VIB-KU LEUVEN
CENTER FOR
MICROBIOLOGY

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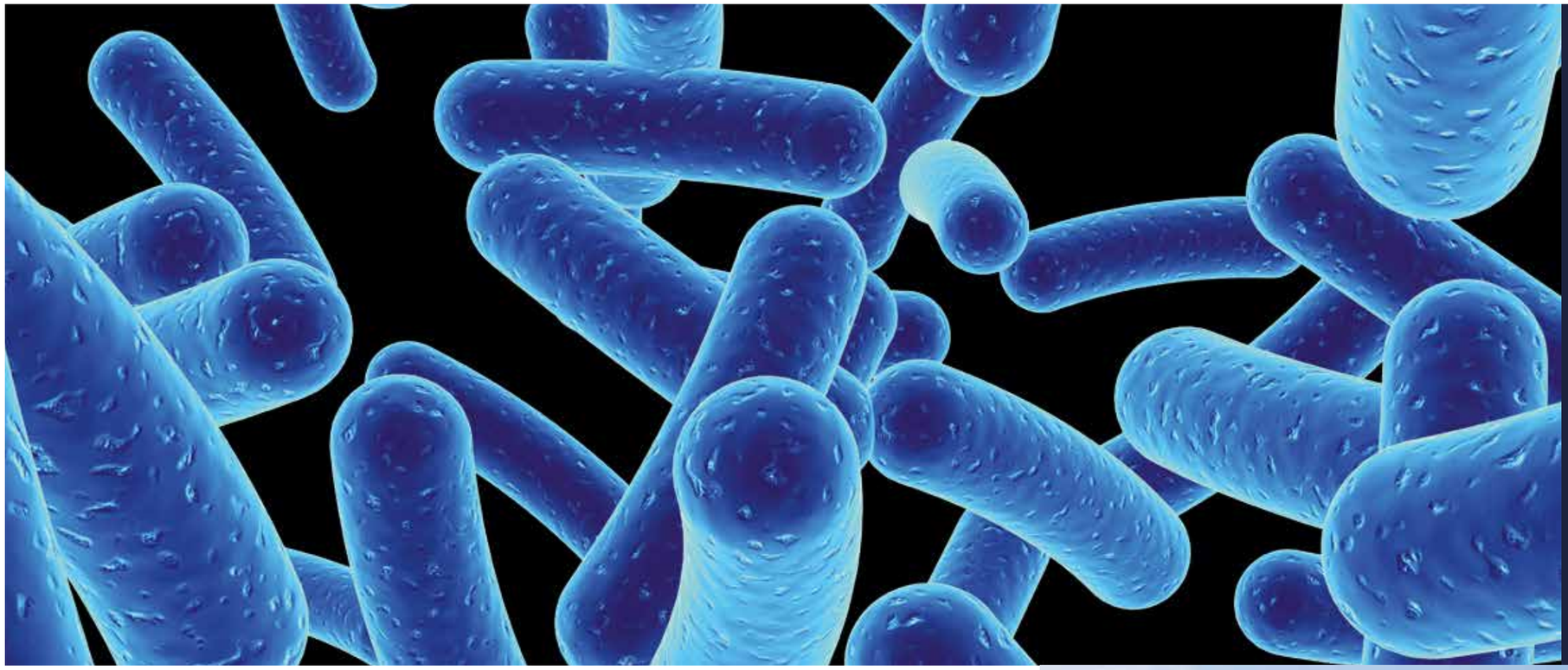


CONTENTS

RESEARCH STRATEGY

LITTLE THINGS MAKE A BIG DIFFERENCE

The VIB-KU Leuven Center for Microbiology combines leading basic research on micro-organisms with translational research and industrial valorization. Using its extensive knowledge of molecular biology and biochemistry, the center's research provides novel insights into prokaryotic and eukaryotic biology, ecology, genetics, genomics, metabolism and pathology. In addition, we are generating superior industrial microbes and microbial products, and are developing novel antibiotics and treatment schemes to fight resistant pathogenic microbes.

SCIENTIFIC VISION

Many of life's basic mechanisms were first discovered in micro-organisms, which are an important model system for cells in higher organisms. Micro-organisms can make us sick and, despite the evolution of antibiotics, more research is needed to control infectious diseases. On the other hand, many micro-organisms are beneficial: intestinal microbes, for example, are essential for the digestion of food and play a crucial role in our health. And let's not forget the role micro-organisms play in the production of fermented beverages and foods, biofuels, pharmaceuticals and bioplastics. Research at our center aims to combine these different aspects by increasing our basic understanding of microbes and higher organisms, and by translating this knowledge into environmental, industrial and medical applications.

MISSION

The VIB-KU Leuven Center for Microbiology aims to be a global leader in the broad field of microbiology.
Our goals are to contribute to our understanding of microbial physiology, genetics, evolution and ecology, for both benign and pathogenic microbes; to use microbes as models to unravel general biological mechanisms; and to pursue industrial and clinical applications of microbes, microbial communities and microbial products (including, for example, the development of antibiotics, probiotics and superior industrial microbes).

BROAD EXPERTISE AND IMPACT

The key areas in which we are currently active include:

- Sensing and signaling mechanisms
- Microbial metabolism and metabolites
- Molecular mechanisms underlying evolution and genetic change
- Microbial ecology and microbial populations
- Antibiotic resistance and persistence
- Generation of superior industrial microbes
- Applications of synthetic biology in microbes
- Clinical microbiology and microbiome research

These areas correspond with our current research groups, which are all led by world leaders in their respective fields. Every year, our team publishes more than 50 papers in leading scientific journals, including *Cell, Science* and *Nature*. The findings of the research performed in the center lead to several patent applications per year. In addition, our translational research and patents yield a significant income and have led to several start-up companies and industrial partnerships.

Kevin Verstrepen, Science Director

RESEARCH GROUPS

A non-profit institute with multiple sites, VIB unites world-class researchers in teams and research centers that are embedded in five universities in Flanders. VIB's scientists conduct groundbreaking biomolecular research in life sciences, leading to sustained scientific progress and contributing to a better world.

All VIB centers consist of several research groups, each with a specific field of expertise. At VIB, researchers are stimulated to collaborate across disciplines and beyond the borders of their own center or even institute.

The VIB centers perform world-leading basic research into some of the most poignant biological questions of our time. It is VIB's strong conviction that fundamental scientific research – often guided by serendipity – can result in major, sometimes unforeseen, breakthroughs.

