VIB

ANNUAL REPORT 2019

SCIENCE AS DRIVER FOR ECONOMIC GROWTH

Scientific knowledge and technological innovations are the motor of economic progress. A recent study of our economic impact clearly demonstrates that VIB is a prime example of this statement. The survey clearly states that the wider economic impacts of VIB in medical and agricultural innovation are globally significant. VIB's efforts in science communication and policy development have an important influence on underpinning the work of the institute.

The study also specifies that for every 1 € that VIB receives in core funding from the Flemish government, it generates an economic contribution of more than 11 €. From a government point of view, this represents a substantial return on investment.

Science meets science

VIB's scientific endeavors and its academic excellence form the solid base for everything we do at VIB. In 2019, we have taken major strides in single-cell analysis and have gained insight in the mechanisms of cellular functionality. Researchers have mapped several cell types, ranging from mouse brain macrophages to endothelial cells, in so-called single-cell atlases. In the field of cancer, scientists have devised new treatment strategies to counter therapy resistance. And in plant science, our researchers have found a way to significantly enhance the processability of plant biomass. In the chapter 'Science meets science' on page 8, you can discover more VIB breakthroughs realized in 2019.

To further increase its international footprint in 2019, VIB extended its translational research initiative, the Grand Challenges program. This program finances research projects that will lead to novel applications with substantial societal impact, based on three sustainable development goals of the United Nations: zero hunger, good health and well-being, and climate action. In 2019, three extra projects were selected for funding: Spartacus – a better treatment for spondyloarthritis, BBB - targeting drugs to the brain, and Mimosa – microbes to tackle inflammatory bowel disease.

Science meets technology

The five-year evaluation of the VIB core facilities revealed that the VIB cores are a leading example in Europe. An international and interdisciplinary panel of technology experts reviewed the quality of the services of VIB's core facility program and gave the program high praise and some future-focused recommendations. The evaluation confirmed the importance of the cores as enablers for breakthrough research by supporting scientists with the best state-of-the-art technologies and highly skilled staff.

VIB's Tech Watch team promoted the development of its Technology Innovation Lab to evaluate high-end technology platforms together with researchers in the VIB centers and the cores. Due to its success, the Single Cell Accelerator received a financial boost through collaborations with life sciences companies, enabling its further expansion. With this program VIB scientists gain access to funding to evaluate, develop and integrate emerging breakthrough single-cell technologies.

Science meets business

VIB's Innovation & Business team has shaped our technology transfer activities into a project-driven approach in which research results are assessed to determine, create and realize business opportunities. These opportunities come in many forms: industry partnerships, licensing agreements, R&D cooperations, new ventures, etc. This approach again proved very successful in 2019. Testimony of this success are two new start-ups, Augustine Therapeutics and Montis Biosciences, a record number of R&D collaborations with an all-time high of 21 M€ in industrial income, and three inward investments. Furthermore, several therapeutic licenses were concluded with biotech and pharma companies to develop new therapies for patients.

Over the past years, VIB has been the driving force to forge Flanders' world-class position in life sciences. The Flemish biotech cluster has become a booming ecosystem which attracts a wide variety of businesses and which greatly enhances Flanders' reputation on a global scale.

Science meets people

VIB goes to great length to create a stimulating working environment where everyone is treated with respect and understanding, where people can flourish. Leadership is also of paramount importance to VIB, with a clear focus on genuine people-oriented leadership, with attention to communication, feedback, career guidance and coaching.

Our outreach activities are set to inform the public at large of VIB's groundbreaking research and proves that science is not just for scientists, but touches the lives of everyone. VIB's Conferences & Outreach team organizes events during which visitors are immersed in the wonderful world of life sciences. Newsletters, brochures and facts series inform our stakeholders on the ins and outs of biotech, and its societal and economic impact.

At VIB we are committed to making a difference, we all work towards one common goal: making the world a better place!

Ajit Shetty, Chairman of the Board of Directors
Jo Bury and Johan Cardoen, Managing Directors

AN EYE FOR QUALITY

Being a research institute partly funded by public money, VIB takes its social responsibility very serious. Every effort is made within the organization to ensure that all processes run as smoothly and efficiently as possible.

At VIB, we rely heavily on peer review to assess the quality of our research. Scientific Advisory Boards which consist of highly qualified specialists in the research domains of the VIB centers, visit our research centers twice every five years to advise them on their research strategy and activities.

The quality of our research is also assessed by means of a monitoring tool (balanced score card) which benchmarks results against performance targets which are predetermined by the Flemish Government. This provides the management with an instrument to evaluate results and to adjust where necessary.

VIB also invests significantly in high-quality infrastructure, enabling our scientists to conduct their research in the best possible conditions. VIB additionally co-invests in bio-incubator and accelerator space to ensure that young biotech companies can grow and only need to focus on their research.

Access to competitive funding

Researchers at VIB increasingly depend on competitive grants for funding, and year after year the funding landscape becomes even more complex. Each grant comes with its own requirements, policy and eligibility criteria. Competition between scientists is fierce, so we make every effort to support our scientists with the necessary expertise. Therefore, VIB's International Grants Office is involved in following the development of EU and international funding programs, in order to guide VIB scientists to those funding calls that fit their needs. The Grants Office invests in training and high-level grant support to all VIB researchers with the aim to increase our success rate and secure international research income for VIB. In 2019, the Grants Office teamed up with representatives of the VIB research centers who already had expertise in grants support to put together a virtual Grants Team. The team also compiled a database with all life sciences funding opportunities available to our scientists and a funding booklet which contains a practical overview of funding possibilities for postdocs.

Grand Challenges Program moving forward

In the first two decades of its existence, VIB has been very successful in both knowledge creation by means of its basic research and in translating this knowledge into societal and economic impact through a professional process of pro-active technology transfer.

Thanks to its current maturity, VIB can now pursue new strategic initiatives to achieve the next level of translation towards value creation and ultimately impact.

To this end, VIB proposed 'the VIB Grand Challenges Program' (GCP) in its strategic plan 2017-2021. This program is a new translational initiative (applied research) starting from major societal challenges and the underlying projects are induced by 'reverse' translational questions and issues which are triggered in daily practice. These projects are, so to speak, developed 'backwards', starting from the patient or crop and leading to new

insights and practical applications. The success of the program depends on transdisciplinary collaborations with skilled top-teams outside VIB (hospitals, strategic research centers, etc.) to realize preset goals in delivering high impact solutions. Each of the selected projects can receive funding up to 2 M€ for an initial period of three years.

The VIB-GCP projects involve an iterative process in which new observations are translated into new testable hypotheses and validated solutions. Throughout the process, VIB expertise and technology are main drivers to impact pertinent challenges in healthcare and agriculture, framed within the United Nations Sustainable Development Goals.

So far, there have been three institute-wide calls for GCP projects. External experts in the field assess all project applications from two distinct evaluation perspectives: scientific quality and valorization/utilization potential.

In 2019, three projects selected in the second call were announced:

- Spartacus: better treatment for spondyloarthritis.
- BBB: targeting drugs to the brain.
- Mimosa: microbes against bowel inflammation.

A third call was launched in 2019, and the projects selected during this round will be announced in June 2020.

Much attention is given to stakeholder engagement and involvement. In 2019, different outreach events were organized. In addition, a first stakeholder consultation moment (round table), where patients and researchers could share their experiences, was implemented in a patient information day for over 100 PID patients (in collaboration with patient organization Bubble ID and the Center for Primary Immune Deficiencies – UZGent).

