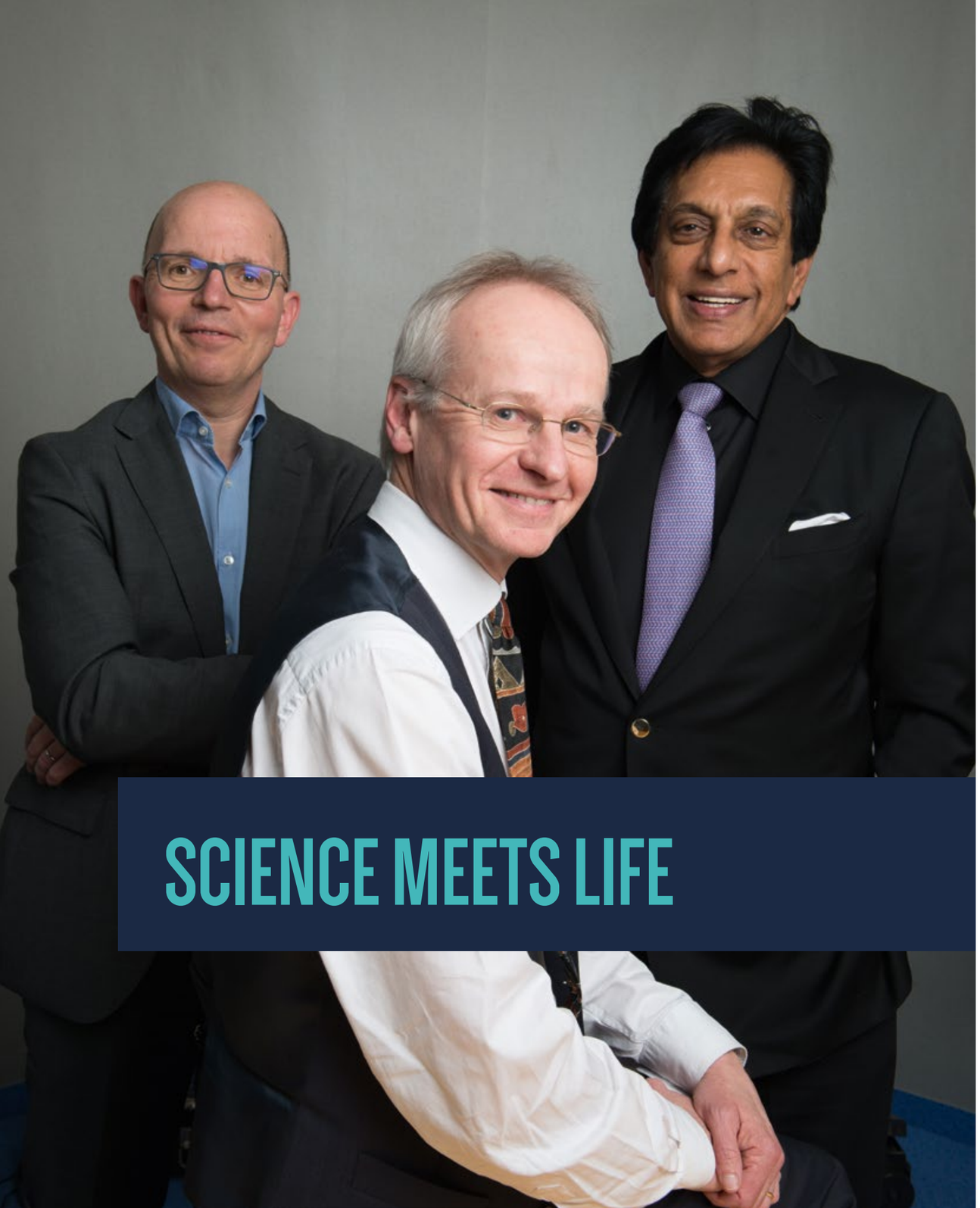
VIB

ANNUAL REPORT 2016



SCIENCE MEETS LIFE

VIB's basic research is inspired by the grand societal challenges and focuses on two primary needs of mankind: healthy living and sustainable food production. Our scientists, grouped in thematic Research Centers, study the molecular mechanisms of human health and disease, and of plant growth and development. A better understanding of these mechanisms will lead to improved diagnostics and therapies and, ultimately, disease prevention and better crops and food products.

Our team of tech transfer professionals ensures that research results are translated into added value for our economy and tangible benefits for society.

An exciting year

Our researchers are pioneers in their fields and they are often early adopters of new technologies. Interdisciplinary research and interactions between different research groups have become essential, given the complexity of life sciences research today. Although our focus is on basic research, the outcome often leads to innovative therapies or diagnostics. In many other cases, new research is built on the results of previous studies and then leads to practical applications.

To list all the important breakthroughs here is an impossible task, but the following findings at least give a flavor of the impact of our research:

- VIB scientists identified two cancer-specific long non-coding RNAs (NEAT1 and SAMMSON), which hold promise as potential anticancer therapeutic targets. What is remarkable in their findings is that these two targets are required for the growth of cancer cells but are not needed for normal cell function.
- VIB scientists have developed a proprietary technology that enables the development of target-specific designer molecules which can switch off the specified target. The technology was demonstrated using a designer molecule against VEGFR2, a well-known cancer target. The scientists showed that this new molecule kills the cancer cells and also stops tumor growth in mice. Because these principles apply to virtually any protein, their approach may be used not only to develop future cancer therapies, but also to treat drug-resistant and many other infections.
- VIB scientists have unraveled the mechanism that causes cellular defects in the most common hereditary form of dystonia. These findings shed new light on this poorly understood condition and may form an entry point for the development of a new medical approach to treatment.
- VIB scientists have discovered a potential new treatment for intractable epilepsy and have found out that increasing the concentration of specific fats in the brain could suppress epileptic seizures.
- Worldwide, the majority of gastric ulcers and cancer cases are caused by the stomach bacterium *Helicobacter pylori*. VIB scientists have provided detailed structural and functional insights into how the BabA protein of the pathogen interacts with specific sugars in the stomach. This breakthrough creates a basis for the rational design of novel drugs to combat *H. pylori* infections.

2016 was also a productive year with regard to our tech transfer activities. Our industrial collaborations generated a turnover of 13.3 million euro and a new start-up was created: Aphea.Bio. This brings the total number of VIB spin-offs to 19, with a collective capital investment of 930 million euro.

The entire institute was audited and received an outstanding evaluation report for the fourth time in a row. Our future strategy, "VIB beyond borders", will further consolidate our position as a leading life sciences research institute and will increase our global impact. Based on this positive evaluation and our ambitious strategic plan, the Flemish government is giving VIB its full support with a 34% increase in our funding for the next five years.

2016 was also marked by the celebration of our 20th anniversary. We celebrated this memorable occasion with the "Science meets life" symposium and the Biotech tour, a cross-country road trip with an exhibition showcasing VIB's research.

We have every reason to be proud of what VIB has achieved over the last 20 years. We will continue in the same pioneering spirit with the ultimate goal of making the world a better place.

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

VIB in brief

VIB is an entrepreneurial non-profit, multi-site research institute, with a clear focus on groundbreaking research in life sciences. Our scientists study the molecular mechanisms that regulate the functions of the human body, plants and microorganisms. This research leads to innovative insights into normal and abnormal/pathological life processes, which have potential uses in the development of novel therapeutics, diagnostics, applications and technologies.