However, scientific research should benefit society as a whole. That is why each research group is also encouraged and supported in framing their work in a socially relevant, applicable context. As such, each group has a substantial interest in a translational research line, where they aim to develop their basic findings in a way that can make a big impact on various societal challenges.

In short, the VIB centers aim to do cutting-edge basic research and translate the results into advances for the benefit of everyone.

In the presentation of the research groups below, it will become clear that each group in the VIB-KU Leuven Center for Microbiology performs trailblazing basic research that leads to significant translational potential.

Through a fundamental focus on all aspects of microbial life, the VIB-KU Leuven Center for Microbiology is able to pursue a variety of applied perspectives, from food production and industrial compound improvements to human health.

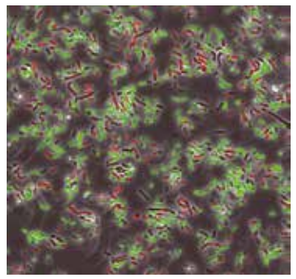
RESEARCH GROUPS

JAN MICHIELS
MOLECULAR BASIS FOR BACTERIAL PERSISTENCE

Antibiotics have revolutionized medical practice by successfully combating life-threatening infectious diseases. However, many bacterial pathogens have become resistant to different classes of antibiotics, often making treatment problematic. In addition to the problem of genetic resistance, antibiotics are unable to completely sterilize genetically susceptible bacterial populations because of the presence of a small fraction of non-growing, transiently antibiotic-tolerant 'persister' cells. Persisters are an important but neglected clinical concern; they underlie antimicrobial therapy failure and recurrence of chronic infections such as *Escherichia coli* urinary tract infections and *Pseudomonas aeruginosa* lung infections. This is especially relevant when persisters cannot be cleared by the immune system because of restricted access (e.g. in biofilms or intracellular infections) or an impaired immune response.

The primary focus of the Michiels lab is to uncover the basic molecular principles of bacterial persistence and how bacteria enter or exit this state. Understanding the underlying molecular mechanisms may help with the development of new therapeutic approaches to combat pathogenic bacteria. From an evolutionary point of view, the scientists in the lab explore how bacterial populations adapt persistence characteristics by genetic mutations or epigenetic modifications during fluctuating antibiotic regimens. In this context, the researchers also examine the link between persistence and the evolution of genetic antibiotic resistance. Their focus lies on the model bacteria *E. coli* and *P. aeruginosa* and several other pathogenic species.

The researchers use genetic approaches combined with 'omics' analyses (large scale genome sequencing, transcriptomics, proteomics and metabolomics) and advanced microscopy, as well as bioinformatics examinations and mathematical modeling. Research is performed at both population and single-cell levels as well as during interaction with the eukaryotic host in cellular and animal models.



BASIC RESEARCH QUESTIONS STUDIED

- How can bacterial antibiotic persistence be understood at the mechanistic and single-cell level?
- Do bacterial persistence levels change depending on the antibiotic treatment frequency and what are the evolutionary dynamics in *in vitro* and *in vivo* contexts?
- Can we develop animal models for persistence research?
- What is the relationship between bacterial persistence and the development of genetic antibiotic resistance? Can we model this in a clinical context?
- Can we determine the mechanistic basis of stress tolerance in bacteria including long-term survival, ethanol stress and desiccation?
- How does the cell division cycle in *E. coli* coordinate envelope homeostasis, DNA replication and cell division?

TRANSLATIONAL RESEARCH TOPICS ADDRESSED

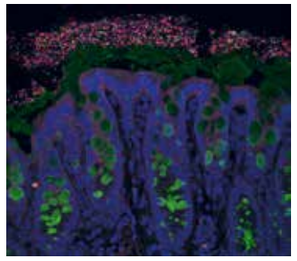
- Development of improved strains and methods for seed inoculation and coating of alfalfa and soybean.
- Development of superior strains for increased production of bio-based chemicals.
- Unlocking cryptic biosynthetic gene clusters using gene editing, synthetic biology and novel culturing approaches to discover new antibiotics.
- Development of new approaches and techniques for high-throughput screening of bacteria for new antibiotics and bio-based chemicals.

JEROEN RAES
HEALTH AND THE GUT MICROBIOME

The functioning of the human body involves a complex interplay of human processes and 'services' rendered to us by the 1,000 trillion microbial cells we carry. Disruption of this natural microbial flora is linked to infection, autoimmune diseases and cancer, but detailed knowledge about our microbial component remains scarce.

Recent technological advances such as metagenomics and next-generation sequencing make it possible, for the first time, to study the various microbiota of the human body at a previously unseen scale. These advances have allowed the initiation of the International Human Microbiome Project, aiming at a genome-level characterization of the totality of human-associated micro-organisms (the 'microbiome').

The Raes lab combines large-scale, next-generation sequencing with novel computational approaches to investigate the functioning and variability of the healthy human microbiome at the systems level and study its alteration in disease. In this context, the researchers discovered the existence of discrete gut flora types (enterotypes) and have linked one of these to inflammatory diseases as well as depression. The lab studies the predictive power of microbial markers for diagnosis and treatment response in various intestinal and chronic conditions, supported by an automated microbiomics platform. Besides this, they pursue the development of novel microbiota modulation strategies, supported by a large in-house bacterial culture collection and fermentation unit. They also develop novel methods for the investigation of community properties based on 16S sequencing, metagenomics, metatranscriptomics and metametabolomics.



BASIC RESEARCH QUESTIONS STUDIED

- What is the population-level variation of the human microbiome and what causes this variation?
- What are the underlying ecological rules and dynamics shaping microbiome composition and functioning?
- How does the microbiota change in disease and how does it contribute to the pathological phenotype?
- What is the role of eukaryotic species in the microbiome?

RESEARCH GROUPS

- What is the role of the microbiome in the gut-brain axis?
- How can we modulate the microbiota?

TRANSLATIONAL RESEARCH TOPICS ADDRESSED

- Identification of diagnostic and prognostic disease markers based on microbiome analysis.
- Development of devices for microbiome sampling and analysis.
- Identification and cultivation of targets for microbiome manipulation in disease and suboptimal health.
- Microbiome services for industry.

