Enabling great science

Great science needs great minds, and these great minds need a stimulating environment to thrive. And what is great science if its results do not find their way to products and solutions that can help to solve some of the world’s challenges in healthcare and agriculture? This is reflected in the vision of VIB, as we firmly believe that breakthrough research in the molecular mechanisms of life will lead to a better quality of life, economic growth and sustainable societal well-being.

So, this brings us to the four important pillars of VIB which encompass science, technology, business and people.

Science meets science

Conducting world-class science is the foundation of VIB’s livelihood. To keep up VIB’s level of excellence, we attract the world’s most talented researchers and ensure that they have the best possible working environment. This environment entails far more than state-of-the-art tools and technologies; we are convinced that a diverse workforce contributes immensely to great science. That is why VIB seeks to attract the most brilliant people, regardless of age, gender, religion, or nationality. The dynamics of diverse teams can lead to new perspectives and creative insights that in turn can lead to breakthrough science. For the years to come, diversity – and in particular striving towards the right gender balance – will remain one of the key issues to address at VIB.

Science meets technology

VIB scientists have access to the most advanced technologies on the market, even before they are commercially available. We know that this is one way of keeping our researchers one step ahead of the competition. VIB’s Tech Watch team scouts the market for the most disruptive technologies to give our scientists the best possible competitive advantage. The Core Facility Program ensures that high technology access is made sustainable; it sees to it that the VIB research community can rely on high-end equipment supported by expert technologists to guide VIB research teams in every step of their research.

Science meets business

Over the years, VIB has shaped the biotech ecosystem, not only in Belgium, but far beyond. VIB’s Innovation & Business team takes technology transfer to heart and explores all the possible avenues to bring research results to the market. They guide researchers every step of the way, be it by negotiating R&D agreements and licensing agreements with industry or, in the best scenario, by creating a new start-up company. VIB’s start-up record shows that it has been very successful with 20 blooming young companies that confirm this business development strategy. The team has also attracted a good number of foreign companies to set up operations in Belgium. In 2018, Inari Agriculture and MouSensor have decided to establish business in Randers.

Science meets technology

The research results of 2018 are a testimony to the success of this approach. VIB has taken great strides in all its research disciplines. If we are to highlight just a few breakthroughs we can say that VIB researchers have shed a new light on immunotherapy and treatment of cancer, new treatment strategies for neurodegenerative diseases and novel mechanisms in plant development and growth. We invite you to read more in the chapter on VIB’s research where you will find an overview of some of VIB’s most impactful publications.

In 2018, the first projects were launched in the framework of VIB’s Grand Challenges program, which was introduced to increase VIB’s global impact on science and society. This program is designed to support disruptive translational projects, starting from real needs and problems. Based on intensive and continuous interaction between scientists from different expertise fields, we search for practicable solutions with maximum social impact. To keep up the momentum, a new call for projects was launched in June 2018.

Science meets people

Great science cannot be accomplished without investing in people and their well-being, but it also leads nowhere if it is not communicated to a variety of stakeholders.

In addition to several measures to ensure diversity through all its levels, VIB has a comprehensive training program to keep all colleagues up to speed, whatever their background or function. At VIB we think it is important that all our colleagues can benefit from continuous training to shape their skills and competences to develop their career. We give all our staff ample opportunity to invest in their self-development; we believe that this will contribute to a feeling of well-being which will benefit the organization in general.

And last but not least, VIB wants to be part of the public debate about biotech. In 2018, especially the CRISPR-ruling by the European Court of Justice caught the eye of the media. Consequently, VIB took the lead in a European-wide action to build awareness, addressing both the public at large and policy makers. In addition, VIB also showcased its research and tech transfer successes at several events.

At VIB we go the extra mile to create a thriving environment for our scientists and all the people who support them in doing world-class research. Together we achieve excellence, together we are VIB.

Ajit Shetty, Chairman of the Board of Directors
Jo Bury and Johan Cardoen, Managing Directors
At VIB, we continuously invest in creating an effective research environment that fosters successful and performant world-leading research. Such an environment does not only consist of state-of-the-art infrastructure and access to the latest technologies, but it also heavily relies on the right behaviors, a collaborative attitude and good governance. Research excellence is underpinned by a culture of integrity, suitable development opportunities for scientists and safe working conditions.

Since its inception, VIB has forged strong relationships with the Flemish universities to initiate and develop multi-disciplinary efforts that address key challenges in both fundamental and applied research. VIB’s eight thematic research centers are thriving science hubs that unite the best scientific minds. VIB pools world-class biotechnological knowledge and facilitates both internal and external collaborations between its centers, the industry, and other research institutions. VIB actively encourages technology transfer and supports its researchers in converting their findings into potential products for various markets. The Innovation and Business team provides key support in creating platforms and access to the latest technologies, and performant world-leading research. Such an environment that fosters successful research quality however can only be ascertained by peer review.

Projects selected in the second call could receive financing to obtain a maximal impact over the different thematic areas. In June 2018, the Grand Challenges program launched its second call for project applications. Via new calls VIB strives to obtain a maximal impact over the different thematic areas. Projects selected in the second call could receive financing as early as the third quarter of 2019.

In 2018, three research projects were selected which are in full swing:
- Pointillism, improving immune response of the tumor microenvironment
- Sustainable agriculture
- Epidemic control

In the frame of the ‘grand challenges strategy’, VIB seeks to stimulate international, transdisciplinary, multi-institutional collaborations with external partners.

Despite addressing wide-ranging challenges that impact society on a global scale, the program will be funded bottom-up, with scientific directors proposing the best candidate project out of their respective center and going through a dedicated two-step review procedure with external experts in the field scoring the projects and a high-level transparent governance group proposing a final consensus selection to the Board.

