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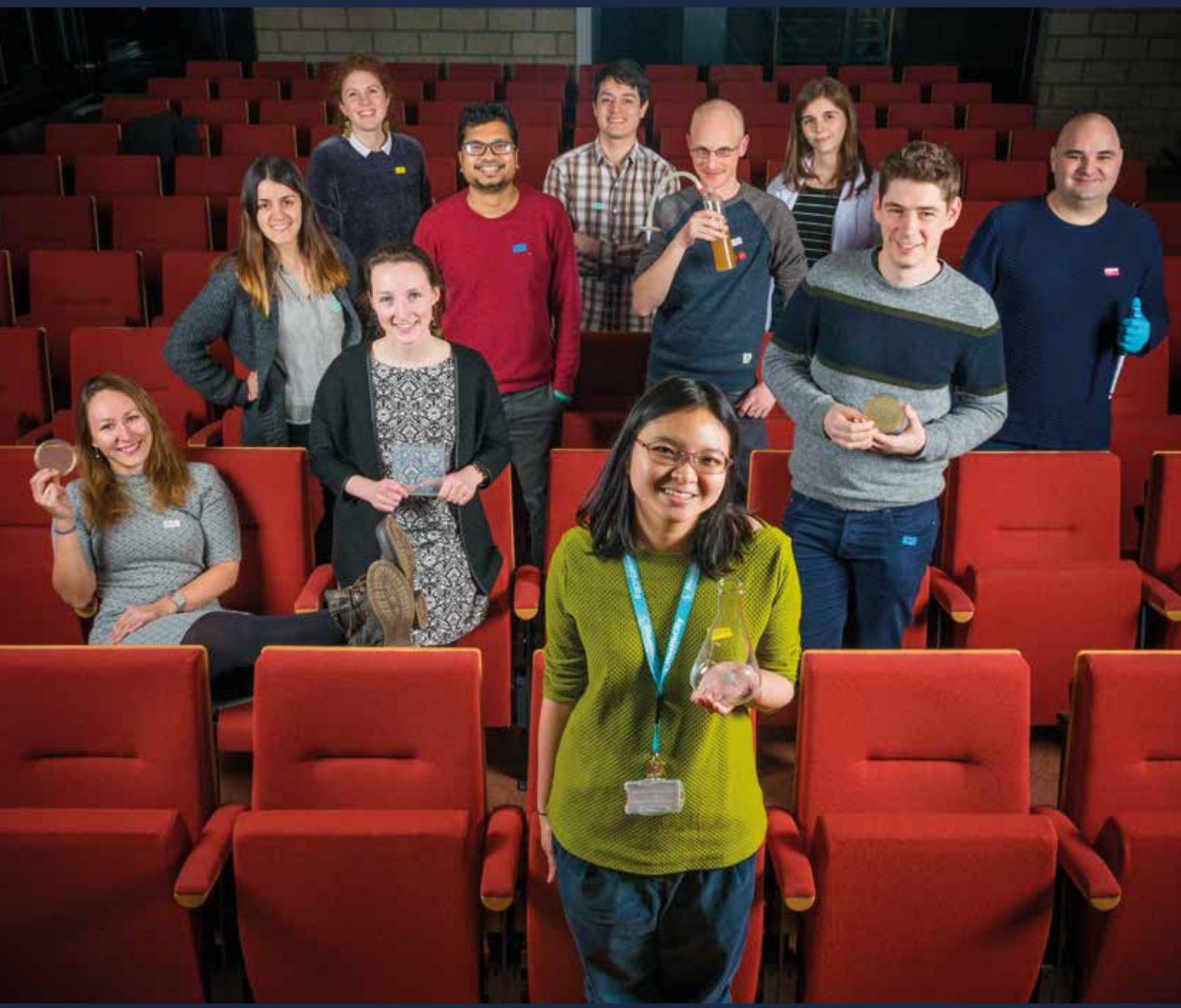


MICROBIOLOGY

WHAT IS TRUE FOR E. COLI IS TRUE FOR THE ELEPHANT

But we study microbes because elephants don't make you sick, nor do they make beer

I vividly remember upsetting quite a few people a few years back at a VIB group leader retreat. Along with several other group leaders, I was asked to give a presentation in a session on future trends in science. As expected, the session turned out to be a recital of the obvious, with people predicting more genome sequencing, more big data, more CRISPR/Cas, more single-cell research. The audience was slipping into a deep, possibly irreversible, coma. That was, until I half-jokingly stated that there's an easy answer for anyone not working in the field of microbiology: simply look at what microbiologists are doing right now to know where other fields will be headed in the coming five years. Coma transformed into fury. Someone stood up and shouted that microbes don't even have neurons and that it is therefore rather unlikely that they would be good predictors of where the field of neurobiology would head to. Plant scientists, cancer specialists and immunologists nodded enthusiastically.

Even though I was mostly joking, there is some truth to my point. Many new techniques and scientific trends begin with microbes, simply because microbes are such easy, versatile and inexpensive models. Want to sequence or synthesize a complete genome, study how single cells behave in a population, or explore how basic processes work? Better put some microbes under your scope! One glance at the list of microbiologists that have won Nobel Prizes supports my claim: gene regulation, transcription, cell cycle control, telomeres, protein trafficking, and, in the near future, CRISPR/Cas. As Jacques Monod said: what is true for *E. coli* is true for the elephant!

In addition to being excellent models, microbes are fascinating creatures in their own right. The sheer variety of microbes, and the things they can do, stretches the limits of our imagination. Some grow in extreme conditions at the bottom of oceans, in hot springs or in the very air we breathe. Some have developed metabolic routes to gather energy from sunlight, metal and rocks. Some can divide within a few minutes. Some are key in the production of human foods and beverages, as well as in many industrial processes. Others colonize larger organisms – sometimes as symbionts, sometimes as parasites and pathogens.

Kevin Verstrepen

It is no wonder then that the VIB Center for Microbiology is doing so well, in terms of both basic research as well as translational achievements. In this edition of VIBnews, you'll get to discover a few recent examples of what the microbiology team is doing – from studying gene regulation, pathogenesis, antibiotics and antibiotic resistance to the microbial ecology of the human gut and industrial fermentations. We highlight some recent papers, the expertise of a new group leader, Jan Michiels, the search for yet another group leader, and the installation of what must be VIB's most fun piece of equipment: our new experimental brewery.

Cheers to microbes!

Kevin Verstrepen, VIB-KU Leuven Center for Microbiology

MICROBIOLOGY

SCIENCE MEETS SCIENCE

SCIENCE MEETS TECHNOLOGY

SCIENCE MEETS BUSINESS

SCIENCE MEETS PEOPLE

EVENTS

On the cover: Francesca Bellinazzo, Stijn De Graeve, Liselot Dewachter, Adam Feyaerts, Jiyeon Si, Jan Steensels, Marija Stojiljkovic, Toon Swings, Selien Schots and Jorge Vazquez Vazquez (VIB-KU Leuven Center for Microbiology)

THE CENTER FOR MICROBIOLOGY: FIGURES AND FACTS

106 PEOPLE

4 LOCATIONS IN LEUVEN

5 GROUPS

26 NATIONALITIES

RESEARCH TOPICS

Kevin Verstrepen Lab:
Using systems biology approaches to study genes and genetic networks, signal transduction and gene regulation, (epi)genetics, evolution, ecology and microbiomes; and using the same technologies to generate improved microbes for the production of fermented food, beverages and biofuels.

Patrick Van Dijck Lab:
Candida albicans and *Candida glabrata* virulence factors such as nutrient sensing; morphogenesis; biofilm formation and adhesion. Molecular interactions between fungal and bacterial pathogens; plant trehalose metabolism.

Jan Michiels Lab:
Molecular principles and socio-evolutionary aspects of bacterial persistence; novel antimicrobials and antipersister molecules; cell cycle control; conjugative horizontal gene transfer; genetics of microbial tolerance towards different stressors (including ethanol); on-seed survival of nitrogen-fixing rhizobia.

Johan Thevelein Lab:
Novel molecular mechanisms involved in nutrient sensing and signaling for growth and metabolic control in yeast and their biomedical significance; polygenic analysis of industrially-important traits of yeast and development of superior industrial yeast strains for commercial fermentations.

Jeroen Raes Lab:
Variation of the gut microbiome in health and disease; population cohort studies; gut microbiology; dietary modulation of the gut microbiota; biomarker research; bioinformatics.

>100,000 yeast strains
>100,000 bacterial strains
>20,000 gut microbiome samples

NEW

Spin offs → Global Yeast, Aphea.Bio

COLLABORATIONS

LEUVEN	Frederic Rousseau and Joost Schymkowitz, Patrik Verstreken, Adrian Liston and Bart Ghesquière
BRUSSEL	Wim Versées and Remy Loris
GENT	Wout Boerjan, Tom Beeckman, Dirk Elewaut, Lars Vereecke, Steven Maere, Yves Van de Peer, Peter Vandenabeele, Geert van Loo and Andy Wullaert
HASSELT	Markus Kleinewietfeld

Jan Michiels

ID KIT: JAN MICHIELS

Jan defended his doctoral thesis in molecular microbiology in 1993 and became a group leader at KU Leuven in 2001. He steadily expanded his team through competitive grants and a growing pile of strong publications. In the meantime, Jan also served on several research councils and science societies.

Research focus: *bacterial genetics, evolution, ecology, interactions and pathogenesis, with a special emphasis on the mechanisms underlying tolerance to stress and antibiotics*
Motto: *Pour accomplir de grandes choses il ne suffit pas d'agir, il faut rêver; il ne suffit pas de calculer, il faut croire. (Anatole France).*

INTRODUCING JAN MICHIELS: THE VIB-KU LEUVEN CENTER FOR MICROBIOLOGY'S NEWEST MEMBER

Last year the VIB-KU Leuven Center for Microbiology was expanded with the addition of a fifth lab, led by Jan Michiels. As part of the Center, Jan and his team aim to uncover the molecular principles of bacterial persistence. But more than just this research focus, Jan's motivation and expertise are also a perfect fit for the Center.

MICROBIOLOGY WITH MAXIMAL IMPACT

Jan: "When I heard that Kevin was looking for additional groups, I didn't waste a second to send in my application. I believe that interaction with other groups in the Center, the VIB community and its core facilities will stimulate all of us to work together in innovative ways and explore new research alleys. Via Tech Watch, the 20 scientists in my group will be able to test new technologies much faster than before."

Kevin adds: "The combination of various topics, technologies and methodologies is indeed what makes us strong, and enlarges the impact of our work. Together, we study all things micro-organisms: the way they act as model systems for cells in higher organisms, their resistance to antibiotics, their essential role in keeping us healthy and their impact on flavor in beer, wine, cheese and chocolate."

A PERFECT MATCH

Jan's enthusiasm is not a one-way street: Kevin and the other group leaders immediately agreed that Jan would be a perfect addition to the Center. "We received over 100 applications, but Jan's was unanimously selected. First of all, he and his team are doing very exciting research, which in the past few years has led to some cool breakthroughs and strong publications in the field of antibiotic resistance and bacterial genetics – this is complementary to our other labs," Kevin explains. "Secondly, because his lab was already fully embedded within KU Leuven, he was able to hit the ground running. But most importantly, Jan is a fun colleague we all look forward to working with."