JOHAN THEVELEIN
GENETICS AND BIOCHEMISTRY OF NUTRIENT SENSING AND SIGNALING IN YEAST

Research in the Thevelein group is focused on two major topics: the molecular genetics and biochemistry of nutrient sensing and signaling in yeast, and the development of novel genetic technologies and their application for the generation of superior industrial yeast strains.

As well as serving as substrates for the production of energy and building blocks, nutrients exert dramatic regulatory effects on cells. Although several signaling pathways triggered by specific nutrients have been elucidated in great detail, much less is known about how different nutrients can act together on a single pathway to control cellular processes such as cell growth and fermentation.

The group's research has resulted in elucidation of the glucose-sensing network that controls the cAMP - Protein Kinase A (PKA) pathway in yeast. This pathway affects many important cellular targets. The cAMP - PKA pathway also plays an important role in mammalian cells as a signal transmitter for the action of hormones and other environmental signals. A major outcome of research into the mechanisms by which other nutrients affect the PKA pathway has been the discovery of nutrient transceptors: proteins that combine the functions of transporter and receptor.

The researchers have also developed pooled-segregant whole-genome sequence analysis for polygenic analysis of complex yeast traits with commercial importance: ethanol tolerance, maximal ethanol accumulation capacity, thermotolerance, low glycerol/high ethanol ratio, acetic acid tolerance, flavor compound production, etc. The superior alleles identified in this way in natural yeast strains with superior properties are used for the targeted improvement of industrial yeast strains by 'natural self-cloning'.

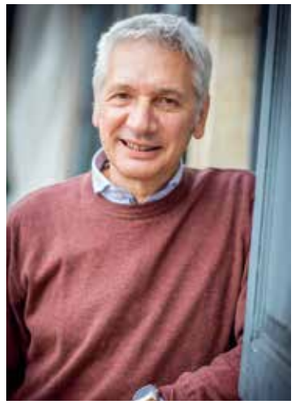
The group also uses yeast as a tool to study mammalian genes with medical importance, such as genes involved in neurodegenerative diseases.

BASIC RESEARCH QUESTIONS STUDIED

- What are the molecular mechanisms in nutrient transceptor/eIF2B-eIF2 interaction?
- How does the nutrient transceptor/eIF2B-eIF2 interaction control protein synthesis and cell growth?
- Does the apically located beta-adrenergic receptor in intestinal epithelial cells function as a glucose receptor for stimulation of glucose uptake from the gut?
- How does the novel class of glucose transport inhibitors that have been isolated within yeast cells function mechanistically?
- Does the novel class of glucose transport inhibitors act synergistically with chemotherapeutics and in how many cancer cell types do they inhibit proliferation?

TRANSLATIONAL RESEARCH TOPICS ADDRESSED

- Development of whole-genome transformation into a targeted technology for predictable improvement of industrial yeast strains.
- Improving the performance of our proprietary second-generation bioethanol strain with different feedstocks.
- Development of yeast cell factories for production of chemicals with second-generation feedstocks.
- Expression of lignocellulolytic enzymes in our proprietary second-generation bioethanol strain.
- What is the importance of acetic acid production for the probiotic potency of *Saccharomyces boulardii*? (Collaboration with Jeroen Raes.)



PATRICK VAN DIJCK
NUTRIENT SENSING IN *CANDIDA ALBICANS* AND STRESS TOLERANCE IN PLANTS

A primary research focus of the Van Dijck lab is nutrient sensing and signal transduction pathways in the human fungal pathogens *Candida albicans* and *Candida glabrata*. The main target of study is the cAMP - PKA pathway, but other glucose or amino acid-induced pathways are also under investigation. There is a strong focus on methionine and how this amino acid affects morphogenesis, an important virulence factor. In order to study these pathways, the team is developing genome-wide *Candida*-specific protein-protein interaction tools, including FRET-based biosensors.

Over the last few years, the group has been studying biofilms of *Candida sp*. Biofilms are a major problem in hospitals as more and more patients receive various implants which are ideal substrates for the attachment and formation of a biofilm. Using a newly developed subcutaneous rodent model system, the researchers have tested anti-biofilm drugs and are currently investigating the effect of biofilms on the host immune system. The model system also allows the group to identify genes that are specifically required under *in vivo* conditions, and screen for novel antifungals (e.g. using collections of essential oils). Resistance to such antifungals is already a

RESEARCH GROUPS

challenge and will certainly become a major problem in the near future. The lab's scientists have identified the major reason why *Candida* cells are tolerant to a major antifungal and are working to develop strategies to counter this.

The second, more recent, main research focus is plant trehalose metabolism. Trehalose is known for its stress-protecting characteristics. Despite the very low trehalose levels in plants, they express 21 genes (in *Arabidopsis*) that show homology to microbial trehalose biosynthesis enzymes. The group aims to understand the role of these genes in plant development and stress tolerance. With their knowledge of the trehalose metabolism, they hope to generate plants with a better stress tolerance.

BASIC RESEARCH QUESTIONS STUDIED

- What are the molecular mechanisms by which methionine and glucose affect the yeast-to-hyphae transition in *Candida albicans* and adhesion in *Candida glabrata*?
- What is the reciprocal effect of bacteria and *Candida albicans* during oral, gut and catheter-associated mixed-species biofilms?
- What is the molecular mechanism that causes tolerance towards the antifungal drug fluconazole?
- What is the role of specific enzymes in glycerol metabolism and is there a link with trehalose metabolism?

TRANSLATIONAL RESEARCH TOPICS ADDRESSED

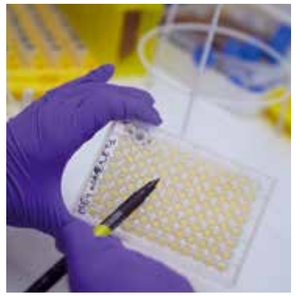
- Use of the bioluminescence-based *in vivo* biofilm model system to screen for novel anti-biofilm compounds.
- Development of high-throughput screening systems for the identification of anti-microbial compounds. (Collaboration with Kevin Verstrepen.)
- Development of a strategy to identify active (for any screenable phenotype) compounds in a mixture of non-active compounds using a collection of 200 essential oils as a model system.
- Development of a yeast-based system for the detection of cannabinoids.
- Use of essential oils for post-harvesting protection.

KEVIN VERSTREPEN
SYSTEMS BIOLOGY

Some properties of living organisms evolve and diverge at a much higher pace than others. The Verstrepen lab's research seeks to elucidate the mechanisms underlying hyper-evolvable properties, which often lie at the border between genetics and epigenetics. The team also exploits these principles to generate superior industrial microbes.

