayed in Antwerp to follow this up with a PhD in the lab of Christine Van Broeckhoven. During her postdoc she traveled to the Mayo clinic in Florida, US. She moved through the academic ranks and became full professor in the Department of Neuroscience in Mayo Clinic in 2014. In 2019, she will join VIB as the new science director of the VIB-UAntwerp Center for Molecular Neurology. She is President of the International Society for Frontotemporal Dementias and is a member of the Medical Advisory Council of the Association for Frontotemporal Degeneration. She has received the Paolo Gontijo Medicine Award and the Sheila Essey Award for ALS Research. She is also the recipient of the 2016 Potamkin Prize for Research in Pick's, Alzheimer's and Related Disorders of the American Academy of Neurology.

QUICKSCAN

1

**#Climate change #Plant growth
#Thermosensing**

Plant growth and flowering time are in part determined by environmental temperature. The combined expertise of the labs of Ive De Smet (VIB-UGent Center for Plant Systems Biology) and Kris Gevaert (VIB-UGent Center for Medical Biotechnology) allowed setting criteria for plant thermosensors that recognize a temperature cue and that trigger a specific response. To identify novel thermosensors structural analysis of DNA, RNA or proteins will be crucial.

Vu *et al.*, Trends Plant Sci. 2019



2

**#TOR kinase #Nutrient signalling
#Plant growth**

The target of rapamycin (TOR) kinase is an ancient metabolic sensor that orchestrates growth at the cellular, tissue and organismal level. To elucidate how TOR functions in plants, the Functional Interactomics lab of Geert De Jaeger (VIB-UGent Center for Plant Systems Biology) combined an extensive protein complex screen with phosphoproteomics for the proteome-wide discovery of upstream regulatory mechanisms and downstream targets, revealing both conserved as well as plant-specific TOR signalling events.

Van Leene *et al.*, Nature Plants 2019

3

#Vaccine #Mice #Immunization

Vaccination is one of the most efficient and cost-effective disease prevention strategies. However, most vaccines are administered by needle injection, which requires trained medical staff. In collaboration with a Dutch biotech company, the group of Xavier Saelens (VIB-UGent Center for Medical Biotechnology) demonstrated that nanoporous ceramic microneedle arrays can be used to effectively deliver an influenza vaccine intradermally, which resulted in a robust, protective immune response in mice. Microneedle patches thus represent a promising, self-applicable pain-free device to deliver vaccines.

Schepens *et al.*, Eur J Pharm Biopharm 2019

4

**#Errors of Metabolism #Nutritional therapy
#Metabolomics**

Congenital disorders of glycosylation (CDG) are rare genetic metabolic disorders arising from defects in how the body processes sugar. One of the main treatments currently used is D-Galactose therapy which exerts its beneficial effects in individuals diagnosed with a mutation in Phosphoglucomutase-1. PhD student Silvia Radenkovic and colleagues from the Metabolomics Core led by Bart Ghesquière (VIB-KU-Leuven Center for Cancer Biology), used tracer metabolomics to discover that D-Galactose rewires cellular metabolism and replenishes the pools of critical UDP-sugars, causing a restoration of the protein glycosylation processes. These findings open new avenues for improved nutritional therapy for other individuals diagnosed with similar defects.

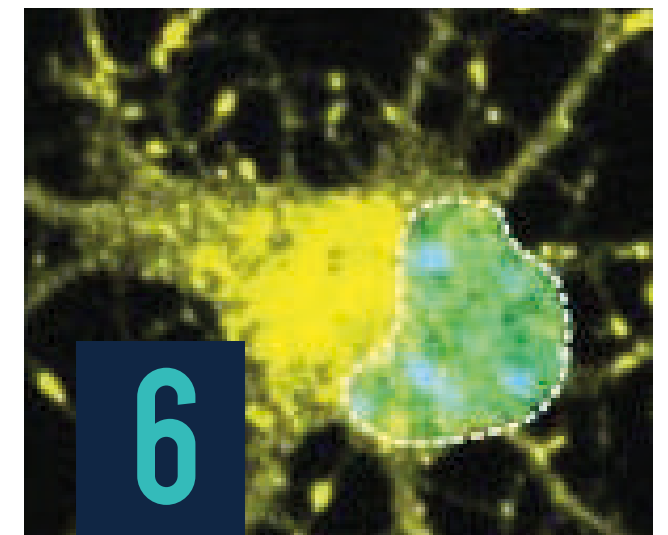
Radenkovic *et al.*, American Journal of Human Genetics 2019

5

**#Dementia #DPP6
#Neuronal hyperexcitability**

Rita Cacace, a postdoc in the group of Christine Van Broeckhoven (VIB-UAntwerp Center for Molecular Neurology), investigated a neurodegenerative dementia family previously linked to chromosome 7q63. She observed a genomic inversion which dislocated the coding sequence of the dipeptidyl peptidase 6 gene (DPP6) from its regulatory region causing loss of DPP6 protein. Resequencing of DPP6 in patients identified rare mutations leading to premature termination codons predicting transcript degradation. Additionally, rare coding variants were enriched in patients. Protein expression studies in autopsy brain tissue and in vitro assays, revealed variant-dependent DPP6 loss. It was shown in primary neurons of mice that loss of DPP6 causes neuronal hyperexcitability. These findings pave the way to the study of the homeostasis of neuronal firing in neurodegenerative dementia.

Cacace R *et al.* Acta Neuropathologica 2019



#DSCAM #Nuclear import #Down syndrome

Down syndrome cell adhesion molecule (DSCAM) receptors serve important neurodevelopmental functions including control of axon growth, branching, neurite self-avoidance, and neuronal cell death, but their signal transduction mechanisms remain poorly understood. The Dietmar Schmucker lab (VIB-KU Leuven Center for Brain & Disease Research) has identified a novel membrane-to-nucleus signaling mechanism by which DSCAM receptors can alter the expression of regulators of neuronal differentiation and synapse formation and function. Considering that chromosomal duplications lead to increased DSCAM expression in trisomy 21, these findings may help uncover mechanisms contributing to intellectual disability in Down syndrome.

Sachse *et al.*, EMBO J 2019

7

#Morphology #Peptide #Inflammation

Candida albicans, a common fungal commensal residing mostly on mucosal surfaces, becomes a deadly pathogen in immunocompromised patients, partly as a result of its capacity to change morphology. A collaborative study performed in the labs of Andy Wullaert (VIB-UGent Center for Inflammation Research) and Patrick Van Dijck (VIB-KU Leuven Center for Microbiology) discovered that a small pore-forming peptide only produced on hyphae of *C. albicans* activates the Nlrp3 inflammasome resulting in pro-inflammatory cytokine production. This work provides a molecular link between *C. albicans* morphogenesis, host recognition and immune response in the control of fungal infections.

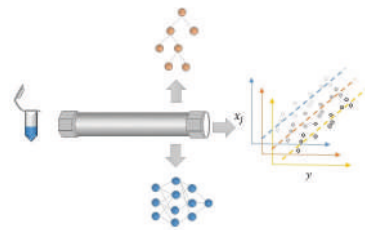
Rogiers *et al.*, mBio 2019

8

#Single cell #Trajectories #Benchmarking

By combining single-cell profiling and computation trajectory inference tools, it is now possible to investigate the dynamics of individual cells at an unprecedented and purely data-driven detail. The Yvan Saeys Lab (VIB-UGent Center for Inflammation Research) has done a comprehensive benchmark of 45 different methods for trajectory inference. They highlight the complementarity of tools, provide guidelines for method users, and indicate open challenges in the field. All software tools are freely available from dynverse.org.