The Grand Challenges program is inspired by the 17 sustainable development goals determined by the United Nations. More specifically, through the Grand Challenges program, VIB seeks to contribute to the ‘zero hunger’, ‘good health and well-being’ and ‘climate action’ goals. As a result, projects in the following fields are actively encouraged:
- Innovative biomarkers
- Innovative treatments
- Targeted treatment strategies
- Epidemic control
- Sustainable agriculture

In 2018, three research projects were selected which are in full swing:
- Overcoming the main current diagnostic challenges in hepatology practices
- Translational science initiative on primary immune deficiencies
- Pointillism, improving immune response of the tumor microenvironment

In each of these projects, various VIB groups collaborate with several external partners from universities and university hospitals across Flanders. This form of cooperation ensures that new hypotheses can be tested starting from observations, issues and needs from practice, leading to new insights that can concomitantly be validated in a clinical setting with the final aim to result in benefits for patients.

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Supporting research excellence
To maintain the highest standards in research, VIB has established clear policies, procedures and practices to support its researchers. A first example of this is VIB’s international grants’ office, which was kicked off in May 2018, to bundle expertise and boost all activities related to international grant applications at VIB. In close collaboration with the grants pilot teams in the centers, this international grants’ office has already set up several new activities such as ERC Concept brainstorm meetings well in advance of European Research Council (ERC) deadlines, hands-on workshops on ‘how to write a successful grant application’, etc. The team supported 19 ERC and 37 MSCA (Marie Skłodowska-Curie actions) applications with a success rate of 2 to 3 times the EU average. The office is currently developing a strategy to maximize the return from the upcoming Horizon Europe as well as other major international funding bodies.

VIB’s Science and Technology team has set up standards for monitoring and benchmarking our research to measure the impact of VIB’s science output. While key performance indicators provide the metrics to gauge scientific impact, research quality however can only be ascertained by peer review. Each VIB research center has a high-quality scientific advisory board (SAB), specialized in the research domain of the center and the research groups involved. At least once every two years, within VIB’s 5-year cycle, an on-site visit by the SAB is scheduled for each VIB research center. As such, four research centers were peer reviewed in 2018.

Informing policy makers in Flanders and beyond
VIB goes to great lengths to inform policy makers of the latest developments in biotechnology so that they can take decisions based on scientific facts rather than perception. A prime example that shows the importance of this is the ruling of the European Court of Justice (ECJ) in July 2018, in which it states that organisms obtained by gene editing techniques, such as CRISPR, are in principle subject to the same regulations as GMOs. According to VIB plant researchers, this ruling puts sustainable agriculture in Europe at risk. Since the ruling, VIB has taken the lead among other European research institutes to engage with policy makers and politicians at all levels and to provide them with crystal clear information on genome editing, and CRISPR in particular. In October, VIB issued a position paper on CRISPR, which has been officially endorsed by 100 institutes and 785 individuals.
VIB devotes substantial attention to the practical implications of the research that is being done in its centers. Clinical applications, business collaborations, and spin-off creation are aspects that are continuously developed in close contact with various units at VIB headquarters.

All this, however, is driven first and foremost by the world-class scientific research that is being done by VIB scientists. Their work is internationally renowned and is regularly recognized as cutting-edge. To showcase the pioneering research VIB scientists dedicate themselves to, the following selection of papers will give you a birds-eye view of the scientific landscape uncovered in ever more detail at VIB.

**Immunology**

**An ID card for immune cells**

Macrophages are a type of white blood cells that attack foreign particles. They are an essential part of our immune system. This group of immune cells is characterized by great diversity.

The group led by Martin Guilliams, recently found a conserved feature shared by all macrophages: the expression of the transcription factor ZEB2, a protein that controls the transcription of genetic information from DNA to messenger RNA. They used mouse models to show that loss of ZEB2 led to the disappearance of macrophages from different tissues. In other words, ZEB2 ensures that macrophages maintain the identity they need in the tissues they protect.

Scott et al., Immunity, 2018

**Attacking multiple targets in the fight against asthma**

Asthma is a chronic inflammatory airway disease in which airways become inflamed, narrow and swollen and produce extra mucus, which makes it difficult to breathe. In clinical trials using biologicals against IL-4 receptor (IL-4R) α or IL-5, only a subset of patients with moderate-to-severe asthma responded favorably.

The Lambrecht & Hammad group together with the company argenx are the first to test an approach that uses a single antibody to attack IL4-R and IL-5 at the same time. Using a llama-based antibody platform, they generated two antibodies, one to target IL4-R and one to target IL-5. Next, they introduced both antibodies into a mammalian cell system from which they could isolate a bispecific antibody. This antibody was then tested in a mouse model for asthma. Their results show that such bispecific antibodies target multiple cytokine pathways and act as superior inhibitors of asthma features in comparison to monotherapies.

Godar et al., Journal of Allergy & Clinical Immunology, 2018

**Mechanical stress determines arthritis hotspots**

Many pro-inflammatory pathways leading to arthritis have global effects on the immune system rather than only acting locally in joints. The reason behind the regional and patchy distribution of arthritis thus represents a longstanding paradox.
An alternative pathway for steroids

Steroids are essential. They regulate the fluidity and flexibility of cell walls and serve as signaling molecules during growth and development. The biochemical pathway that leads to steroids is a key component in the evolution of eukaryotes and can be found across the eukaryotic branches in the tree of life. The flavoprotein squalene epoxidase (SQE) catalyzes the first oxygenation reaction in this pathway. However, several eukaryote genomes lack an SQE-encoding gene.

The Goossens & Vandepoele groups discovered and characterized an alternative SQE (AltSQE). AltSQE was identified through the screening of a gene library of the diatom *Phaeodactylum triquetrum* in an SQE-deficient yeast. This discovery provides an alternative element for the conserved steroid biosynthesis pathway, raises questions about eukaryote metabolic evolution, and opens routes to develop selective SQE inhibitors to control hazardous organisms.

Pollier et al., Nature Microbiology, 2018

Medical biotechnology

Fighting tumors with mRNA

Cancer immunotherapy can induce durable antitumor responses. However, many patients remain unresponsive to the current immunotherapies that are based on so-called checkpoint inhibitors. A growing body of evidence indicates that checkpoint inhibitor unresponsiveness correlates with a lack of CD8+ T cells inside the tumor.