Apart from standard genetics and biochemistry, the group also incorporates mathematical models, bioinformatics and evolutionary theory to help explain and understand their results.

The primary model organism used by the team is baker's yeast, *Saccharomyces cerevisiae*. However, in collaboration with other groups, they are also studying other yeasts, and, for some research lines, are confirming our findings in human cell lines.



BASIC RESEARCH QUESTIONS STUDIED

- What are the mechanisms that determine the speed of gene regulation, and how is this influenced by past experiences ('memory' or 'hysteresis')?
- Genetic buffering and network evolution.
- The role of insects as vectors for microbes, and adaptation of microbes to insect vectors. (Collaboration with Jeroen Raes.)
- The mutagenic effect of ethanol. (Collaboration with prof. Sandra Nuyts at the medical campus.)
- Genetics and genomics of industrial yeasts.

TRANSLATIONAL RESEARCH TOPICS ADDRESSED

- Generation of superior industrial yeasts through large-scale hybridization and marker-assisted breeding.
- Generation of novel industrial microbes by interspecific breeding.
- Development of novel approaches for high-throughput screening of microbes (using lab-on-chip & microfluidics approaches).
- Use of synthetic biology to engineer novel biosynthetic pathways and generate superior industrial microbes.

RESEARCH IMPACT & SCIENTIFIC OUTPUT

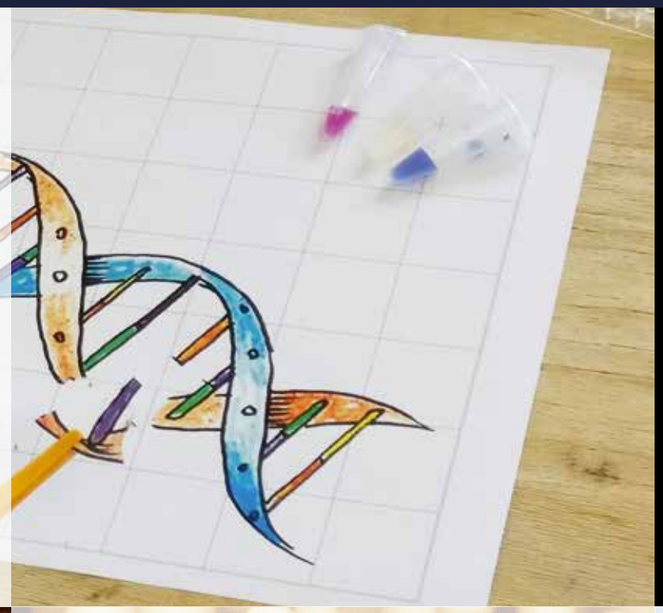
SELECTED PAPERS

While VIB invests strongly in socially beneficial translational research, this would not be possible without the world-class fundamental research done in its centers. Investigating the basic biological mechanisms of life, across the great diversity of organisms, lies at the core of scientific progress and the social and technological advances that flow from it. The VIB-KU Leuven Center for Microbiology aims to understand the smaller organisms with which we share our world. Researchers in the center have elucidated many mysteries in the microbial world, and they will continue to do so. They have also used their fundamental knowledge to develop novel industrial applications in areas as diverse as food production and disease therapies. Below, we present a brief selection of impactful papers detailing their work. Many more can be found on the center's website (http://www.vib.be/en/research/departments/Pages/VIB-KU-Leuven-Center-for-Microbiolgy.aspx)

Swings T, *et al.* (2018). CRISPR-FRT targets shared sites in a knock-out collection for off-the-shelf genome editing. *Nat Commun*, 9(1):2231 (IF 12.35)

Conventional CRISPR techniques require a unique guide RNA for each genetic modification. This can be a constraint for the implementation of the technology, in terms of both time and cost.

In this study, the Michiels team demonstrates a novel technique (CRISPR-FRT) by generating a guide RNA against the flippase recognition target (FRT) site, a common genetic element shared by multiple genetic collections. CRISPR-FRT thus provides a broad platform for fast, scarless, off-the-shelf genome engineering.



Falony G, *et al.* (2016) Population-level analysis of gut microbiome variation. *Science*, 352(6285): 560-4. (IF 37.21)

The microbiome is often studied in the context of disease. However, little is known about microbiome variation in a healthy population.

In this paper, the Raes team analyzes two independent and extensively phenotyped cohorts: the Belgian Flemish Gut Flora and the Dutch LifeLines-DEEP study. Gut microbiota composition correlates with a range of factors including diet, use of medication, red blood cell counts, fecal chromogranin A and stool consistency. The data may lead to biomarkers of normal gut communities.

B. Gallone, *et al.* (2016). Domestication and divergence of *Saccharomyces cerevisiae* beer yeasts. *Cell*, 166(6):1397-1410.e16. (IF 28.8).