The concept of VIB is based on close collaboration with the universities of Ghent, Leuven, Antwerp, Brussels and Hasselt. Thanks to these unique partnerships, VIB builds on collective scientific expertise and experience in life sciences research.

Over the years, life sciences have become part of our everyday lives and there is no doubt that science has become deeply interwoven with our daily routines. Scientific knowledge can improve the quality of life at many different levels, from the routine workings of our daily existence to global societal challenges such as healthy living and sustainable food production. In light of this fact, we go to great lengths to inform the public about our research results and tech transfer achievements.

Our mission and core values

It is our mission to conduct pioneering biomolecular research in life sciences. By doing so, we encourage sustainable scientific progress and contribute to a better world.

We strive for excellence in all areas of our research and encourage our scientists and employees to be entrepreneurial and creative in their thinking. Our focus on innovative technologies ensures that our research is genuinely groundbreaking, and our entrepreneurial tech transfer approach ensures that breakthroughs in science are translated into value for society. We stimulate public engagement and transparent communication to build trust and mutual understanding.

840 PUBLICATIONS

SCIENCE

276 PUBLICATIONS IN TIER 5 JOURNALS

CORE FACILITIES **10**

TECHNOLOGIES

INVESTED IN TECH WATCH PROJECTS **500 K**

5 PARTNER UNIVERSITIES → 75 RESEARCH GROUPS

1 INSTITUTE

66 NATIONALITIES ← 1,606 COLLABORATORS

TOTAL INCOME

%53 FLEMISH GOVERNMENT

%47 OTHER INCOME

TECH TRANSFER

930 M CAPITAL INVESTED IN SPIN-OFFS

706 EMPLOYEES IN START-UPS

PUBLIC ENGAGEMENT

PARTICIPANTS IN VIB CONFERENCES **1,460**

ARTICLES PUBLISHED IN THE PRESS **585**

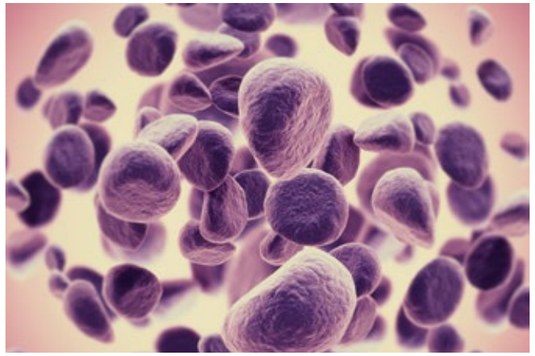
SCIENCE MEETS SCIENCE

CURIOSITY-DRIVEN RESEARCH

VIB researchers play in the top league of their discipline and our scientific research is continuously benchmarked with the world's leading experts in various sub-fields from other life sciences institutes. Research at VIB is conducted at the frontier of the global scientific endeavor.

The summaries on the following pages are just a small sample of the groundbreaking research published by our experts in 2016.

Cancer biology



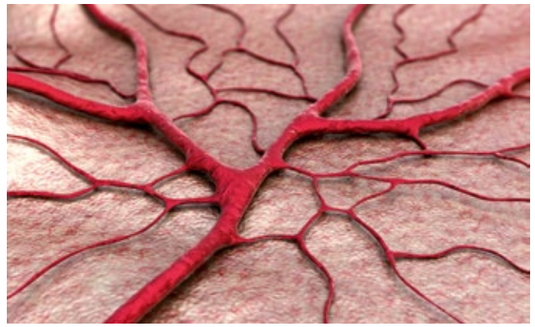
Clear link between cell metabolism and the spread of cancer

A team led by Massimiliano Mazzone has demonstrated that the metabolism of macrophages can be attuned to prevent the spread of cancer. Macrophages are types of white blood cells that attack foreign micro-organisms; as such, they are an essential part of our immune system. Besides their positive effect on pathogens, macrophages can also play a negative role in cancer biology. Tumors contain a lot of specific macrophages that play a decisive role in the formation of blood vessels. In tumors, these vessels traditionally have a chaotic and dysfunctional buildup. As a result, cancer cells are more likely to escape through the vessels, enter the bloodstream and invade other organs.

The key is to make these macrophages more prone to "steal" sugar from the cells forming the tumor's blood vessels. Changing the macrophages' metabolism creates a 'glucose competition' between the macrophages and the tumor's blood vessels. As a result, the macrophages can eat the glucose instead of the blood vessel cells. Because the latter are no longer overstimulated, they are able to form more regular vessels. This creates a structured and strong vessel barrier around the tumor, preventing cancer cells from escaping to the bloodstream and invading distant organs.

Further research is being carried out in cooperation with experts specialized in blood vessel formation and in metabolism to study the impact of cell metabolism for future tumor therapies.

Wenes et al., *Cell Metabolism, 2016*



Normalizing tumor oxygen supply could be a key factor in the fight against cancer

In general, the onset of cancer is well understood: due to chance or carcinogenic factors, the DNA of a single cell mutates, followed by the rapid expansion of abnormal cells. These genetic mutations disturb normal cell function, but are beneficial for the growth and survival of cancer cells. Apart from these genetic changes, tumor cells also differ epigenetically. Although epigenetic changes don't affect the genetic code, they can strongly disturb the function of a gene in a similar way, in favor of cancer cells. Until now, the origin of these epigenetic changes largely remained a mystery. Scientists from the lab of Diether

Lambrechts investigated one frequent epigenetic alteration: hypermethylation, or the excessive addition of methyl groups to DNA. Hypermethylation silences the expression of tumor-suppressing genes, thereby enabling the abnormal behavior of cells and the excessive growth of tumors. This study shows that these epigenetic alterations are caused by the tumor environment and, more specifically, by oxygen shortage – which is called "hypoxia". Oxygen is essential for the enzymes that normally remove the methyl groups from DNA. When there is oxygen shortage, too much methylation is retained, causing hypermethylation. While the study focused primarily on breast tumors, it was also demonstrated that this mechanism has a similarly broad impact in bladder, colorectal, head and neck, kidney, lung and uterine tumors.

Subsequent research in mice showed that interfering with tumor oxygen supply is sufficient to stop the progression of epigenetic alterations. To take the research a step further, the lab is now testing whether analysis of tumor DNA can be used to predict tumor oxygenation.

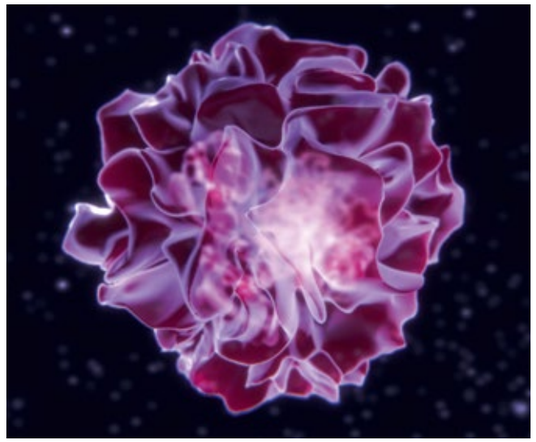
Thienpont B. et al., *Nature, 2016*

Immunity and inflammation

Novel dendritic cell identification method paves the way to an anti-tumor cell-based vaccine

In the human body, so-called dendritic cells are responsible for activating our immune system. To do this, they process specific molecules (antigens) and present these selectively to antigen-specific T cells. This unique role makes the dendritic cell the main cellular target in vaccination strategies. Unfortunately, identifying dendritic cells is very challenging, since many different markers are used in different tissues and species. This leads to a lot of confusion and impedes the application of preclinical dendritic cell research for the design of novel therapies.