GROWING AND DIVERSIFYING

Adding Jan's group to the center is an important, but not a final step for Kevin. "We will soon launch a call to attract a sixth group leader. It would be nice to find a female PI, as all our current group leaders are Belgian, white males. Although most life science institutes are struggling to get female applicants, or applicants from underrepresented minorities, that's no excuse, and we are doing everything we can to change this. For instance, together with our HR department, we write the call that women are in the same way attracted as men and contact possible candidates personally."

Stijn Mertens and Kevin Verstrepen

A TASTE OF SCIENCE IN VIB'S HYPER-MODERN BREWERY

In a state-of-the-art experimental brewery, Kevin Verstrepen (VIB-KU Leuven Center for Microbiology) and his team investigate yeast behavior in large volumes of beer. The brewery bridges the gap between the lab and the industry: it allows scientists to study fermentation in depth and test how their newly developed industrial yeasts behave.

Our new experimental brewery is somewhat hidden between the Dijle river and KU Leuven's Arenberg Campus. "It keeps the smell away from the crowds", brewing engineer Stijn Mertens chuckles. The building houses many large fermentation vessels, of which fourteen are lined up behind a big window. "Brewing beer inherently requires several vessels, but on top of that, we use these fourteen fermenters to compare different yeast variants on one batch of brewed medium", Stijn explains. "This way, we create better yeasts, helping brewers perfect existing beers or create new ones."

FLEXIBLE TESTING ENVIRONMENT

Creating top-class yeast is largely a matter of persistent testing. "Up until now, fermentation processes were examined in lab conditions on small amounts of beer", Kevin says. "But the problem is that yeast tends to act differently in a 1-liter flask than in a 50,000-liter fermenter. So, with help from AB Inbev and about 20 other industrial partners, we built the experimental brewery."

"What makes our installation unique is its potential to run tests on all types of beers and compare many different yeasts at once", Stijn explains. "Whereas traditional breweries are made to deliver just one specific brew with one yeast, our infrastructure is more flexible, ready to handle beers with different and extreme alcohol percentages and flavors."

SETTLING IN AT THE BREWERY

The beer industry is already reaping the benefits of VIB's experimental lab. "Several yeasts that we developed, including some producing superior or novel aroma, are already used for commercial beer production", Kevin says.

"Another trend is the production of beers with extremely high or low alcohol content. In this respect, we also want to investigate stress resistance of yeasts: how do they react to high amounts of alcohol, pressure and extreme temperatures?"

Additionally, the brewery is the perfect place to observe how yeasts adapt to their environment. "Yeasts can reproduce sexually, but also non-sexually, by creating clones of themselves", Stijn explains. "During this process, mutations start occurring in the population, giving rise to complex Darwinian evolution of sublineages. That's how beer yeasts acclimatize to life in the brewery. By sampling them, we are able to uncover their mutation patterns. And as they reproduce every two hours, these evolutions are highly visible, making our studies even more exciting."

Based on an article of KU Leuven Campuskrant by Tine Bergen

BREW IT YOURSELF

To get a real taste of beer brewing, master's students in biochemistry and biotechnology at the University of Ghent can attend a practicum from the Nico Callewart Lab (VIB-UGent Center for Medical Biotechnology). Postdoc Hendrik Grootaert explains how it works: "First, we teach a group of 20 students how to compose a recipe, on both practical and biotechnical levels. We then provide them with ingredients and let them brew their own beer in a traditional way: fermentation in plastic buckets. Students' imagination is endless," postdoc Francis Santens continues. "This year, we've seen brews with raspberry, thyme and even orange zest flavors. Although not all experiments succeed, some beers are actually really tasty!"

Philippe Muyters, Johan Hanssens, Jo Bury and Christine Van Broeckhoven

HOW THE FLEMISH GOVERNMENT SETS THE EXAMPLE IN RESEARCH VOLUNTEERING

To examine diseases such as dementia, Alzheimer's, diabetes and Parkinson's, every volunteer counts – not in the least when that volunteer is Philippe Muyters, Flemish Minister for Work, Economy, Innovation and Sports. Together with one hundred civil servants, he participated in two large-scale VIB studies.

"The vital work VIB scientists deliver every day puts Flanders on the map as an innovative biotech region", Muyters proudly says. "All too often, however, we forget how much these scientists need our help. Yet, lending a hand is easy: sending in samples or participating in small tests will make a difference. That's why the Government of Flanders actively chips in – hoping Flanders' citizens will follow their lead."

A GUT FLORA FEELING

The human body hosts 100 trillion bacteria – over one thousand times the number of people on earth. Most of these species live in our intestines, protecting us from various diseases. Jeroen Raes (VIB-KU Leuven Center for Microbiology) plays a pioneering part in unraveling the essential role of these gut flora. "Our research hinges on the engagement of volunteers donating stool samples. With the Flemish Gut Flora Project, we aim to collect and analyze at least five thousand stool samples. The more people join our quest, the more insight we gain into the relationship between gut bacteria and health."

THE GROWING PROBLEM OF ALZHEIMER'S

Muyters and the Flemish civil servants also participated in a study by Christine Van Broeckhoven (VIB-UAntwerp Center for Molecular Neurology) on dementia. The condition is taking on pandemic proportions: the 47 million patients worldwide today are expected to rise to 131.5 million by 2050. In Flanders-Belgium, in the age group 60-64 years, 1% run the risk of dementia, a number that doubles every five years. But treatment for the disease is yet to be found. "To properly investigate how dementia works, we need data from both patients and healthy people", Christine explains. "Citizens donating blood samples or joining memory tests are invaluable to our research."

"Many of these studies stand or fall by the cooperation from citizens. With very little time or effort, you can help advance science and society as a whole."

Philippe Muyters

MORE INFO ON HOW TO TAKE PART CAN BE FOUND AT WWW.VIB.BE/IKWERKMEE.

Patrick Van Dijck

FOCUS ON FUNGI: UNDERSTANDING *CANDIDA ALBICANS*

At the VIB-KU Leuven Center for Microbiology, Patrick Van Dijck and his team study a peculiar type of fungus: Candida albicans*. This organism is the cause of several common ailments, like white tongue and vaginal infections. Alarmingly, under specific circumstances, the fungus also becomes a vicious killer.*

Patrick: "For most of us, *C. albicans* is a common fungus in our gut. If introduced into the bloodstream of patients with a weakened immune system, it can turn into a deadly pathogen, killing 40 to 60% of them. We seek to understand the virulence factors of the fungus to develop therapeutic strategies."

THE IMPLANTS ISSUE

One of those virulence factors is the formation of biofilms: natural protective layers that communities of cells create to protect themselves against adverse environmental factors. These biofilms shelter *C. albicans* from the patient's immune system and from specific antifungal drugs. Patrick: "Implants, such as catheters or hip replacements, are ideal substrates for *C. albicans* to attach to and form biofilms. As more patients get implants, this becomes a big problem."

"Today, when a biofilm is formed, the only solution we have is to replace the implant. For a simple catheter, that's doable, but for other implants, such as heart valves, the consequences are much bigger." Over the last few years, Patrick and his team have become leading experts in the study of these films. They have developed an *in vivo* rodent model system that allows them to investigate the effects of biofilms on the immune system and to test anti-biofilm drugs.

ANTIFUNGAL DRUG RESISTANCE

Another issue tackled in the lab is antifungal drug resistance. Patrick: "When patients don't react to a drug, they are given a higher dose. But *C. albicans* responds by developing new resistance mechanisms, which leads to a vicious circle until the dose can't be upped anymore, and the patient dies from the fungal infection."

The team is close to understanding the reason for *C. albicans'* tolerance to the most widely used antifungal drug, fluconazole. "Unraveling the molecular mechanisms behind this tolerance allows us to screen for novel compounds that would, together with fluconazole, result in a fungicidal combination."

MORE THAN FUNGI

Instead of merely focusing on fungi, the team is also looking into the molecular interaction between bacteria and fungi. "Scientists tend to study one or the other," Patrick says. "But that doesn't make sense, since bacteria and fungi live together in the human body. Multiple mutual effects are at play between the two, which impacts the influence of these organisms on the patient. I strongly believe that to truly advance in science, we need to bring both worlds together."

RESEARCHERS FROM THE LAB OF KEVIN VERSTREPEN TELL US MORE ABOUT THEIR RECENT STUDY

TANDEM REPEATS: USEFUL FOR SURVIVAL, BUT NOT EASY TO WORK WITH

Although protein degradation receives much less attention than protein synthesis, breaking down damaged, unnecessary and harmful proteins is just as important as generating new ones. In fact, changes in protein degradation and protein half-lives can cause neurodegeneration and cancer. A key degradation system depends on the addition of a 'ubiquitin tag' to proteins that need to be degraded. Interestingly, the eukaryotic stress-induced polyubiquitin gene UBI4 is composed of tandem repeats, with each repeat encoding a ubiquitin moiety.

Rita Gemayel and her colleagues in the Kevin Verstrepen lab (VIB–KU Leuven Center for Microbiology) show that the number of ubiquitin units encoded by the UBI4 gene differs greatly between different species, and even within a species, including different yeast strains as well as humans.

Did your study uncover any surprising new insights into *UBI4* tandem repeats?
Kevin: "Tandem repeats have been a longstanding topic in the lab. When we screened the yeast genome to find all repeats located within coding regions, we were surprised to find that the *UBI4* gene did not just contain a repeat, but instead solely consists of one big tandem repeat!
We found that the unusual structure of the *UBI4* gene allows yeast cells to quickly produce more copies of ubiquitin and rapidly respond to sudden environmental stress.

"Even more, the number of ubiquitin repeats that is optimal for stress survival differs between stress conditions, indicating that natural variation in repeat units may optimize the chance for survival. Natural instability in the number of ubiquitin repeats encoded by *UBI4* may also serve as an elegant alternative to copy number variation, enabling cells to rapidly tune the ubiquitin production rate in times of stress."

Did you run into any challenges during the project?
Rita: "Because of their intrinsic instability and the problems with sequencing and amplification, working with tandem repeats gave me a lot of headaches. But after a while, I learned how to make things work. Perhaps we should publish a paper on how to live with difficult repeats".

Gemayel *et al.*, Nat.Comm. 2017

THE YEAST IS YET TO COME

Although it may seem like just another mundane fungus, yeast plays a leading part in many VIB studies. Some scientists use it as a model for tumor cells, while others aim at uncovering the genes of specific yeast strains to find out where flavors come from. Whatever the research goal, yeast often comes in handy.

Last fall the Johan Thevelein group from the VIB-KU Leuven Center for Microbiology relied on yeast cells to suggest a possible relationship between sugar and cancer, and during the same period, they also identified the yeast genes behind rose and honey flavors in beer and wine.