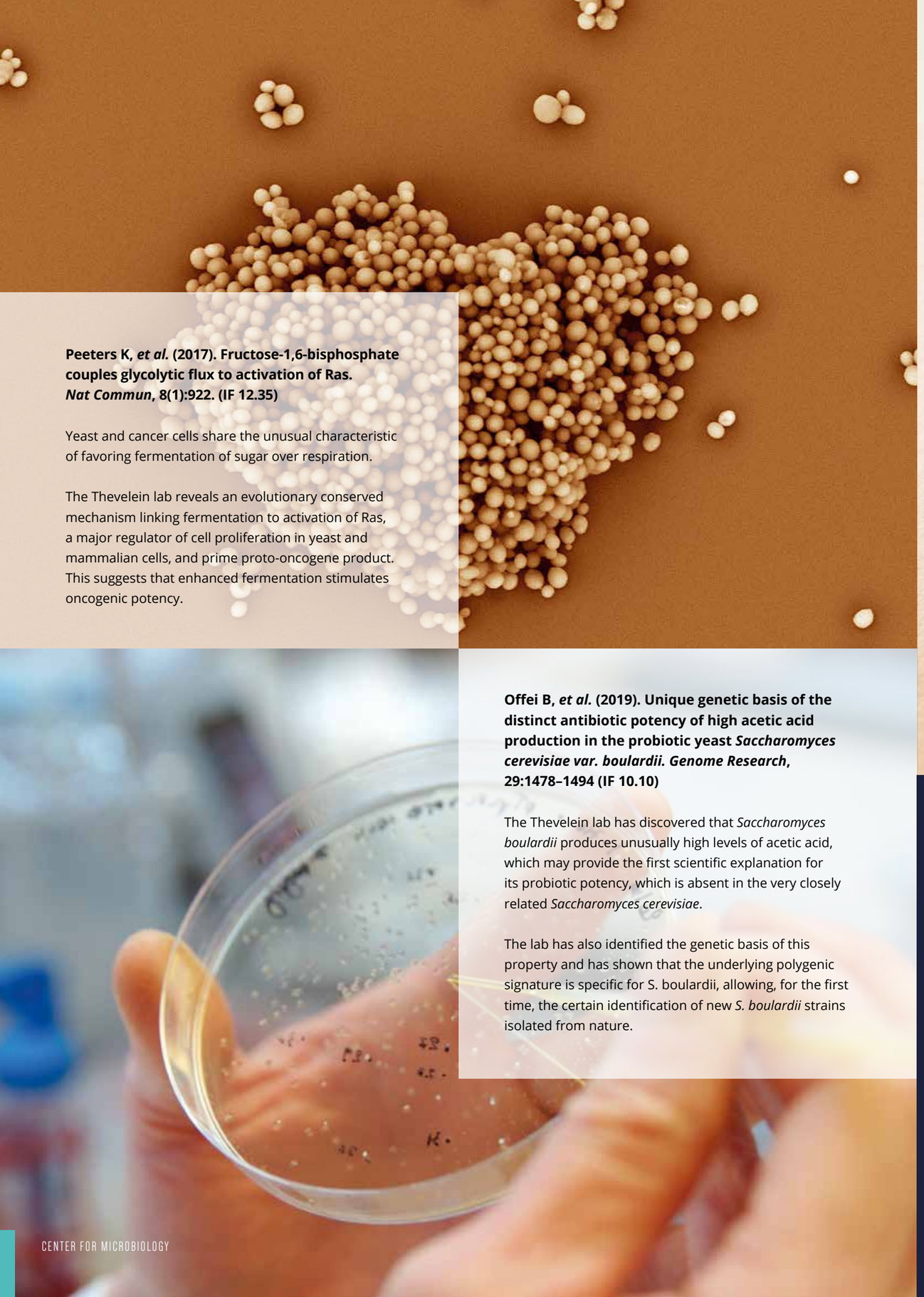
The genetics of the domestication process are well-documented in pets, crop, and livestock. However, domestication of another group of very relevant organisms, microbes, has thus far been neglected.

In this paper, the Verstrepen group begins to remedy this through large-scale phenotyping and genome analysis of 157 yeast strains. Their analyses reveal that today's industrial yeasts can be divided into five sublineages that are genetically and phenotypically separated from wild strains and originate from only a few ancestors through complex patterns of domestication and local divergence.

Demuyser L, *et al.* (2017). Mitochondrial cochaperone Mge1 is involved in regulating susceptibility to fluconazole in *Saccharomyces cerevisiae* and *Candida species*. *mBio*®, 8(4): e00201-17. (IF 6.69)

Although they are mostly neglected compared to bacterial infections, fungal infections pose a serious threat to the human population. Only a few therapies are available, and resistance of the pathogen to these drugs is a frequently encountered problem.

The Van Dijck group shows here that iron metabolism and formation of important iron-sulfur clusters are involved in regulating susceptibility to fluconazole, the most commonly used antifungal drug.



Peeters K, *et al.* (2017). Fructose-1,6-bisphosphate couples glycolytic flux to activation of Ras. *Nat Commun*, 8(1):922. (IF 12.35)

Yeast and cancer cells share the unusual characteristic of favoring fermentation of sugar over respiration.

The Thevelein lab reveals an evolutionary conserved mechanism linking fermentation to activation of Ras, a major regulator of cell proliferation in yeast and mammalian cells, and prime proto-oncogene product. This suggests that enhanced fermentation stimulates oncogenic potency.

Offei B, *et al.* (2019). Unique genetic basis of the distinct antibiotic potency of high acetic acid production in the probiotic yeast *Saccharomyces cerevisiae var. boulardii. Genome Research*, 29:1478–1494 (IF 10.10)

The Thevelein lab has discovered that *Saccharomyces boulardii* produces unusually high levels of acetic acid, which may provide the first scientific explanation for its probiotic potency, which is absent in the very closely related *Saccharomyces cerevisiae*.

The lab has also identified the genetic basis of this property and has shown that the underlying polygenic signature is specific for S. boulardii, allowing, for the first time, the certain identification of new *S. boulardii* strains isolated from nature.

GRANTS & AWARDS

Over the past three years, members of the five research groups in the VIB-KU Leuven Center for Microbiology have been awarded over fifty grants and awards combined. The high-quality science of the center's members has been recognized at both national and international levels. The center has been extraordinarily successful in obtaining competitive grants and fellowships from Research Foundation Flanders (FWO), at all levels, from graduate students to advanced research projects.

In addition, students affiliated with the center have had their work recognized at international conferences through poster and presentation prizes, as well as conference and meeting grants. For their science communication skills, they have achieved top places in the PhD Cup, a competition that aims to identify the early-career scientists who are best capable of distilling their work into a short, engaging talk for a general audience.

The group leaders have attracted many external funding opportunities, including multiple EC Horizon 2020 as well as ERC grants and grants by other international organizations such as EMBO, BAEF and NIH.

Jeroen Raes held the Belgian Francqui Chair for the academic year 2016-2017 at the University of Antwerp. Each year, the Francqui Foundation enables all Belgian universities to invite two visiting professors to present a series of high-level lectures. Jan Michiels holds a Franqui Research Professorship for the period from 2017 to 2020.

Another example of recognition by scientific peers is the honorary professorship from Nottingham University's School of Biosciences held by Kevin Verstrepen.