Therefore, the teams of Martin Guilliams, Bart Lambrecht and Yvan Saeys (VIB-UGent) joined forces with the teams



of Florent Ginhoux (SIgN, Singapore) and Bernard Malissen (CIML, France) to design a universal, high-throughput and standardized method for the identification of dendritic cells in mice, macaques and humans. The toolbox resulting from this collaboration makes use of a minimal set of markers to subdivide conventional dendritic cells into two functionally distinct subsets across tissues and species (cDC1s and cDC2s). This means that a large number of additional markers can still be used to further characterize the functional specialization of cDC1s and cDC2s across tissues and during inflammation.

This new methodology was subsequently used by Jo Van Ginderachter's group to gauge the presence of dendritic cells in tumors. This allowed the identification of cDC1s and cDC2s within human and mouse tumors. Importantly, when these cells were isolated and used as a cell-based vaccine to immunize mice against a subsequent tumor challenge, tumor growth was considerably retarded. Remarkably, cDC1 and cDC2 acted through distinct molecular mechanisms, and some types of tumors were more susceptible to cDC1 vaccination while other tumors were more susceptible to cDC2 vaccination. This success could lead to new cancer immunotherapies.

Guilliams M. et al., *Immunity, 2016*
Laoui D. et al., *Nature Communications, 2016*

Cytokine IL-33 drives allergic sensitivity in neonatal lung

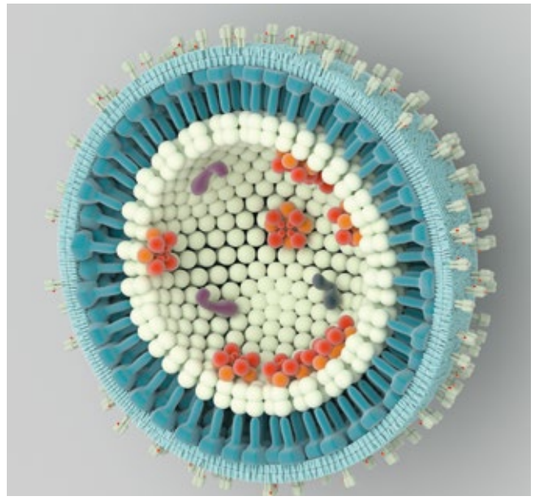
Scientists from the labs of Bart Lambrecht, Hamida Hammad (VIB-UGent) and Erasmus University (NL) have found evidence that interleukin-33 (IL-33), a protein created by lung epithelial cells, is a key driver of allergic sensitivity in the lungs of newborns. While it remains a scientific puzzle how allergy develops early in life, this study has uncovered new insights into immune responses that could prove key in understanding – and fighting – allergy and asthma in infants and young children.

The human immune system responds to the presence of pathogens in two main ways: the non-specific innate immune response to destroy pathogens rapidly, and the specific adaptive or acquired immune response. The adaptive immune response is composed of humoral immunity, mediated by antibodies produced by B cells, and cellular immunity, mediated by T cells. Allergies and asthma are the result of a hyperactive T helper 2 cell-mediated immune response, but their initial triggers have not yet been pinpointed. Allergic asthma often starts in early childhood and when allergens are first encountered, the lungs of young children are still developing. This study's findings shed light on the process of allergy development in early life, demonstrating that spontaneous high IL-33 production in the developing lung promotes a wave of type 2 cellular immunity and lowers the threshold for innate immune responses

to allergens. As asthma is a common and sometimes fatal immune disorder in young children, information relating to underlying causes or triggers of the disease could prove critical to therapies that treat it, or even prevent its emergence.

de Kleer et al., *Immunity, 2016*

Medical Biotechnology



Viral particles used to trap intact mammalian protein complexes

The team of Sven Eyckerman developed Virotrap, a viral particle sorting approach for purifying protein complexes under native conditions. This method catches a bait protein together with its associated protein partners in virus-like particles that are budded from human cells. This approach eliminates the need for cell lysis and protein complexes are preserved during purification.

Conventional approaches to analysis of protein complexes have several shortcomings. For example, mass spectrometry–based strategies require lysis conditions to break open cell

membranes that often affect protein-protein interactions. Inspired by virus biology, the Eyckerman lab came up with a creative solution. It is well known that the natural process of HIV particle formation also captures a number of host proteins. The scientists used this observation to their benefit by hacking a completely safe form of the virus to abduct intact protein complexes from the cell. By fusing a bait protein to the HIV-1 GAG protein, interaction partners become trapped within virus-like particles that bud from mammalian cells. Standard proteomic approaches are used next to reveal the content of these particles. Fittingly, the team named the method "Virotrap".

The Virotrap approach is exceptional as protein networks can be characterized under natural conditions. By trapping protein complexes in the protective environment of a virus-like shell, the intact complexes are preserved during the purification process. The researchers used the method for confirmation of known binary interactions and for mass spectrometry-based identification of novel protein partners for both bait proteins and small molecules.

Eyckerman S. et al., *Nature Communications, 2016*

Microbiology

Beer yeasts are dogs, wine yeasts are cats

A group of multi-disciplinary researchers, under the leadership of Kevin Verstrepen and Steven Maere, found that yeasts used for beer and winemaking were domesticated in the 16th century, around 100 years before the discovery of microbes. Together with a US research team, the Belgian teams analyzed the genomes and fermentation characteristics of more than 150 industrial yeasts used to produce different beers, wines and breads. The results show that the hundreds of beer and wine yeasts available today are the result of brewers and winemakers unconsciously selecting variants that can consume specific sugars, tolerate industrial conditions and produce the flavors they want.

The scientists found that yeast strains were selected to provide beers with desired industrial characteristics. Another interesting find was the fact that wine yeasts, even though they share their origins with beer yeasts, show fewer signs of domestication. This is probably because wine yeasts are only used to ferment grape juice once a year; for the rest of the year, they survive in and around the winery, where they may interbreed with feral yeasts. Beer yeasts typically live happily in the brewery throughout the year and have no contact with their feral family members. In that sense, beer yeasts are like dogs, completely "tamed", whereas wine yeasts resemble the wilder character of cats.

Mapping out the genome structure of yeasts in food and drinks allows a better understanding of the mechanics and applications of yeasts. As a result, it opens up new possibilities to breed yeasts to enhance flavors, aromas or conservation techniques.

Gallone B. et al., *Cell, 2016*

World's first population-level microbiome study reveals links between lifestyle and gut flora

The Flemish Gut Flora Project, one of the largest population-wide studies on gut flora variation among healthy volunteers, has presented its first major results. Through the analysis of more than 1,000 human stool samples, a team of researchers led by professor Jeroen Raes (VIB-KU Leuven) has identified 69 factors associated with gut flora composition and diversity. Most of these covariates are related to transit time, health, diet, medication, gender and age. Integration of the Flemish Gut Flora Project results with other data sets gathered around the world revealed a set of 14 types of bacteria that make up a universal core microbiota present in all individuals.