The Saelens group described a generic antitumor therapy that is based on the intratumor delivery of mRNA that codes for the necroptosis executioner mixed lineage kinase domain-like (MLK5) protein. This intervention stalled primary tumor growth and protected against tumor formation in mouse melanoma and colon carcinoma models. Moreover, the mRNA treatment...
Structural biology

Ranking receptor activators

In humans, G protein-coupled receptors (GPCRs) are the largest protein family of receptors that detect molecules outside the cell and activate internal signaling pathways and, ultimately, cellular responses. These receptors are structurally very dynamic, which makes it difficult to design small molecules that interact with them to influence, for example, disease processes.

In this study, the Steyaert lab reported on Nanobody®-enabled fragment screening and fragment elaboration for the efficient discovery of GPCR-activating molecules. Their data demonstrate the feasibility to predict the pharmacological impact of a receptor-binding molecule through Nanobody-based methods of screening. This method facilitates the identification of novel therapeutic compounds and represents a cornerstone technology for Confo Therapeutics, a spin-off of the Steyaert lab.

Pardon et al., Angewandte Chemie, 2018

Multifunctional crystals

The formation of condensed (compacted) protein phases is associated with a wide range of human disorders, such as eye cataracts, amyotrophic lateral sclerosis (ALS), sickle cell anemia and Alzheimer’s disease. However, condensed protein phases can also contribute to research and biotechnology as crystals. They are harnessed by structural biologists to elucidate protein structures or used as delivery vehicles for pharmaceutical applications. The properties of crystals can vary substantially between different forms or structures (polymorphs) of the same macromolecule.

A team led by Mike Sleutel used time-resolved cryo-transmission electron microscopy to image crystal development and uncover the pathways that lead to polymorphs. Using this new knowledge, they managed to control the system by selectively forming desired polymorphs. These insights suggest ways of controlling crystal formation, aiding the development of protein-based drug delivery systems and macromolecular crystallography.

Pardon et al., Angewandte Chemie, 2018

A new actor in blood vessel sprouting

Endothelial cells (ECs) line the walls of blood vessels. Emerging evidence reveals that EC metabolism controls the sprouting of new blood vessels (angiogenesis). Recent research suggests that the amino acid glutamine might be important for this process, but its exact role in real-life blood vessel formation is still unclear.

The Carmeliet group sought to elucidate this mystery. They used mice with a deletion in the gene that controls glutamine synthase, a substance that is needed to build glutamine. The mice showed deficiencies in vascular development and during angiogenesis in inflammatory disease. Next, the researchers tested their findings in human umbilical vein cells, which corroborated their results from the mouse model. This also revealed that limiting glutamine synthase decreased the mobility of umbilical ECs. These findings revealed that, in addition to the known formation of glutamine, glutamine synthetase shows unknown activity in endothelial cell migration during pathological angiogenesis.

Eelen et al., Nature, 2018

A mutation that drives disease

The protein LZTR1 is mutated in human cancers and developmental diseases, yet its mechanism of action remains unknown.

That was the starting point for this investigation by the Sablina group. They found that problems with LZTR1 led to the development of Noonan syndrome symptoms in mice. To find out why this happened, the researchers trapped LZTR1 complexes from intact mammalian cells. This helped them discover that the LZTR1 protein associated with RAS, another protein type that is important for cell proliferation. Disease-associated LZTR1 mutations disrupted this association. This new understanding may help to identify patients who might benefit from RAS pathway inhibitors and inform new therapeutic approaches for these patients.

Steklov et al., Science, 2018
To gain insights into the biology of MRD, the Marine group applied single-cell RNA sequencing to malignant melanoma cells isolated from patients. They identified distinct drug-tolerant states, varying combinations of which co-occurred within MRDs from biopsies of patients on treatment. They also found that preventing a receptor called RXRG from functioning reduced MRD. Their data identified key drivers of resistance and illustrated the therapeutic potential of MRD-directed therapy.

Rambow et al., Cell, 2018

**The mutation series of leukemia**

T-cell acute lymphoblastic leukemia (T-ALL) is a common childhood malignancy caused by clonal proliferation of immature T cells. Analysis of T-ALL genomes with various technologies has revealed that 10–20 protein-altering mutations are typically present at diagnosis. However, it is currently unclear in which order these mutations are acquired and in which progenitor cells this is initiated. The Cools lab used targeted single-cell sequencing of total bone marrow cells and progenitor cells for four T-ALL cases. They detected a dominant leukemia cluster at diagnosis, accompanied by a few smaller clusters harboring only a fraction of the mutations. With a graph-based algorithm the group managed to determine the order of mutation acquisition. This study is a powerful demonstration that targeted single-cell sequencing can elucidate the order of mutation acquisition in T-ALL and that T-ALL development can start in a multipotent progenitor cell.

De Bie et al., Leukemia, 2018

**Signals that enhance leukemia development**

Survival rates for T-cell acute lymphoblastic leukemia (T-ALL) are currently close to 90% in children, but adults still have a poor prognosis. Current therapy is associated with both short-term and long-term side effects, especially devastating for children. Therefore, there remains an urgent need to uncover the molecular mechanisms underlying T-ALL in order to identify therapeutic targets and to develop personalized targeted therapies.

The Cools group used a transgenic mouse model and a human cell line to show that a genetic fusion associated with an overexpression of transcription factors is linked to T-ALL. Using integrated ChIP-sequencing, ATAC-sequencing, and RNA-sequencing data, they demonstrated that the proteins TLX1 and STAT5 cooperate to activate genes that may lead to cancer. Their results suggest that targeting these proteins can reduce relevant gene expression and induce leukemia cell death.

Vanden Bempt et al., Cancer Cell, 2018

**Towards therapy without relapse**

Many patients with advanced cancers achieve a good response to therapeutics yet retain minimal residual disease (MRD), which ultimately results in relapse. Why and how some people relapse is not always clear.