From left to right: Frederik Van Leemputte, Johan Thevelein and Maria Remedios Foulquié Moreno

THE WARBURG EFFECT

After nine years of joint effort alongside Wim Versées and Peter Tompa from the VIB-VUB Center for Structural Biology and Veerle Janssens (KU Leuven), Johan and his team were able to provide evidence for the positive correlation between sugar and cancer. They discovered that a major intermediate of sugar breakdown, fructose-1,6-bisphosphate, is a potent stimulator of the Ras proteins, which in overactive form are well-known activators of cancer. Their study is published in *Nature Communications*.

Frederik Van Leemputte (PhD student and co-first author of this publication): "Our research mainly focused on how the Warburg effect, the phenomenon in which cancer cells rapidly break down sugar, stimulates tumor growth. It was already well known that the stronger the Warburg effect, the more aggressive the tumor becomes. For the first time we have now identified a logical molecular explanation for this correlation."

As you might have guessed, yeast cells proved to be the key to these results. Yeast contains the same Ras proteins that are commonly found in mammalian cells, which can cause cancer in their mutated form. Moreover, just like cancer cells, yeast has a preference for breakdown of sugar by fermentation rather than respiration. The fungus is therefore an attractive model organism for cancer research.
"We observed that sugar degradation is linked to the activation of Ras proteins, stimulating the multiplication of both yeast and cancer cells," Johan explains. "Although it's still too early to make statements about the possible consequences for cancer treatments and adjusted diets, our discovery delivers very valuable novel insights."

"Pooling the expertise from various labs, we were able to deliver wonderful work at an impressive speed. These strategic collaborations are, in my opinion, the power of modern science in action."
Frederik Van Leemputte

A MOLECULAR WHIFF

In the very same lab, postdoctoral fellow Maria Remedios Foulquié-Moreno investigates how specific yeast strains shape the flavors in beer and wine.
Maria: "Although most aromas in wines come from the grapes, the metabolism of yeast can alter those, adding secondary flavors. And the yeast itself also contributes its own flavors. In beer, yeast is the main source of the aroma produced during fermentation."

Using their polygenic analysis platform and the CRISPR/Cas9 technology, Maria and her colleagues have now identified the specific yeast genes that produce high levels of phenylethyl acetate (2-PEAc). The name of this compound may not ring a bell, but the aroma probably does. Maria: "When a wine smells of roses or honey, this is mainly caused by 2-PEAc."

However, why some yeasts produce more of this compound than others remained unknown – until now. Maria: "We found that two genes – TOR1 and FAS2 – were directly related to the high production of 2-PEAc. This was quite unexpected, as neither of them had been associated with this rose-like aroma before."

These findings may be used to grow yeasts that produce new flavors. Maria: "In the past, enhancing industrial strains for desirable aromas has been a real challenge. Scientists usually rely on cross-breeding to select specific genes, but this is time-consuming, expensive, and may cause other unwanted changes in the yeast. By using the CRISPR/Cas9 technology, we can now engineer production of desirable aromas without affecting other traits."

Peeters, Van Leemputte, Fischer *et al.* Nature Communications, 2017
Trindade de Carvalho *et al.* mBio 2017

Front row from left to right: Gunter Kathagen, Gwen Falony and Doris Vandeputte
Back row from left to right: Kevin D'hoe, Sara Vieira-Silva and Jeroen Raes

IT'S THE INSIDE THAT COUNTS: QUANTITATIVE MICROBIOME PROFILING

Many illnesses – like Crohn's disease – are associated with gut flora alterations. And not only the type of bacteria in our bowels, but also their quantity matters. Introducing Quantitative Microbiome Profiling, Jeroen Raes (VIB-KU Leuven Center for Microbiology) and his team take a leap towards the quantitative assessment of microbiome composition.

The changes in amounts of gut bacteria are usually described as proportional shifts in microbiome composition. "The problem with these percentages is that they cannot tell you whether a particular bacterium is actually becoming more abundant under specific conditions", Jeroen explains. "A proportional increase in one species could just as well imply that other taxa are declining. This makes it very difficult to link microbiome data to health and diseases. With Quantitative Microbiome Profiling, we are one step closer to solving this issue."

RISKY BUSINESS

The development of the new methodology was financed by a KU Leuven CREA grant, aimed at stimulating young scientists to explore groundbreaking, but also risky research lines. Gwen Falony, staff scientist in Jeroen's lab, is one of those enthusiasts: "Creating new methods is always tricky: you never know if it will work until you try. Thanks to the CREA initiative, we were able to take a chance, which turned out to be quite successful."

Quantitative Microbiome Profiling allows fast and accurate determination of the bacterial load in a fecal sample. Jeroen: "By parallelization of microbiome sequencing with flow cytometry enumeration, we generate true quantitative microbiome profiles expressed as numbers of cells per gram, rather than percentages. We hope this technique will put gut flora research on the fast track."

"Our research makes it impossible to continue ignoring the elephant in the microbiome room: proportional data."
Gwen Falony

ROOTED IN THE FLEMISH GUT FLORA PROJECT

Essential for the interpretation of quantitative microbiome findings was the Flemish Gut Flora Project. In this population-wide monitoring study, Jeroen and his team collected over 3,000 fecal samples from healthy volunteers. Assessment of microbiome variation in a non-diseased population enabled the identification of a new, often disease-associated microbiota community type characterized by a low microbial load.

Postdoc Doris Vandeputte: "We found 50 times less bacteria in samples from patients suffering from Crohn's disease compared to healthy volunteers, quite a spectacular result. Further research will be targeted at determining whether this actually causes such diseases, and if so, how to prevent it."

A NUMBERS GAME

During the Flemish Gut Flora Project, Jeroen and his team got unexpected help from university college PXL Hasselt. Jeroen: "Students and personnel voluntarily started collecting stool samples at the school. Their initiative has been essential to the success of our study. Indeed, to be able to conduct representative research, we need as many samples as we can get." The same goes for our current follow-up study '150 Days of Gut Flora', which aims to map out various microbiota compositions over a longer period of time. Once again, help from citizens is indispensable. Every sample counts."

More info on www.vib.be/gutflora.
To join the project, simply register at www.vlaamsdarmfloraproject.be.

Vandeputte *et al.*, Nature 2017
Wilck *et al.*, Nature 2017

GUT FLORA ARE SENSITIVE TO SALT

The Nature issue that highlighted Quantitative Microbiome Profiling also included a publication from the ECRC Berlin, under participation of Markus Kleinewietfeld (VIB Center for Inflammation Research -UHasselt).

The study describes how salt reduces the number of specific gut commensals in mice. Markus: "We found that high salt intake depletes lactobacilli in mice and thereby indirectly affects immune cells that play a key role in autoimmune diseases and hypertension. Although these results offer potential for therapy development, more research is needed to unravel the complex interaction between nutrition, gut flora and immunity, and how all those factors impact diseases. This is just the start."

MICROBIOLOGY THROUGHOUT VIB

The Sofie Goormachtig group focuses on the fascinating world of plant-microbe interactions

Soil is extremely diverse in terms of microbial life, and it is fascinating that roots engage in mutualistic interactions with some of these, but repel others. We still have no clear idea how this discrimination works. In nutrient-poor environments, plants heavily rely on microorganisms for growth. A key example are legumes that grow as pioneer plants in poor soils but require symbioses with nitrogen-fixing rhizobia in order to do so. Plants even develop new organs: the nodules to host the microbes! Plant roots communicate with surrounding microbial life through chemical signal exchanges. We only know little about the language they speak.

Sofie Goormachtig (VIB-UGent Center for Plant Systems Biology): "Communication is the basis of life. Without excellent communication, you do not survive, or you stay very unhappy. Just look at humans... The same holds true for plant roots communicating with the surrounding microbial life."

Crop protection via single domain antibodies

Chemical crop protection is still widely used to control plant diseases, despite its adverse effects on human health, and on environment and resistance development on the pathogen side. In that context, the Bruno Cammue Lab (KU Leuven and VIB-UGent Center for Plant Systems Biology) investigated, in a joint effort with the VIB spin-off company AgroSavfe, the potential of camelid single domain antibodies (VHHs) to control plant diseases. VHHs were generated that specifically bind to fungal glucosylceramides (fGlcCer), known through the Cammue lab's research as specific binding sites for the antifungal plant peptides termed plant defensins and important pathogenicity factors. *In vitro* these anti-fGlcCer VHHs were shown to inhibit the growth of one of the most devastating fungal plant pathogens, *Botrytis cinerea*, as well as reduce disease caused by this pathogen on tomato leaves. This data supports the potential of the VHH-based approach as an alternative strategy to combat plant diseases.

De Coninck *et al.*, Front. Microbiol. 2017

First Belgian Germfree and Gnotobiotic mouse facility opened in Ghent

The VIB-UGent Center for Inflammation research (IRC) has successfully launched a germfree mouse facility, through the joint efforts of VIB, UGent and UZ Gent. The facility represents a great asset for studying physiological and immunological functions related to microbiota. Many inflammatory, metabolic and even neurological disorders are characterized by distinct shifts in microbiota composition (termed 'dysbiosis'). Using germfree and gnotobiotic mouse technology, we are now able to perform functional causality studies in a plethora of disease models. The facility is coordinated by Lars Vereecke.

(VIB-UGent Center for Inflammation Research).

Stimulating root development and nutrient acquisition by interfering with the soil microbial community

In the Root Development Group of Tom Beeckman (VIB-UGent Center for Plant Systems Biology), one research topic focuses on the role of the plant root system in soil nutrient acquisition and its plasticity to increase nutrient access. The microbial community in agricultural soils is being recognized as a major contributor to changing plant nutrient levels. Taking the microbiome contribution into account, the final goal is to identify new strategies to improve fertilization and nutrient use efficiency by plants. A more elaborate description of such strategies has recently been published in *Current Opinion in Biotechnology.*

Beeckman *et al.*, Curr. Opin. Biotechnol. 2018

A link between the microbiome and neurological diseases

Over the last few years, the impact of the gut microbiome on our health, including neurological manifestations and referred to as gut-brain axis, has been increasingly recognized. Roosmarijn Vandenbroucke (VIB-UGent Center for Inflammation Research) reports that gastric *Helicobacter suis* colonization in mice is associated with behavioral changes, including cognitive decline. Analysis of the mechanisms revealed that this is due to breakdown of the gastrointestinal barrier, increased leakage of TLR4 ligands in the periphery and subsequent loss of brain barrier integrity, specifically at the blood-cerebrospinal fluid (CSF) barrier.

Emerging evidence is pointing to a crucial role for the microbiome in Parkinson's disease. PhD student Arnout Bruggeman will soon start a placebo-controlled randomized clinical trial of fecal microbiota transplantation in Parkinson's disease patients in close collaboration with Debby Laukens (Gastroenterology, UZGent) and Patrick Santens (Neurology, UZGent). Microbiome analyses will be done in collaboration with the Jeroen Raes lab (VIB-KU Leuven Center for Microbiology). The ultimate goal of this project is to address the impact of microbiota on motor and non-motor Parkinson's disease symptoms and progression.