SCIENCE

720 PUBLICATIONS

95 PHD GRADUATIONS

260 PUBLICATIONS IN TIER 5 JOURNALS

TECHNOLOGIES

CORE FACILITIES **10**

TECH WATCH PROJECT APPLICATIONS APPROVED **43**

5 PARTNER UNIVERSITIES → 86 RESEARCH GROUPS

1 INSTITUTE

76 NATIONALITIES ← 1,614 COLLABORATORS (FTES)

TOTAL INCOME

% 51 FLEMISH GOVERNMENT

% 49 OTHER INCOME

TECH TRANSFER

3 INWARD INVESTMENTS

2 NEW START-UPS

24.6 M € TOTAL INDUSTRIAL INCOME

OUTREACH

4,000 VISITORS TO BIOTECH DAY

1,455 PARTICIPANTS AT VIB CONFERENCES

SCIENCE WITH IMPACT

VIB's impact on society and the biotech ecosystem springs forth from the world leading science that is being done in all its centers. With this science as firm base, clinical applications, business collaborations, and spin-off creation are continuously developed in close contact with various units at VIB headquarters.

The selection of papers here serves to illustrate the internationally recognized and cutting-edge work that VIB scientists from all VIB centers engage in. Their pioneering work is routinely published in leading scientific journals in several fields of the life sciences.

IMMUNOLOGY & INFLAMMATION

DISSOLVING PROTEIN CRYSTALS AGAINST ASTHMA

Normally, proteins do not crystallize in the body, but there are some instances where this process does occur. Charcot-Leyden Crystals are made from the protein Galectin-10 and were discovered in the airways of asthmatics as early as 1853. However, the crystals have been largely ignored by scientists, and their actual link to disease remained unknown.

The groups of Bart Lambrecht and Savvas Savvides have now established that the crystals, which are highly abundant in airway mucus, stimulate the immune system and promote the inflammation and altered mucus production that is often seen in the airways of asthmatics. Together with the biotech company argenx, they developed antibodies that can dissolve these crystals to reduce key asthma features.
Persson *et al.*, Science, 2019

TRACKING SINGLE CELLS

By combining single-cell profiling and computation trajectory inference tools, it is now possible to investigate the dynamics of individual cells at an unprecedented and purely data-driven detail.

The Yvan Saeys Lab has done a comprehensive benchmark of 45 different methods for trajectory inference. They highlight the complementarity of tools, provide guidelines for method users, and indicate open challenges in the field. All software tools are freely available from dynverse.org.
Saelens *et al.*, Nature Biotechnology, 2019

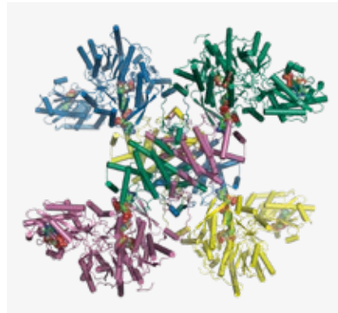
MAPPING MACROPHAGES

Our brains do not only contain neurons, but also a variety of immune cells that play an important role for its functioning. Even a century after their discovery, one type of such immune cells – brain macrophages – continue to spark fascination.

Researchers from the Jo Van Ginderachter and Yvan Saeys labs combined single-cell transcriptomics with high-dimensional cytometry, fate-mapping and microscopy to reveal the origin and diversity of brain macrophages. This revealed the striking diversity of brain macrophages and found unexpected microglia. Remarkably, these 'hidden' microglia resembled those normally associated with disorders such as Alzheimer's disease.
Van Hove *et al*, Nature Neuroscience, 2019

ENZYMES IN 3D

Organisms across all kingdoms of life crucially rely on a molecule called acetyl-CoA that fuels essential biochemical processes in cells, such as the production of fatty acids and cholesterol. However, acetyl-CoA is not always easily available. To produce it, the enzyme ATP citrate lyase (ACLY) is needed.



The research team of Savvas Savvides and Kenneth Verstraete has unraveled the three-dimensional structure and molecular mechanism of ACLY. The reported findings could help targeting ACLY in cancer and metabolic diseases such as atherosclerosis. The structure of ACLY also unmasked a crucial evolutionary relationship that radically changes our understanding of the origins of cellular respiration.
Verschueren *et al.*, Nature, 2019

PLANT SYSTEMS BIOLOGY

UNDERSTANDING RADIAL GROWTH

Besides obvious longitudinal growth, plants also enlarge in the radial sense. This thickening of plant stems and roots provides physical support to plants, provides us with wood and cork, and plays a major role in sequestering atmospheric carbon into plant biomass.

The lab of Bert De Rybel contributed to our understanding of plant radial growth by showing that DOF-type transcription factors control oriented divisions in specific procambium cells, suggesting that this seemingly homogenous tissue contains zones of high proliferation and quiescence. This will assist plant breeding for higher yield and atmospheric carbon capture through biomass increase.

Miyashima *et al.*, Nature, 2019
Smet *et al.*, Current Biology, 2019

CURCUMIN FOR BETTER BIOMASS PROCESSING

To enhance the industrial processing of plant biomass into energy and valuable chemicals, plants can be engineered to contain alternative and easier-to-degrade lignins. Importantly, this intervention must not affect plant yield.

Researchers from the team of Wout Boerjan have now discovered that curcumin, a molecule natively produced by turmeric, can act as a building block for the lignin polymer, thereby significantly enhancing plant biomass processability.

Oyarce *et al.*, Nature Plants, 2019

BLOCKING ENDOCYTOSIS

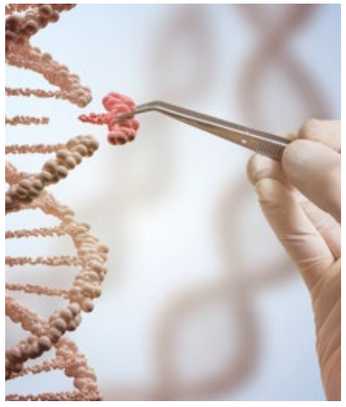
Plant cells absorb many important substances through a process called endocytosis, which is essential for nutrient uptake, passing on cellular signals and plant–microbe interactions. However, the vital nature of endocytosis makes it challenging to be studied using methods from classical genetics.

The team of Jenny Russinova found a new chemical, ES9, that blocks endocytosis and discovered that this small molecule binds to clathrin, a protein that plays a major role in the formation of coated vesicles, small 'organs' in cells. Further *in vitro* binding studies and X-ray crystallography confirmed this interaction.

Dejonghe *et al.*, Nature Chemical Biology, 2019

A CRISPR KNOCKOUT

Knocking out genes is a great way to learn what they do. After all, if you prevent a gene from doing its job and you notice changes, it's very likely the gene has something to do with it. There is a caveat, though. If a scientist mutates a gene that is required for growth and/or reproduction, the mutant plants are often very sick or even die.



The teams of Thomas Jacobs, Moritz Nowack, and Tom Beeckman have now devised a CRISPR-based tissue-specific knockout system, CRISPR-TSKO. This system enables the generation of specific mutations in particular plant cell types, tissues, and organs. The efficiency of CRISPR-TSKO opens new avenues to discover and analyze gene functions during the life of plants while avoiding the effects of system-wide loss of gene function.

Decaestecker *et al.*, Plant Cell, 2019

MEDICAL BIOTECHNOLOGY

EDIBLE VACCINES

Therapeutic antibodies are increasingly being used in the clinic for the treatment of various diseases. Yet, oral to gut targeting of antibodies remains a challenge due to their incapability to survive digestion and reach gastrointestinal tissues.

Now, the team of Nico Callewaert has developed a new antibody technology that combines the advantages of antibody-based therapies with the convenience of oral drug administration. Importantly, these antibodies are manufactured using yeast in a process as straight-forward as food-manufacturing. This may have uses in various areas, from fighting gut infections, treating inflammatory and metabolic disorders, to the development of microbiome altering food supplements.