Stool transit time showed the strongest association to gut flora composition. Diet was also an important factor, with most associations related to fiber consumption. Other project results invite deeper investigation, such as the relationship between the gut flora and factors linked to oxygen uptake capacity. Medication also had a strong link to the gut flora profile.

These results are essential for disease studies. Parkinson's disease, for example, is typically associated with a longer intestinal transit time, which in turn impacts microbiota composition - showing the importance of including confounders in clinical microbiomics studies. These and many other observations can help scientists in their research into future therapies.

Although the Flemish Gut Flora Project has enormously enriched our knowledge on gut flora composition, it only explains 7% of gut flora variation. An enormous amount of work still needs to be done to map the entire gut flora ecosystem. The Raes Lab is already planning follow-up studies, including new large-scale research projects that will explore the evolution of gut flora over time.

Falony G. et al., *Science, 2016*

Neuroscience

New insights into the development of Alzheimer's

A research team led by Wim Annaert has presented new insights into the roles of different γ-secretases in the development of Alzheimer's disease.

The accumulation of the short protein fragment amyloid-β into amyloid plaques is a known pathological hallmark of Alzheimer's. These protein fragments are generated by secretases, enzymes that cleave proteins into smaller pieces.

Slightly different forms of γ-secretases exist and this study now demonstrates that they are active in different parts of the cell. In contrast to the γ-secretases that contain the presenilin1 protein and are localized at the cell membrane, γ-secretases containing presenilin2 are active in lysosomes.

Hence, presenilin2-γ-secretase not only cleaves other types of proteins but, because of its localization, it generates a pool of intracellular Aβ, including the longer and more toxic forms of Aβ.

Remarkably, it was completely unanticipated that the existence of slightly differently composed γ-secretases could contribute to two different pools of toxic Aβ species.

This study provides a foundation for developing new cellular and *in vivo* disease models, allowing researchers to address the contribution of intracellular Aβ accumulation to the development of Alzheimer's, particularly in the early stages.

Sannerud R. et al., *Cell, 2016*

Catching a tumor in a spider's web

New research at VIB's Switch Laboratory has revealed a novel designer molecule that inhibits a well-validated cancer driver through the mechanism of amyloid formation. This work demonstrates that amyloid structures can be used to develop an innovative class of biotechnological molecules that are able to fight a wide array of diseases.

Proteins in boiled eggs, beer foam and spider silk all share a similar structural element: amyloid. These structures are active in humans as well, playing a role in processes such as melanin production and cellular hormone storage. However, amyloids are also associated with diseases like cataracts, Alzheimer's and blood clotting disorders. The Switch Laboratory, led by Frederic Rousseau and Joost Schymkowitz, has now invented a design principle that could be used to destroy the function of virtually any protein based on the properties of amyloids.

The first validated result of this new technology is called vascin, a designer amyloid that targets a well-known player in cancer metabolism. The way it works could be compared to "catching tumors in a spider's web". By artificially imitating the formation of protein clumps, the target molecule can be inhibited.

Because these principles apply to virtually any protein, this approach may be useful not only in developing future cancer therapies, but also in treating drug-resistant infections.

VIB's tech transfer team is already exploring the next steps to translate this groundbreaking technology, branded Pept-in™, into direct benefits for patients.

Gallardo R. et al., *Science, 2016*

Children of a parent with frontotemporal dementia or ALS have increased risk at a younger age

The most common genetic cause of the brain diseases frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS) is a mutation in the C9orf72 gene. Researchers, headed by Christine Van Broeckhoven, have demonstrated that if an affected parent passes on this mutation, the children run a higher risk of being affected at a younger age than the parent. This research is based on the team's previous results, which showed that the same C9orf72 mutation leads to both FTD and ALS (Gijselinck I. *et al*., The Lancet Neurology, 2012). As this mutation occurs in a substantial group of ALS and FTD patients, it is important to extract as much knowledge about the mutation and the disease process as possible.

The mutation in C9orf72 consists of a repetition of a short DNA sequence GGGGCC which can expand up to several thousands of repetitions in patients. The previous study demonstrated that the age of onset is determined by the number of GGGGCC repeats: the more repetitions, the earlier the age of onset. In C9orf72 families in which the affected parent had a late age of onset and their affected children an earlier age of onset, the researchers provided evidence that the GGGGCC repeat in the C9orf72 gene expanded from a short sequence of repeats (less than 200) to a long one (more than a thousand).

A new clinical study on 36 C9orf72 families analyzed the age of onset in patients from two to four generations. The research revealed that there was a significant difference in the ages of onset between successive generations. In most families, the children were affected by the disease at a younger age, but there were no indications that the disease was progressing more quickly. Additionally, in families with both FTD and ALS patients, if the parent had FTD the child was more likely to have FTD, and a similar principle applied to ALS.

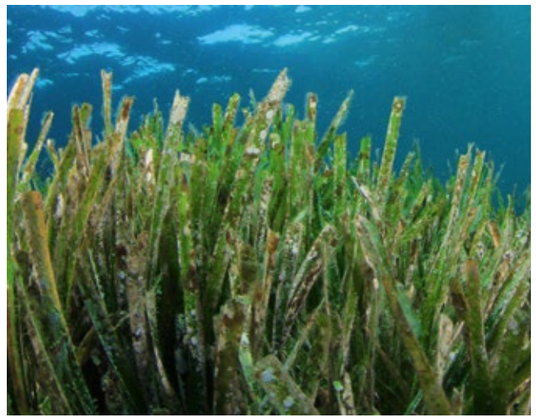
Gijselinck I. et al., *Molecular Psychiatry, 2016*

Van Mossevelde S. et al., *JAMA Neurology, 2017*

Plant Systems Biology

Seagrass genome study to boost ecological insights into marine ecosystems

Seagrasses provide the foundation of highly productive ecosystems which can be found along the coasts of all continents except Antarctica. In colonizing sedimentary shorelines of the world's oceans, seagrasses found a vast new habitat free of terrestrial competitors and insect pests, but they had to cope with new structural and physiological challenges related to full marine conditions. An international research team completed the first comprehensive genome analysis of *Zostera Marina*, the most widespread seagrass species throughout the temperate northern hemisphere. By sequencing *Z. marina*, the researchers gathered unique insights into the genomic gains and losses that helped it to achieve the necessary adaptations for a marine lifestyle. To begin with, the seagrass species lost the entire repertoire of stomatal genes. Inhabiting a light-attenuated, submarine environment, *Z. marina* also lost ultraviolet resistance genes — used to sense and respond to UV damage — along with the phytochromes related to light detection.



Having unraveled the genomic basis of *Z. marina*'s complex adaptations to life in ocean waters, these findings can advance ecological studies on how marine ecosystems might change due to global warming.

Olsen J.L. et al., *Nature, 2016*

Where death is a new beginning

Plant roots may be less obvious than the more visible flowers and leaves, but they are no less important to the plant. The roots anchor the plant in soil, take up nutrients and water, and support a soil ecosystem that profoundly impacts plant growth. Understanding the molecular framework that drives root branching helps to design strategies to improve crop root systems.