Gorlé *et al.*, Brain Behav. Immun. 2017

Structural molecular biology of bacterial cell surfaces

The Han Remaut Lab (VIB-VUB Center for Structural Biology) looks at bacterial cell surface components and processes because of their prime role in bacterial physiology and host-pathogen interaction on the one hand, and as a source for new biomaterials and biotech applications on the other hand. "In the Structural & Molecular Microbiology group, protein structure and function studies are deeply rooted in their (micro) biological context, reflecting my dual interest and training in biology and biochemistry", says Han. Main topics include chronic and inflammation-associated colonization by pathogenic Escherichia coli and Helicobacter pylori, and bacterial amyloid assembly and biotechnology.

REPORTER ON THE ROAD: LEARNING FROM MICROBES: ADAPTING TO CHANGING ENVIRONMENTS

THEY OFTEN SAY: "FIRST LOVE NEVER DIES." WELL, THIS MIGHT BE TRUE, AT LEAST FOR ME.

August 2011. It is a warm Monday with sunny skies; it's summer break. What more could a student want? Still a bit hungover from the night before, I take my bike and rush to the Bio-Incubator in Heverlee. I'm almost late on my first day. Together with some of my classmates, I officially kicked off my master's thesis work in the lab of Kevin Verstrepen on that day. I would start pursuing my ultimate childhood dream: to study evolution. Yes, I was the geeky kid that read *On the Origin of Species* at the age of 13, and now, I could finally work on biology's most beautiful theory myself.

Pretty much every genome is riddled with so-called *'junk'* DNA, mostly consisting of tandem repeats, transposons and other funky DNA elements. But from an evolutionary point of view, this makes no sense. Could there be some overlooked function to this so-called junk? In his previous work on yeast, Kevin had found that, indeed, such tandem repeats could be beneficial to an organism. I planned to follow up on this work and study how these repeats allow yeasts to adapt to changing environments.

INFECTIOUS EXCITEMENT – I HOPED

It was a tough year. We had – but we also wanted – to work hard and give it our best shot. I learned the ins and outs of yeast genetics, and of working with tandem repeats. I fell in love with what I was doing. I had never been so excited about anything in my entire life. This was what I wanted to do, period. In January of that year, I submitted my FWO proposal. I wanted to continue working with yeast through my PhD. The project was basic science, we had cool data, my grades were good: it was the perfect shot at a fellowship! How could anyone not be excited about this awesome project?

A small caveat: I really needed to get this grant. An applied grant at IWT would be not possible for such a fundamental project, and unfortunately, the PhD students before me had had bad luck with their applications and were being paid by the lab. There was no more budget left for me. It would mean getting a grant, or no PhD.

MOVING FORWARD, GRANT OR NO GRANT

Well, the review committee was clearly not as excited as me about the project proposal. My world collapsed. What now? After a few weeks of disillusion, I decided to make the best of it. Even though nothing would be as cool as what I was doing, I might find an interesting alternative. In applying to every neuroscience lab in Gasthuisberg, I was consistently told that all PhD positions were taken. But finally, against all odds, I was eventually able to squeeze into one lab. The year before scientists discovered that a tandem repeat expansion underlies most familial ALS cases, which was a breakthrough in the study of this dreadful disease. However, given that ALS was not considered a tandem repeat disorder before, ALS researchers generally knew quite little about these DNA elements. This is how I convinced Ludo Van Den Bosch and Wim Robberecht that my expertise in yeast could, perhaps surprisingly, help them figure out how this tandem repeat causes the disease.

FALLING IN LOVE ALL OVER AGAIN

Five years flew by. The experience I had gained in Kevin's lab gave me an edge in this new and fast-evolving field. Together with collaborators at VIB and abroad, we were able to make some fascinating discoveries that opened up novel niches and illuminated the complex biophysics of protein aggregation in ALS. During my PhD, I ended up working with yeast, fly, zebrafish, mice and cell cultures. I jumped from genetic screening to hardcore biophysics. I am sure I gave Ludo and Wim headaches from time to time with my endless list of "side projects" and "quick experiments".

I never believed it could happen, but I was falling in love again. Yes, my heart still ached a bit at the thought of the project I'd left unfinished in Kevin's lab. But here at Gasthuisberg, new doors had opened for me, as was the case in Brussels, Ghent and Antwerp through numerous collaborations within VIB. There was so much exciting stuff out there!

WHEN LIFE GIVES YOU LEMONS... DO SCIENCE!

I am a creature of habit. When I like something, I won't easily change. Indeed, most Friday nights, I could usually be found among the same group of colleagues in the same bar, drinking the same beer, rocking out to the same 80s tunes. In science, I am pretty similar. When something grabs my interest, I won't let go of it easily. But from time to time, one must change, broaden one's horizons, etcetera. Good luck finding a position in science with expertise in only one specific thing! Science is becoming increasingly multidisciplinary, and it's important to have that extra knowledge "baggage" to tackle complex questions.

In retrospect, not getting that grant wasn't nearly as bad as I'd initially thought. It's never fun to leave a project behind unfinished, but in return, I learned plenty of new and exciting things. When yeast is faced with a shortage in glucose, it will be disillusioned for a while, but it will eventually look around for other sugars to eat and new niches to conquer. My environment had also changed, forcing me to adapt, just like my beloved yeast cells. I learned to deal with rejection and made the best of my situation. Even though I continued to focus on tandem repeats, switching to new model organisms gave me an entirely new toolkit and set of techniques that I might not have gained otherwise. More importantly, I realized that one closed door does not equal a dead end – just a detour. Passion for science will always find a way.

February 2017. It is a sunny winter day in California. I have just received a fellowship to continue my work on tandem repeats in ALS. However, I also picked up yeast work again, and labs from across the US are sending samples to fuel my side project on the evolution of repetitive protein sequences.

First love never dies.

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

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

Marcelo Vinces

PUTTING EVIDENCE-BASED SCIENCE EDUCATION INTO PRACTICE

VIB ALUMNUS MARCELO VINCES EXPLORES THE INTERSECTION OF SCIENCE, EDUCATION AND POLICY.

*As a postdoctoral fellow in Kevin Verstrepen's lab at VIB-KU Leuven, Marcelo Vinces used brewer's yeast to study the biological function of highly mutable repetitive 'junk' DNA sequences. Although he left VIB in 2011 to work at the National Science Foundation (NSF) through an AAAS Science and Technology Policy Fellowship, part of his heart remained in Belgium. He arrived at the interview in a KU Leuven sweater with Kristof Calvo's book 'F*ck de zijlijn' at hand. "A much better politician than Donald Trump," he says with a wink, "and the perfect way practice my Dutch."*

The step from being a successful microbiology researcher to a role in public service must have been gigantic.
"Not so much for me, no. I have always been engaged in policy issues: broadening participation and increasing diversity in STEM fields, communicating science to wider audiences, but also teaching and working with students at various education levels.

"The AAAS fellowship is open to PhDs in science and engineering and allows them to spend one or two years in the US federal government. The idea is twofold: scientists and engineers experience how the US government functions and how policy is formulated. At the same time, scientific thinking and expertise is lent to the federal government.

"My motivation was to connect my research experience with the bigger picture of where science and academia fit into society. It was an eye opener. I became interested in supporting science and education at the institutional level, instead of becoming a professor and teaching 'my' class, and 'my' students. The NSF work allowed me to think about the next step in my professional life."

That next step being Oberlin College in Ohio?
"Exactly. At Oberlin College, I established the Center for Learning, Education and Research in the Sciences (CLEAR), an interdepartmental resource for faculty and students. With the support of an HHMI grant of $800,000, CLEAR provides ongoing support for faculty development and curriculum development. It also helps students strengthen their understanding of quantitative and formal reasoning skills.

"For example, CLEAR provides peer support for basics such as math and graphs, but also for advanced skills, such as modeling. These skills are common in different disciplines and necessary for interdisciplinary research. They come in handy in virtually all academic fields and in almost every profession."

Oberlin College is, at least in Europe, not the most well-known US college or university. What's so special about it?
"Oberlin was the first college to grant undergraduate degrees to women and, historically, was a leader in the education of African Americans. Oberlin is a small, highly selective, liberal arts undergraduate school with an impeccable reputation. Per capita, Oberlin sends as many or even more students to PhD programs in the sciences as renowned institutes like MIT and Caltech. Of Oberlin's alumni, 22 are members of the US National Academies of Sciences. That is a huge number for such a small college.

"There is something special about the science education program at Oberlin. It attracts science students with broader societal views. The students are more creative and think out of the box."

Why is that?
"The college is better-known – fortunately and unfortunately – for its arts and music programs and his home to a world-renowned music conservatory. The unfortunate part is that many students ignore the fact that Oberlin is also strong in sciences. The fortunate part is that Oberlin attracts an interesting group of students. They might major in sciences, but are at the same time very interested in music, culture and society. A lot of the science students I worked with were also doing theatre and composing music."

As CLEAR's first director, you had to start from scratch. And now, five years later, you are leaving CLEAR and Oberlin. Why?
"In the beginning, I had to establish partnerships with offices and departments across campus to form learning communities to advance inclusive excellence and transformative learning approaches in all STEM fields and at all levels of the curriculum. I believe we did a good job, as five years later in 2017, we received a $1 million grant through HHMI's Inclusive Excellence Initiative. This grant will support CLEAR's aim to advance Oberlin's historic role in inclusive education by enhancing the climate and success of a diverse student population in STEM.

"It was also a good time to leave. The CLEAR program is in good shape, there are exciting plans and an excellent new director. It is hard to let go of your babies, but moving to Chicago – where my partner moved – will bring me new challenges and opportunities. I want to do the same work, but in Chicago there are bigger institutions and universities, and thus bigger challenges."

Where do you see yourself in the future? Will you return to the lab and your experimental work, be a science educator, or work in science policy?
"I would say yes to all of the above. I miss experimentation, for sure. One of the things I would really like to do is apply my research skills to the educational setting. Why not do controlled experiments on the effectiveness of educational strategies? Evidence-based teaching: that's my future!"

COUNTERACTING THE EFFECTS OF TNF RECEPTOR-I HAS THERAPEUTIC POTENTIAL IN ALZHEIMER'S DISEASE

From left to right: Sophie Steeland, Charysse Vandendriessche, Griet Van Imschoot, Elien Van Wonterghem, Nina Gorlé and Roosmarijn Vandenbroucke

Alzheimer's disease (AD) is the most common form of dementia and increasing evidence has shown that neuroinflammation is an important and early hallmark of the pathogenesis. It has been suggested that tumor necrosis factor (TNF), a pro-inflammatory cytokine, might be detrimental in AD, though the results coming from clinical trials on anti-TNF inhibitors are inconclusive. Roosmarijn Vandenbroucke (VIB-UGent Center for Inflammation Research) reported that TNF, via activation of its receptor TNFR1, is the main inflammatory upstream mediator of the AD-associated changes at the choroid plexus and that targeting TNF/TNFR1 signaling has therapeutic potential.