Virdi *et al.*, Nature Biotechnology, 2019

A PROTEIN TAG TO STUDY THE IMMUNE SYSTEM

To keep control of the expressed proteins, cells can attach a chemical 'tag' onto a protein to modify its activity. ISG15 is such a tag. However, the molecular function of ISG15 is elusive, since the identity of the modified proteins and their exact sites of modification are still unknown. The team of Francis Impens took advantage of the technology developed to identify ubiquitin modification sites for the identification of ISG15 modification sites. With the newly developed method, scientists can now identify and study proteins tagged with ISG15, allowing them to unravel its many functions in fighting disease, potentially leading to novel antimicrobial drugs.

Zhang *et al.*, Nature Communications, 2019

STRUCTURAL BIOLOGY

DISMANTLING BACTERIAL ARMOR

What if we could fight pathogenic bacteria by stripping down their protective armor? *Bacillus anthracis*, the etiological agent of anthrax has a proteinaceous armor known as the S-layer.

An interdisciplinary study by the team of Han Remaut has shed light on the assembly and composition of this S-layer. Thanks to these insights, a new strategy to tear the armor apart using specific nanobodies was developed. When applied *in vivo*, these Nanobodies® worked as nanobiotics able to cure anthrax in mice. This study represents the first *in vivo* evidence that the disruption of bacterial S-layer integrity during infection has therapeutic potential.

Fioravanti *et al.*, Nature Mirobiology, 2019

MEGABODIES REVEAL $GABA_A$ STRUCTURE

The Jan Steyaert lab has developed an innovative plug-and-play technology to graft functional Nanobodies® on several scaffolds with diverse properties to build Megabodies. Such Megabodies are game changing research tools in cryo-electron microscopy.

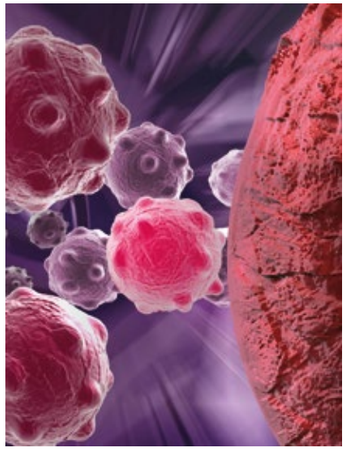
Here, the team applied the Megabody technology successfully, which leads to major new insights in the structure and functional mechanisms of human $GABA_A$ receptors. These receptors are the main mediators of rapid inhibitory neurotransmission in the vertebrate nervous system. They are among the most important human drug targets as they bind compounds with anticonvulsant, anti-anxiety, analgesic, sedative, and anaesthetic properties.

Masiulis *et al.*, Nature, 2019

CANCER BIOLOGY

METASTASIS THROUGH THE LYMPHATIC SYSTEM

When breast cancer cells spread through the body, they do so mainly through the lymph system that normally removes excess fluid and waste products from our tissues. Growing tumors often put physical pressure on their environment, which makes these lymphatic vessels leaky and easier accessible for tumor cells.



Now, scientists from the Massimiliano Mazzone lab identified a novel subset of immune cells, called Podoplanin-expressing macrophages (PoEMs), that change the tissues near a tumor in a way that promotes the spreading of cancer cells. Getting rid of these PoEMs in a mouse model strongly reduced the ability of breast cancer cells to move to other parts of the body.
Bieniasz-Krzywiec P. *et al.*, Cell Metabolism, 2019

TEACHING NORMAL CELLS TO FIGHT CANCER

Current chemotherapies aim at killing rapidly proliferating cancer cells. However, such therapies are often only temporarily effective because cancer cells quickly evolve drug resistance. The Hippo signaling pathway has been implicated in tumor growth, sparking interest in the pathway as a potential therapeutic target.

In a study of liver cancer in genetically manipulated mice, the Georg Halder team discovered that the role of this pathway in tumorigenesis is more complex than previously appreciated. They found that whether tumor cells survive or are eliminated depends on competing signals produced by the tumor and surrounding tissue.
Moya et al., Science, 2019

PYRUVATE AS CANCER FOOD

Most cancer patients die due to metastasis formation. The local tumor environment is a crucial determinant of metastatic growth. The environment in which the cancer cells are embedded, the extracellular matrix (ECM), is a major component of this niche. Cancer cells remodel the ECM by hydroxylating collagen to promote their own metastatic growth.

The team of Sarah-Maria Fendt discovered that breast cancer cells rely on the nutrient pyruvate to remodel the lung metastatic niche. This study identifies the pyruvate metabolism as a new target for novel and selective strategies to inhibit metastasis formation without affecting healthy cells.
Elia *et al.*, Nature, 2019

TOWARDS A SAFER THERAPY FOR LEUKEMIA

T-ALL—short for T-cell acute lymphoblastic leukemia—is a form of cancer characterized by the presence of too many immature white blood cells. T-ALL mainly affects children and is rapidly fatal if left untreated. Current chemotherapy is very effective but causes long-term side effects, so there is an urgent need for less toxic targeted therapies.

The teams of Jan Cools and Bart De Strooper found that the relative abundance of two different versions of one of the gamma-secretase complexes was strikingly different in leukemia cells versus healthy cells. This discovery led them to explore whether inhibiting only this specific version of the complex would prove to be a safer treatment option. They saw that targeting only one type of complex was both effective and safe in mouse models and in leukemia cells from T-ALL patients.
Habets *et al.*, Science Translational Medicine, 2019

NEUROSCIENCE & MOLECULAR NEUROLOGY

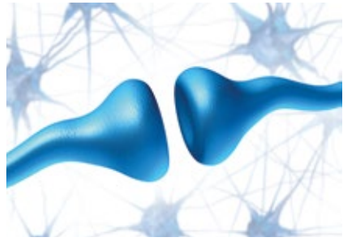
A LOOK AT CELLULAR DIVERSITY

Our genomes are controlled by combinations of regulatory molecules that 'switch on' target genes in our DNA. These regulatory molecules bind to so-called enhancer and promoter regions in our chromosomes. Understanding when and how they are activated, can teach us a lot about the cellular diversity in our bodies.

The Stein Aerts lab developed cisTopic, a probabilistic framework that provides insight into the mechanisms underlying regulatory heterogeneity within cell populations. The results allow the optimization of cell clustering and enhancer categorization, the identification of cell subpopulations and enhancers that represent shared epigenomic programs.
Bravo González-Blas *et al.*, Nature Methods, 2019

SIGNAL TRANSMISSION IN ALZHEIMER

Alzheimer's-affected brains are riddled with so-called amyloid plaques: protein aggregates consisting mainly of amyloid-β. Although the pathological role of the amyloid-β precursor protein (APP) in Alzheimer's disease is well-studied, the physiological role of this protein has remained elusive.

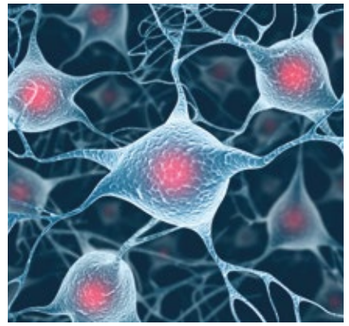


The teams of Joris de Wit and Bart De Strooper have uncovered that the secreted part of the amyloid precursor protein modulates neuronal signal transmission through binding to a specific receptor, $GABABR_{1a}$. Binding suppressed synaptic vesicle release and modulated synaptic transmission and plasticity in mice, hinting that modulating this receptor could potentially help treat Alzheimer's or other brain diseases.
Rice *et al.*, Science, 2019

HUMAN NEURONS IN MOUSE BRAINS

The brain cortex, the outside layer of our brain often referred to as grey matter, is one of the most complex structures found in living organisms. But how neural circuits develop in the human brain has remained almost impossible to study at the neuronal level.