Saelens *et al.*, Nat Biotech 2019



09

#Asthma #Allergen immunotherapy #GM-CSF

Allergic asthma is caused by an aberrant immune response to airborne allergens, such as proteins derived from house dust mites (HDM). The Hamida Hammad and Bart Lambrecht Lab (VIB-UGent Center for Inflammation Research) showed in mice that prophylactic inhalation of one HDM allergen, Der p 2, completely prevented asthma development induced by the full HDM extract containing multiple allergens. Der p 2 treatment mediated tolerance by blocking the release of lung GM-CSF, a cytokine crucial to endow dendritic cells with an allergy-promoting function. These insights might be exploited to improve allergen-specific immunotherapy.

Haspeslagh *et al.*, J Allergy Clin Immunol 2019

10

#Liquid chromatography #Machine learning #Data-driven modelling

Liquid Chromatography (LC) separates molecules based on their physicochemical properties and plays a key role in the analysis and identification of peptides and metabolites. Predicting how an analyte will behave in LC systems therefore eases its identification. Members of the Lennart Martens lab (VIB-UGent Center for Medical Biotechnology) investigated which machine learning algorithms and analyte feature representations are best at predicting LC separations, and found that the most commonly used model is not optimal, instead proposing a rarely used but superior alternative.

They also found evidence for the usefulness of combination learning techniques for LC predictions.

Bouwmeester *et al.*, Anal Chem 2019

3 NEW PROJECTS SELECTED IN VIB GRAND CHALLENGES PROGRAM

The VIB Grand Challenges Program is a translational research program with which we aim to significantly increase the societal impact of VIB. We are convinced that this can be done by teaming up with experts outside VIB who have complementary expertise (clinic, agriculture, engineering, etc.). Together we can exploit our knowledge, expertise and toolbox to generate new, otherwise untapped avenues to create added value for society.

Three projects were selected in addition to the three that are already running.

Microbiota modulation strategies in Inflammatory Bowel Disease management

- Formulate microbiota modulating strategies in inflammatory bowel disease and set up a validation pipeline that starts in the lab and ends in the clinic.
- VIB groups: Jeroen Raes, Johan Thevelein (VIB-KU Leuven Center for Microbiology)
- Non-VIB partners: Séverine Vermeire (UZ Leuven), Peter Bossuyt (Imelda General Hospital Bonheiden)

Targeting drugs to the brain

- Identify Nanobodies® that can cross the blood-brain barrier or the blood-cerebrospinal-fluid-barrier by receptor-mediated transcytosis in a smart *in vivo* screen that bypasses the current limitations of lab models.
- VIB groups: Bart De Strooper (VIB-KU Leuven Center for Brain & Disease Research), Roosmarijn Vandenbroucke (VIB-UGent Center for Inflammation Research), Sebastian Haesler (NERF, imec, KU Leuven and VIB), Maarten Dewilde (VIB Discovery Sciences)
- Non-VIB partners: Johannes Van Loon, Tom Theys, Peter Janssen, Paul Declerck, Nick Geukens, Frederik De Smet (KU Leuven/ UZ Leuven)

SPondyloArthritis inducing drug free Remission by early TNF Alpha bloCkade Under guidance of Single cell RNA sequencing

- Investigating the possible superiority of early treatment of psoriatic SpA patients with biologic treatment as compared to standard of care.
- VIB groups: Dirk Elewaut, Filip Van Den Bosch, Philippe Caron, Peggy Jacques, Koen Venken, Martin Guilliams (VIB-UGent Center for Inflammation Research)
- Non-VIB partners: Ruth Wittoek (UGent/UZ Gent), Rik Lories, Frederik De Smet (KU Leuven/ UZ Leuven), BeGIANT consortium (9 major rheumatology units covering most of Flanders: 2 centers in Bruges (AZ Sint-Jan, AZ Sint-Lucas), 2 centers in Gent (UZ Gent, Maria Middelaes), 2 centers in Antwerp (ZNA, Sint-Augustinus), 1 center in Leuven (University Hospital), 1 center in Hasselt (Reuma Instituut/Jessa Ziekenhuis) and 1 center in Aalst (Stedelijk Ziekenhuis).

The September edition of VIBTimes will focus on the Grand Challenges Program.

IN CONVERSATION WITH PETER PIOT,

ONE OF THE NEW MEMBERS OF VIB'S INSTITUTIONAL ADVISORY BOARD

Sukato is an Ebola survivor from the 1976 Ebola outbreak (when Peter went as part of the team to investigate the outbreak when "Ebola" was named). Sukato is now the lab technician in the Yambuku hospital.

From the start, VIB has aimed high in its ambitions: perform excellent research, realize impact for society and create a good and striving work environment for its scientists. This has always been and will remain a challenge in which VIB can count on the support of its Institutional Advisory Board (IAB). The IAB consists of prominent international scientists and managers who regularly formulate recommendations to VIB on its institutional policy and the board will be joined by three new IAB members. Peter Piot starts as of 2019, Aviv Regev and Daria Mochly-Rosen will join the IAB in 2020. We had the pleasure to speak with Peter Piot during his first on site visit as brand new IAB member.

It is an honor to welcome you to our institutional advisory board (IAB). What was your first idea when you were invited to join the IAB? What made you decide to join?

"I have a lot of respect for VIB because I'm convinced that VIB has

been a game changer in science in Flanders, certainly in my field of life sciences and biotechnology. It has introduced a non-politicized excellence-driven type of research and ensured that we can support the best researchers which will be good against brain drain."

"I also think VIB is taking large steps towards translation and that is where my current interests lie, and I know a few of the groups, particularly those working in infectious diseases. Reasons enough, the only reason I hesitated is I'm overcommitted. But this

But this doubt has passed, and I hope to learn as much as I can contribute."

How important/valuable do you consider such an Advisory Board for an institute as VIB?

"Any organization now and then needs an outside look from 'critical friends', people who are willing to say what they think, but do so in the spirit of encouraging improvement. When you're in the daily rat race, you sometimes lose perspective on the longer-term view. Sometimes you lose perspective of what's going very well, but also on what needs to be fixed."

"Where VIB is quite international in terms of its researchers, one of the limiting factors is the fact that the institute – and its top management – is Flemish. That could slow down further development, so having an institutional advisory board is, as for any other organization, very important."

"I see my role a bit as a bridge between the international members and the local community, since after all I'm still a Belgian. This institute is world-class, but the world doesn't always know it, and even within Flanders people don't always know. I hope I can contribute by spreading the message that this is one of the best life sciences and biotechnology institutions in the whole world."

You were active abroad as

With Paul Nurse (Francis Crick Institute, London, UK) as chair, and Detlef Weigel (Max Planck Institute for Developmental Biology, Tübingen, Germany) as vice-chair, the IAB can also count on Kay Davies (MRC Functional Genomics Unit, Oxford, UK) and Huda Zoghbi (HHMI Investigator, Professor Baylor College, Houston, US).

We are very proud to welcome three new members bringing expertise on technology, tech transfer and

Executive Director of UNAIDS and Under Secretary-General of the United Nations when VIB was initiated (1995). Did you have any expectations at that time of what this new institute could mean for research, for Flanders, and for society?

"I was still part-time in Antwerp when VIB was founded and what I liked immediately was that it was breaking down the silos and the barriers between various universities and disciplines, and that it had as sole criterion scientific excellence. And of course, the societal usefulness. I also remember that there was a lot of skepticism, which now proves to be unjust."

Translating research results into applications has always been the aim of VIB. Now, with VIB Discovery Sciences and the Grand Challenges program, we are taking two additional steps to increase the societal impact of VIB. What is your view on these initiatives?