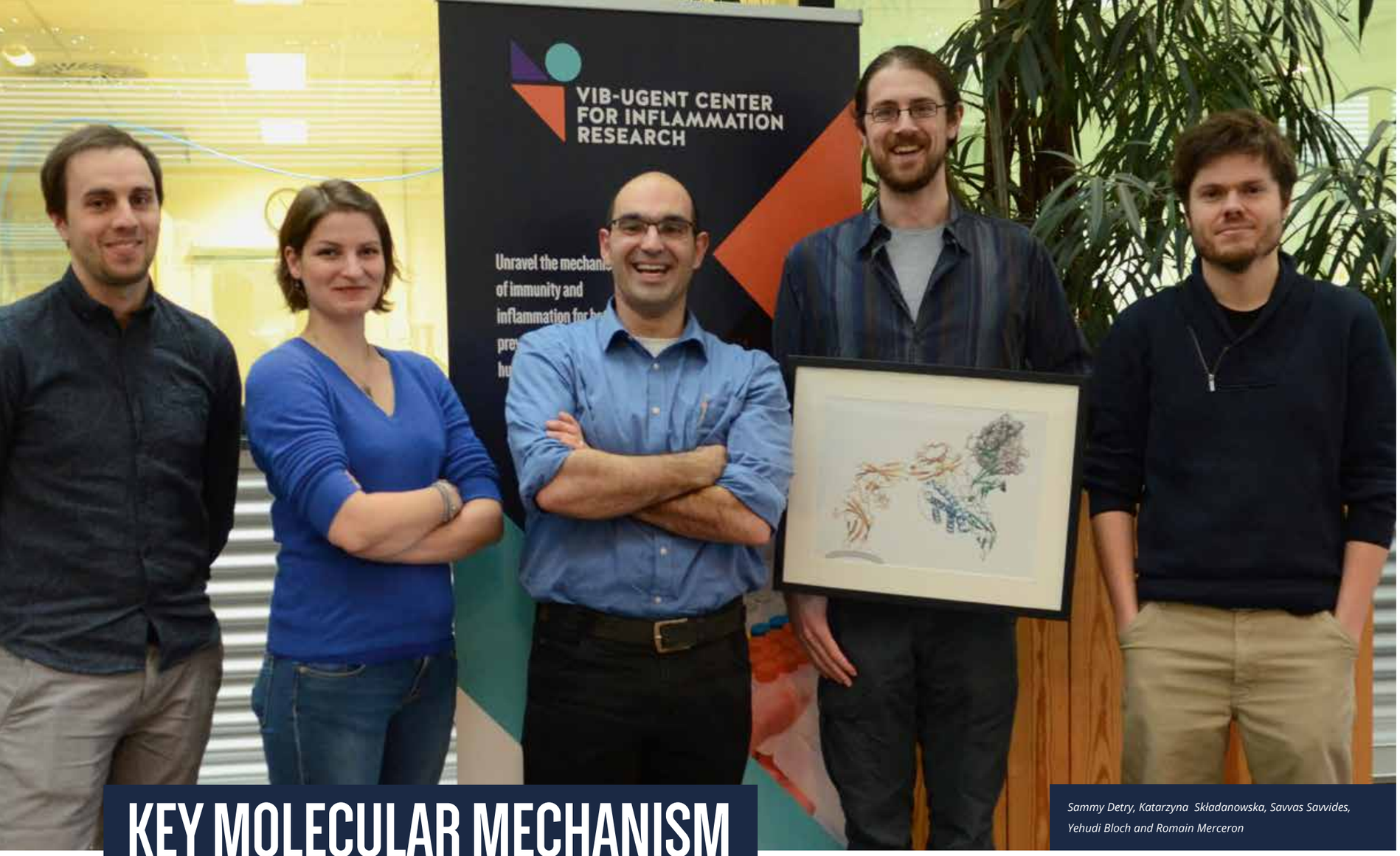
Together with her team Roosmarijn focuses since a few years on an often neglected structure in the brain called the choroid plexus which contains a monolayer of tightly connected choroid plexus epithelial (CPE) cells forming the blood-cerebrospinal fluid (CSF) barrier. Previous research from the team has shown that AD is associated with changes in CPE cell morphology and a compromised blood-CSF barrier. Now, based on gene expression analysis of choroid plexus tissue of AD patients compared to healthy persons and subsequent mouse studies, they found this specific role of TNF.

Roosmarijn: "We could confirm the detrimental role of TNF/TNFR1 signaling in two murine AD models: intracerebroventricular (icv) injection of oligomerized amyloid beta and transgenic APP/PS1 mice. TNFR1 contributes to the morphological damage of CPE cells in AD and TNFR1 abrogation reduces brain inflammation and prevents blood–CSF barrier impairment. In APP/PS1 transgenic mice, TNFR1 deficiency ameliorated amyloidosis and improved microgliosis. Strikingly, genetic and pharmacological blockage of TNFR1 with an in-house generated Nanobody did not only prevent the AD-associated inflammation, it also rescued against the induced cognitive impairments. Therefore, our data indicate that TNFR1 is a promising therapeutic target for AD treatment."

An important limitation of the current study is the fact that the anti-TNFR1 Nanobody® was directly injected into the brain, thereby circumventing one of the major challenges of successful therapy for central nervous system (CNS) disorders: drug delivery across the tight brain barriers.

Roosmarijn: "To address this, we are currently focusing on novel potential strategies to deliver therapeutics into the brain. For this, we exploit the CPE cells as delivery route. Within the European Horizon 2020 B-SMART project and a recently granted SBO project, we are generating Nanobodies against different targets involved in transport across the blood-CSF barrier. After identification of an ideal candidate, this Nanobody will be coupled to nanoparticles that carry RNA therapeutics to target Alzheimer's disease and of course also to the TNFR1-inhibiting Nanobody used in our current study."

Steeland *et al.*, EMBO Molecular Medicine 2018



Sammy Detry, Katarzyna Składanowska, Savvas Savvides, Yehudi Bloch and Romain Merceron

KEY MOLECULAR MECHANISM OF AUTOIMMUNE AND INFLAMMATORY DISEASES

An international team of researchers led by Savvas Savvides (VIB-UGent Center for Inflammation Research) has unraveled a crucial aspect of the molecular basis of autoimmune and inflammatory diseases such as psoriasis, rheumatoid arthritis and Crohn's disease. Focusing on the immunomodulatory cytokine IL-23 they discovered that its pro-inflammatory activity, which underlies a wide range of inflammatory diseases, critically depends on structural activation of the cytokine by its receptor, IL-23R.

The prevalence of psoriasis, rheumatoid arthritis, inflammatory bowel diseases, and multiple sclerosis, has been rapidly expanding over the last few decades. For instance, an estimated 125 million people worldwide are affected by psoriasis and another 100 million by rheumatoid arthritis, while the presence of inflammatory bowel diseases (Crohn's disease and ulcerative colitis) in ethnic populations and previously unaffected geographical regions is growing at alarming rates. The cytokine IL-23 – a specific type of immunomodulatory protein – plays a crucial role in these diseases. Consequently, IL-23 has become the focus of therapeutic strategies against such diseases.

REVERSED ROLES: WHEN RECEPTOR ACTIVATES CYTOKINE

Since the first description of IL-23 about a decade and a half ago, the structural and molecular basis for the mechanisms underlying the pro-inflammatory activity of IL-23 remained unclear. Savvas and his team have now shed light on the unique way that IL-23 interacts with at least one of its receptors. In general, cytokines activate receptors. But surprisingly, in the current study, the opposite appeared to be true.

Savvas: "We were surprised to find that both IL-23 and its receptor change drastically to create an intimate cytokine-receptor interface. In this interface, the receptor uses a functional hotspot on IL-23, enabling it to recruit an essential co-receptor for pro-inflammatory signaling. The binding site of the co-receptor on IL-23 also emerged as an unexpected finding. What we have now discovered about the pro-inflammatory complex mediated by IL-23 appears to be a new paradigm in the field."

CONTINUED COMBINED EXPERTISE

The study was spearheaded by PhD student Yehudi Bloch and grew into a joint effort between research groups at the University of California (Davis, USA), Ghent University Hospital, and Savvas' team at VIB and Ghent University. The researchers relied on integrative structural biology, combining methods to describe protein structures in atomic detail with complementary biochemical, biophysical, cellular and in vivo studies.

Savvas: "These initial research milestones from our program on IL-23 will be the cornerstone for further research in our own labs and elsewhere. After all, many questions still remain unanswered. For instance: how does IL-23 bind with other possible co-receptors? Furthermore, our insights are expected to fuel the development of new therapeutic strategies against IL-23."

Yehudi Bloch *et al.*, Immunity 2018

HOW TREATING ECZEMA COULD ALSO ALLEVIATE ASTHMA

Scientists from VIB-UGent have discovered insights for a possible new therapy for eczema that also reduces the severity of asthma. The findings are an important next step in understanding the relationship between the two inflammatory diseases and to developing effective therapies.

Children with atopic dermatitis (AD), a type of eczema of the skin, show an increased risk of developing asthma later in life. This phenomenon, also known as atopic march, raises questions on whether therapies can be developed that not only tackle AD, but also prevent the onset of other allergic diseases. Intrigued by this possibility, Julie Deckers spitted it out for her PhD with Karolien De Bosscher (VIB-UGent Center for Medical Biotechnology) and Hamida Hammad (VIB-UGent Center for Inflammation Research) as promotors.

MARCHING FROM THE SKIN TO THE LUNGS

House dust mites are known culprits in the development of both AD and asthma, as exposure to the mites induces inflammation. The researchers created a mouse model to look further into the relationship between the two diseases.

Julie: "As predicted, our test showed that house dust mite-induced skin inflammation leads to aggravated levels of allergic airway inflammation. Yet, to our surprise, this response significantly differs from the reaction to direct exposure of house dust mites in the lungs without prior skin inflammation. These results have given us a deeper understanding of the complexity of the atopic march."

ONE THERAPY TO RULE THEM ALL

The real challenge, however, was to investigate whether the relief of skin inflammation might influence the subsequent development of asthma. The team therefore combined two anti-inflammatory compounds – corticosteroids and PPARγ agonists – into one potential treatment in mice.

Julie: "The combined therapy effectively alleviated AD, but was insufficient at preventing allergic asthmatic response in the lungs. However, the treatment did significantly reduce the severity of the asthma by counteracting one aspect of the specific immune response in the lungs. In this way, the therapy represents a potent remedy against allergic skin inflammation and the aggravation of atopic march."

The team is now looking for industrial partners to develop clinical trials for the therapy, making the leap from mouse to man. At the same time, they plan to further investigate the exact mechanisms driving the progression from AD to asthma in order to develop alternative therapies that can halt the atopic march.

Deckers *et al*., Journal of Investigative Dermatology 2017

SCIENTISTS SHED LIGHT ON A TUMOR-SUPPRESSIVE PROTEIN IN METASTASES

Massimiliano Mazzone

A new study conducted at the VIB-KU Leuven Center for Cancer Biology in Belgium has labeled the protein Caveolin-1 as a high-potential pursuit in the fight against cancer. Many research projects have already implicated this protein in both tumor-promotive and suppressive functions, but its exact role remained elusive. By examining macrophages at the sites of metastases, the scientists have now described the 'anti-metastatic surveillance' role of Caveolin-1 for the first time.