A collaboration between the labs of Pierre Vanderhaeghen and Vincent



Bonin investigated human cortical neuron development, plasticity and function, using a mouse/human chimera model in which xenotransplanted human cortical pyramidal neurons integrate as single cells into the mouse cortex. Furthermore, these cells were active and exhibit human 'tempo' in their activity. Their findings provide new insights into human neuronal development, and open novel experimental avenues for the study of human neuronal function and diseases.
Linaro *et al.*, Neuron, 2019

STUDYING HUMAN MICROGLIA IN MICE BRAINS

Microglia cells, brain cells that are responsible for brain 'maintenance', are thought to play an important role in the development of Alzheimer's disease. But they are not easy to study. Culturing them in a petri dish neglects the complex environment in which they usually function, and model organism, such as mice, have microglia that are too different from human ones to draw robust conclusions.

Here, the Bart De Strooper team shows that embryonic stem cell-derived human microglia successfully engraft the mouse brain. Upon exposure to oligomeric Aβ, a wide range of Alzheimer's disease risk genes are expressed that are not readily studied in current mouse models for the condition. This work provides a unique humanized animal model that will allow elucidating the role of genetic risk in the pathogenesis of Alzheimer's disease.
Mancuso *et al.*, Nature Neuroscience, 2019

A NEW MECHANISM OF NEURODEGENERATION

Charcot-Marie-Tooth disease (CMT) is an inherited neurodegenerative condition that affects 1 in 2,500 individuals. Currently, however, it is still lacking effective treatment options. Over 90 genes are implicated in the pathology so far and these are involved in a variety of processes. This complexity makes it a difficult condition to study and treat.

New research by the Albena Jordanova team has demonstrated that an important group of molecules known as aminoacyl-tRNA synthetases – which help in translating RNA into proteins – can interfere with the transcription of DNA into RNA. This interference was found to be at the core of CMT disease in both fly and cellular models.
Bervoets *et al.*, Nature Communication, 2019

INFORMATION FLOW IN THE BRAIN

We use information about the world around us to guide our behavior.

To get from detection to action, visual information is passed from the retina in our eye to different downstream brain regions. The nervous system consists of many different cells that work together in circuits.

The team of Karl Farrow has unraveled how our brain processes visual information. They identified specific roles for distinct neuronal cell types in passing on information from the eye to downstream brain regions that guide behavior. The researchers deciphered a projection-specific logic where each output pathway from a brain area called the superior colliculus sampled a distinct and limited set of retinal inputs. Such knowledge is essential to understand how sensory information guides our actions and decisions.
Reinhard *et al.*, eLife, 2019

REPLAY FOR BETTER MEMORY

When we experience something important, we usually remember it better over time. This enhanced memory can be the result of stronger memory encoding during the experience, or because of memory consolidation that takes place after the experience. But how replay contributes to the consolidation of experiences in a familiar context is unknown.

Researchers from the team of Fabian Kloosterman have now demonstrated that large rewards can selectively enhance performance during familiar but demanding spatial memory tasks. Post-learning hippocampal replay thus selectively reinforces spatial memory of highly rewarded locations in a familiar context. These insights could open future opportunities for treatments that help to strengthen memories.
Michon *et al.*, Current Biology, 2019

ASTROCYTES HELP THE BRAIN PROCESS INFORMATION

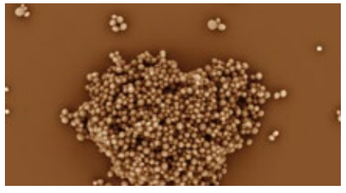
When we are aroused the hormone noradrenaline is secreted, which helps us to better remember emotional situations compared to neutral ones. Noradrenaline is released across the entire brain and stimulates astrocytes, which listen and respond to locally active neurons. But how do astrocytes integrate this brain-wide signal with the specific activity of local neuronal networks?

A collaboration between the teams of Vincent Bonin and Matthew Holt revealed that noradrenaline plays a key role in how astrocytes track distinct information during behavior. The researchers found that astrocytes can integrate information on arousal state and sensory experience. These results also show that astrocytes can integrate two kinds of information – sensory and behavioral information.
Slezak *et al.*, Current Biology, 2019

MICROBIOLOGY

MEDIEVAL SUPER YEASTS

Despite being beautiful and intriguing creatures, interspecific hybrids are mostly sterile and thus an evolutionary dead end. Such interspecific hybridizations are rare and seem to be favored by the domestication process.



In a joint effort, the teams of Kevin Verstrepen and Steven Maere discovered that yeasts used for the production of traditional Belgian beers are hybrids between *Saccharomyces cerevisiae* and *Saccharomyces kudriavzevii*. The hybrid yeasts combined important characteristics of both parental species, with the fermentation capacity of normal beer yeasts and the stress tolerance and capacity to form special aromas of more feral ancient yeasts. Analyzing the genomes of these as-yet unknown beer yeasts revealed details of how interspecific hybridization can drive evolution.
Gallone et al., Nature Ecology & Evolution, 2019

A GUT FEELING FOR MENTAL HEALTH

The relationship between gut microbial metabolism and mental health is a controversial topic in microbiome research. The notion that microbial metabolites can interact with our brain - and thus behavior and feelings - is intriguing, but gut microbiome-brain communication has mostly been explored in animal models, with human research lagging behind.

Researchers from the lab of Jeroen Raes described a novel approach to assess the gut-brain potential encoded in metagenomic datasets. This allowed the assembly of the first neuroactivity catalogue of human gut microbes and the identification of groups of microorganisms that are linked to quality of life and depression. The results provide population-scale evidence for microbiome associations with mental health.
Valles-Colomer et al., Nature Microbiology, 2019

WAKING UP SLEEPING BACTERIA

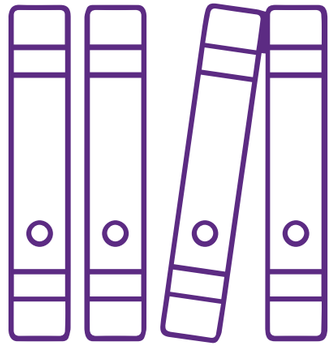
Bacterial populations harbor a small fraction of transiently antibiotic-tolerant cells, so-called persister cells. Upon exit from the persister state, they can recolonize the host leading to relapse of the infection. It is currently unknown how this exit from the persister state is regulated. Research by the Jan Michiels group unraveled the molecular basis of the mechanisms of persister awakening. Persister cell development is promoted by forming pores in the bacterial cell membrane. This results into a rapid loss of energy, pushing the bacteria into a low energy state or deep sleep. Importantly, this pore formation is only possible when two HokB peptides are linked together. These findings may lead to the design of antipersistence therapies.
Wilmaert et al., Molecular Cell, 2019

GUT MICROBES AND BOWEL INFLAMMATION

Over the years, many research groups worldwide have attempted to describe microbiota alterations associated with diseases. Especially IBD is a hot topic in microbiome research. Inflammatory bowel disease (IBD) groups several conditions characterized by chronic inflammation of the intestinal tract, including ulcerative colitis and Crohn's disease.