The Lambrechts lab presented a 52,698-cell catalog of the TME transcriptome in human lung tumors at single-cell resolution. This was validated in independent samples where 40,250 additional cells were sequenced. By comparing with matching non-malignant lung samples, they revealed a highly complex TME that profoundly molds stromal cells. In providing a comprehensive catalog of stromal cell types and by characterizing their phenotype and co-optive behavior, this resource provides deeper insights into lung cancer biology that will be helpful in advancing lung cancer diagnosis and therapy.

Lambrechts et al., Nature Medicine, 2018

**Neuroscience**

**Sleep patterns and parkinson’s disease**

Parkinson’s disease patients report disturbed sleep patterns long before motor dysfunction occurs. Interestingly, dopaminergic replacement therapy in Parkinson’s disease patients can significantly restore motor function but is insufficient to remedy sleep pattern disturbances. This suggests that sleep defects originate from dysfunction of distinct circuitry. However, the origin of sleep defects in Parkinson’s disease remains elusive.

The Verstreken group used fruit fly models of the disease to map sleep pattern defects to specific neuronal activity. They found problems with the so-called neuropeptidergic neurons, a specific type of neuron that regulates sleeping patterns. Disturbed lipid trafficking in these neurons disrupted the production of vesicles of neuronal-signaling proteins. Because of this, sleep patterns and circadian disturbances arise in Parkinson’s disease. The researchers found that restoring the lipid balance restored normal sleep patterns. Unlike for dopaminergic neurons, the neuropeptidergic problems are caused by neuronal dysfunction, not degeneration, which implies that they can be corrected. This could be a real paradigm shift in the Parkinson’s disease field.

Valadas et al., Neuron, 2018

**An atlas of the aging brain**

Aging has a significant and diverse impact on the brain. But how the diversity of cell types and regulatory states in the brain change during aging remains largely unknown. Describing these processes at a cellular level is challenging but could enable new insights into aging and other disease progressions.

To map these hidden lands of understanding, the Aerts lab presented a single-cell transcriptome atlas of the entire adult Drosophila melanogaster brain sampled across its lifespan. They identified 87 initial cell clusters that were validated by targeted cell-sorting. During aging, RNA content declined
Alzheimer’s disease is a highly prevalent and incurable neurodegenerative disease with a long pre-symptomatic phase of several decades. The gene ABCA7 was identified as a risk factor for Alzheimer’s through genome-wide association studies. Mutations in ABCA7 are up to five times more frequent in Alzheimer’s patients. But how specific variants of ABCA7 influence the disease remained elusive. Researchers from the Van Broeckhoven lab addressed this knowledge gap by investigating repetitive regions in the DNA sequence of ABCA7 in a Belgian cohort of 1529 patients. They found an association between the length of a tandem repeat that affects both ABCA7 expression and function and the risk for Alzheimer’s. Their findings underline the importance of studying repetitive DNA in complex disorders and expand the contribution of genetic and transcript variation in ABCA7 to AD.

Davie et al., Cell, 2018

Making the right connections
Pyramidal neurons are named after their cell body, which is shaped like a pyramid with multiple long protrusions. Like large trees, these protrusions extend through multiple brain tissue layers where they make connections with both neighboring and more distant neurons. This precise organization of connectivity is essential for normal brain function, but the mechanisms that orchestrate it are not well understood. The de Wit lab identified a new protein interaction that mediates the formation of one very specific type of synapse, namely that between so-called mossy fibers and pyramidal neurons located in a specific region in the hippocampus, the brain area central to learning and memory. These new research findings represent another step towards an increasingly detailed view and understanding of the brain, new research findings represent another step towards an increasingly detailed view and understanding of the brain.

Davie et al., Cell, 2018

Tandem repeats and Alzheimer’s disease
Alzheimer’s disease is a highly prevalent and incurable disease. This single-cell brain atlas covered nearly all cells in the normal brain. It provides the tools to study cellular diversity alongside other Drosophila and mammalian single-cell datasets in a unique single-cell analysis platform: SCope. These results, together with SCope, allow comprehensive exploration of all transcriptional states of an entire aging brain.

Davie et al., Cell, 2018

Research from the Bonin lab set out to explore how our brain handles all this moving around. They approached the question aided by micrometer-sized silicon devices, called Neuropixels. These new probes allowed them to record the electrical activity of hundreds of neurons simultaneously instead of the handful that is customary in most neuroscience laboratories. They found that neurons in the thalamus are just as strongly affected by movement as those in the cortex, suggesting that locomotor modulations are much more widespread than previously appreciated.

Aydin et al., Nature Communications, 2018

Moving around arranges brain cells
What we see is not only determined by what is there, but also depends on whether we are paying attention, whether we are moving, excited or interested. When we move around our brain must process a lot of information at once. How does it do that?

De Roeck et al., Acta Neuropathologica, 2018

Unlocking the genome
The human body consists of trillions of cells and each of them contains all the DNA that makes us unique as human beings. At any given time, most of our DNA is wrapped around histone proteins and stacked into chromatin. It requires a lot of regulation to unpack, unwind, and translate the right pieces of DNA at the right time.

De Malmazet et al., Current Biology, 2018

Our big brains
Over the last million years of evolution, the human brain underwent a considerable increase in size and complexity, resulting in the exceptional cognitive abilities of the human species. This brain enlargement is largely due to an increase in the number of neurons in the cerebral cortex, the outer part of the brain. But it has remained a daunting task for scientists to identify which human-specific gene changes may underlie the unique aspects of human brain evolution.

Jacobs et al., Nature Genetics, 2018

Mouse see, mouse do
What we see guides what we do. After all, most behaviors are a response to something in our environment and we are quite visual creatures. To understand more about how we respond to what we see around us, we need to look at the brain areas that process visual input and output changes in our behavior.