The lab of Massimiliano Mazzone lab has been focusing on the tumor microenvironment for some time now, gradually disentangling topics such as tumor oxygen shortage, angiogenesis (the formation of blood vessels) and macrophages (a type of white blood cell) and anti-cancer immunity. This fundamental groundwork has now been stimulated by a European ERC grant on metabolic immunoregulation in cancer and tumor immunotherapy.

THE GATEKEEPERS OF OUR LUNGS

While the role of tumor-associated macrophages at each step of cancer progression is already well-established, the biology of 'metastasis-associated macrophages', their counterparts at the sites of cancer metastases, has been almost neglected. Understanding this field, however, is of the utmost relevance, as metastases cause no less than 90% of human cancer deaths.

In this research, the team describes for the first time the mechanism of Caveolin-1 in metastatic macrophages. They saw that upregulation of this protein in the lung environment clearly hinders metastatic growth.

Massimiliano: "A surprising outcome, since macrophages are traditionally associated with cancer progression. But at the same time, the anti-metastatic, patrolling function of Caveolin-1 makes sense when one considers the relevance of the immune system in the lungs as the first barrier against (inhaled) pathogens and external bodies. You could say Caveolin-1 is a gatekeeper: high expression can protect the body against foreign bodies and diseases, while downregulation is prometastatic."

CAVEOLIN-1 AS A GATEKEEPER

Previous studies already associated the loss of Caveolin-1 with more aggressive proliferation – and worse patient outcomes – in several types of cancer. The findings of the Massimiliano Mazzone lab directly confirm the suggestion that this protein may yield promising therapeutic perspectives.

Massimiliano: "We have now learned that there is a huge difference in immunity at the metastasis compared to the primary tumor. And since metastasis is what kills most cancer patients, this research avenue deserves much more attention – which describes perfectly the direction of our next research projects!"

Celus *et al*., Cell Reports 2017

QUICKSCAN

1

#GIT2 #Thymus #Aging

Aging is one of the most complex processes in biology. The molecular events that comprise aging are organized into 'small-world' networks that are interconnected by keystone or 'hub' proteins. The Stuart Maudsley Lab (VIB-UAntwerp Center for Molecular Neurology) has demonstrated that the G protein-coupled receptor kinase interacting protein 2 (GIT2) acts as an aging keystone. Genomic alteration of GIT2 expression in mice accelerates systemic aging and induces premature thymic involution – a classical marker of aging. GIT2-mediated immune dysfunction is caused by altered clock gene time sensing across multiple tissues.

Siddiqui *et al.*, Aging 2017

2

#Plant growth regulation #Short-term stress response #Gene regulatory networks

Plants have to cope with environmental fluctuations and accordingly fine-tune their growth and development through the regulation of molecular networks that are largely unknown. The lab of Dirk Inzé (VIB-UGent Center for Plant Systems Biology) detailed a complex, highly interconnected network of 20 *Arabidopsis* transcription factors at the basis of leaf growth inhibition upon mild osmotic stress. Phenotypic analysis identified novel growth-promoting genes, some of which stimulated organ growth even more when combined. This work offers new perspectives for selecting stress-tolerant crops.

Van den Broeck *et al.*, Mol. Syst. Biol. 2017

3

#Plant gene regulation #Systems biology

Although various experimental methods exist to map gene regulatory networks in *Arabidopsis thaliana*, their limited throughput renders our knowledge about regulators for many genes incomplete. PhD student Shubhada Kulkarni from the Klaas Vandepoele group (VIB-UGent Center for Plant Systems Biology) introduced TF2Network, a tool that exploits the vast amount of transcription factor binding site information to detect potential regulators for a set of co-expressed or functionally related genes.

Kulkarni *et al.*, Nucl. Acids Res. 2018

4

#GlycoCirrhoTest #Hepatocellular carcinoma #Cirrhosis

In cooperation with the group of Hans Van Vlierberghe (UGent/UZ Gent), the Nico Callewaert Lab (VIB-UGent Center for Medical Biotechnology) assessed GlycoCirrhoTest for the risk of hepatocellular carcinoma (HCC) development in compensated cirrhosis patients. This study demonstrates that a simple serum blood test based on the analysis of serum glycomics predicts a 5-year 12-fold enhanced risk for the development of HCC in these patients. This enables a more intensive screening for HCC.

Verhelst *et al.*, Clin. Cancer Res. 2017

5

#C9orf72 #ALS #RNAtoxicity

C9orf72 expansion is the most frequent genetic cause of ALS and FTD, but it is unclear which pathogenic mechanism it elicits: repeat RNA toxicity or dipeptide protein (DPR) toxicity.

The team of Ludo Van Den Bosch (VIB-KU Leuven Center for Brain & Disease Research) used a zebrafish model to answer this question, and found that neurodegeneration arises, at least in part, from RNA toxicity that is independent of DPRs. Assuming that both play a role, the team proposes that approaches targeting both modalities have the highest therapeutic potential, as opposed to targeting DPR toxicity alone.

Swinnen *et al.*, Acta Neuropathol. 2018

6

#Tau #Neurotransmission

The lab of Patrik Verstreken (VIB-KU Leuven Center for Brain & Disease Research) showed last year that Tau mislocalizes to presynaptic terminals in human disease conditions, causing early defects in synaptic transmission. In a new study, they have now identified an interaction between Tau and the presynaptic vesicle protein Synaptogyrin-3. This interaction restricts synaptic vesicle mobility, driving defects in neurotransmission in fly and mouse models of Tauopathy.

McInnes *et al.*, Neuron 2018

7

#Cancer Immunotherapy #Interferon

Clinical use of type I interferon (IFN) is curbed by its complex toxicity pattern. Anje Cauwels and her colleagues from the Jan Tavernier Lab (VIB-UGent Center for Medical Biotechnology) developed AcTaferons (AFN = Activity-on-Target IFN) displaying focused, cell-specific signaling. AFN-targeting using a tumor-specific antigen prevents tumor growth, and when targeted to dendritic cells a broad-spectrum antitumor effect is seen against melanoma, breast carcinoma and lymphoma, all without any detectable toxic side effects. In combination therapies, complete tumor regression and immunity are obtained. Hence, AFNs represent a new class of safe and generic, off-the-shelf cancer immunotherapeutics.

Cauwels *et al.*, Cancer Res. 2018

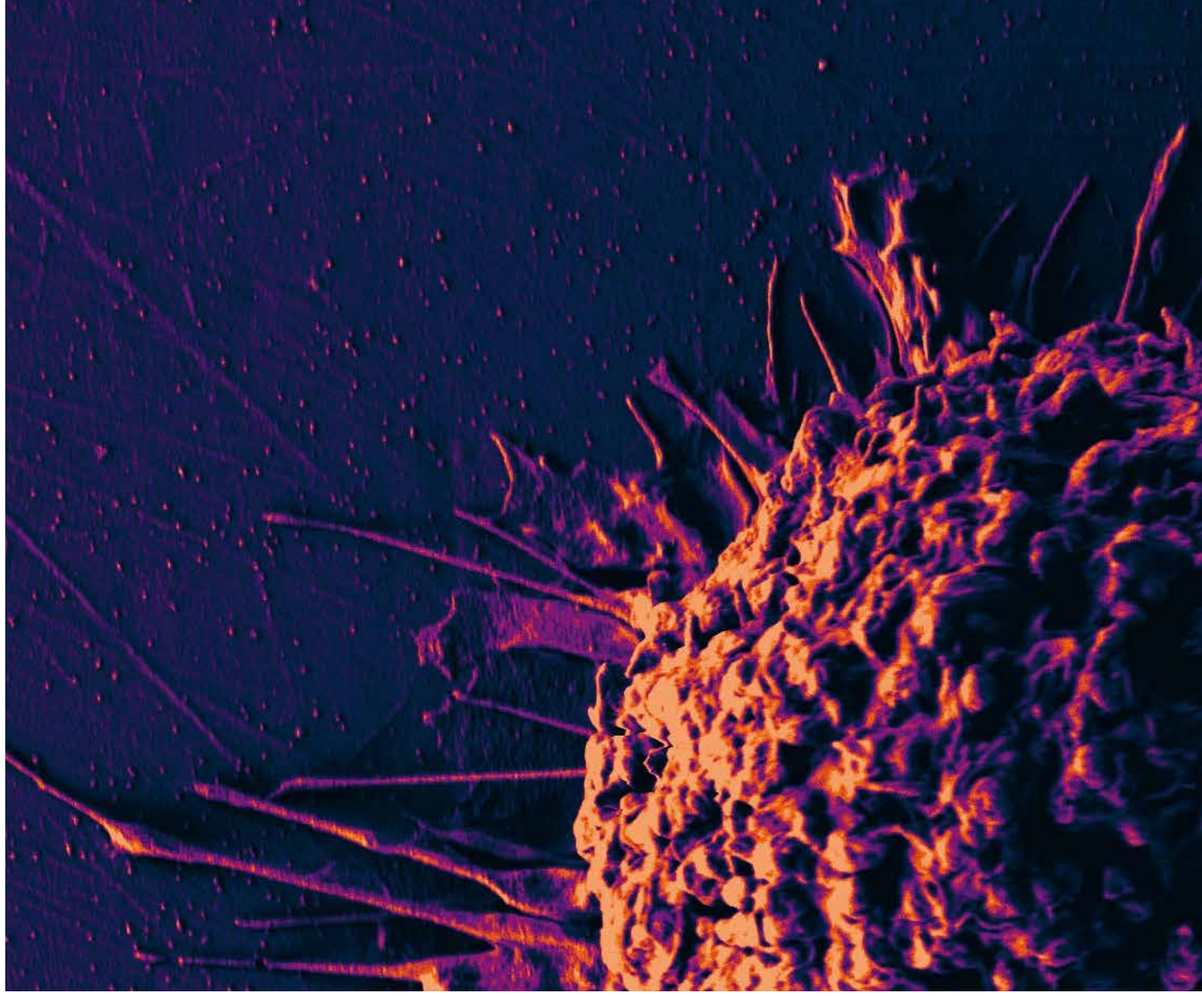
Cauwels *et al.*, OncoImmunology 2018

8

#Leukemia #JAK_3 #Mutations

PhD student Sandrine Degryse and her colleagues of the Jan Cools Lab (VIB-KU Leuven Center for Cancer Biology) observed that one-third of JAK_3-mutant T-cell leukemia cases harbor two JAK_3 mutations, some of which are monoallelic and others that are biallelic. Analysis of these double mutants in primary mouse T cells demonstrated that JAK_3 mutants can increase their limited oncogenic potential through the acquisition of additional mutations in the same JAK_3 allele, or by losing the wild type allele.

Degryse *et al.*, Blood 2017



9

#Vessel dysmorphia #Glioma #Stroma

Gliomas are aggressive and abundantly vascularized tumors. Longitudinal intravital imaging revealed progressive vessel dysmorphia during glioma growth due to dynamic macrophage recruitment and re-polarization. The Holger Gerhardt lab (VIB-KU Leuven Center for Cancer Biology) found that targeting this stroma response resulted in vessel normalization and improved efficacy of chemotherapy, suggesting that the combination of these therapeutic modalities could improve the outcome of glioma treatment in the clinic.