The team of Jeroen Raes used their newly developed quantitative microbiota profiling method and the Flemish Gut Flora Project catalogue to describe gut microbiome alterations in inflammatory bowel disease and primary sclerosing cholangitis. Patients had an increased prevalence of an altered microbial community type – Bacteroides2 – surprisingly also previously linked to depression.
Vieira-Silva et al., Nature Microbiology, 2019

SCIENTIFIC IMPACT 2019



721 PUBLICATIONS

260 PUBLICATIONS IN TIER 5 JOURNALS (BREAKTHROUGH PAPERS)

105 HIGHLY CITED PAPERS (>100 CITATIONS IN CURRENT 5 YEARS' PERIOD)

95
PHD GRADUATIONS

27 RUNNING ERC GRANTS

5 STARTING GRANTS

14 CONSOLIDATOR GRANTS

8 ADVANCED GRANTS

13 RUNNING MARIE SKŁODOWSKA-CURIE ACTIONS

A SELECTION OF INTERNATIONAL RECOGNITIONS

- 4 YOUNG INVESTIGATOR AWARDS
- AGILENT THOUGHT LEADER AWARD
- BAILLET LATOUR GRANT
- AAAS FELLOW
- CAREER AWARD SCIENCE COMMUNICATION

TECHNOLOGIES WITH IMPACT

Know-how is valuable. At VIB, we have bundled specific expertise in core facilities, to provide our scientists with state-of-the-art technologies and equipment on a quality and scale that is beyond the capacity of individual research groups and even research centers. Furthermore, the core facilities are open to the wider scientific community, laying the foundations for collaboration and impact.

Core evaluation

To ensure continued high-quality services, the cores are subjected to a five-yearly evaluation. In November 2019, the on-site visit took place and the cores received high praise – and future-focused recommendations – from an international, interdisciplinary panel of technology experts. The review concluded that VIB's core program is operating at the very highest level and is recognized as a gold standard in Europe for how core facilities should be implemented and operated.

The expertise present in the different VIB Core Facilities is often complementary. Coupled with the increasing interest in single-cell studies, the VIB cores have contributed virtual service engine called Singularity. This service platform provides access to state-of-the-art flow cytometry, single-cell RNA sequencing, and advanced data processing workflows as a one-stop solution. After all, single cell work is no longer just transcriptomics- and genomics-driven but has spread out to all 'omics' disciplines. This clear trend prompted the cores to join forces in 2019 and start building a well-integrated multi-omics platform that should enable an individual researcher to acquire all this integrated info from one single sample.

In 2019, the VIB Screening Core launched NextGenQBio. This state-of-the-art platform is unique in Belgium and combines several cutting-edge technologies. The centralized platform connects high-throughput screening technologies with high-content imaging. This screening module is integrated with a centralized cell culture platform for automated culturing of a broad range of cell types. To accurately handle the biological data points that are generated, a package of comprehensive bioimaging analysis software and IT infrastructure for data storage completes the setting. In the years to come, NextGenQBio will provide major insights into the basic biological mechanisms of complex systems and facilitate the translation of these insights into drug discovery programs.

Strategic collaborations

The VIB Tech Watch initiative continues to give VIB researchers a competitive advantage since scientific breakthroughs are often preceded or paralleled by developments in the tools and technologies that enable new scientific hypotheses to be addressed. The Tech Watch team skims the market for new, emerging technologies that can have the potential to boost the research and IP output at VIB.

In 2019, the success of the Technology Innovation Lab, a Tech Watch initiative to further facilitate and derisk the uptake of ground-breaking technologies, resulted in many collaborations with technology companies such as Mission Bio, Sphere Fluidics, Refeyn, GALT and Nanoview Biosciences. The launch of the Single Cell Accelerator in 2018 was a key driver of this, as the accelerator program is now fully operational.

The competitive advantages created by the Tech Watch initiatives have sparked significant interest in the industry and resulted in numerous new partnerships. As part of the Single Cell Accelerator program, Janssen Pharmaceutica already entered in a partnership with Tech Watch in 2018. Given the success of this collaboration the partnership has been expanded.

Another collaboration announced in 2019 was with BGI Group headquartered in Shenzhen, China. BGI is the world's largest genome research organization innovating at the forefront of genomic technologies. Through this strategic collaboration, VIB and BGI will establish joint research programs and conduct co-developments on innovative applications of single cell sequencing, health monitoring omics and more.

A collaboration with IMEC was established, with the two institutes joining forces to develop a game changing technology platform for automated single cell multi-omics analysis with the aim to spin out a company, with 1 FTE to be hired in 2020.

SCIENCE-BASED BUSINESS FOR ECONOMIC IMPACT

VIB's Innovation and Business team guides the development of innovative research towards applications and products that benefit patients, farmers, and consumers. In 2019, the team continued its growth trajectory. On top of that, a marked acceleration occurred in terms of spin-off creation and high value deal-closing. Business development activities, such as R&D and license deals, generated the highest income ever: 21 M€. This record amount reaffirms VIB's position as a business partner of choice and a source of innovation within the life sciences ecosystem.

These business efforts do not only generate, but also increase, the economic and societal impact of VIB research in the local biotech ecosystem and beyond Flanders. An external economic impact study covering the past six years (2013–2018) provides an excellent illustration of this: for every 1 € of core funding from the government in Flanders, VIB generated an economic return of 11 €. In 2018, VIB activities contributed over 1 B€ to the global economy, with over two thirds of that number going directly into the economy of Flanders.

Added economic value comes in many shapes: collaborations and strategic alliances with a multitude of companies, technology licensing, creating start-ups, creating incubator space, and attracting international companies and funds to drive investments towards Belgian life sciences industry.

In 2019, VIB spin-offs employed more than 850 people. These spin-offs have thus far generated over 1.27 B€ in equity investments, with at least an equal, non-dilutive amount secured through partnership agreements. Mergers and acquisitions deliver another substantial capital injection that contributes to the growth of the biotech ecosystem in Belgium.

VIB's patent portfolio

Patent applications are a parameter for innovation, and this illustrates the forward-looking nature of VIB research. In 2019, VIB's IP team submitted 29 priority applications.

VIB currently manages a patent portfolio of 234 active patent families, the majority of which are monitored in-house.

Spin-offs for progress

The past year saw the birth of VIB spin-offs Augustine Therapeutics and Montis Biosciences.

Augustine Therapeutics, a spin-off from VIB and KU Leuven, is focused on the discovery and development of innovative therapeutics for patients with Charcot-Marie-Tooth disease (CMT) and other neuromuscular conditions. The company is rooted in the ground-breaking research of the VIB-KU Leuven lab of Ludo Van Den Bosch and from a collaboration between the labs of Joris de Wit and Bart De Strooper (both VIB-KU Leuven). A seed funding round of 4.2 M€ catalyzed the collaborative effort of VIB, KU Leuven, V-Bio Ventures and PMV, joined by Advent France Biotechnology (FR) and Gemma Frisius Fund.

Augustine Therapeutics is a great example of VIB's approach to company co-creation with business partners and investors. In addition to providing capital, the investors remain involved in the startup's day to day management. The VIB Discovery Sciences team is taking the

lead in the preclinical development of the new therapeutics, while the founder VIB labs contribute to the biological understanding underlying these projects.

Montis Biosciences, founded by VIB, KU Leuven and Droia Ventures, is based on the research from the labs of Peter Carmeliet and Massimiliano Mazzone (both VIB-KU Leuven Center for Cancer Biology). The novel spin-off's mission is to investigate and therapeutically exploit interactions between perivascular macrophages and tumor vasculature, in order to drive and sustain immune reactions against solid tumors.

Seed funding of 8.4 M€ allows Montis Biosciences to progress towards clinical studies and expand its screening and assay platform to identify and validate additional promising targets. For the seed financing, the founders were joined by a strong international consortium of investors Polaris Partners (US), ALSA Ventures (UK) and Pfizer Ventures (US). For both Polaris and ALSA it is the first time that these funds invest in a Belgian-based biotech company.

Raising capital

In 2019, several VIB spin-offs have attracted financial investments to expand their activities and progress their research programs. With these investments, new product and therapy pipelines can be set up.

VIB spin-off Confo Therapeutics started in 2015 based on technology developed at VIB/VUB. Many stakeholders participated in a 30 M€ series A2 financing investment round, which was led by BioGeneration Ventures (NL) and Wellington Partners (DE). The company will use the acquired funds to accelerate its drug discovery activities and to develop compounds that modulate G-protein coupled receptors (GCPRs) to produce drug candidates for clinical trials.