De Roeck et al., Acta Neuropathologica, 2018

To investigate this, the Farrow lab zoomed in on the organization of neurons in the superior colliculus, a midbrain structure that mediates orientation responses to visual cues. The researchers imaged neuronal activity of individual neurons in mice that were looking at moving visual stimuli on a screen. The group found that direction-selective neurons cluster anatomically by preferred direction. This finding suggests that the way neurons are organized in the brain is very much linked to how animals interact with their world.

De Malmazet et al., Current Biology, 2018

The Aerts lab set out to study this regulation and find out what actually does the regulating. The group used a combination of computational biology and in vivo experiments. They found that access to the DNA regions that are relevant for epithelial cells is governed by a protein called Grainyhead. Grainyhead is necessary to ‘unlock’ these specific DNA regions, which consequently allows other players to move in and turn genes on or off. This knowledge encourages an exploration of whether this lock-and-key system can open up or close off other parts of the genome in a controlled way. This could be helpful for example in regenerative medicine, to direct cells to turn on specific genetic programs for skin cells or any other type of cells.

Aerts et al., Nature Genetics, 2018

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The Vanderhaeghen group took up the challenge. The researchers used a tailored RNAseq analysis for specific and sensitive detection of the human-specific genes of interest. In that way, they were able to identify a whole repertoire of duplicated genes that are involved in the development of the cerebral cortex in humans. Among these, the researchers focused on NOTCH2NL, a cluster of human-specific genes related to the NOTCH2 receptor. The Notch pathway is well-known as a key player in organ development, including that of the brain. Using a stem-cell-based model for cortical development, the scientists found that NOTCH2NL genes stood out for their ability to promote expansion of cortical stem cells, which in turn generated more neurons.

Suzuki et al., Cell, 2018

Microbiology

From the past to your offspring’s future

Cells constantly adapt to environmental fluctuations. These physiological changes require time and therefore cause a lag phase during which the cells do not function optimally. Interestingly, past exposure to an environmental condition can shorten the time needed to adapt when the condition re-occurs, even in daughter cells that never directly encountered the initial condition. To unravel that process, the Verstrepen lab used the molecular toolbox of *Saccharomyces cerevisiae* to systematically elucidate the molecular mechanism underlying such history-dependent behavior in transitions between glucose and maltose. In contrast to previous hypotheses, the behavior did not depend on persistence of proteins involved in the metabolism of a specific sugar. Instead, presence of glucose induced a gradual decline in the cells’ ability to activate respiration, which is needed to metabolize alternative carbon sources. These results revealed how trans-generational transitions in central carbon metabolism generate history-dependent behavior in yeast and provide a mechanistic framework for similar phenomena in other cell types.

Cerulus et al., eLife, 2018

Gene editing made easy

CRISPR technology is the most recent great leap in gene editing. It can be programmed to target specific sequences of genetic code with a guide RNA (gRNA) and to edit DNA at precise locations, thus allowing research scientists to permanently modify genes in living cells. However, this approach presents some challenges, such as constraints on the sequences that can be targeted, the possibility of off-target effects and the requirement of a unique guide RNA for each target gene.

The Michiels lab set out to address those challenges. They realized they wouldn’t need a new gRNA for each gene if they targeted a universal sequence found in gene knockout collections. The sequence they targeted is found in many genetic collections of medically important bacteria and even in some fruit fly collections. By generating a gRNA against the flippase recognition target (FRT) site, a common genetic element shared by multiple genetic collections, CRISPR-FRT circumvents the previous design constraints to provide a broad platform for fast, scarless, off-the-shelf genome engineering.

Swings et al., Nature Communications, 2018
SCIENTIFIC IMPACT 2018

723 PUBLICATIONS
250 PUBLICATIONS IN TIER 5 JOURNALS
102 HIGHLY CITED PAPERS (>100 CITATIONS) IN THE PAST 5 YEARS

102 PHD GRADUATIONS

35 RUNNING ERC GRANTS
7 STARTING GRANTS
16 CONSOLIDATOR GRANTS
7 ADVANCED GRANTS
5 PROOF-OF-CONCEPT GRANTS

RUNNING MARIE SKŁODOWSKA-CURIE ACTIONS
9

FLEMISH GOVERNMENT 27%
INDUSTRY 15%
INTERNATIONAL+OTHER 16%
UNIVERSITIES 24%
FELLOWSHIPS 18%

3 MAJOR INTERNATIONAL AWARDS
BRAIN PRIZE
HEINEKEN PRIZE
LEOPOLD GRIFFUEL PRIZE

9

PUBLICATIONS IN TIER 5 JOURNALS
HIGHLY CITED PAPERS (>100 CITATIONS) IN THE PAST 5 YEARS
35 RUNNING ERC GRANTS
7 STARTING GRANTS
16 CONSOLIDATOR GRANTS
7 ADVANCED GRANTS
5 PROOF-OF-CONCEPT GRANTS

FLEMISH GOVERNMENT 27%
INDUSTRY 15%
INTERNATIONAL+OTHER 16%
UNIVERSITIES 24%
FELLOWSHIPS 18%

RUNNING MARIE SKŁODOWSKA-CURIE ACTIONS
9

3 MAJOR INTERNATIONAL AWARDS
BRAIN PRIZE
HEINEKEN PRIZE
LEOPOLD GRIFFUEL PRIZE

9

21
A first core was already established in 2000 and over time, a true Core Facility program was developed. The VIB Cores, supported by the ‘Technology Watch’ program, are instrumental in guaranteeing VIB scientists’ access to the latest and greatest tools and field-specific technologies. The different cores gather expertise in state-of-the-art servicing in, for example, transcriptomics, genomics and proteomics, protein and antibody engineering, advanced light & electron microscopy, and in assay design & proof-of-concept screens. This technoscientific expertise, which would be costly and almost impossible to replicate in individual research groups, is made available to the VIB life sciences research community and beyond.