"As much as I am a big believer in blue skies science, discovery for the sake of improving knowledge, we must also become better at filling the gap between the academic type of science and results that can improve people's life, whether it's in plant science – better foods, or improved medicine, vaccines... VIB has already made great contributions. With those new initiatives VIB is moving to version

2.0 or 3.0. I think that is a logical next step because society will want to see improvements not only in knowledge, but also in applications."

Basic researchers sometimes feel reluctance towards translation. You must have experienced this as well. How do you deal with this?

"Well, I think we need the whole spectrum. One should not force a basic researcher to focus on translation immediately. In any case, you never know what some esoteric type of discovery could lead to. But the reverse is also true. People who would like to do translational research, connect more with entrepreneurship and innovation... We need both and I don't see a conflict. It's very important that there is dialogue. The fact that both aspects can coexist under the same roof, as is the case for VIB, is very important and a major strength."

In your career you must have experienced the importance of external factors (politics, economic issues, crises...) in the process of translating promising research results into new applications. How do we, as researchers or research institution, best deal with this?

"In Europe there are a lot of restrictions. Here, we probably need to do a better job as scientists and have a real dialogue: involve people,

translational research into the IAB: Peter Piot (London School of Hygiene & Tropical Medicine, London, UK), Aviv Regev (MIT, Broad Institute, Boston, US) and Daria Mochly-Rosen (Stanford University's SPARK program, San Francisco, US).

We also wish to thank Børge Diderichsen (Novo Nordisk, DK), Luis Serrano (CRG, Barcelona, Spain) and Erin O'Shea (President HHMI, Harvard University, US) for their involvement the past 5 years.

provide information without being arrogant and pretending that we know it all. This engagement with the public, politicians and other stakeholders should be part of every scientist's job. But scientists often speak in terms and acronyms that even scientists from another discipline don't understand, and they are usually not good in politics. That is where VIB as organization can really take position and support its researchers."

"At the same time, now that VIB is growing and becoming more important in the world, the institute should have explicit policies on conflict of interest, on gender.... Action points nobody is against, but which need to be worked on to make them happen. Also, when your science leads to an interesting application, you need to think about how the largest number of people can benefit from this. There's of course a limit to what VIB can do, but it's important that we collectively think about this. This is also a role for the IAB in my opinion."

The largest number of people, that includes of course people in developing countries. How can we make sure that they also get access to breakthroughs from VIB researchers?

"This is always a priority in my mind, but don't forget people in high-income countries like the US where a lot of people don't have health insurance. A good way to deal with this is via access policies. Many universities, many research institutions or foundations like the Gates foundation or the Wellcome Trust, use this. In negotiations with an industrial partner there is a clause included ensuring access to a wider range of people, not always easy. For me, it's important that we

can discuss this, preferably before a crisis. I am not naïve. It costs hundreds of millions of euros to develop a new vaccine or medicine and bring it to market. But we also have to think about how we can find the best of all worlds to benefit people. All these are new and good challenges ahead for VIB."

You were one of the speakers in our recent conference 'The 1918 Influenza pandemic: historical and biomedical reflections'. How important and enriching are such initiatives that bring together different disciplines on one mutual topic of interest?

"I am a strong believer. Today's problems are so complex that it's very rare that one discipline can find a solution. Health issues for instance. In a sense it can be easy if there is a vaccine. But you also need to make sure that people accept the vaccine. Heidi [his wife Heidi Larson, director of the Vaccine Confidence Project, London School of Hygiene & Tropical Medicine] works on the fact that a lot of parents refuse to have their kids vaccinated. But if you think of other problems like dementia, where there is no single treatment, or obesity, diabetes, also major health issues. It is not only about availability of cures, but also about aspects such as the business side and behavioral change."

"I prefer to go to conferences with people who are a bit different than I am, because that's when I learn something."

What lessons have you learned in your rich career (researcher Ebola and AIDS, UNAIDS director, Director London School of Hygiene and Epidemiology, writing books) that you want to share with the VIB community?

"Believe in a dream. Go for it. Be ambitious. Don't give up. We only hear about success stories, but behind every success there are many, many failures. When your first grant proposal is rejected, or your first paper, or your fiftieth. Do not give up. And work with others. One of the things I feel strongly about is that one should read widely, beyond one's specialty. It's important to look around beyond the topic you're working on. And of course, have fun!"



WHO IS PETER PIOT?

Peter Piot is the Director of the London School of Hygiene & Tropical Medicine and Professor of Global Health. He was the founding Executive Director of UNAIDS and Under Secretary-General of the United Nations from 1995 until 2008 and was an Associate Director of the Global Program on AIDS of the WHO. He has a medical degree from the University of Ghent (1974), and a PhD in Microbiology from the University of Antwerp (1980). He has received numerous scientific and civic awards including an honorary doctorate from seven universities. He was ennobled as a baron in Belgium in 1995 and received an honorary knighthood KCMG in the UK in 2017.

VIB HIGHLY CITED PAPERS

To illustrate the international renown of VIB research, the following is a selection of highly-cited papers originating in VIB research groups. Citations are a way to explore the reach and influence of a scientific study. In general, scientific teams whose work has citation counts in the top 1% of the research field are recognized as 'highly cited'.

The fact that several VIB scientists are included in this category is a testimony to the excellence of VIB research. VIB congratulates all those researchers who have made an impact on life sciences research worldwide.

POPULATION-LEVEL ANALYSIS OF GUT MICROBIOME VARIATION.

"The Flemish Gut Flora Project was one of the first population-wide microbiota sampling efforts ever. When we launched the project in 2013, no manuals or protocols were available to manage a study at such scale. From sample collection to data analysis, we needed to design every single step from scratch. I remember the pioneering spirit in the team, somewhere in-between self-confidence and recklessness, with moments of collective despair and extreme excitement. The dataset we collected was unprecedented and, in many ways, it still is. With all hands on deck and 16 hours shifts, we wrote the actual paper in little more than two weeks. Compared to everything we built up the years before, the final wrapping was a piece of cake."

Gwen Falony (VIB-KU Leuven Center for Microbiology)



"This paper was a game-changer for our lab. We are internationally recognized as one of the main players in the field and this has multiple opened doors for e.g. EU projects and industry collaborations. But most importantly, it's been a project in which the whole lab was involved and has created a fantastic collaborative spirit in the group – something I care deeply about, probably even more than the papers themselves."

Jeroen Raes (VIB-KU Leuven Center for Microbiology)

BONE MARROW-DERIVED MONOCYTES GIVE RISE TO SELF-RENEWING AND FULLY DIFFERENTIATED KUPFFER CELLS



"Using novel tools allowing the specific depletion of macrophages in the liver (Kupffer cells) we demonstrated that adult monocytes could generate bona fide long-lived Kupffer cells. This research highlighted that nurture by the local environment rather than the nature of the progenitor is a key factor in macrophage differentiation, which really changed the way we thought about tissue-resident macrophages and led us to some of the hypotheses we are currently testing in the lab."

Charlotte Scott (VIB-UGent Center for Inflammation Research)



Eleonora Leucci

"This paper is a collaboration with Alain Beschin from the VUB and together we report that Clec4F is a Kupffer cell-specific gene and that we could use that specificity to make the first knock-in mice that permit the specific depletion of Kupffer cells in vivo. In the next paper we also reported the generation of Clec4F-CRE mice that permit the knock down of any gene of interest in Kupffer cells in vivo. These tools for the basis of much of the ongoing research in our lab."