VIB spin-off Biotalys (previously Agrosavfe) is a biotech-company that seeks to transform food protection with the ultimate goal of shaping a sustainable and safe food supply. It generates a new generation of protein-based biocontrol solutions for key crop pests and plant diseases that can affect stages across the entire production chain. The products developed through their unique and versatile technology platform provide safe, sustainable and efficient protection for seeds, crops, and food. With 35 M€ of series C financing raised in 2019, Biotalys can upscale its efforts in developing, registering, and commercial production of its products. The first product is a biofungicide scheduled for a 2022 launch on the US fruit and vegetable market, rapidly followed by release in Europe and other regions. Early in 2020, Biotalys announced the second closing of its Series C financing round, bringing the total amount to 45 M€.

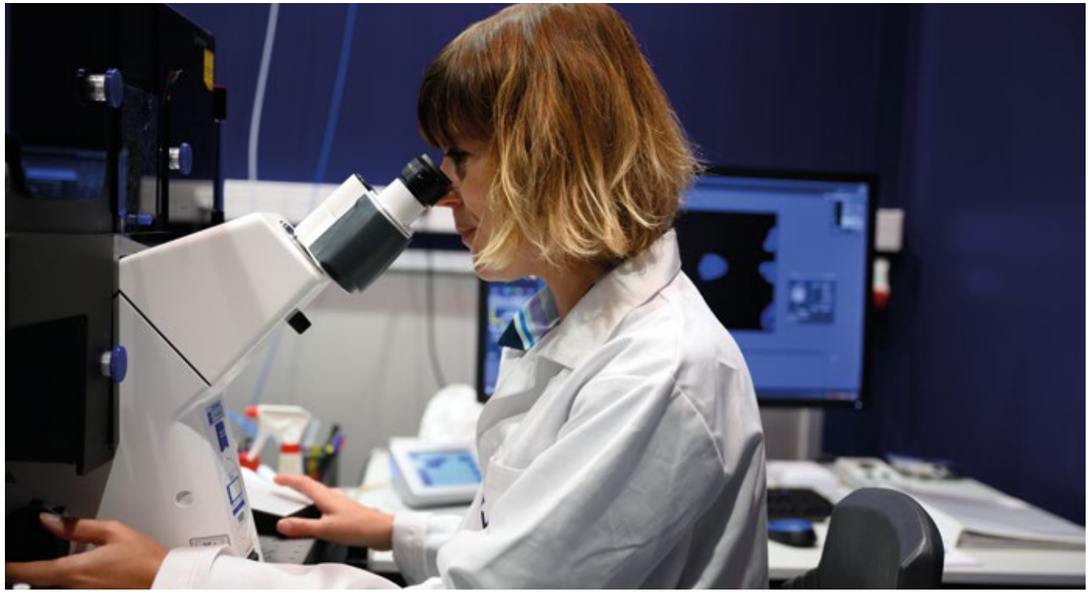
Collaborating with industry

One of VIB's core missions is to advance its science to create benefits for patients, farmers and consumers. Being a research institute, VIB needs to partner with companies to accomplish that goal. In 2019, VIB concluded more than 180 agreements with industry and realized an industrial income of more than 24.6 M€ in total.

The research groups of Bart Lambrecht and Savvas Savvides (VIB-UGent Center for Inflammation Research) have found that the Charcot-Leyden crystals, highly abundant in airway mucus of asthma patients consist out of Galectin10 and stimulate the immune system in a particularly pathogenic manner. Together with the biotech company argenx, the teams developed antibodies that can dissolve these crystals and reduce key asthma symptoms. argenx and VIB are co-developing these ARGX-118 antibodies from lead to clinical drug candidate.

The team of Xavier Saelens (VIB-UGent Center for Medical Biotechnology) has been able to provoke necroptosis in cancer cells with the protein MLKL – delivered by synthetic mRNA – and awaken an anti-tumor immune response. They teamed up with eTheRNA Immunotherapies, a Belgian biotech company specialized in mRNA technology to fully explore the possibilities of their finding.

The Jan Steyaert team (VIB-VUB Center for Structural Biology) developed an innovative plug-and-play technology to graft functional single domain antibodies on several scaffolds with diverse properties to build Megabodies, which are game-changing research tools for the high-resolution structure determination of molecules in solution. Confo Therapeutics, a VIB founded emerging drug discovery company, entered into an agreement with VIB for an exclusive, worldwide license to VIB's 'Megabody' technology for applications on GPCRs.



This year also witnessed the commercial launch of new diagnostics based on VIB research.

At the world's first Liver Glycomics Congress in 2019, the UK-based medical diagnostics firm Helena Biosciences announced the launch of the Glyco Liver Profile test. This novel diagnostic test for chronic liver diseases based on the analysis of serum proteins has been developed by the Nico Callewaert team (VIB-UGent Center for Medical Biotechnology).

The diagnostic license on MSI (microsatellite instability) markers from Diether Lambrechts lab (VIB-KU Leuven Center for Cancer Biology) to Biocartis has led to a commercial launch of the Idylla™ MSI Assay for *in vitro* diagnostic use in colorectal cancer.

Drawing international attention

Flanders is a region well-known for its biotech expertise. More importantly, Flanders is equally well-known for its willingness to share this expertise. This combination of knowledge and collaborative spirit draws regular international attention of foreign companies looking to expand and establish local facilities. In 2019, VIB contributed to attracting three companies to establish bases in Flanders: StixFresh, Asylia Diagnostics and Handl Therapeutics.

Derisking to accelerate product development

VIB Discovery Sciences is a strategic initiative that mitigates the risk of setting off on the path towards the execution of translational projects, thereby increasing the success rate of translational research. Working closely with VIB group leaders, the VIB Cores, and external partners with complementary expertise they 'derisk' the initial stages of translational projects.

In 2019, the Discovery Sciences team was actively involved in a VLAIO project grant for Oncurious of close to 1 M€. In collaboration with VIB Discovery Sciences, Oncurious will continue the pre-clinical development of its pipeline of next generation cancer immunotherapies.

The new startup Augustine Therapeutics also benefits from a close collaboration with VIB Discovery Sciences, which is taking the lead in the preclinical development of new therapeutics.

ECONOMIC IMPACT

22 START-UPS

2 NEW SPIN-OFFS IN 2019

1.3B € CAPITAL INVESTMENT

850 DIRECT EMPLOYEES

INFRASTRUCTURE

BIO-INCUBATOR GHENT

6,500 M^2

10 COMPANIES

216 EMPLOYEES

BIO-INCUBATOR LEUVEN

9,375 M^2

16 COMPANIES

382 EMPLOYEES

BIO-ACCELERATOR GHENT

18,000 M^2

4 COMPANIES

575 EMPLOYEES

VIB

INTELLECTUAL PROPERTY

618 TOTAL NUMBER OF PATENT APPLICATIONS

234 TOTAL NUMBER OF ACTIVE PATENT FAMILIES

INDUSTRIAL INCOME

125M € OVER THE LAST 5 YEARS

INWARD INVESTMENTS

3 INWARD INVESTMENTS IN 2019

2B € CAPITAL INVESTMENT

800 DIRECT EMPLOYEES

SUPPORTING THE BIOTECH ECOSYSTEM

INTERNATIONAL SCHOOLS

99 GHENT PUPILS

54 LEUVEN PUPILS

TALENT POOL

5 UNIVERSITIES

4 STRATEGIC RESEARCH CENTERS

PEOPLE-ORIENTED LEADERSHIP

As a research institution, VIB can have the best infrastructure, the most sophisticated equipment and state-of-the-art technologies, but without our people, without their passion, energy, perseverance, work ethic and creativity, we are nowhere. That is why we want to ensure that our scientists and all who support them can work in a stimulating environment where everyone is treated with respect and understanding. Where people can develop their talents to boost their career. This vision also underlies the importance that VIB attaches to leadership; genuine people-oriented leadership, with attention to communication, a transparent feedback culture, career guidance, well-being and coaching.