The newest member of the core family is the cryo-electron microscopy facility housed at the VIB-VUB Center for Structural Biology, headed by professors Jan Steyaert and Han Remaut. This core facility houses a new kind of cryo-electron microscope (cryo-EM), one of just three in the world. The microscope, installed with the help of a four-million-euro grant from Research Foundation - Flanders (FWO), allows images of proteins, the building blocks of the human body, to be produced with atomic precision. Greater knowledge about the function and structure of proteins may enable a better understanding of diseases and the development of methods to combat these.

The new facility was officially opened on September 21st, 2018 by Flemish Minister of Labor, Economics, Innovation and Sport Philippe Muyters. The guest of honor at the inauguration was professor Richard Henderson (Medical Research Council, Cambridge, UK), recipient of the 2017 Nobel Prize for Chemistry for ‘developing cryo-electron microscopy for the high-resolution structure determination of biomolecules in solution’. The microscope will be run as a multi-user, 24/7 facility under the expert supervision of prof. Rouslan Efremov.
Forging alliances

VIB has entered into a partnership with Akoya Biosciences to explore multiplexed spatial analysis of single cells. Akoya Biosciences, a private biotech start-up, announced that VIB will be one of its first partners for exploring the CODEX™ (CO-Detection by indexing) technology in Europe. This technology is one of the few technologies that can provide a spatial and quantitative analysis of up to 50 biomarkers of individual cells in complex tissues. It is a key component in VIB’s recent focus on ground-breaking single-cell research. The CODEX™ platform transforms traditional fluorescent microscopes into powerful high-dimensional tissue imaging stations that can analyze tissue architecture and heterogeneity through multiplex staining. Characterizing the interaction of single cells and their corresponding microenvironments is of major interest to VIB and is also one of the key goals of the newly established Single Cell Accelerator (SCA) program at the institute. This program aims to expand VIB’s expertise in single cell research by optimizing, validating and developing novel technologies and establishing recently commercialized platforms within VIB’s Technology Innovation Lab.

The Akoya partnership significantly boosts VIB’s single cell expertise, which is of great value for the biotech and pharma industry. This expertise is apparent for major players in these industries. Janssen Pharmaceutica NV, part of the Janssen Pharmaceutical Companies of Johnson & Johnson, is the first pharma partner in the SCA. This new collaboration will help VIB and Janssen Pharmaceutica to combine forces for the development and evaluation of emerging single-cell technologies, which will allow both parties to excel rapidly in the single-cell field. The newly developed methodologies will also be disseminated across the VIB centers to make an institute-wide impact.

THE VIB TECHNOLOGY ECOSYSTEM
Forging a solid biotech ecosystem

Through strategic Intellectual Property filings, various industrial collaborations and spin-off activities, VIB plays a role of importance in shaping the biotech ecosystem in Belgium and beyond. The Innovation & Business team ensures that innovative research is translated into tangible products and services that find their way to patients, farmers and consumers. Financial return from tech transfer activities is reinvested in VIB’s basic research programs to perpetuate the science-expertise-business cycle.

The creation of added economic value takes various forms. It involves engaging in collaborations and strategic alliances with a multitude of companies, ranging from (bio)pharma to agri-biotech and food-processing companies and from SMEs to multinationals. It also means creating start-ups as a new economic activity and attracting international companies and funds to invest in Flanders, both resulting in capital investments and the creation of extra jobs in our region.

In 2018, VIB spin-offs employed 875 people. Since their launch, the spin-offs generated over €1.2 billion in equity investments, along with at least as much capital that has been secured through partnerships. What’s more, the value of merger and acquisition transactions amounts to even larger volumes, with the acquisition of Ablynx for €3.9 billion as a prime example.

Leaping forward

Early in 2018, the VIB-VUB spin-off Ablynx was acquired by the pharmaceutical giant Sanofi. The activities of Ablynx are maintained in Flanders as the Ghent biotech company is included within the existing company structure of Sanofi.

Ablynx works on a portfolio of Nanobody®-based therapeutic programs in several major disease areas, including inflammation, hematoloy, immuno-oncology, and oncology. Nanobodies® are a class of antibody-derived therapeutic proteins based on single-domain antibody fragments. These unique molecules have potential uses in the treatment of a range of serious life-threatening human diseases. In October 2018, Ablynx launched its first product, caplacizumab, to treat the life-threatening blood clotting disorder aTTP. Good to know, the same technology also laid the basis for VIB spin-offs AgroSavfe and Confo Therapeutics and Belgian biotech company Camel-IDs.

Orionis Biosciences is a VIB-UGent start-up that focuses on the development of new drugs for the treatment of certain autoimmune diseases and pathologies linked to certain types of cancer. The company holds the rights to a series of technologies needed to develop innovative drugs which were originally developed by its scientific co-founder Professor Jan Tavernier (VIB-Ugent Center for Medical Biotechnology) and research partners. In 2016, the company attracted €5 million of start-up funds from a consortium of international investors led by Excel Venture Management.

In 2018, Orionis Biosciences continued its upward trajectory. On April 30th, the company successfully acquired additional financial backing in a $25 million series B funding round. Both existing investors such as V-Bio ventures and a group of new investors, have participated in the new funding round that allows Orionis Biosciences to further the company’s mission.

Confo Therapeutics started in 2015 based on technology developed at VIB/VUB. The company has now extended a Series A capital round to further expand its activities in the use of ConfoBodies™ to develop improved therapeutic options against G-protein coupled receptors (GPCRs). The capital injection involved participation of existing investors (including V-Bio ventures and VIB) as well as new ones.

Attracting international biotech companies

To have, and be willing to share, technological and scientific expertise can encourage foreign companies to have a closer look and establish local facilities to benefit from the expertise and know-how on offer. The past year has seen two such new investments by international companies.