Martin Guilliams
(VIB-UGent Center for Inflammation Research)

Scott *et al.*, Nature Communications 2016

MELANOMA ADDICTION TO THE LONG NON-CODING RNA SAMMSON

"Going from SAMMSON discovery, to its mechanism of action, to the preclinical study, our paper is one of the most complete papers in the field to date. Moreover, the pulldown technique that we described in the paper is now a chapter in the prestigious Methods in Molecular Biology and 5 students visited my lab last year to learn this technique. Lastly, we paved the way to the study of primate-specific lncRNAs in an in vivo relevant model."

Eleonora Leucci
(KU Leuven, Department of Oncology)

Leucci *et al.*, Nature 2016



Karolien Van Huynegem, Pieter Rottiers, Lothar Steidler, Klaas Vandembroucke and Sabine Neiryck

ALL VIB ALUMNI ARE INVITED TO JOIN THE VIB ALUMNI GROUP ON LINKEDIN.

LOTHAR STEIDLER

WINNER OF THE SECOND VIB ALUMNI AWARD

The VIB Alumni Award recognizes a meritorious alumnus with a strong impact on society. Out of 14 candidates, nominated by VIB employees and alumni, the VIB Alumni Board preselected three candidates. A jury of four distinguished emeriti – Marc Van Montagu, Désiré Collen, Joël Vandekerckhove and Hugo Van Heuverswyn – together with guest jury member Maggie De Block, Belgian Federal Minister of Public Health, named Lothar Steidler the winner of the second VIB Alumni Award. Lothar Steidler is currently Chief Technology Officer at ActoBio Therapeutics.

Steidler started his scientific career in the group of Erik Remaut. In the early nineties he combined two research topics of the Walter Fiers Lab: microbial genetic engineering and cytokines. He genetically modified the bacterium *Lactococcus lactis* to create a safe live vector for expressing and locally delivering potential disease modifying therapeutics. Steidler became a globally known pioneer in this technology and was decades ahead of the current microbiome boom.

“Steidler was never afraid to operate at the frontline of technology in a very competitive international environment with high risks, not only due to several unknown factors in his science, but also because of the vast economic and financial challenges. Therefore, Steidler, who co-founded Actogenix, one of VIB’s spin offs, in 2006, absolutely deserves this award”, says a jury member.

Using genetically modified bacteria as a drug vector is a bold idea. Where did the inspiration come from?

“Sometime during 1992, I was finalizing my PhD; I was looking for new scientific excitement. My ambition was to cure diseases, but not to follow well-trodden paths. I started to experiment with recombinant strains of the bacterium *Lactococcus lactis* as an expression system for human and murine cytokines. Instead of purifying them for subsequent use as biological medicines, I had the idea to use the bacterium as a vector system to locally deliver the cytokines, first in mice and, ultimately, maybe even into human patients.”

“*Lactococcus* is an ideal candidate. It is probably the most innocuous microorganism on the planet, used extensively in the production of cheese and other fermented food products. It is consumed in high amounts by nearly every population on earth and by every age group. So the bug has a proven zero profile when it comes to toxicity.”

“The first breakthrough came in 2000 with a publication in Science¹. The paper describes the delivery of a therapeutic dose of interleukin-10 by a genetically engineered *Lactococcus* strain in two mice models for inflammatory bowel disease (IBD). At that time, purified IL-10 was a prime candidate for treating IBD in human clinical trials.”

Most academic scientists would leave it with the Science paper, but you proceeded towards human clinical trials. A risky career choice?

“Law – fortunately - protects the words of poets and authors eternally but new scientific ideas are only protected for a limited amount of time. If you issue a patent, this protection is roughly 20 years. So once you have published an idea, there is a tremendous time pressure to find out whether your invention really works and can be of benefit to society.”

“On the other hand, to push your idea into a marketable product, you have to pass what insiders tend to call the ‘valley of death’: you hardly publish papers, you lack money to pursue your idea(s) and, in my case, I was confronting regulatory authorities with an entirely new concept. Don’t forget that genetically modified plants, at least in Europe, have been going through a very rough phase since the mid-nineties. We came with a genetically engineered bacterium to directly treat diseases. That notion was far from evident.”

But ActoGenix / ActoBio Therapeutics® managed to convince regulatory authorities in the US, Belgium, the Netherlands, Sweden and other countries to allow genetically modified *Lactococcus* for clinical trials.

“Yes, and we understood it was important to prevent the bacterium from escaping and surviving in the sewer systems to prevent unwanted exposure. So, we built a sort of suicide switch. A pig model proved that this containment strategy worked well.”

“In 2006, a second breakthrough came with the first clinical trial, involving 10 patients with severe Crohn’s disease. Henri Braat, Maikel Peppelenbosch, and Sander van Deventer conducted this trial in a strict containment ward at the Academic Medical Center (AMC) in Amsterdam. The trial showed that the transgenic *Lactococcus* disappeared from the volunteers’ stools shortly after taking the last capsule.”

“After that initial trial we got approval for deliberate release in the environment. Obviously this is essential if you want to conduct multicenter trials or treat patients with this – or any - technology.”

The AMC Crohn’s disease trial was a landmark study and received wide public attention. For VIB it was also the signal to set up Actogenix. But you had left Ghent and VIB in the meantime.

“I was given a great opportunity to work at the University College of Cork (Ireland) but VIB convinced me to come back to Belgium to help start up Actogenix. Pieter Rottiers, Sabine Neiryck, Karolien

Van Huynegem, and Klaas Vandenbroucke (all ex-VIB), had become - and still are - my ‘partners in crime’ during this exciting and adventurous period running up to and culminating in Actogenix, in 2015, when Intrexon Corporation acquired Actogenix, and recently when the unit was rebranded to ActoBio Therapeutics®.”

“The original *Lactococcus* delivery technology became known as “ActoBiotics™”, a proprietary unique drug delivery platform combining the advantages of highly selective protein-based therapeutic agents with local delivery by the well-characterized, safe, food-grade *Lactococcus lactis*. Besides interleukins, other potential biological drugs were added to the platform, including trefoil factors, proinsulin, glutamic acid decarboxylase, TNF antibodies and many others. With hundreds of chromosome-modified *Lactococcus* strains, we have a rich library of therapeutic agents.”

“At ActoBio Therapeutics® the main focus is currently on immunotherapy and tolerance induction/desensitization, besides interventions in metabolic disease. Our most advanced program is on oral mucositis, a disease resulting in painful inflammation and ulcers in the mouth, throat and esophagus. This type of inflammation is often caused by cancer chemotherapy. In a phase IIb trial on patients with head and neck cancer, ActoBio Therapeutics®, in collaboration with Oragenics Inc., is testing a *Lactococcus* strain releasing trefoil factor 1. This human protein stabilizes and protects the mucus layer in the mouth. The product is formulated as an oral rinse solution.”

Surprisingly, type 1 diabetes is also on your list of candidate diseases to treat.

“Absolutely. We engineered a *Lactococcus* strain to deliver proinsulin and the tolerance-enhancing cytokine IL-10. Studies have already demonstrated that this strain, in combination with an anti-CD3 monoclonal antibody, successfully restores normal blood sugar levels in diabetic mice. A clinical trial is now assessing the safety and tolerability of this strain administered in patients with type 1 diabetes mellitus.”

“Besides those clinical programs we have strains in preclinical development for inflammatory bowel disease, chronic rhinosinusitis, food allergies, and celiac disease. On top of this there are early development programs in phenylketonuria, metabolic

disease, and autoimmune skin disease.”

Looking back, what do you see as the most important contribution of VIB to your career?