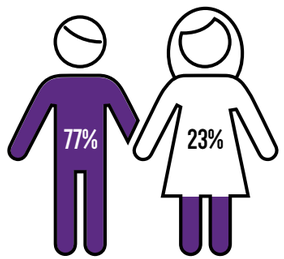
GENDER AT VIB: CURRENT SITUATION

VIB ALL

HQ

HQ MANAGEMENT

PHD STUDENTS



PIS

POSTDOCS & STAFF SCIENTISTS

S&T PERSONNEL

GENDER BALANCE AND DIVERSITY

VIB's international recruitment policy ensures a continuous influx of the most talented people from diverse backgrounds, nationalities, and cultures. Such a diverse workforce brings a wide array of perspectives to the table, which stimulates out-of-the-box thinking and creativity.

In order to achieve a better gender balance, VIB has taken various initiatives in previous years that have paid off in 2019. One of these initiatives is the Gender Action Plan (GAP), which foresees in the recruitment of ten young female group leaders who receive funding for five years together with a career support package. In 2019, VIB managed to recruit ten female group leaders (out of twelve recruitments) of which 3 within the GAP. This momentum will be continued in 2020 to further increase the number of women in leadership positions.

With the recruitment of these ten female group leaders, the gender balance is moving in the right direction, i.e. 23% female and 77% male PIs (whereas we only had 15% female group leaders in 2018).

TRAINING

The aim of Training@VIB is to offer comprehensive training, workshops, and individual coaching to all VIB researchers and supporting personnel. In addition to scientific training, we are convinced that training in transferable skills is equally important. Therefore, the training offer consists of four distinctive areas: science, skills, bioinformatics and coaching/leadership.

ENGAGING EMPLOYEES

Good internal communication and well-informed colleagues pave the way to creating enthusiastic VIB brand ambassadors. At VIB, we pay close attention to the needs of our people and we aim to build a close-knit VIB community. An important internal communication initiative that was launched in 2019 is the organization of so-called 'town hall meetings' in all VIB research centers, during which the general management informs all collaborators of the state of affairs of VIB.

OUTREACH

VIB's work in science communication is an important influence in shaping the public attitude towards the pioneering research at the institute. Public perception has a tangible impact on policy makers and misconceptions among the general public can quickly affect government policy.

Spreading the word on the work of VIB's scientists and biotechnology applications is one of the organization's key tasks. It has a dedicated Conferences & Outreach team that is responsible for communicating complex matters in a simple but scientifically based manner to a wide audience. This public engagement is important, allowing VIB to share its research, to inform and educate people, and to provide evidence to taxpayers that their money is being wisely invested.

Biotech day

Biotech Day 2019 was a great success. Over 4,000 visitors enjoyed a range of presentations and activities that provided a glimpse into the marvelous world of microbes. Researchers and companies from all over Flanders gathered at campus Arenberg, Leuven to give the general public a (sometimes literal) taste of the power and relevance of microbes.

The visitors were as varied as the topics and activities. Clearly, the interest in biotechnology is alive and well in Flanders. Both the many tastings and the experimental brewery were popular. The presentations, long and short, attracted an auditorium-filling audience, and the escape room captivated the attention of young and old.

Science Day

Another event where VIB promoted its biotech research was the national Science Day. During this day scientists from all over the country explain how science and technology affect our daily lives. As is the case every year, VIB scientists were eager to contribute, with, for example, biotech quizzes, ketchup DNA, secret escape rooms, and much more.

Facts series

Through the Facts Series, VIB's communication team provides in-depth, but comprehensible information on various scientific topics. In 2019, two Facts Series brochures were completed that aligned closely with public and political interest: CRISPR-Cas genome editing in plants, and CRISPR-Cas genome editing in medicine.

Conferences

To produce impactful science, scientists themselves also have to stay informed about the latest developments within and beyond their fields. Regular interaction and knowledge-sharing among the internationally dispersed scientific community is a key component of a scientific career.

VIB regularly organizes conferences of international importance to give its members, as well as the scientific community as a whole, a fertile breeding ground for ideas and collaborations. The VIB Conference Series has had another successful year. With the help of the dedicated conferences team, over 2,100 scientists visited these conferences, which attracted significant industrial interest and corporate funding, with 93 companies sponsoring the VIB Conference Series.

Apart from the VIB Conference Series program, the conferences team also provided support for various VIB science events, which in total attracted 647 participants.

FACES OF VIB

As a center of excellence, VIB's primary focus is basic research: unravelling the molecular mechanisms that define health or disease. Over the years it has become apparent that translating scientific findings into concrete solutions or applications for patients and consumers leads to sustainable societal and economic impact. Many VIB researchers play a key role in this process and are happy to share how they experience their contribution to a better world.

Jeroen Aerts
Life Science Technology Specialist

"During my PhD we developed an immunotherapy against cancer by provoking a specific kind of cell death (necroptosis) in cancer cells. After obtaining proof-of-concept results in experimental mouse models, we teamed up with the intellectual property team of VIB to file a patent. The collaboration with VIB-HQ went smoothly and I was closely involved with the patent filing process. This gave me the opportunity to learn about the complex world of intellectual property. Next, the VIB business development team made it possible to start a research collaboration with eTheRNA. As a young researcher it is really cool that your research is of interest to a company that is already in clinical stage with their treatment."

Lien Van Hoecke
Postdoctoral Scientist, VIB Center for Inflammation Research (previously VIB-UGent Center for Medical Biotechnology)

"Working with industry is mutually beneficial. For companies, this means extra exposure and linking their name to the VIB quality seal. For us, our industrial projects often attract a lot of media attention which can (and has) sparked new collaborations, attract students, build the lab's reputation… Industry collaborations can also lead to new 'fundamental' research projects, and we notice that companies that we collaborated with use our lab as a talent pool. So, being in a lab with a lot of industry contacts can be good for your future career. But, most of all, it is just fun to chat about science with people from industry, which in our case ranges from CEOs of mid-caps to the monks of the Trappist breweries."

Jan Steensels
Postdoctoral scientist, VIB-KU Leuven Center for Microbiology

"It gives great satisfaction to see that your basic science is turning into potential applications through a company that is steadily growing. The company has the means to execute aspects of the science that are not possible for us such as large-scale field experiments. These activities are complementary to our activities. It is highly interesting to get to know these last steps of the pipeline that are required to bring basic science into application."

Sofie Goormachtig
Principal Investigator, VIB-UGent Center for Plant Systems Biology

"The economic impact study showed that excellent research and tech transfer activity, combined with a focus on cluster development, result in clear economic impact. The study – which was carried out by an external consultant – showed that for every € invested by the Flemish government 11€ flows back to the economy, creating 8,500 jobs in this region. The study also noted that the impact is increasing over time. The economic activity creates a return to government through social security contributions and taxes. This return is more than 4 times higher compared to the total investment of the government in VIB."

Rik Audenaert
Chief Financial Officer

"As I come from a family with a demyelinating form of CMT, I had decided early on that I would join a CMT lab to contribute to the research. I joined Ludo's lab after searching for quite some time for a CMT research lab where I felt the science was leading to a breakthrough. When I came across the HDAC6 inhibition therapeutic strategy implemented by Ludo and Constantin d'Ydewalle, I knew this would be big. Since joining the lab, I have worked amongst others trying to extend the therapeutic strategy to other forms of CMT, in particular the demyelinating forms of CMT. Additionally, I have been using induced pluripotent stem cells to help model the disease in a better manner. Previous lab

alumni, such as Veronick Benoy and Lawrence Van Helleputte, and myself helped to understand the overall therapeutic benefits of HDAC6 inhibition in inherited and acquired peripheral neuropathies. All this led to the establishment of Augustine Therapeutics. This is a very important chapter in my life, as I really believe that the therapy it has to offer patients with axonal forms of Charcot-Marie-Tooth disease (CMT) will be life-changing."