As plant roots grow through the soil, lateral roots branch out to reach more water and nutrients. The tip of the growing root is covered by a root cap. The root cap senses the nutrient and water status of the soil the root is traversing, as

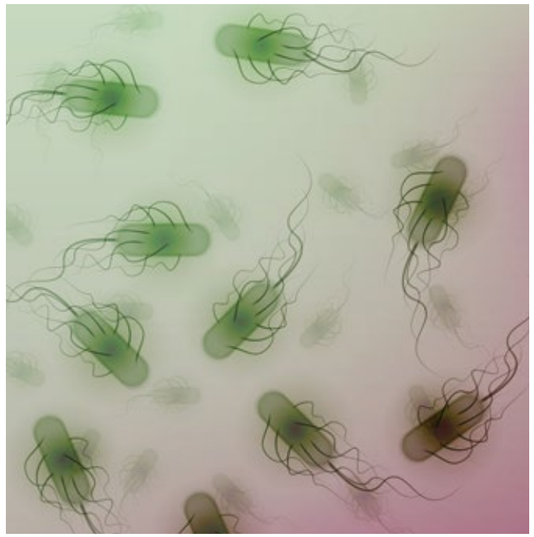
well as obstacles it may encounter, and directs root growth accordingly. The research team of Tom Beeckman showed that cycles of programmed cell death in the root cap of *Arabidopsis* drive the patterning of lateral root formation. Their findings suggest that the location at which a lateral root develops is predefined by specific root cap cells that periodically die off as a group, hereby releasing signals to the surrounding root tissues.

Xuan W. et al., *Science, 2016*

Structural biology

Researchers take a new step towards non-antibiotic bladder infection therapies

A cross-border team of scientists has gained fresh insight into the development of bladder infections, also known as cystitis. *Escherichia coli* – the main bacterial cause of cystitis – has been found to use two complementary types of hair-like structures or pili to adhere to bladder cells, depending on the inflammation state of the tissue.



The importance of type 1 pili for the attachment of *E. coli* to healthy bladder cells and the onset of cystitis is well known. VIB researchers, guided by Han Remaut, explored the workings of another *E. coli* pilus type, called "F9" pilus. They set out to identify the binding sugars used by the bacterium's F9 pili to adhere to bladder cells and, together with a team led by Scott Hultgren at cWIDR (USA), showed that these receptors become exposed on the bladder surface as the infection develops and causes bladder inflammation. When the pili were not present, the *E. coli* had a 10000-fold disadvantage in holding on in the bladder during late stage or chronic bladder infections. Consequently, *E. coli* bacteria appear to have a complementary pair of pili utilized for bladder interaction during early and late stages of infection. The bacterium can thus anticipate infection-induced changes in the bladder tissue.

The use of F9 pilus inhibitor molecules may be particularly interesting during advanced urinary tract infections. A critical next step would be to get urinary tract tissues from patients and find out if there is a parallel between the observations we made in mouse models and bladder infection in humans. In time, this could help to find new inhibitor molecules that could be used as therapies when antibiotics are no longer efficient.

Conover M.S. et al., *Cell Host Microbe, 2016*

Scientists track down possible new treatment for epilepsy

Groundbreaking research into the molecular mechanisms underlying pathologies such as epilepsy has revealed that increasing the concentration of specific fats in the brain could suppress epileptic seizures. This finding is the result of a cross-disciplinary collaboration between the groups of Patrik Verstreken, specialized in brain research, and Wim Versées, specialized in structural biology.

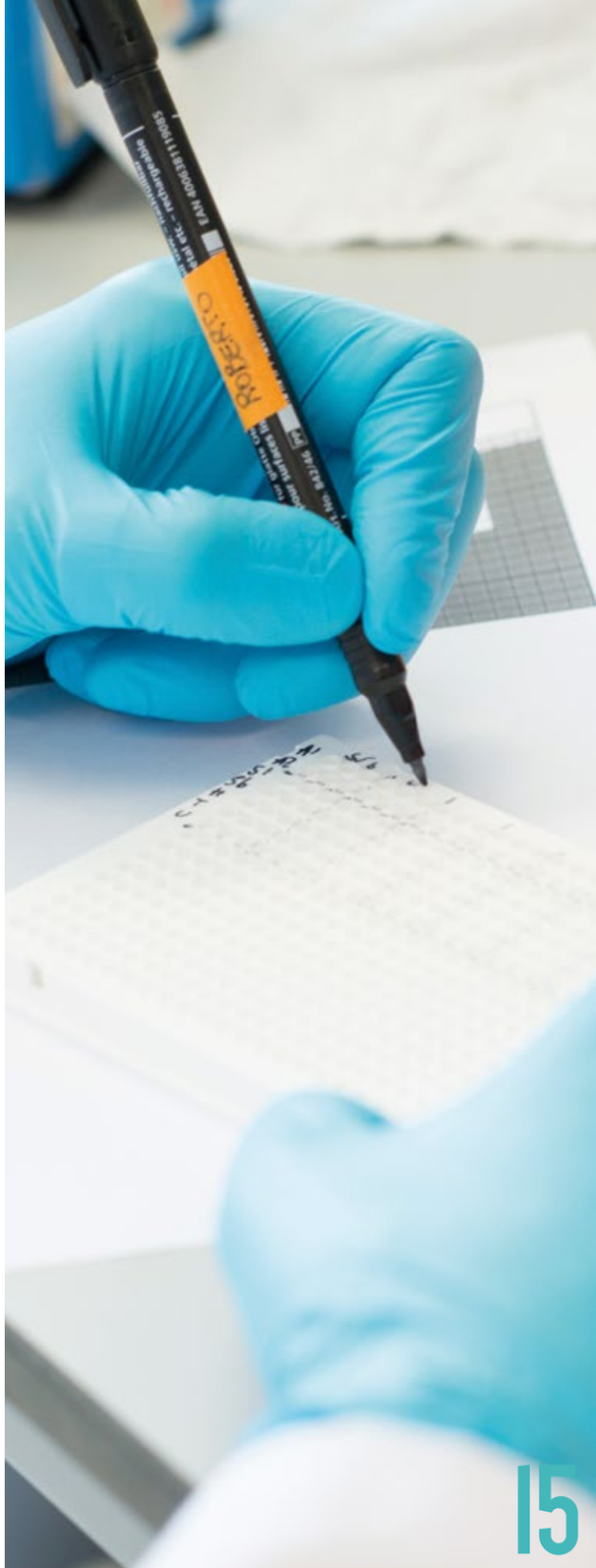
Earlier research involving fruit flies had already demonstrated that a protein known as 'Skywalker' plays a crucial role in maintaining communication between brain cells. An almost

identical protein operates in the human brain under the name "TBC1D24", a genetic mutation of which causes a deviation known as the DOOR syndrome.

By joining forces, the scientists were able to figure out the three-dimensional structure of Skywalker, making it possible to study the protein in atomic detail and giving them completely new insights into its precise function. They also discovered that the human protein TBC1D24 connects with specific brain fats. And more importantly, this connection is impaired in over 70% of patients with a TBC1D24 mutation.