Mathivet *et al.*, EMBO Mol. Med. 2017

VIB TECH WATCH INNOVATION LAB UPDATE: 10x GENOMICS' TECH FUELS SINGLE-CELL STUDIES AT VIB

The 10x Genomics' GemCode Technology makes it possible to study the genetic and transcriptional information of an organism at the single-cell level. Early in its development, this technology was spotted by the VIB Tech Watch initiative, which gave the VIB scientists a competitive advantage. Over the last few months, scientists from multiple VIB research centers have used the technology to investigate biology at a scale never seen before.

UNPRECEDENTED INSIGHTS AT AN UNPRECEDENTED SCALE

The field of cancer biology will be significantly impacted by this technology. "It was previously believed that tumors form a uniform, homogeneous population," says Diether Lambrechts (VIB-KU Leuven Center for Cancer Biology). "However, large-scale single-cell data allowed us to generate a catalog of the tumor microenvironment transcriptome at single-cell resolution. Specifically, we were able to identify multiple discrete cell populations."

Peter Carmeliet (VIB-KU Leuven Center for Cancer Biology) agrees: "10x Genomics' single-cell technology has allowed us to obtain unprecedented insight into the metabolic signature of tumor endothelial cell subpopulations." Bart Lambrecht (VIB-UGent Center for Inflammation Research) is also confident that the hundreds of parameters obtained on individual cells will eventually result in the discovery of biomarkers for the successful treatment of immune-mediated diseases.

ONE EXPERIMENT, THOUSANDS OF INDIVIDUAL CELLS PROFILED

The technology is broadly applicable and will affect multiple fields in life sciences. Abbas Jariani, PhD student in the lab of Kevin Verstrepen (VIB-KU Leuven Center for Microbiology), used the 10x Genomics GemCode to analyze yeast populations. He is enthusiastic about his first results: "We gathered transcriptome data for thousands of individual yeast cells in just one experiment!"

The same holds true for the research performed in the lab of Stein Aerts (VIB-KU Leuven Center for Brain & Disease Research), who comments on his recent work (Davie *et al.*, 2017, BioRxiv): "The 10x Chromium allowed us to profile the transcriptome of more than 100,000 fruit fly brain cells, achieving a nearly 1x cell coverage of the entire brain. In combination with our computational method SCENIC, this dataset enabled the discovery of cell-type transcription factor networks at single-cell resolution."

AN ENTHUSIASTIC RESPONSE

The value of this platform for the VIB scientists is reflected in the fact that multiple VIB centers have now incorporated the 10x Genomics GemCode into their workflows. In addition, interest in this technology is continuously increasing, illustrated by the more than 100 scientists who attended the 10x Genomics VIB workshop in October 2017, held in Ghent.

VIB looks forward to the ongoing collaboration, in which the newest applications for this technology will be explored. Halina Novak, VIB Tech Watch and Innovation Manager: "The Chromium System and GemCode technology have multiple applications, from single-cell genomics, whole genome and exome sequencing to the assembly of full-length single-cell V(D)J sequences for investigating the immune system. Ultimately, this will allow many researchers across life sciences to rapidly advance their research."

GENERATING NOVEL RESEARCH QUESTIONS

Multiple new research questions and accompanying technological challenges arise from the new single-cell sequencing studies. For example, the recent discovery of numerous discriminatory tumor biomarker panels favor targeted sequencing approaches to increase throughput while lowering cost. Even more so, the interest in spatial localization of RNA and proteins *in situ* to validate the single-cell sequencing data is increasing. Below is a list of a few companies on the Tech Watch radar that provide advanced solutions for next-generation single-cell applications:

AKOYA BIOSCIENCES has developed the CODEX technology platform (will be evaluated by the 'VIB Tech Watch Flexible Innovation Lab' from March 2018) to visualize up to 50 proteins *in situ* using oligo-labeled antibodies and a fluidic staining device (Y Goltsev, *et al.*, Biorxiv, 2017).

IONPATH has developed a technology for *in situ* detection of up to 50 proteins, DNA and/or RNA in parallel at subcellular resolution based on mass spectrometry (Angelo *et al.*, Nat Med, 2014).

FLUIDIGM has developed the Hyperion system, which combines CyTOF with imaging capabilities, allowing *in situ* detection of up to 37 proteins at subcellular resolution.

MISSIONBIO has developed the Tapestri platform to perform 'SiC-seq' for targeted single cell gene panel DNA sequencing (Lan *et al.*, 2017, Nat. Biotech) and 'Abseq' for single cell protein profiling using droplet microfluidic barcoding (Shahi *et al.*, 2017, Sci Rep).

We are watching 70 additional companies active in single-cell analysis technologies.

To keep up with the hottest technology trends in Life Sciences, follow the Tech Watch team on Twitter: @VIBTechWatch.

Sofie De Prijck and Niels Van Damme (VIB-UGent Center for Inflammation Research)

TWO MEN ON A MISSION: JOOST SCHYMKOWITZ AND FREDERIC ROUSSEAU ON THE DAWN OF AELIN THERAPEUTICS

Frederic Rousseau and Joost Schymkowitz

"NOTHING IS MORE SATISFYING THAN TRANSFORMING KNOWLEDGE INTO MOLECULES THAT MEET HUMAN NEEDS"

'Catching tumors in a spider's web': that metaphor was used by Joost Schymkowitz and Frederic Rousseau (both VIB-KU Leuven Center for Brain & Disease Research) in a 2016 press release following a Science publication on their peptide-based protein knockdown technology. Fast forward to 2018: our 20th spin-off Aelin Therapeutics has just been launched, and Joost and Frederic's coveted technology platform is now up and running.

Having raised 27 million euro, the most funding ever for a VIB spin-off, the expectations for Aelin Therapeutics are high. But Joost and Frederic have full confidence in their platform for Pept-ins™, designer molecules able to neutralize disease-related proteins by collecting them in inactive clumps. These clumps, called amyloids, were the subjects of their research projects as early as 2004.

When did you first realize that your research project could hold great promise?
Frederic: "That happened quite gradually. But around 2006, we began to understand that our concept of mimicking amyloid formation to inactivate proteins could apply to virtually any protein – and, by consequence, potentially impact a wide array of diseases. Rudy Dekeyser (VIB's cofounder and codirector until 2012 – Ed.) was one of our very first ardent enthusiasts, lending a lot of support during those early years. But although the enormous potential of our idea was clear, we all knew that transforming this idea into a technology platform would be a huge endeavor."

Could you briefly describe the path from idea to start-up?
Joost: "We first tested our proof of concept in a common bacterial model system, after which we submitted our data to the VIB Innovation & Business Team. They were immediately intrigued and very enthusiastic, and a first patent application was readily drafted by Jan Demolder. The support of the Innovation & Business team was also instrumental in helping us secure early funding. That led to a first series of publications showing the potential of our approach in a wide range of applications. For instance, with Jenny Russinova of the VIB-UGent Center for Plant Systems Biology, we demonstrated protein functional knockdown in transgenic plants expressing Pept-ins. And with Johan Van Eldere at the UZ Leuven we managed to kill multi-resistant clinical bacterial strains by clumping together their proteins."

Frederic: "In a later stage, when the technology platform was more advanced, protecting the many possible fields of application was a real feat. Not so much for us, but for our IP team. Hannes Iserentant and Jan Demolder have done an incredible job in that respect. When it came to valorization and creating a business model for a spin-off, we enjoyed the close collaboration with Els Beirnaert and Griet Vanpoucke from VIB's Innovation & Business team. During many years, we learned a lot from each other. Pitching the story to investors together was always very productive but also enlightening. For example, we discovered that many venture capital funders are not simply interested in investing, but also have a clear vision on making a societal difference."

Can you take stock of some highs and lows during that journey?
Joost: "Starting with the latter: the biggest challenge in the early days was simply persuading ourselves that our approach really worked, especially because the quality of the peptides we ordered from companies was very variable. And yes, we encountered quite a few dead ends. We often thought back to something Rudy said: 'In biotech, the bumps are the road'. The highs more than offset the lows. Seeing our paper published in *Science* in 2016 was a massive boost as well."
Frederic: "A breakthrough was the moment we bought a peptide synthesizer and started making our own peptides in-house. And, of course, we are very excited that the spin-off has been launched! Being part of a record investment in a very innovative idea and seeing the team gradually being built is a great feeling."

Who came up with Aelin, by the way? And what does it mean?
Joost: "That's Fre's idea! Aelin is actually a mix of different etymologies: the Greek root means 'light' and the Latin root means 'different'. It illustrates the novel and unique nature of Pept-ins and our hope to bring therapeutic molecules to the market that meet urgent medical needs."

A nice ambition indeed. Could you elaborate a bit?
Frederic: "There's scientific consensus that we're approaching a post-antibiotics era. That's where our potential therapeutics come in, because they offer a very different approach to fight antibiotic-resistant diseases. In the years to come, we plan to work hard to make that happen. After all, making game-changing discoveries is exciting, but bringing them to the real world is even more satisfying!"

Joost: "While we continue to work as advisors for Aelin, we'll keep on exploring other applications for our Pept-ins in our labs – in close collaboration with Aelin, of course."

Gallardo *et al.*, Science 2016

AELIN THERAPEUTICS IN FACTS

FOUNDED: December 6, 2017
BASED ON THE WORK OF: Frederic Rousseau and Joost Schymkowitz
FOCUS: novel modality in drug development in order to create a completely new class of antibiotics and first-in-class therapeutics against high-value undruggable human targets
INVESTEMENT: 27 M€
INVESTORS: LSP (the Netherlands), PMV (Belgium), Novartis Venture Fund (Switzerland), Boehringer Ingelheim Venture Fund (Germany) and Fund+ (Belgium)
LOCATION: Bio-Incubator Leuven
CEO: Els Beirnaert
NUMBER OF COLLABORATORS BY THE END OF 2018: 10

WEBSITE: www.aelintx.com

VIB AND CD3 JOIN FORCES WITH BELGIAN BIOTECH COMPANY GALAPAGOS FOR NOVEL DRUG DEVELOPMENT

VIB, the KU Leuven Center for Drug Design and Discovery (CD3) and Galapagos NV have signed an exclusive license and collaboration agreement for the development of novel MALT1 inhibitors as therapeutics in inflammatory and/or oncological diseases.

VIB EXPERTS IN MALTI PUT THEIR HEADS TOGETHER

This new partnership builds on the small molecule MALT1 protease inhibitors jointly identified and developed by CD3 and VIB and is based on the world-leading expertise at VIB on MALT1. The VIB teams of Thijs Baens and Peter Marynen at VIB-KU Leuven, and Rudi Beyaert at VIB-UGent, have an extensive track record in high-impact publications on MALT1. They identified MALT1 as an important regulator of the NF-κB signaling pathway and demonstrated its potential as a drug target for inhibition of its proteolytic activity in the treatment of auto-immune disorders and certain types of cancer.