“When I was 15 years old, two of VIB’s founders – Marc Van Montagu and Walter Fiers – immensely inspired me with their interviews on television. They were talking about cutting and gluing genes, trans-kingdom from one species into another. I was literally gobsmacked and decided then and there that I would become a genetic engineer. Of course, that was way before the creation of VIB, which gave the Flemish biotech landscape as a whole a real boost.”

“The most important contribution of VIB to my career is that its directors and staff believed in our technology and founded Actogenix. Without this company, I might have become a professor in Ireland or something else somewhere else, who knows.”

Finally, as a ‘seasoned genetic engineer’ what is your advice to young researchers?

“Live your dream. If your ambition is to invent and try to cure a disease, well, do so. Don’t be surprised to find that the path is full of obstacles – which, in all honesty, may be great fun to solve, keep that in mind – and that it takes much longer than originally anticipated. Also be critical to yourself: if you end up in a loophole, get out of it. That also happened to me. At some point I was thinking that engineered *Lactococci* could deliver vaccines. I was not the only one. There was a large European consortium with over a hundred academics, professors and researchers, thinking exactly the same. It may not have been my best idea.”

“And finally, the biggest error that you can make is to think that you are an expert in everything. As a scientist in a company, your job is to profoundly understand the science and the technology, and to be among the best in your field. You will never get to the deepest understanding of the legal aspects, because you are not a lawyer. Or the business aspects, if you are not trained or talented in business administration. As a scientist, you are the inventor. But after all, that is where it all starts.”

¹ Steidler L, Hans W, Schotte L, Neiryck S, Obermeier F, Falk W, Fiers W & Remaut E (2000). Treatment of murine colitis by *Lactococcus lactis* secreting interleukin-10. *Science* 289(5483):1352-5.



RAMPING UP THROUGHPUT AND SENSITIVITY OF SINGLE-CELL ANALYSIS WITH THE CELSEE GENESIS PLATFORM

Single-cell analysis technologies are booming due to a growing recognition that bulk population analysis is insufficient to capture the vast cellular heterogeneity present. Currently available single-cell omics platforms tend to rely on microfluidics and the encapsulation of cells in droplets to barcode nucleic acids and proteins that belong to the same cell. These established technologies have their shortcomings, such as a limited capture efficiency and an effect on cell viability and function.

The newest addition to VIB's Single-Cell Accelerator program, the Celsee Genesis platform, is available

to overcome these hurdles and enables massively scaled single-cell isolation, and transcriptomics and proteogenomics on millions of cells per sample. Celsee's technology is based on a gravity-induced, micro-well isolation technique which maintains cellular integrity and viability.

Currently, the company has micro-analysis slides available containing up to a million wells. Oligo-labeled microbeads and/or oligo-tagged antibodies are added to each well allowing analysis of a cell's transcriptome and surface proteome.

TechWatch reached out to the VIB community and opened a targeted call for groups interested in using the Celsee technology. Four different VIB centers submitted project proposals. Together with VIB's Technology Innovation Lab, these early adopters will evaluate the Celsee platform. Eventually, the goal is to offer all VIB scientists the opportunity to use this technology for affordable, high-throughput single-cell analysis.

COLLABORATE WITH THE SEQUENCING FACILITIES TO EXPLORE NANOPORE SEQUENCING PLATFORMS

Long-read sequencing technologies such as the Oxford Nanopore Technologies' (ONT) platforms aim to use biological nanopores to shed light on the complex genomic regions that are difficult to analyze using traditional next-generation technologies. This direct sequencing approach allows real-time analysis of native DNA and RNA sequences.

Mojca Strazisar, Expert Scientist at the Neuromics Support Facility (VIB-UAntwerp Center for Molecular Neurology) and one of the early adopters of the ONT PromethION platform, confirms: "Screening and validation of structural variants and genome assembly are just one of the many applications of the ONT platforms. The possibility to sequence unmodified long reads allows scientists to obtain an excellent overview of the role of genetics in phenotype determination".

Stefaan Derveaux, Core Facility Manager at the VIB Nucleomics Core, couldn't agree more: "Nanopore sequencing is transforming the field and allows VIB

scientists to study full-length end-to-end sequences in a single read, making it possible to perform accurate characterization and quantitative analysis of all isoforms in a sample."

In 2019, VIB scientists will collaborate with the Nucleomics Core and Neuromics Support Facility to explore the ONT GridION and PromethION platforms. Each GridION flow cell produces an average of 10-12 Gbs of sequencing data, with the possibility to run up to 5 flow cells simultaneously. Whereas one PromethION flow cell generates on average >75 Gbs sequencing data. The PromethION can run up to 48 flow cells in parallel, leading to a potential 4 Tbs per run.

Yu-Chun Wang, Technology Implementation specialist at VIB, emphasizes: "VIB is one of the first research institutes that provide access to both the GridION and PromethION platforms for long read sequencing in Europe".

VIB AND SPHERE FLUIDICS PARTNER ON PICODROPLET TECHNOLOGY

To strengthen its position at the frontiers of single-cell research, VIB is partnering with the UK-based Sphere Fluidics to test and evaluate their picodroplet single-cell analysis platforms.

Sphere Fluidics uses its proprietary microfluidics technology to generate picodroplets which serve as miniature test tubes for single cells. The picodroplets are stabilized using biocompatible surfactants, allowing the incubation and growth of individual cells within. High performing cells can be identified using optical detection methods

and isolated for downstream characterization. Sphere Fluidics' Cyto-Mine instrument is a fully automated benchtop instrument which allows millions of individual cells to be manipulated, incubated, analyzed and sorted in a single day. Using Cyto-Mine, researchers can drastically reduce the time it takes to identify highly valuable or rare variants, and their biological products, among vast cell populations. As such, the Sphere Fluidics technology has various applications within antibody

discovery, cell line development and synthetic biology. It can also be adapted for precision genome editing. VIB's Tech Watch team and several VIB research groups are collaborating with Sphere Fluidics to test and evaluate a more flexible research platform which allows for picodroplet single-cell assays and downstream isolation. This research instrument is a less automated version of the Cyto-Mine instrument that allows increased experimental flexibility.

INWARD INVESTMENTS



In order to build a thriving biotech ecosystem, VIB aims to attract international life sciences companies. In doing so, the institute continues to fulfil a role as a catalyst for the growth and development of the biotech cluster in Flanders.

To have, and be willing to share, technological and scientific expertise can encourage foreign life sciences companies to have a closer look at the biotech industry in Flanders. This can convince international players to establish local facilities, so they can benefit from the talent pool, expertise and know-how on offer. The past year has seen two such new investments by international companies.

Inari Agriculture

First is Inari Agriculture, a company that is revolutionizing plant breeding by tapping into natural genetic diversity. The company has chosen to expand its research activities in Europe with the opening of a laboratory in Bioscape, a new life sciences incubator in Ghent. By partnering up with VIB and ILVO, Inari has access to high-caliber expertise in plant biology and genomics as well as state-of-the-art phenotyping

and greenhouse facilities. Inari aims to take advantage of the local talent and resources in their efforts to increase water and nitrogen-use efficiencies in crops such as maize, soy and wheat.

Yesse Technologies

The second company to touch down in Flanders for the launch of a local branch is Yesse Technologies, a company that works on a nose-on-a-chip technology and aims to provide an objective way to measure odor. Beyond the obvious interest from the fragrance and flavor industry, there are strong indications that this can also be used to diagnose conditions such as Parkinson's disease. To drive continued refinement of its smelling technology, Yesse Technologies has entered in a collaboration with imec (Leuven, Belgium) to integrate their biology with state-of-the-art silicon chip technology.