Based on this discovery, the scientists increased the concentration of specific brain fats in fruit flies with a Skywalker mutation and observed that the epileptic seizures in the sick fruit flies were completely suppressed. This means that increasing specific brain fats at the synapses of patients with a TBC1D24 mutation is a possible strategy for preventing epileptic seizures. Although this research focuses on people with TBC1D24 mutations, one can assume that these findings could be relevant to various forms of epilepsy.

Fischer B. et al., *Nature Structural & Molecular Biology, 2016*



SCIENCE MEETS TECHNOLOGY

TECHNOLOGY AS DRIVER OF WORLD-CLASS SCIENCE

There is no doubt that scientific breakthroughs depend not only on interdisciplinary collaboration, curiosity-driven research and creativity, but also to a large extent on technological advancement. We realize how important it is for our scientists to have access to technological expertise and state-of-the-art infrastructure.

VIB's culture of dedication to innovation is distinguished by two focal points: Tech Watch and institutional Core Facilities.

Tech Watch: assessing the potential of technologies

The task of our Tech Watch team is to observe, track and assess emerging technologies from a wide field of life sciences disciplines. They identify scientific and technological innovations with the potential to accelerate our basic research. Several programs have been established allowing VIB scientists to gain privileged access to hi-tech opportunities, by exploring pre-commercial, prototype stage technologies, granting access to recently commercialized technologies or supporting them to develop new technology platforms.

Over the years, the team has built an extensive network of technology companies and every year it assesses thousands of innovations. After an initial evaluation, the team selects a few technologies that show the most potential, which are then subjected to thorough and detailed testing.

Competitive edge

The Tech Watch team also negotiates specific agreements for technology access with a large number of companies, giving our scientists a competitive advantage. One example of such an innovative technology is the 10x Genomics' Chromium™ Instrument which is currently being tested by several VIB groups. The instrument has many uses but is mainly being used as a tool for single-cell RNA-sequencing (scRNA-Seq). This technology is emerging as a key technology in genomics, providing a better understanding of the function of an individual cell in the context of its micro-environment. scRNA-Seq yields extremely rich and fine-grained data sets, which can be used to interrogate cellular heterogeneity. Many VIB research questions can now be addressed through access to this innovative instrument.

In addition to boosting omics research at VIB during 2016, Tech Watch also catalyzed the use of Genome Editing

technologies. Many CRISPR-libraries as well as CRISPR-modified cells and mice were generated with support from Tech Watch. Given the breakthrough potential of CRISPR to catalyze life sciences research, we expect that Tech Watch can further leverage this technology to sustain VIB's growth for years to come.

Institutional Core Facilities: providing expert services

The institutional cores are one of the flagship initiatives of VIB, providing scientists with sophisticated and expensive technologies and infrastructure which individual research groups would be unable to manage, let alone afford. By offering cutting-edge equipment, expertise and experience, the cores make it possible to execute technology-demanding and interdisciplinary projects. Their expert staff team up with our researchers to help them to achieve their scientific ambitions.

In 2016, the cores further strengthened VIB's portfolio by investing in several high-end infrastructure settings, including the PacBio Sequel, several new microscopes, a HPF module and a state-of-the-art mass spectrometer, etc. With the launch of the Metabolomics core, our omics activities now span almost the complete spectrum and together offer the potential for multi-omics profiling studies.

Together is better

The VIB Core Facilities are engaged in several type of excellence-based partnerships. At regional level, they co-invested in state-of-the-art screening and proteomics infrastructure together with Cancer Research Initiative Ghent (CRIG). At European level, they continued to benefit from active involvement in Core for Life (C4L), where they have built several benchmark tools to further improve respective omics pipelines.

In July 2016, a landmark paper was published with the C4L colleagues in EMBO Reports, entitled "Institutional core facilities: prerequisite for breakthroughs in the life sciences".

SCIENCE MEETS BUSINESS

INNOVATION AND ENTREPRENEURSHIP GO HAND IN HAND

People in and around VIB are well aware of our mission: basic research as a starting point for tangible solutions that benefit society. But translating a novel finding or technology into an innovative drug or agricultural application doesn't happen overnight. VIB's tech transfer team translates research results into new economic ventures which, in time, lead to products that can be used in medicine, agriculture and other applications.

Patent portfolio: VIB as innovator

Our groundbreaking research often leads to inventions. The process of tech transfer starts with safeguarding these inventions by means of Intellectual Property Rights.

Patent applications are often used as a measure of innovation. In 2016, VIB's IP Management team submitted 42 new priority applications. VIB's current patent portfolio contains 252 active patent families with commercialization potential, while 37 patent families have already been transferred to VIB start-ups and other companies.

Collaborations with industry: VIB as business partner

The rise of the global knowledge economy has intensified the need for strategic partnerships between research institutes and industry. In order for these collaborations to be successful, they should be based on long-term relationships that merge the discovery-driven culture of VIB and the innovation-driven culture of life sciences companies.

Over the years, VIB has developed a vast network of reliable business partners. In 2016, we generated a turnover of 13.3 million euro through industrial activities. We signed 137 partnership agreements with industry partners, 47% of which are located in Flanders. Thanks to industrial investment, we employed 73 VIB knowledge workers (full-time equivalents).

VIB as creator of start-ups

Tech transfer offices of universities and research institutes play a central role in the biotech ecosystem, as many young start-ups aspire towards the successful commercialization of an academic discovery. At VIB, entrepreneurship has almost become second nature and, as a result, we have an impressive track record in creating successful start-up companies.

VIB has been involved in starting up 19 companies since its inception. These include 12 venture capital supported companies, 3 non-venture capital supported enterprises, 2 real estate initiatives, the FlandersBio trade association and the V-Bio Ventures investment fund. In total, these ventures employ 706 people and have raised 930 million euro in capital investments.

In 2016, VIB founded one start-up company, Aphea.Bio. Aphea.Bio positions itself as a technology platform company focused on the identification of micro-organisms that have a positive effect on plant health (abiotic stress) and crop yield, and which can be used as biostimulant and/or biocontrol agent.

Exits

In February 2016, the VIB-UGent spin-off Q-Biologicals was acquired by Amatsigroup (FR) in order to strengthen their product offering for the pharmaceutical and biotech industry. Q-Biologicals focuses on production and purification of biologicals.

VIB as catalyst for biotech ecosystem

- **V-Bio Ventures**

  In December 2016, V-Bio Ventures announced the final closing of its V-Bio Ventures Fund 1 ARKIV ("V-Bio Ventures") fund, with over 75 million euro in capital commitments. This successful fundraising makes V-Bio Ventures one of the largest European first-time life sciences investment funds.

  V-Bio Ventures is a dedicated life sciences venture fund that identifies, builds and finances start-up and early-stage companies with high growth potential. V-Bio Ventures has a close working relationship with VIB, one of the founders of this fund. V-Bio Ventures will continue to focus on investments throughout Europe in biopharmaceutical, pharmaceutical, diagnostics and agricultural sectors, and will build a portfolio of companies drawn from VIB's research pipeline and elsewhere.