Robert Ciaran Prior
PhD student, VIB-KU Leuven Center for Brain & Disease Research

"VIB research is often considered too early-stage for investors or corporate partners to engage because the uncertainties are high. Therefore, we invest a lot of time working together with the VIB scientists in 'derisking' their research results to compile a solid data and IP package backed by reproducible proof-of-concept data in relevant industry-standard models. Another challenge is to find the right management team. We're looking for white ravens here: while the technology or invention is the foundation for a new venture, it's the team that needs to turn it into a success. Being able to attract a great management team is the proof that we've done our homework properly in building a solid investment case! New ventures are an important way to translate the results of basic VIB research into applications and – eventually – novel medicines, diagnostics, or improved crops. Starting biotech companies in Flanders has a huge impact on the local ecosystem: not only do they attract significant investments to the region; they lead to direct employment in the biotech scene."

Griet Vanpoucke
Head of New Ventures

"So far, the collaboration between VIB and argenx has been very fruitful. For me personally – with a background in fundamental structural biology research – it is a unique and rewarding experience to be so closely involved in the different phases of the drug development process. Targeting pathogenic protein crystals with antibodies is a rather unconventional approach and this means we sometimes need to come up with novel and creative experiments. We have biweekly meetings with argenx where we discuss the progress in an open and collegial atmosphere as a single team. One of the major challenges right now is that mice do not possess a similar protein as human Galectin10, which makes the evaluation of the *in vivo* therapeutic efficacy in an animal disease model difficult. However, I am optimistic that we can overcome this challenge in near future."

Kenneth Verstraete
Staff scientist, VIB-UGent Center for Inflammation Research

"For me, the collaboration with Oncurious has been a very positive experience because it feels like a team effort with the common goal to successfully translate a conceptual strategy, supported by preclinical results, into the clinic. Understanding the underlying mechanisms of tumor micro-environment modulation will contribute to the overarching goal of developing new therapeutic approaches to boosting the immune system in tumors. This research may lead to a therapy that enables cancer-fighting immune cells to penetrate tumors and destroy malignant cells. We have regular interactive meetings with the company in which we exchange our progress, discuss challenges and try to find solutions to move to the next steps."

Gabriele Bergers
Principal Investigator, VIB-KU Leuven Center for Cancer Biology

GOOD GOVERNANCE

VIB has established a 'Good Governance Charter'. The full text of the charter is public and can be consulted on our website (vib.be). Our principles of good governance are regularly tested and adjusted.

This means that we are able to capitalize on local and international developments in this context and meet the needs of all our stakeholders.

BALANCE SHEET

(€ THOUSANDS)

ASSETS	31.12.2019	31.12.2018	31.12.2017	2019-2018 %
Intangible fixed assets	1 091	907	968	20%
Tangible fixed assets	32 466	33 707	31 699	-4%
Financial fixed assets	35 882	34 789	25 191	3%
Contracts in progress	14 090	11 491	8 646	23%
Amounts receivable within one year	20 698	18 196	16 587	14%
Investments	83 715	73 500	68 625	14%
Cash at bank and in hand	37 911	40 461	31 010	-6%
Deferred charges	4 009	13 025	14 348	-69%
TOTAL ASSETS	229 862	226 076	197 074	2%

LIABILITIES

Allocated funds	108 475	103 761	87 452	5%
Investment grants	31 517	31 991	29 462	-1%
Amounts payable after one year	10 232	12 264	5 360	-17%
Amounts payable within one year	50 361	53 379	54 205	-6%
Accrued charges and deferred income	29 277	24 681	20 595	19%
TOTAL LIABILITIES	229 862	226 076	197 074	2%

PROFIT AND LOSS STATEMENT

(€ THOUSANDS)

Operating income	**114 405**	**108 503**	**99 612**	**5%**
Turnover (from contract research)	32 243	30 085	25 382	7%
Contracts in progress (+/-)	2 599	2 846	1 476	-9%
Grants and subsidies	76 769	73 217	69 987	5%
Other income	2 794	2 355	2 767	19%
Operating expenses	**-109 138**	**-101 854**	**-94 107**	**7%**
Raw materials and consumables	-12 066	-11 076	-9 478	9%
Services and other goods	-26 592	-26 589	-23 393	0%
Remuneration, social security costs and pensions	-60 301	-54 944	-51 425	10%
Depreciation	-9 333	-8 484	-8 866	10%
Other operating expenditures	-846	-761	-945	11%
Financial income	**970**	**1 138**	**688**	**-15%**
Financial charges	**-9**	**-957**	**-633**	**-99%**
Extraordinary income	**2 359**	**24 114**	**18 557**	**-90%**
Extraordinary expenditure	**-3 873**	**-14 635**	**-8 325**	**-74%**
PROFIT/LOSS FOR THE FINANCIAL YEAR	4 714	16 309	15 792	-71%

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. As such, 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 a close partnership with five Flemish universities – Ghent University, KU Leuven, 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 can be found at www.vib.be

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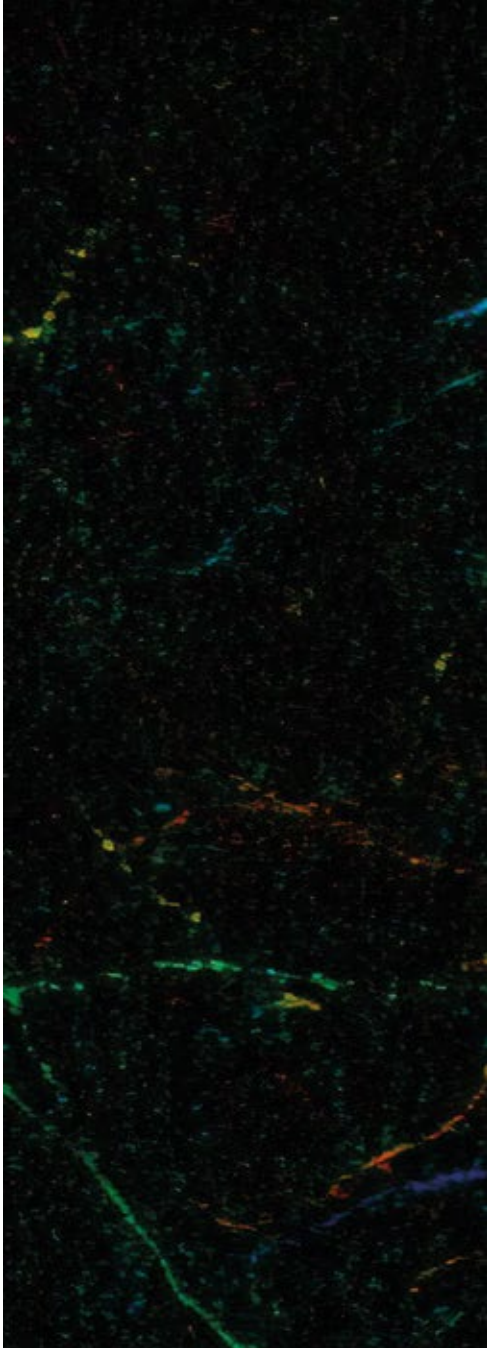

The image on the cover shows human neurons implanted in the brain of a mouse by means of a new process. By measuring their calcium signals over a short period of time, we can represent the cell body and the dendrites with certain colors.

Image: Ben Vermaercke, VIB-KU Leuven Center for Brain & Disease Research