Inari Agriculture is a company that is revolutionizing plant breeding by tapping into natural genetic diversity. The company has chosen to expand its research activities in Europe with the opening of a laboratory in Bioscape, a new life sciences incubator in Ghent. By partnering with VIB and ILVO, Inari has access to high-caliber expertise in plant biology and genomics as well as state-of-the-art phenotyping and greenhouse facilities. Inari aims to take advantage of the local talent pool and resources in their efforts to increase water and nitrogen-use efficiency in crops such as maize, soy and wheat.
MouSensor, a company that works on a nose-on-a-chip technology, aims to provide an objective way to measure odor. Beyond the obvious interest from the fragrance and flavor industry, this can also be used to diagnose disease. There are, for example, hints that Parkinson’s Disease patients have a specific odor even before other symptoms appear. To drive continued refinement of its smelling technology, MouSensor has entered into a collaboration with imec (Leuven, Belgium) to integrate the MouSensor Biology with state-of-the-art silicon chip technology. This R&D partnership was awarded with a €1.05 million grant from Flanders Innovation & Entrepreneurship (VLAIO). The company has set up a subsidiary in Belgium to facilitate the imec collaboration and fuel its own chip R&D.

Building confidence with data
Translating basic life sciences research data into drug and agri-tech innovations remains 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 because the uncertainties are high. Naturally, for-profit players make their decisions based on an estimation of profitability. They insist on robust target validation, e.g. evidence that modulating specific therapeutic targets will lead to beneficial effects. On the other hand, companies often don’t have the depth of expertise in basic biology as we do at VIB.

Our strategic initiative VIB Discovery Sciences intends to bridge this gap, to increase the success rate of translational research. VIB Discovery Sciences is a team of senior industry-trained technical scientists with significant expertise in drug discovery biology and agrochemical biotechnology. The team is fully embedded in the Innovation & Business unit of VIB and helps to design and execute translational projects. The experts engage in a proactive way with VIB scientists and kick-start early translational work packages, after a valorization analysis by the VIB Innovation & Business team. Intense collaboration with the group leader, the VIB Cores and external partners with complementary expertise is an essential component of these efforts. In addition, VIB Discovery Sciences has also developed a network of external experts and CROs that can be consulted to validate data and results. As such, VIB Discovery Sciences follows one of VIB’s aims, addressing unmet societal needs and seeking the relevant companies or non-for-profit partners to achieve this.

An example of their work is the involvement in the projects of Oncurious, a VIB spin-off focusing on the development of innovative oncology treatments. The VIB Discovery Sciences team has taken the lead in new projects in the company’s pre-clinical research and drug development programs. This work will result in a pipeline of next-generation immuno-oncology drugs targeting a broad spectrum of cancers. The partnership between VIB Discovery Sciences and Oncurious illustrates how VIB’s expertise can be applied to preclinical work and sets the early stage for translational success.
ECONOMIC IMPACT

INTELLECTUAL PROPERTY
- Total number of patent applications: 618
- Total number of active patent families: 259

INDUSTRIAL INCOME
- € over the last 5 years: 125M

INWARD INVESTMENTS
- € capital investment: 1.3B
- Direct employees: 660

INFRASTRUCTURE
- Bio-incubator Ghent: 6,500 M², 10 companies, 186 employees
- Bio-incubator Leuven: 9,375 M², 20 companies, 333 employees
- Bio-accelerator Ghent: 18,000 M², 4 companies, 575 employees

SUPPORTING THE BIOTECH ECOSYSTEM
- International schools: 65 Ghent pupils, 48 Leuven pupils
- Talent pool: 5 universities, 4 strategic research centers

20 START-UPS
- € capital investment: 1.2B
- Direct employees: 875

SUPPORTING 20 START-UPS
- € capital investment: 1.2B
- Direct employees: 875

BIO-INCUBATOR GHENT
- 6,500 M²
- 10 companies
- 186 employees

BIO-INCUBATOR LEUVEN
- 9,375 M²
- 20 companies
- 333 employees

BIO-ACCELERATOR GHENT
- 18,000 M²
- 4 companies
- 575 employees
Science is not just for scientists. Quite the contrary, it is for everyone. To do their work, scientists often receive funds from governmental sources, which, in turn, derive from the public. Scientific researchers are well-aware of this money trail and most of them are eager to engage with the public to show what they are doing, and why it is worthwhile. This is why VIB stimulates and supports scientific outreach at all levels.

SuperNova
The SuperNova festival is a public festival on ‘Het Eilandje’ in Antwerp. This one-of-a-kind immersive experience took place on September 29-30, 2018 and VIB signed up for duty. Visitors were able to explore VIB’s single cell research through an interactive installation. Inspired by the recent breakthrough of Stein Aerts and his team of the VIB-KU Leuven Center for Brain & Disease Research, a giant brain ‘puzzle’ brought the concept of single-cell technology to life. At the Tech Fair, VIB showcased its scientific highlights with a captivating exhibition, designed to offer a fresh view of VIB’s groundbreaking research and the Innovation & Business team’s realizations.

Biotech Day
In 2018, Biotech Day focused on personalized medicine. The event, held in Antwerp this time, was a great success, attracting over 3,000 visitors. VIB and the University of Antwerp opened their labs to the public to provide a glimpse of the world-leading research on dementia, various other brain diseases, and regenerative medicine. Interested visitors had their thirst for knowledge further slaked with biotech talks and meet & greet sessions.
Day of Science

Another event where VIB promoted its biotech research was the Day of Science. Various researchers gather here to explain and show how science and technology contribute to daily life. VIB scientists were more than eager to contribute, with, for example, blind dates with researchers, biotech quizzes, DNA Minecraft, funky beer brewers, and much more.

Conference Series

Of course, communication among scientists is very relevant as well. To stay up-to-date in rapidly developing fields, scientists should regularly interact with (international) colleagues. Conferences are an excellent way to facilitate such a continent-spanning knowledge exchange. VIB contributes to this by regularly organizing conferences of international importance. The VIB Conference Series has had another successful year. With the help of the dedicated conferences team, over 1,800 scientists visited these conferences, which attracted significant industrial interest and corporate funding.