- **Attracting foreign companies**

  Flanders has a well-established track record of discoveries and innovation in biotechnology. As a result, several Flemish biotech companies have become key players on the international market. Together with FlandersBio, VIB is considered one of the main drivers of the local biotech ecosystem. This success also reflects abroad and draws international companies to Flanders. VIB has successfully supported a number of companies that have settled in Flanders, which now employ up to 470 people and have raised 569 million euro of capital investments.

In 2016, two concrete inward investments were realized through the mediation of the Flanders Welcome Team Life Sciences (with representatives from VIB, FIT, VLAIO and FlandersBio). The first is Octimet Oncology. This company acts as a translational accelerator, creating value for investors and patients by providing rapid clinical proof of concept for cancer therapies through innovative clinical development strategies and patient-centered biomarker approaches. Octimet Oncology is located at the Janssen Innovation Campus in Beerse. The second business is Softhale, a company established in Diepenbeek. Softhale develops innovative medical products to optimize administration of medication mainly for the treatment of asthma and COPD.

VIB Discovery Sciences builds confidence with data

Translating findings into concrete solutions for patients and consumers is one of VIB's key drivers. To increase the success rate of translational research, VIB has endorsed the start of a strategic initiative called "VIB Discovery Sciences".

Translating basic life sciences research data into drug and agro-biotech innovations is an unpredictable process: while the potential societal gain is high, the success rate is often frustratingly low. At an early stage, the private sector is hesitant to engage in a business venture because the uncertainties are high. They insist on robust target validation, e.g. evidence that modulating specific therapeutic targets will lead to beneficial effects. However, companies often lack the depth of expertise in basic biology that we have within VIB. And naturally, for-profit players make their decisions based on an estimation of profitability. At VIB, we aim to address unmet societal needs and seek the relevant companies or not-for-profit partners such as charities to advance such projects.

SCIENCE MEETS PEOPLE

PUBLIC ENGAGEMENT

We strongly believe in an interactive approach to keep the public abreast of what we do at VIB. Public engagement helps to maximize the flow of knowledge and learning between our institute and society. It can help to build trust and mutual understanding. By communicating openly, we can address concerns about certain controversial topics such as the use of animals in research. It is also a way to involve the public with our scientific work.

We have developed several initiatives that target various audiences. On the one hand, we hope to inspire schoolchildren and their families to take an interest in life sciences. We aim to convince policymakers of the impact of our research and the need for public funding, and to demonstrate our groundbreaking research to peers in academia and industry.

On the other hand it is important for our scientists to be part of public dialogue and debate, as their research touches upon our daily lives in many ways. Public lectures and meetings with patient organizations help to build genuine understanding and appreciation. They also encourage people to become actively involved in our research by, for example, donating blood or stool samples.

New VIB logo: enhancing VIB's brand to strengthen our reputation

In 2016 we launched our new brand identity, which encompasses all VIB centers and cores and makes us recognizable as one research institute. This strong and consistent institutional brand allows us to project one and the same image to all stakeholders and thus reinforce our position as a world-leading center of excellence in life sciences research.

VIB Conference Series: sharing knowledge with peers

The VIB Conference Series unites the best speakers in their specific field of science or technology, who share their views on the latest trends in life sciences. The series attracts an international audience from both academia and industry. Meanwhile, VIB conferences have earned an excellent reputation and are attended by a growing number of participants. In 2016, we organized five conferences in total. Two of these were Tools & Technologies conferences – one on Genome Engineering & Synthetic Biology and the other on Advances in Cell Engineering, Imaging & Screening. The rest were Science conferences: Applied Bioinformatics in Life Sciences, The Brain Mosaic, a conference in the field of neuroscience, and, last but not least, a Cell-VIB symposium on the Hallmarks of Cancer.

20 years of VIB: celebrating two decades of excellent research

In October last year, we celebrated our 20th anniversary in style. We organized a symposium called "Science meets life" at BOZAR, Brussels. The symposium addressed the importance of life sciences research and its impact on society, industry and our future in general. It highlighted the consecutive steps in the process of translating results of basic research into viable products and solutions. Speakers from different walks of life shared their views on the importance of scientific research. The day ended with a festive concert conducted by Dirk Brossé, who composed a musical piece for the occasion: "The DNA of music".

Biotech tour: bringing VIB research to town

The VIB Biotech tour was a captivating exhibition bringing VIB research and tech transfer closer to people. The exhibition visited five major cities in Flanders over a period of five months. We went from university campuses to hospitals, from libraries to cultural centers. In each of the cities in which we have a partner university, we organized a biotech talk, during which VIB researchers discussed citizen science, how to address challenges such as healthy living and sustainable food production, etc. Both the exhibition and the talks attracted an interested audience and often led to lively discussions.

Commitment to our teams

Creating a stimulating environment

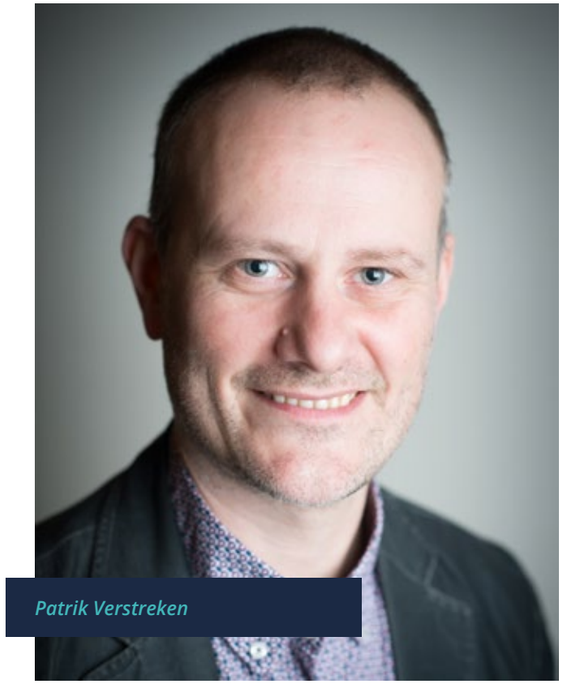
Scientists who embark on a career at VIB do not just have access to state-of-the-art facilities and the most innovative technologies. They can also rely on the necessary training and support in every step of their career. We believe that it takes more than an academic degree to become an excellent scientist. That is why, in addition to science and bioinformatics courses, Training at VIB also provides a series of courses that focus on soft skills. A coaching program addresses personal and professional development in individual sessions tailored to specific needs, while skills training sessions concentrate on transferable skills ranging from research ethics to preparing for a grant overview.

Strong leadership to inspire extraordinary results

As part of VIB's strategy for the future, the research groups were re-clustered into thematic Research Centers to stimulate a multidisciplinary approach and increase cross-pollination and interaction between researchers. This will reflect positively in VIB's international and societal impact.

Strategic leadership and scientific mentorship will be required to ensure that collaboration across borders is encouraged and that the decision-making process follows a bottom-up approach.

And who better to share their views and ideas than some of our "new" science directors?



Patrik Verstreken

Patrik Verstreken – Science Director,
VIB-KU Leuven Center for Brain & Disease Research

The mission of our center is to force a breakthrough in the cure of neuronal and neurodegenerative disorders. To get there, we need a thorough knowledge of normal brain function, the determination to turn this into a solid understanding of disease mechanisms, and the facilities and know-how to translate basic research into new therapies.