HMPV DEAL WITH JANSSEN PHARMACEUTICALS, INC.

Since its discovery in 2001, Human metapneumovirus (hMPV) has been a leading cause of acute respiratory tract infection, causing significant morbidity, and mortality in certain clinical settings. Monoclonal antibodies, effectively targeting other viral infections, represent a potential therapeutic and prophylactic route to treat and

prevent hMPV infections. However, no hMPV-specific antivirals are on the market today.

The team of Xavier Saelens (VIB-UGent Center for Medical Biotechnology) now entered into an agreement with Janssen with the aim to produce potent prophylactic hMPV-neutralizing nanobodies.



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CONFO THERAPEUTICS FORMS SCIENTIFIC ADVISORY BOARD AND RAISES 30 MILLION EURO

Emerging drug discovery company and VIB/VUB-spinoff Confo Therapeutics announces the formation of its Scientific Advisory Board (SAB) with four key appointments: Radu Aricescu (MRC Laboratory of Molecular Biology, Cambridge), Peter Kolb (Philipps-Universität Marburg), Graeme Milligan (University of Glasgow) and Jan Steyaert, founder of Confo Therapeutics and science director of the VIB-VUB Center for Structural Biology, who will serve as Chairman of the SAB.

Confo Therapeutics is building a portfolio of first-in-class programs based on its proprietary Confo® technology. This technology makes use of camelid single domain antibodies or CONFO® bodies to

stabilize G-protein coupled receptors (GPCRs) in a particular conformation of interest as a superior starting point for drug discovery.

Johan Cardoen (VIB Managing Director): "Truly great to see that Jan Steyaert, founding father of the technology that laid the basis of Confo Therapeutics, and other key opinion leaders will advise on the scientific direction of the company."

To accelerate its research trajectory, Confo Therapeutics has recently attracted a capital injection of 30 million euro, an exceptional success for an incipient company. With this financial backing, the company will proceed to phase I trials faster than anticipated as well as attract additional employees.

TRANSFERRING KNOWLEDGE AND KNOW-HOW VIA THE XIMBIO PLATFORM

Recently VIB has entered into an agreement with Ximbio. Ximbio is the world's largest non-profit reagent technology transfer service where scientists can exchange knowledge and maximize commercial opportunities for the research reagents they have created. It is an initiative from Cancer Research UK and is an international hub for the efficient transfer of various research technologies and products.

Institutes that partner with Ximbio submit research reagents or tools (e.g. cell lines, mouse models, vectors, bacteria, etc.). Ximbio handles the subsequent storage, promotion, documentation such as material transfer agreements, invoicing, shipping etc. for all its clients' products.

To VIB, Ximbio represents a global online platform that helps to distribute many interesting research tools. This collaboration is expected to greatly advance the spread of VIB's knowledge and know-how.



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REPORTER ON THE ROAD: NEW MODEL ORGANISMS IN THE BATTLE AGAINST CLIMATE CHANGE

A lot of research in the life sciences relies on model organisms. Scientists often work with a specific plant, fungus, bacterium, mammal, invertebrate, or cell line. Decades of research have allowed each respective field to develop all the required tools to breed, test, and manipulate these model organisms. By studying them in close detail we have been able to develop an amazingly in-depth, yet continuously expanding, view on biology. In a way, model organisms are the true champions of science.

Currently, only a select group of organisms holds this elite 'model' status. However, if we look around us, there is such a wide variety of organisms alive. I don't think that any one of us doubts the exciting biology out there waiting to be discovered. Yet, going back to the lab we often find ourselves studying the same model organisms over and over. While I will by no means argue that model organisms have not provided incredible value for the life sciences, I believe it is time for life scientists to step out of their comfort zone. Moreover, with the ever-decreasing cost of sequencing and the broad applicability of CRISPR/Cas9, I would argue that now is a great time to pursue research in 'new' organisms.

The lab of Sue Rhee at the Carnegie Institute of Science (Washington D.C., US) is interested in how plants adapt to changing environments, especially considering climate change. While the work of Sue initially almost exclusively involved *Arabidopsis*, her lab is now pursuing a new path forward. In the 70's, two

plant scientists at Carnegie and Stanford created a mobile laboratory, which was essentially an RV stuffed with lab equipment. With this vehicle, they travelled throughout California. This allowed them to measure photosynthesis rates in plants in their natural habitats. "When measuring the photosynthesis Death Valley plants, they found something really interesting," says Sue. "*Tidestromia oblongifolia*, a desert plant that can not only withstand the excruciating heat in Death Valley, but thrives there, has the highest documented optimal temperature for photosynthesis in plants." She adds: "That record temperature of 47°C hasn't been broken yet."

If we want to arm our crops against the detrimental effects of climate change, looking at evolution for solutions to this problem seems to be an ideal place to start. Sue says: "Rediscovering those seminal papers, I knew this could be something exciting. However, we needed to start from scratch, as no one had really looked closely at this organism in almost

four decades". Growing desert plants in the lab does sound challenging though, and the lab indeed had to partner with companies to pull it off. They now have custom-built incubation chambers that can reproduce the high temperatures and light intensities of the desert environment. "We essentially recreated a mini-Death Valley in our greenhouse," Sue explains. As they can now grow the plants in the lab, the next step will be to sequence the genome and transcriptome. This will allow them to start elucidating the molecular mechanisms of how desert plants can thrive under such extreme conditions.

Climate change is happening, and we need to start considering how we will maintain agricultural production in the future. Making crops more resistant to stress conditions could be one of the solutions. While this will obviously involve research on the major crops themselves, we should not neglect the plants that are already evolutionary endowed with mechanisms to resist drought and heat. "Nobody cares about desert plants," Sue jokes. She continues: "But I believe that they will be a part of the solution to making our crops resistant against the effects of climate change. I believe all real solutions for problems like this will come from basic science. We will need to continue to make funding agencies and governments aware of the need for supporting fundamental biology if we want to be able to tackle the challenges ahead of us".

Besides its effect on agriculture, global warming may present us with problems on other fronts as well. Neglected tropical diseases are expanding towards more temperate regions. For example, Florida and neighboring states have seen increasing incidences of parasitic infections that one mostly associates with the tropics. These infections are caused by protists,

small organisms with a – still – very mysterious biology. *Naegleria fowleri* is one such parasitic protist. It is also known as 'the brain-eating amoeba', since it occasionally infects humans, wreaking havoc in the brain leading to the death of the patient within days. There is no treatment for the condition, and as *Naegleria* prefers warmer waters of lakes and pools, it is expected that global warming may lead to an increased incidence of such infections. While hanging out at a happy hour here at Stanford, this organism came up in discussion. Two postdocs from neighboring labs, Broder Schmidt and Keren Lasker, and I had a crazy idea: What if we could pioneer this organism as a novel model system to gain insights into early eukaryote evolution, and at the same time use that knowledge to think about treatment options for *Naegleria* infections? Digging into the literature we found a *Naegleria* species that is not infective, and we are now able to culture these amoebae in the lab. As we speak, we are sequencing its genome and setting up multiple omics experiments.

So why are we doing this? Even though this side project of ours might not immediately lead to big breakthroughs, we are convinced that if more scientists would spend some time studying non-model organisms, we would dramatically expand our understanding and appreciation of biology. If no one ever bothered studying a weird type of DNA repeats that were present in numerous bacterial genomes, we would not have CRISPR/Cas9 today. Evolution has come up with this enormous diversity in life forms. Within this diversity lie many secrets yet to unravel, secrets that will not only amaze us, but also provide key insights to address present and future challenges.