THE CENTER IN NUMBERS

7 PATENTS FILED OVER THE LAST THREE YEARS

1 ERC GRANT

PARTNER IN
AD-GUT PROJECT
SYSCID CONSORTIUM

63 TIER 5 PAPERS TIER 25 86
1138 CITATIONS

25 PHD'S AWARDED

5.6 MILLION EUR
INDUSTRIAL FINANCING
INCLUDING MAJOR PARTNERSHIP DEALS

3.5 MILLION EUR
INTERNATIONAL FINANCING

3 YEAR AVERAGE

24 POSTDOCS
11 BELGIAN
13 NON-BELGIAN

55 PHD'S
36 BELGIAN
19 NON-BELGIAN

EXPERTISE & TECHNOLOGIES

EXPERTISE

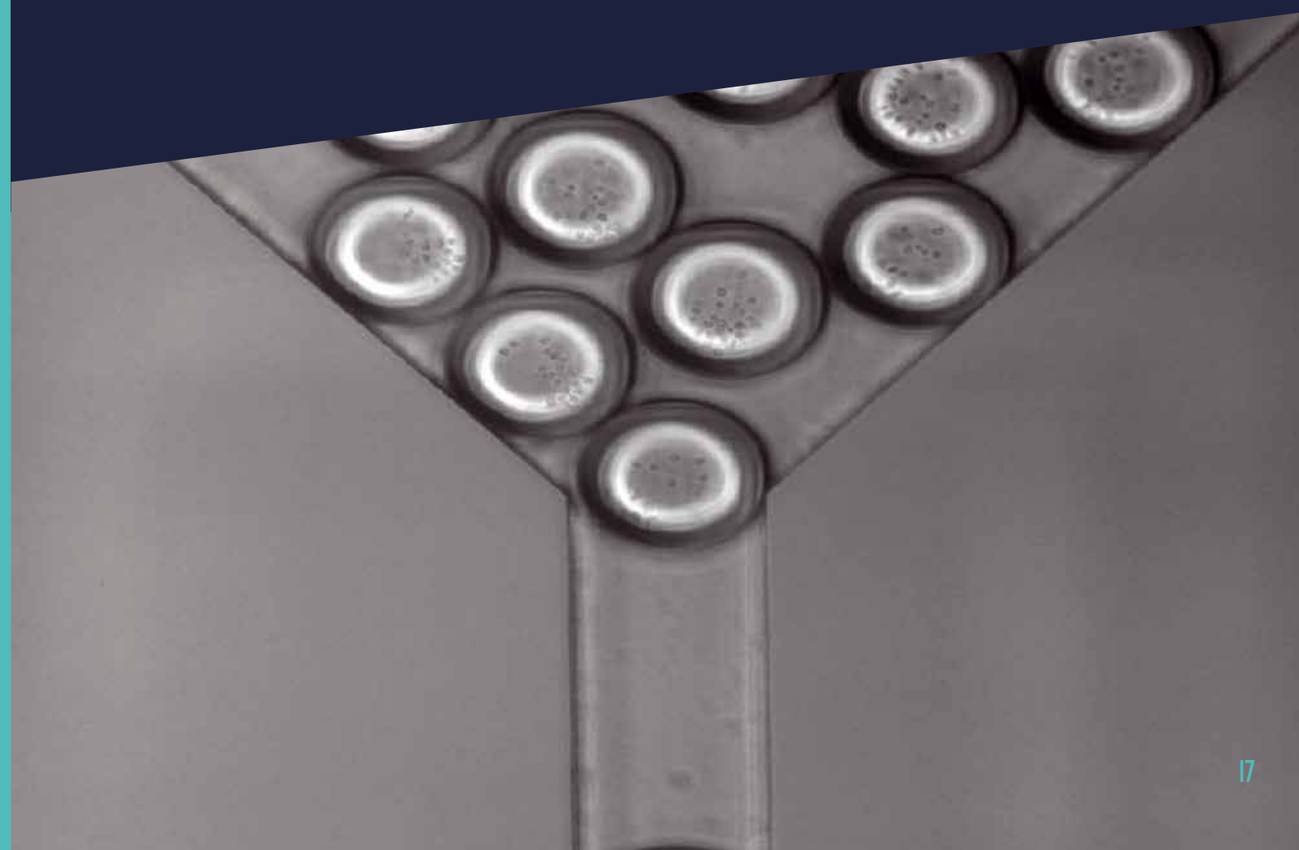
The groups at the VIB-KU Leuven Center for Microbiology possess combined expertise in many aspects of micro-organism biology. They are also especially adept in translating their findings to industrial contexts and advances in technology. This enables the labs at the center to offer several services to other scientists and interested companies.

... LEADS TO TECHNOLOGY DEVELOPMENT

As an indication of the breadth of expertise present in the center, there are many ways in which the center's members share their know-how so that colleagues can tap into these resources.

SORTING CELLS

The need to be able to study individual cells of, for example, yeast, has spurred the center to develop strong expertise in labeling and sorting cells. In the Flow Cytometry and Cell Sorting core facility, this is done by a BD Influx Fluorescence Activated Cell Sorter. To study single-celled organisms, microscopic know-how and tracking techniques are a must. The center has tools for high-quality microscopy (confocal, FRET and BifC), as well as robots and a microfluidics system that allows microscope tracking of populations and switching between different media (CellAsic ONIX2). Finally, the center also developed several *in-vivo* assays for pathogenetic microbes and microbial biofilms.



MONITORING MICROBIOMES

A strong research program in various aspects of the microbiome is reflected not only in the flow of high-impact papers, but also the availability of microbiota services including quantitative microbiome profiling and the accompanying bioinformatics data analyses and integration. This encompasses both animal and soil microbiomes. These services can be used for various applications, ranging from assessing human health to monitoring crop productivity.

BREWING BEER AND INDUSTRIAL YEAST

Yeast, one of the study organisms in the center, plays an important role in various food production processes, such as beer brewing. A 500-liter fully-automated Braukon pilot brewery with water treatment system, 6-drum milling line, 3-vessel brewhouse, and 16 fermenters is available as a testing ground for new beers. The yeast expertise can also be applied for the characterization of yeast genes/proteins of interest in various industrial processes (e.g. bioethanol production).

TECHNOLOGY TRANSFER

Translating research results into tangible products that benefit society is high on the agenda of the VIB-KU Leuven Center for Microbiology. This technology transfer comes in different forms, such as industrial partnerships, research cooperations, licensing agreements and – the cherry on the cake – start-ups. In many cases, the process of tech transfer starts with the possession of unique know-how or expertise, or with filing a patent. Over the last three years, seven patents have been filed for novel findings with potential for industrial application. The center has built a solid reputation which has led to industry collaborations worth several million euro. In some cases, however, the potential of the novel technology warrants the establishment of a start-up. This helps to ensure that the technology in question receives the undivided attention of a specialized team to come to full fruition. Spin-offs also create added value for society in the form of jobs and new products.

globalyeast Selected By Excellence.