I believe that truly innovative research in translational medicine emerges where excellent basic research and medically-oriented research meet. Therefore, it's no coincidence that our center is home to world-leading experts in both fields. This standard of expertise is embedded throughout our organization, which leads to excellence on all levels.

Neurological diseases are becoming a major problem for developed economies. As a result, translating basic research findings into tangible solutions is of great importance. To smoothen this transition, our center teams up with different stakeholders such as patient organizations, clinicians, the life sciences industry, etc.

I am also convinced that technological development is one of the major drivers of scientific research. It goes without saying that we will continue to invest in disruptive technologies and world-class technologists.

I will continue to build and expand a vibrant, ambitious and interactive community in neurosciences; an environment that fosters cross-disciplinary collaboration.

Diether Lambrechts and Chris Marine – **Science Directors, VIB-KU Leuven Center for Cancer Biology**

Our mission is to gain better insights into the biology of cancer initiation, progression and the spread of cancer cells with the ultimate goal of developing more effective and specific anti-cancer therapies. One of our major research focuses is to understand how conditions within the tumor environment influence tumor cells, and vice versa.

To reach this ambitious goal, our top priority will be excellence in curiosity-driven research. We will advocate the highest quality research. This will not only be reflected in highly-cited publications in top journals, but also in the international recognition and visibility of our researchers.

We firmly believe that the best possible cancer research can only be done in close cooperation with clinicians, as this gives us access to primary cancer samples and these collaborations will enable us to translate our basic research findings into relevant applications. Our close proximity to the UZ Leuven university hospital is definitely a major advantage for us.

Having access to cutting-edge technologies is also essential for pioneering research. By re-clustering all cancer groups in our newly formed center, we have created a significant portfolio of state-of-the-art technologies and expertise, which is available to our scientists.

We will also actively seek to exploit valorization opportunities such as the validation of novel diagnostic or predictive biomarkers in phase 2/3 clinical studies with pharmaceutical companies. In close cooperation with VIB's tech transfer team, we will consider the possibility of developing some of our scientific breakthroughs into start-up companies.

Chris Marine and Diether Lambrechts

We see the co-directorship as an added value for our center. As we started our VIB career in different research groups, we have distinct cultural and scientific backgrounds, which means that we have complementary expertise and management skills. However, we share the same management principles: we believe in a horizontal management structure and hope to engage our group leaders in decision making. We also think that the research groups will benefit from efficient administrative support and the implementation of a budget model that encourages and rewards highly productive group leaders and innovative research lines.

Kevin Verstrepen – **Science Director, VIB-KU Leuven Center for Microbiology**

The center for Microbiology is composed of diverse research groups, each approaching microbes from different complementary angles – from infectious diseases to model systems, from molecular biology to systems biology, and from wet-lab experiments to computational approaches.

Our center's research focuses on three main areas. Firstly, we use microbes as model systems to unravel the basic principles of life. Secondly, we study how microbes cause disease and how we can fight these pathogens. Thirdly, we aim to generate novel and superior microbes for industrial applications, for example the production of food and biofuels.

My job as science director comes with a few challenges, but the flipside is that there are also a lot of fantastic opportunities. On an organizational level, my aim is to implement a management style based on strong and fully independent group leaders who each lead their own research and govern their own budgets. Importantly, we will also foster bottom-up collaboration, interaction and entrepreneurship. Apart from strong basic science, tech transfer is one of the major strengths of our center. One of my ambitions is to keep scientific output and industrial income above VIB targets and international benchmarks. The creation of a new start-up would, of course, be an added bonus.

Kevin Verstrepen

A last major goal is to improve interaction between research groups, not only in my own center, but also with other VIB groups and beyond. I firmly believe that working together with scientists from other groups will not only lead to more exciting breakthrough science, but will also increase the visibility of our groups. Therefore, I gave particular support to a few changes in the overall VIB strategy and funding scheme that I believe will reduce competition and increase collaboration between centers.

Jan Steyaert and Han Remaut – **Science Directors, VIB-VUB Center for Structural Biology**

The mission of our center is to study the structure and dynamics of macromolecular complexes to explain their mode of action in health and disease. We integrate our structural biology work with genetic and cellular studies, aiming to bridge molecular and cellular resolution. We want to excel in translating our findings into biotechnological and medical applications.

We think it is true to say that our center is the prime example of how technologies drive innovation, and how multidisciplinary collaboration and interaction between (VIB)

Jan Steyaert and Han Remaut

research groups lead to scientific breakthroughs, which in turn lead to concrete solutions and value for society. The various spin-offs and technologies that have resulted from our research are living proof of the latter.

As co-directors, we live by the same values. Our center should be an equal-opportunity research organization that fosters scientific curiosity, creativity and integrity. In addition to scientific excellence, we promote ethical responsibility, societal accountability and ecological sustainability. We encourage our researchers to be open to dialogue with society and we foster cultural inclusiveness.

Sharing research equipment and facilities are key to creating a stimulating research environment. We therefore encourage our group leaders to contribute complementary technology and expertise to be shared with other research groups within and beyond VIB. One of our ambitious projects is to launch and operate the first cryo-electron microscopy center in Flanders, sponsored by the FWO-Hercules program. This empowering technology allows researchers to study macromolecular complexes in their native context, even tissues, to provide information on the cellular and molecular level and an in-depth structural-functional analysis.

We will create a stimulating environment for tech transfer, allowing our group leaders to translate their findings into concrete applications. Ablynx, AgroSavfe and Confo Therapeutics, the spin-offs that have already been created based on findings of our center, have generated a considerable impact and visibility for our research, so we definitely want to continue on this route.

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	31.12.2016	31.12.2015
Intangible fixed assets	1.151	1.129
Tangible fixed assets	32.970	31.271
Financial fixed assets	22.797	16.066
Contracts in progress	7.169	8.685
Amounts receivable within one year	12.963	16.127
Investments	53.422	55.572
Cash at bank and in hand	16.942	14.584
Deferred charges	12.106	14.709
TOTAL ASSETS	159.520	158.143

LIABILITIES		
Allocated funds	71.660	70.144
Investment grants	30.334	28.030
Amounts payable after one year	6.045	6.785
Amounts payable within one year	43.101	41.704
Accrued charges and deferred income	8.380	11.480
TOTAL LIABILITIES	159.520	158.143

PROFIT AND LOSS STATEMENT

(€ THOUSANDS)

	2016	2015
OPERATING INCOME	84.853	87.195
Turnover (from contract research)	23.634	24.865
Contracts in progress (+/-)	-1.516	800
Grants and subsidies	60.401	59.721
Other income	2.334	1.809
OPERATING EXPENSES	-84.723	-83.573
Raw materials and consumables	-7.431	-8.263
Services and other goods	-21.124	-21.113
Remuneration, social security costs and pensions	-47.133	-45.704
Depreciation	-8.070	-7.853
Other operating expenditures	-965	-640
FINANCIAL INCOME	1.152	1.435
FINANCIAL CHARGES	-447	-786
EXTRAORDINARY INCOME	926	14.531
EXTRAORDINARY EXPENDITURE	-245	-9.245
PROFIT/LOSS FOR THE FINANCIAL YEAR	1.516	9.557

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 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

VIB

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