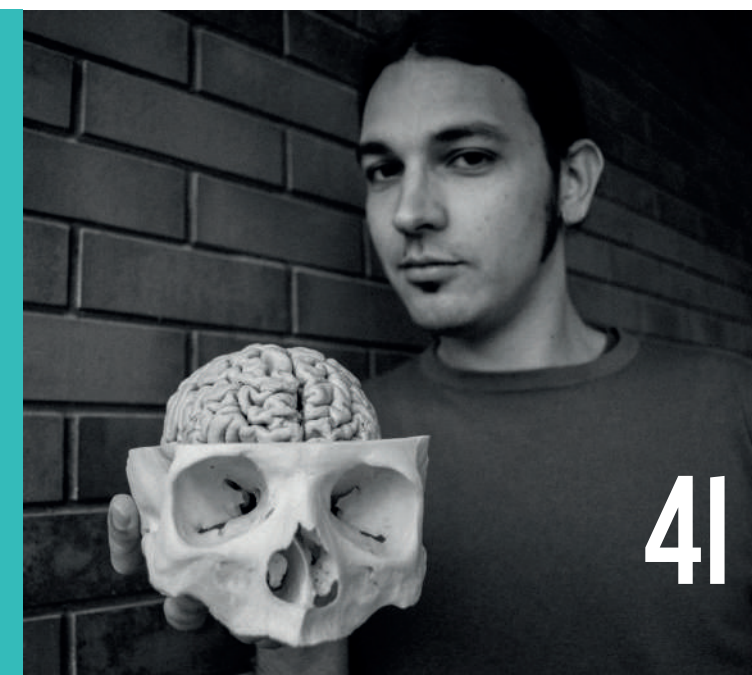
Steven Boeynaems is a VIB alumnus who worked at the Kevin Verstrepen Lab (VIB-KU Leuven Center for Microbiology) and the Ludo Van Den Bosch Lab (VIB-KU Leuven Center for Brain & Disease Research). Recently he traded Belgium for the Californian sun. At Stanford University he keeps pursuing his passion for science and science communication.



@steven.boeynaems



@BoeynaemsSteven



Give
CRISPR
a chance

"With positive activism we achieved public awareness for the need of modern technologies to develop solutions. We distributed flyers that highlighted our message and informed passers-by about the potential of CRISPR."

Gwen Swinnen (VIB-UGent Center for Plant System Biology)

"The event was actively shared on Twitter with the hashtag #GiveCRISPRaChance and we were able to engage many more young researchers to spread the word."

Nick Vangheluwe (VIB-UGent Center for Plant Systems Biology)

"Give CRISPR a chance". This statement reflects what many researchers think after the Court of Justice of the European Union (ECJ) ruled on the 25th of July that organisms obtained by modern forms of mutagenesis such as CRISPR are not exempt from the EU GMO legislation. Many different points of view have been shared via social media and newspapers about the possibilities of CRISPR-based gene editing for agriculture and health care. However, politicians and policy makers at the national and European level have been mainly silent about the ECJ's ruling about CRISPR or responded carefully.

European plant research institutes jointly called for action through a position paper, which was directed

to the European commission on the 24th of January. Many researchers feel that CRISPR gene editing will contribute to the development of solutions for challenges of growing importance such as more climate resilient and more nutritious crop varieties. Given the current ecological and societal challenges we face, such innovations are urgently needed. On Tuesday, March 5, 2019, Science for Democracy organized an awareness event in Brussels, joined by young researchers in plant biotechnology from the VIB-UGent Center for Plant Systems Biology. Even though Belgian authorities from the food safety agency tried to confiscate it, the VIB scientists consumed, together with researchers from across the country, rice pudding - a traditional Belgian dessert - prepared with CRISPR'ed rice.

5 VIB RESEARCHERS RECEIVE A PRESTIGIOUS ERC ADVANCED GRANT

The European Research Council (ERC) is unique in its kind in Europe supporting individual top researchers from anywhere in the world for 5 years to embark on an innovative and highly challenging research project. The ERC Advanced Grants are awarded to exceptional research leaders embarking on a novel high-risk/high-gain project. No less than 5 VIB researchers have been awarded these competitive and renowned benchmarks of scientific excellence.

Lieve Ongena, Senior Science Policy Manager, heading VIB's International Grants Office: "We are extremely proud of this achievement. It is – again – an important international recognition of the high quality and relevance of the research at VIB."

VIB's ERC Advanced grant recipients for 2019 are Dirk

Inzé, Wout Boerjan, Yves Van de Peer (VIB-UGent Center for Plant Systems Biology), Kodi Ravichandran (VIB-UGent Center for Inflammation Research) and Bart De Strooper (VIB-KU Leuven Center for Brain & Disease Research), all of whom receive a research budget of 2,5 million euro to pursue their projects.



Dirk Inzé

Dirk Inzé and his team will explore a novel crossing scheme that allows for a swift evaluation of combinations of potential yield contributing gene variants by unifying 'classical' breeding with gene-centric molecular biology. Dirk looks forward to start developing this new approach: "I am extremely pleased that the ERC allows my team to develop an innovative concept that has the potential to revolutionize crop improvement."

Wout Boerjan and his team will use the CSPP algorithm, an innovative method recently developed in the lab, to predict the structures of metabolites in poplar along with their biosynthetic pathways. Wout voices his enthusiasm: "It is exciting to realize that the data generated in this project will be fundamental for understanding the fascinating biology of trees. We will contribute to topics as diverse as wood formation, tree-environment interactions, and the valorization of wood in the bio-economy."



Wout Boerjan



Yves Van de Peer

Yves Van de Peer and his team will unravel why and how polyploids can outcompete non-polyploids. They will replay the 'genome duplication tape of life' in two different model systems, *Chlamydomonas* and *Spirodela*. Yves says: "Because of a previous ERC grant, we were able to show that polyploidy often is an evolutionary dead end. But, in times of environmental upheaval or climate change, it might confer an evolutionary advantage, possibly explaining why polyploids can, for instance, escape extinction."

Kodi Ravichandran and his team will investigate the role of specific lipids that are part of the cell wall of viable sperm in mammalian fertilization, along with the part played by the complementary receptors on egg cells. "This is a relatively new direction for our group, and although fertilization is so fundamental for species survival, surprisingly, there are still many gaps in our understanding" says Kodi.



Kodi Ravichandran



Bart De Strooper

Bart De Strooper and his team will use mouse-human chimeric mouse models to test the effects of genetic risk factors associated with Alzheimer's disease (AD) on transplanted brain cells derived from patient stem cells. "We're very excited to start this project, which will provide us with humanized models for Alzheimer's disease," Bart says. "We will be able to explore human genetics in human cells in a living brain."

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VIB

DID YOU KNOW

LIFE AT VIB NEVER STANDS STILL. A SEMINAR YESTERDAY, A GROUND-BREAKING PROJECT TODAY, AN INNOVATIVE TECHNOLOGY LAUNCHING TOMORROW... STAY IN THE LOOP WITH THIS OVERVIEW.

Did you know that...