The center's fermentation expertise has led to the initiation of GlobalYeast, a biotechnology start-up based in Brazil that develops products and solutions for the fermentation industry. Their unique insight into fermentation processes is based on the strong knowledge of yeast metabolism and genetics at the lab of Johan Thevelein. The company is involved in multiple collaborations with yeast and fermentation industries worldwide. GlobalYeast provides unique products and services to key markets of the bio-based economy, based on their superior industrial yeast strains and advanced industrial fermentation. The center's fermentation expertise has led to the establishment of GlobalYeast, a biotechnology start-up based in Brazil and Belgium that intends to develop products and solutions for the fermentation industry. Its unique insight into fermentation processes is based on the strong knowledge of yeast metabolism and genetics as well as industrial yeast strain development at the lab of Johan Thevelein. However, the company decided to shift its focus towards development of process monitoring technologies for the bioethanol and bio-based chemicals industries.

NovelYeast

A new spin-off has now been established by the Thevelein lab, NovelYeast, that will focus on the development and commercial implementation of superior industrial yeast strains for the production of bioethanol, other biofuels and bio-based chemicals. The company will also use the extensive knowledge and technical experience of the Thevelein lab with yeast research for other projects in the biomedical and agricultural domains in which yeast can be successfully used as a model and tool.

Aphea.Bio
Applied Nature for Better Agriculture

Soils are filled with micro-organisms which perform myriad important functions that underlie crop growth and yield. In this, the VIB-UGent Center for Plant Systems Biology and the VIB-KU Leuven Center for Microbiology saw fertile ground for the growth and development of the spin-off Aphea.Bio. Founded in 2017, this company exploits natural micro-organisms to increase crop yields and to protect them against specific fungal diseases in a sustainable way. (Logo). Related to this, the Van Dijck lab has implemented iChip technology to isolated non-culturable soil micro-organisms and is currently identifying novel antifungal molecules produced by these bacteria.

Apart from these two companies, prof. Van Dijck was recently appointed as CSO of the company StixFresh, and a Flemish entity of the company was established in April 2019

For many years, Kevin Verstrepen's group has had close ties with several leading breweries, including Anheuser-Busch InBev (AB InBev), the world's largest brewer, based on a mutual interest in finding new yeast variants to unlock new beer flavors and aromas. The yeast and fermentation know-how of his lab has also resulted in the establishment of an experimental brewery with the help of AB Inbev and about 20 other industrial partners. The brewery bridges the gap between the lab and the industry: it allows in-depth study of fermentation and testing of how newly developed industrial yeasts behave. The expertise and yeast databank developed and explored in the experimental brewery provide the foundations for a whole new spectrum of beer flavors, and they also allow testing of yeast fermentation performance at pilot scale. This has led to collaborations between the pilot facility and many national and international breweries, as well as bioethanol and biotech companies.

Kevin Verstrepen and Stijn Mertens in the experimental brewery

TRAINING

While good scientists are specialists on the specific topic they work on, great scientists are able to survey a broader field of knowledge within their domain.

Backed by its research facilities and scientists, VIB offers a range of training courses in the life sciences for all VIB and non-VIB doctoral and postdoctoral researchers.

The driving force for launching this open cross-disciplinary training course now is that, to become a top-notch scientist in the 21st century, it is no longer enough to stay in the lab and to stick to a specific discipline of interest. Success as a scientist increasingly hinges upon a combination of wet lab activities with professional training in additional scientific and so-called parascientific disciplines. The availability of such broad training allows VIB scientists and students to develop into multi-disciplinary scholars.

To expose its students to cutting-edge research from across the broad field of microbiology, the VIB-KU Leuven Center for Microbiology organizes summer schools for master's and PhD students and postdocs on, for example, the ecology and biomedical importance of biofilms. The center was also the main organizer of the human fungal pathogens advanced lecture course in May 2019.

The center hosts monthly seminars. It also hosts 'Meet the Jury' seminars, in which international experts invited to Leuven to evaluate PhD candidates are invited to give a seminar that is open to the public.

The center participates in the organization of international conferences, such as the Microbiology congress (June 2019) and the Trends in Brewing Conference (2015 and 2020).

OUTREACH

Science is not just for scientists. On the contrary, it is of interest to everyone. To do their work, scientists often receive funds from governmental sources, which, in turn, derive from the public. Scientific researchers are well aware of this money trail and most of them are eager to engage with the public to show what they are doing and why it is worthwhile.

Beyond technological and scientific developments and the benefits that flow from them, public outreach is another way for scientists to give back to the community and show their appreciation for the support they receive.

Many members of the VIB-KU Leuven Center for Microbiology engage in outreach events for the public at large, such as 'Dag van de Wetenschap' (science day), 'Biotechdag' (biotechnology day), etc. Several researchers from the center also take part in a VIB education project called 'Wetenschap op Stap' (science on the move), in which scientists visit primary schools to answer questions from pupils and foster enthusiasm for science. This project is one of the STEM (Science, Technology, Engineering and Mathematics) initiatives to encourage youngsters to choose an education in one of the STEM disciplines.

In similar vein, members contribute to the annual 'children's university' event at KU Leuven, which exposes school children to the work carried out at the university.

Finally, researchers at the center have given TED talks and published books on their work for a general audience. The most recent example of this is a book on Belgian beers, 'Belgian Beer: Tested and Tasted'.

PHD STUDENTS & ALUMNI

PHD STUDENTS

"VIB creates an environment that stimulates high-quality research by providing professional support in different ways."

"For example, VIB offers numerous courses that broaden both our technical and soft skills, several of which I participated in. The VIB Tech Watch team brings labs into contact with cutting-edge technologies and facilitates collaborations with industry. Furthermore, VIB provides opportunities to put our research in the spotlight and communicate it to a broader audience.

Our monthly 'Microbes and Booze' seminars stimulate strong interaction between different labs of the center in a very informal atmosphere. Furthermore, VIB organizes multiple events, such as the VIB New Year reception and the VIB seminar, which encourage networking between different centers."

Etthel Windels, PhD student, Jan Michiels lab

"I very much enjoy working in the Center for Microbiology. A PhD in microbiology was something that I really wanted to do. My research topic is very interesting. I use a lot of different techniques and have already had the opportunity to do research in Vienna. Also, the kind environment and friendly people make it a nice workplace.