TRANSLATING KNOWLEDGE INTO TREATMENTS

For the MALT1 program, VIB and CD3 have now exclusively partnered with Galapagos, a leading global biotechnology company with deep expertise in drug development in inflammatory diseases. Galapagos will continue the development of the MALT1 inhibitors towards clinical application in a number of therapeutic indications, supported by a broad collaboration with VIB's Discovery Sciences and CD3.

Johan Cardoen, Managing Director of VIB: "This is a landmark deal for VIB and yet again proves VIB's long-term commitment to translating our scientific insights into value creation and novel therapies to improve patients' lives. We're extremely pleased that Galapagos, one of the prime biotech companies emerging from Flanders' life sciences hotspot, will pursue this asset with its deep expertise in drug discovery and development."

ALZHEIMER'S ANTIBODY DEVELOPED BY VIB GOES US

VIB has signed an exclusive license and collaboration agreement with new-kid-on-the-stock-market Denali Therapeutics. The San Francisco-based biotech company – which raised about 210 million euro on its first day on the stock exchange in December – specializes in treating neurodegenerative diseases through rigorous therapeutic discovery and development.

Denali Therapeutics will build on an antibody developed by Bart De Strooper, Wim Annaert and Lujia Zhou (all VIB-KU Leuven Center for Brain & Disease Research) to create novel therapies for Alzheimer's disease.

BACK TO THE GENETIC BASIS

The firm's baseline says it all: "Denali Therapeutics is taking on diseases that pharmaceutical companies have long tried – and failed – to treat." To succeed where others haven't, Denali Therapeutics looks into the genetic drivers of specific illnesses. Bart: "That same focus also characterizes our work on Alzheimer's and Parkinson's disease. In our lab, we aim to uncover the basic mechanisms behind these conditions and develop antibodies that halt or delay their progression. A prime example of this was Lujia's PhD thesis, in which we created anti-BACE1, an antibody targeting the BACE1 protein that plays a crucial role in the brain of people suffering from Alzheimer's."

TWO-IN-ONE ANTIBODY

However, BACE1 is not the only key factor in the development of the disease. That's why Denali Therapeutics now wants to create a bispecific antibody that targets not one, but two proteins: BACE1 and Tau. Under the license agreement, they have access to the VIB-developed anti-BACE1 antibody as an important component of their product.

The plan is to push the new bispecific antibody from the bloodstream into the brain, where it would hinder the progression of Alzheimer's. To enhance penetration across the blood-brain-barrier and increase exposure in the brain, the product will also incorporate Denali's proprietary ATV™ (Antibody Transport Vehicle) technology. The ATV technology is enabled by intellectual property licensed by Denali from UK-based biotech firm F-star.

NEXT UP: JAPAN

In January of this year, Denali Therapeutics entered into an agreement with Japanese pharma giant Takeda. The latter thereby acquires the right to develop and commercialize therapies for neurodegenerative diseases using technologies and antibodies created by Denali, including the BACE1 program. Bart: "In this way, our anti-BACE1's journey continues: the deal with Takeda gives Denali the resources to push this program forward. At the same time, it illustrates that large pharma companies are not merely following the unfortunate decision of Pfizer to pull out of this field. Rather, it shows that neurodegenerative diseases are considered a priority by Takeda, as they should be.

DENALI™
THERAPEUTICS

VIB AND PLANT IMPACT PLC: ADVANCING SMALL MOLECULE DISCOVERY FOR CROP ENHANCEMENT

Plant Impact plc, based in the UK, US and Brazil, is a company that focuses on research and development in crop enhancement products. The firm now has exclusive development access and a licensing option to VIB891, a class of small molecules identified by the VIB-UGent Center for Plant Systems Biology. VIB-UGent researchers have discovered that VIB891 can almost double biomass in different plant species. The Plant Impact R&D team will carry out a full evaluation, including greenhouse studies and field trials, of these high-potential molecules. Their fundamental role and their impact on diverse aspects of plant development may indicate their suitability for several ongoing Plant Impact product development projects.

"It is gratifying to see fundamental research in plant science lead to the identification of small molecules that have great potential for many agricultural applications. Plant Impact is the ideal partner to realize this potential."

Aurélie Nowack, Business Development Manager at VIB

Arabidopsis

AWARDS

Our scientists are consistently at the forefront of their fields – often making them honored recipients of grants and awards from distinguished institutes from around the world. Below is a quick overview of the most recent wins of VIB researchers. Congratulations!

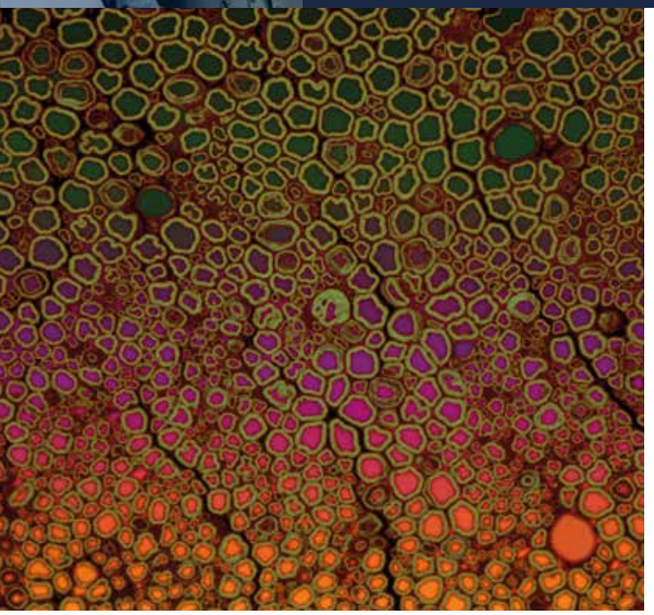
Stein Aerts (VIB-KU Leuven Center for Brain & Disease Research) received a prize in bioinformatics from the Flemish Academy of Medicine for his work titled 'Single-cell gene regulatory networks'. The prize is awarded annually to a Dutch-speaking researcher, and was presented during a ceremony on 24 November 2017 at the 'Big data in life sciences R&D' symposium.

Stein Aerts

@PierreMOREL/FRA

Bart De Strooper (VIB-KU Leuven Center for Brain & Disease Research) won the 2017 European Grand Prix for Alzheimer Research. The EUR 100,000 award was presented by the Alzheimer Research Foundation in Paris in February 2018. It recognizes Bart's excellent high-level research and discoveries related to Alzheimer's disease.

Bart De Strooper



Bob Asselbergh (VIB-UAntwerp Center for Molecular Neurology) won third place in the Olympus Image of the Year Award 2017 for his fluorescent image of a sciatic mouse nerve. Olympus representatives visited the VIB-UAntwerp Center for Molecular Neurology for an interview, and his name and image were published on the Olympus Image of the Year website.

"I found out about the competition through the VIB newsletter and it's my first time ever entering this type of image contest. Given my success rate so far, it surely won't be the last. I was delighted by the fact that one of the jury members found my image very Gustav Klimt-esque."

DID YOU KNOW?

VIB IS A HOTSPOT FOR ENGAGING ACTIVITIES, BREATHTAKING BREAKTHROUGHS AND RENOWNED RECOGNITIONS. STAY IN-THE-KNOW WITH THIS AT-A-GLANCE OVERVIEW. DID YOU KNOW THAT...

MASSIMILIANO MAZZONE, ANNA SABLINA AND SARAH-MARIA FENDT (VIB-KU Leuven Center for Cancer Biology) have each received ERC Consolidator grants of EUR 2 million. These grants, awarded to scientists with the proven ability to run their own labs, allows the three researchers to kick off a high-risk/high-gain project. Congratulations!

DORIS VANDEPUTTE (VIB-KU Leuven Center for Microbiology) summarized her *Nature* article on exploring variations in the number of gut bacteria in 16 tweets. Follow her on Twitter for her latest updates, @DorisVandeputte!

JOLIEN ROOVERS (VIB-UAntwerp Center for Molecular Neurology) is one of the stars in the new 'ikhebeenvraag' ('I have a question') children's book. The book features scientific questions with answers given by researchers in Flanders and an interview with some of them, including Jolien.

DAG VAN DE WETENSCHAP on November 26, 2017 was attended by around 36,500 visitors. VIB's activities reached about 1,700 people through this science-themed event.

THOMAS VOETS (VIB-KU Leuven Center for Brain & Disease Research) received research funding for the 2017-2019 period from the Queen Elisabeth Medical Foundation (GSKE). The award was presented by Her Royal Highness Princess Astrid. GSKE's scientific prizes support Belgian university teams performing basic research in the field of neuroscience.

The LAYING OF THE FIRST STONE of the VIB-UGent FSVM II Research Building took place on February 19, 2018. Philippe Muyters, Flanders' Minister for Work, Economy, Innovation and Sports, did the honors. More details will follow in the next edition of VIBnews.

SOFIE VAN GASSEN (VIB-UGent Center for Inflammation Research) was selected as a new Marylou Ingram Scholar by the International Society for the Advancement of Cytometry (ISAC). The program provides opportunities for leadership training, mentorship training, presentation opportunities, financial support for membership in ISAC (Society), and attending the CYTO conference as well as other valuable professional development activities.

THE BIO IMAGING CORE IN GHENT received about 500 visitors in 2017.

DAMYA LAOUI (VIB Center for Inflammation Research, and VUB Myeloid Cell Immunology lab) was selected through an open call by de Jonge Academie (Young Academy) to become one of 12 new members. She will remain a member until March 31, 2023. Great representation for VIB!

BIOTECH DAY 2018 will take place on October 21, 2018 in Antwerp. With 'customized medicine' as its tagline, the event will cover diverse topics, from neurodegenerative diseases, cancer and personalized medicine to cell therapy and more. The VIB-UAntwerp Center for Molecular Neurology will take center stage at the event, with the possibility for visitors to tour UZA labs.

THE VIB-KU LEUVEN CENTER FOR BRAIN & DISEASE RESEARCH is the proud winner of the crystal bear cupcake prize. The center sold the most cupcakes and collected the most money for National Cupcake Month, amounting to 2,860 cakes and EUR 10,010.

JO BURY GLADLY ACCEPTED THE ALS PEPPER CHALLENGE NOMINATION by Philip Van Damme (VIB-KU Leuven Center for Brain & Disease Research). Together with Johan Cardoen and other brave colleagues from HQ he ate a red chili pepper and at the same time, VIB contributed 1000 euros to the ALS liga. Want evidence? Check out the videos online, including one of minister Philippe Muyters who in his turn was nominated by Jo Bury.

MARK YOUR CALENDAR

Dystonia Europe 25th Anniversary Conference & D-DAYs
April 12-14, 2018 - Brussels

Medical Biotechnology
May 24-25, 2018 - Ghent

Sound of Science
May 27, 2018 - Edegem

Core Technologies For Life Sciences
July 1-4, 2018 - Ghent

Plant Protease and PCD Symposium
September 11-13, 2018 - Ghent

Structural Dynamics in Cellular Communication
September 20-21, 2018 - Ghent

Cell-Nerf symposium: Neurotechnologies
September 30 - October 2, 2018 - Ghent

Biotech Day
October 21, 2018 - Ghent

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