- **Inna Afonina and Rudi Beyaert** (VIB-UGent Center for Inflammation Research) received a 2-year Charcot Fund grant for their project 'Characterization of interleukin-33 (IL-33) as a potential therapeutic target in multiple sclerosis? With this project, they aim to study the pathological role of interleukin-33 in MS, and to analyze the therapeutic effects of a new IL-33 blocker in preclinical mouse models of MS.
- **Alain Goossens** (VIB-UGent Center for Plant Systems Biology) and his team will participate in the EU-funded ENDOSCAPE project, which aims to develop a novel gene delivery technology? This 6.8-million-euro project includes academic and industrial partners from 7 European countries. The role of Alain's team includes the genetic engineering of medicinal plant lines to enable the production of endosomal endoscape enhancers.
- **VIB is welcoming** incoming Marie Curie fellows Freya Svedberg, Patricia Altea Monzano, Sebastián Dumas, Lucía Alberta Servera, Panagiotis Karras and Thomas Moens, and Anna Schröder and Liselotte Dewachter are leaving VIB with a Marie Curie fellowship? Through these competitive 2-year fellowships, scientists have the unique opportunity to kickstart outstanding research careers. While an average of 12% of applications are successful, VIB scientists have an average success rate of 27%.
- **9 VIB researchers** (Evgenia Salta, Wim Annaert, Matthew Holt, Araks Martirosyan, Kristel Slegers, Eline Wouters, Lucia Chavez-Gutierrez, Valerie Uytterhoeven, Sophie Steeland) received funding from the Alzheimer Foundation (Stichting Alzheimer Onderzoek)? These 2-year grants offer fundamental support for our scientists' quests for cures for Alzheimer's disease and
- **Our PID (primary immune deficiency) family day** on Sunday 17 March was a big success? PID patients had the opportunity to

meet each other and the scientists that dedicate their lives to the understanding and treatment of immune disorders. Around 100 patients participated, including Krista Bracke, who received an honorary doctorate from Ghent University later that week.

• **Anje Cauwels** (VIB-UGent Center for Medical Biotechnology) received funding from the Charcot Fund for her study 'In vivo induction of tolerogenic dendritic cells via AcTaferon targeting? With this support, Anje aims to develop a safe, precise, generic way to dampen the immune system in MS patients.

• **Dirk Inzé** (VIB-UGent Center for Plant Systems Biology) and Bart Lambrecht (VIB-UGent Center for Inflammation Research) and their teams received WOW! Awards from the rector of Ghent University on 17 March? These awards are presented to researchers whose work has major impacts on our lives as an ode to what science means to humankind.

• **Dirk Inzé** (VIB-UGent Center for Plant Systems Biology) was listed as one of the '20 most influential people for the EU seed sector'? Dirk received this recognition for his influential research and promotion of innovation at VIB as well as his leadership of a coalition of over 90 scientific institutions following the EU court ruling on mutagenesis.

• **Vinoy Vijayan** (VIB-KU Leuven Center for Brain & Disease Research) was interviewed by EMBO in the 'Life of @EMBOFellows' series? An Indian national, Vinoy lived in 6 countries before joining the Patrik Verstreken Lab for a postdoc.

• **The VIB-KU Leuven Center for Brain & Disease Research** now has an Inclusion & Diversity Committee?

- **The VIB-UGent Eco-team** has digitized VIBnews, kicked out disposable drinking cups, started a cork recycling program and brought vegetarian BBQs to the VIB-UGent Center for Plant Systems Biology? They've even already collected EUR 3,000 after kicking off a new fundraising campaign to protect nature via www.hutsepotbos.be.
- **The annual Lolands Festival** is organized by volunteers to raise funds for ALS research? Learn more about the event at www.lolands.be.
- **Elsa Lauwers** (VIB-KU Leuven Center for Brain & Disease Research) ran the 20 km of Brussels in support of the Demoucelle Parkinson's charity to raise funds for Parkinson's Disease research?
- **PhD students of the VIB-KU Center for Brain & Disease Research** recently launched 'The Optimist'. This publication is a survival journal by and for PhD students, supporting them in the ups and downs of PhD life.
- **René Custers** (regulatory & responsible research manager at VIB) and Lutgarde Serneels (VIB-KU Leuven Center for Brain & Disease Research) have shed light on a new CRISPR documentary at a public screening event organized by 'Dear Tech' in Antwerp? DearTech is a non-political and non-commercial initiative that

explores the latest developments in a wide range of technologies. Learn more at <http://deartech.org>.

- **Chinese and Belgian scientists** have teamed up to set up a laboratory for advanced single cell analysis. The Sino-Belgian Collaboration Laboratory for Single Cell Analysis Technologies opened on Friday at the Chinese National Compound Library in Zhangjiang of Pudong. It was set up by VIB and the Shanghai Institute of Materia Medica.
- **Patrizia Agostinis** joins the VIB-KU Leuven Center for Cancer Biology as new group leader. She will lead a research group focused on the biology of cell death and how improved knowledge in this field can be leveraged to develop new cancer therapies.
- **Heather Rice** (VIB-KU Leuven Center for Brain & Disease Research) has been awarded a junior Faculty Award at the 14th International Conference on Alzheimer's and Parkinson's Diseases and related neurological disorders.
- **Marlies Vanden Bempt**, Grand Challenges coordinator at the VIB-KU Leuven Center for Cancer Biology, claimed the third place at the Falling Walls Lab Leuven with her presentation 'Breaking the Wall of untreatable cancers'.



CONFERENCES 3RD EDITION: 'REVOLUTIONIZING NEXT-GENERATION SEQUENCING'

The 3rd edition of 'Revolutionizing Next-generation Sequencing' has shown first-hand how intertwined technology and science have become.

The organizing committee: Bernard Thienpont (KU Leuven), Jeroen Raes (VIB-KU Leuven Center for Microbiology), Mojca Strazisar (VIB-UAntwerp Center for Molecular Neurology), Silvie Van den Hoecke (VIB TechWatch) and Stefaan Derveaux (VIB Nucleomics Core).

It was an intense two days full of exciting new technologies and discoveries, with excellent lectures by world-renowned scientists and pioneers in the development of novel technologies.

Single-cell omics tools are rapidly pervading every aspect of life sciences, and single-molecule sequencers can now read DNA molecules of over 2 million bases in one go at an ever-improving fidelity. The ingenuity and capabilities of some of the tools presented seemed like science fiction at first, even while producing very real data. The combined measurement of virtually every aspect of biology (e.g. RNA abundance and DNA mutations) within cells in their native tissue is no longer a dream, but a very likely possibility.

Besides the science, plenty of time for networking allowed attendees to meet and greet, discuss novel strategies and plant new seeds for further collaborations.

RNGS19 was an extremely invigorating meeting highlighting many scientific opportunities to come. We cannot wait to see what the future will bring and how the potential presented at the conference will translate into novel future scientific achievements.



FOR THE THIRD TIME DANY CUYT CYCLES 1,000 KM SOLO TO COMBAT CANCER

Dany Cuyt (VIB-UGent Center for Plant Systems Biology) is participating for the third time in the Kom Op Tegen Kanker's (Fight Cancer in English) 1,000-km cycling event as a solo cyclist. Kom Op Tegen Kanker is a high-impact Belgian nonprofit that supports patients, raises cancer awareness, funds research initiatives and stands up for patient rights.

"During the Sportgala 2019 athlete recognition event in Nazareth, Belgium, I was elected Amateur Athlete of the Year 2018, thanks in part to my 3-year consecutive participation in the event. This year, I'm registered for the international ride from Lyon, France to Mechelen, Belgium."

Dany wasn't the only VIB biker this year. Oskar Marin, Bram Boeckx, Dries Verdegem, Roel Vandepoel, Ann Bouché and Koen Veys, together with HQ colleagues Els Hermans and René Custers rode the 1000 km for KOTK as the VIB KU Leuven Center for Cancer Biology team.



MARK YOUR CALENDAR

The Brain Mosaic: Cellular heterogeneity in the CNS (2nd edition)

October 10-11, 2019 - Leuven

Biotech day

October 20, 2019 - Leuven

Next-Generation Protein Analysis and Detection (3rd edition)

December 2-3, 2019 - Ghent

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