I followed the basic course in statistics, which I can recommend to anyone. I had already followed statistic courses, but it was really time for a recap. The course was clear and the teacher was very patient in explaining everything.

This year, I went to the HFP meeting in La Colle-sur-Loupe with almost the entire lab. This was a really nice experience. We got to know each other even better than before, we laughed a lot and had a lot of fun. We were also able to present a poster about our work, which is great for PhD students in the earlier stage of their career.

I would definitely recommend a PhD in our center. The environment is very nice and, if you have a problem, everyone wants to help you. We have expertise in different aspects of microbiology and techniques."

"Studying here will definitely enrich your scientific career."

Stefanie Wijnants, PhD student, Patrick van Dijck lab

"The experience here taught me how to 'do science' properly and has motivated me to pursue a career in an academic field. I participated in several of the courses and training opportunities offered, including the microscopy summer school. Many of these courses have proven very useful.

On the personal side, I am happy to say that I made some very good friends in the lab, and Johan is an excellent supervisor who's always ready to give advice and offer any type of support.

I would definitely recommend joining the center."

"Dealing with problems in science at a high level is not easy, but the center offers plenty of support to help its members carry the load."

Zhiqiand Zhang, PhD student, Johan Thevelein lab

ALUMNI

"It was a great experience to work at the VIB-KU Leuven Center for Microbiology: challenging, encouraging and interesting."

"The center offered me not only professional and scientific training, but also a lot of personal development and communication opportunities."

"The friendly, international environment also helped me with my further career development.

There was a lot of interaction between group members. We had lab meetings, group meetings and one-to-one meetings. VIB provides opportunities for annual reunions and the center also held annual lab meetings including scientific presentations, team building and 'newcomers' parties. All of these provided opportunities for the members of the center to interact.

The center provided many opportunities to attend conferences, such as the VIB annual conference and the NEMO conferences.

Both the center and VIB provided lots of opportunities and support, which is not always the case in other labs."

Dr. Yingying Li, postdoctoral research associate, University of Manchester (UK)

"I joined the center before it was even in Belgium – at Harvard's Bauer Center for Systems Biology in Cambridge, MA, USA. I moved with Kevin and his small group of Americans to start the lab anew in Leuven. I saw it grow over the next four years into an industrial and academic research powerhouse. The friends and colleagues he attracted to the lab became like my family.

Kevin's lab and the VIB provided a fantastic environment and opportunity to grow as a scientist. I helped organize the VIBes in Biosciences PhD student conference. This was a great way to meet other PhD students and gain experience in the logistics of organizing a large meeting.

Our arrival from Harvard to Leuven was, at first, a cultural shock – our lab was physically very separate from the rest of the KU Leuven Microbiology Department, and the VIB Center for Microbiology was still not established. While the shared data club meetings between groups in the Department were exciting, we no longer had the day-to-day interactions with colleagues from other labs that we were used to. We also didn't have many visitors from outside the institute - we had gone from having invited speakers and talks nearly every day to being lucky to have just one per year.

Despite the physical distance from the rest of the department, as Kevin's lab grew, he managed to attract many bright and interesting people to it, and we managed to do quite well with just ourselves."

"Our day-to-day scientific discussions happened constantly, from our group meetings to after work at the pub, and this was a very enriching experience."

"Since the Center for Microbiology began, I can already see from Twitter that it is now offering the kind of day-to-day scientific interaction and invited speakers that we had back at Harvard.

Kevin is a fantastic leader and sets a great example of how to balance personal and professional interests. The people he managed to attract to his group were simultaneously kind and interesting, and brilliant scientists to boot. I couldn't have asked for more.

In 2011-2012, Kevin and colleagues organized a symposium on experimental evolution, with Richard Lenski as an invited speaker. He didn't have any plans for the next day, so my master's student and I brought Rich on a trip to Ghent.
The symposium, and this day of tourism talking so much about science (and everything else) with one of my scientific heroes was an unforgettable experience.

We Americans were so excited to be coming to Belgium, and we knew that Jean Claude Van Damme was one of Kevin's great Belgian heroes so, right after we arrived, we taped a poster of his muscular idol onto the ceiling right above his desk. Unfortunately, instead of staying in place, it soon fell off onto him while he was sitting working. I'm not sure if he had even realized it was there before it fell! Afterwards, he started locking his office, so we never had the chance to put it back up.
I would wholeheartedly recommend that students do their PhD or postdoc at the center. The community and resources provided by the VIB make a fantastic experience for young scientists."

Dr. Aaron New, postdoctoral researcher at the Centre for Genomic Regulation, Barcelona (Spain)

"I didn't really feel that I was working in a 'center', that is, the VIB-KU Leuven Center for Microbiology. Although there were some good initiatives, it certainly didn't help that the center was spread over separate buildings. Conversely, there was and is close collaboration between the two laboratories housed in the same building.

It is probably too early to fully reflect on how the center has shaped my career. The possibility to follow qualitative specialized courses during my PhD was perhaps the greatest help. Indirectly, this has an impact on your further career.
To fully use the opportunities offered, I participated in many training sessions and most were of good to very good quality!"

"I had the opportunity to attend various conferences where I often had the opportunity to present my own research."

"Almost all of the conferences I attended were memorable in one way or another."

Dr. Adam Feyaerts, freelance teacher and business consultant

ABOUT **VIB**

Basic research in life sciences is VIB's raison d'être. VIB is an independent research institute where some 1,500 top scientists from Belgium and abroad conduct pioneering basic research. In the process, they are pushing the boundaries of what we know about molecular mechanisms and how they rule living organisms such as human beings, animals, plants and microorganisms.

Based on close partnerships with five Flemish universities – KU Leuven, Ghent University, University of Antwerp, Vrije Universiteit Brussel and Hasselt University – and supported by a solid funding program, VIB unites the expertise of all its collaborators and research groups in a single institute.
VIB's technology transfer activities translate research results into concrete benefits for society, such as new diagnostics and therapies and agricultural innovations. These applications are often developed by young start-ups from VIB or through collaborations with other companies. This also leads to additional employment and bridges the gap between scientific research and entrepreneurship.

VIB also engages actively in the public debate on biotechnology by developing and disseminating a wide range of science-based information. More information is available at **www.vib.be**