The international conferences of the past year included:
- Genome Engineering and Synthetic Biology
- Applied Bioinformatics in Life Sciences
- Medical Biotechnology
- CellTune 2018@VIB
- Structural Dynamics in Cellular Communication
- Metabolism in Cancer and Stromal Cells

These conferences showcase the breadth of work performed at VIB as well as the international relevance thereof.

Diversity and gender balance

VIB seeks to attract the brightest talent, regardless of age, gender, religion, or nationality. The presence of 76 different nationalities in VIB’s centers is a great testimony to this. Diverse teams enable the cultivation of new perspectives and fuel the creativity that can lead to breakthrough science. VIB actively promotes diversity and inclusion at all levels, not only to enrich the scientific work and insights, but also to enrich the interaction between its members. VIB thrives on diversity and will continue to ensure that it stays this way in the years to come.

Several initiatives have been launched with a specific focus on gender balance. While the gender balance within VIB is in general well balanced, the group leaders form an exception.
Currently, slightly less than 20% of the group leaders are female. However, VIB has committed to remedy this and has set a target of at least 30% female PIs by 2022. To achieve this, VIB has critically assessed its recruitment process and career support packages. Changes in the recruitment process involve active scouting, careful attention to the wording in job advertisements, representing VIB as an attractive workplace for women and mothers (which is often neglected in scientific institutes), ensuring a mixed-gender recruitment panel, and a stronger focus on potential rather than past output.

Following recruitment, VIB strives to ensure a continued focus on gender balance and equality. The strategic plan that builds toward this comprises a variety of initiatives. Notably among these is a workshop on unconscious bias and the Gender Action Plan (GAP), which aims to recruit an additional 10 young female PIs who will receive five years of funding and a broad package of career support resources. Finally, VIB will continue to stress the importance of a healthy work-life balance, including the option of on-campus child support and access to the Bsit app, the possibility to work from home and sensible meeting times, as well as the encouragement of parental leave for fathers.

Faces of VIB

VIB can only thrive thanks to the dedication and commitment of its people, no matter what their function or seniority. The enthusiasm of our employees and their continuous hard work to deliver and support breakthrough science is what makes VIB great. It is with great pleasure that we present just a few of our colleagues who contribute to VIB’s mission.

“As coordinator of one of the VIB Grand Challenge projects, I am excited to be at the forefront of novel scientific and technological developments! Our aim is to find new biomarkers for immunotherapy in cancer, which is not only extremely interesting, but also super relevant for society. I can combine my passion for life sciences with my enthusiasm for science communication and I get to work with the most inspiring people. Every day is a new challenge, and I truly love it.”

— Marlies Vanden Bempt, Grand Challenge coordinator, VIB-KU Leuven Center for Cancer Biology

“At the moment, I spend a lot of time as liaison between the builders and future users of our new research building. I ensure that the wishes of our researchers are considered. I also coordinate center-wide initiatives such as the organization of mock trials for the application of FWO grants, the logistics of the CMB retreat, the CMB newsletter. I am a member of VIB News’ editorial board and the VIB grants pilot team. This role as conduit in different initiatives teaches me a lot and provides the satisfaction of directly contributing to smooth operations within our center.”

— Nele Vervaet, Staff employee, VIB-UGent Center for Medical Biotechnology

“Let’s focus on innovative ideas, act like a team and be authentic; I think it’s a recipe for success.”

— Els Hermans, Business Development Manager, VIB Innovation & Business team

“At the VIB Proteomics Core we identify novel protein targets on a daily basis, contributing to research projects in all VIB centers. It is extremely exciting to work so close to scientific discoveries and to share in the enthusiasm of our users.”

— Francis Impens, Expert technologist, VIB Proteomics Core

“VIB creates an optimal atmosphere to perform high-quality science and provides excellent support in achieving the ultimate goal of my research project, being an improved outcome of antibiotic therapy. Having access to cutting-edge equipment and emerging technologies raises our research to the next level and extends our connections with the industry. Networking activities have resulted in international, multidisciplinary collaborations between our lab and other academic institutes. Furthermore, VIB’s training program, including courses on advanced technologies as well as soft skills, offers numerous opportunities to both develop my personal skills and actively contribute to VIB’s mission to improve societal well-being.”

— Etthel Windels, PhD student, VIB-KU Leuven Center for Microbiology
“Biodiversity is essential for biotech research and biotech research can contribute to maintaining biodiversity. With these two simple messages, the Ecoteam of VIB-UGent started the biotech for nature fundraising campaign. Donations via www.hutsepotbos.be go entirely to a conservation organization and are used to conserve a local nature reserve. So far, we collected over €3,000, sufficient to protect about 700 square meters of nature.”

Ruben Vanholme, Post-doctoral scientist, VIB-UGent Center for Plant Systems Biology

“In my case, as PhD student trying to decipher mechanisms to explain brain neurodegeneration, I need all the help I can get. VIB enables these efforts with training courses by experienced scientists, by organizing seminars to keep us up to date of the latest advances in the field, and by providing us with state-of-the-art core units (VIB Core Facilities) available whenever needed to save the day. In essence, VIB is made by scientists for scientists.”

Alexandros Frydas, PhD student, VIB-UAntwerp Center for Molecular Neurology

“By collaborating with other VIB research groups and VIB Discovery Sciences, and supporting their findings with structural biology, I hope to contribute to integrative and translational research at VIB.”

Inge Van Molle, Post-doctoral scientist, VIB-VUB Center for Structural Biology

“I lead the Single cell Expertise unit at the VIB-KU Leuven Center for Brain & Disease Research, and as such, I actively collaborate and provide expertise, trainings and services for different scales of projects both within and outside our center. We put a lot of focus on technological developments. By combining novel microfabrication technologies such as the droplet microfluidics and by using our strong expertise in cutting-edge molecular biology techniques, we are developing novel assays to address various single cell quantitation challenges, including multi-omics single cell measurements. We strive our best to make every cell count! VIB recently launched the ‘Single Cell Accelerator’ initiative, to which we contribute our expertise to keep the single cell research at VIB at the forefront. Through this initiative and via internal collaboration at our research center, we are currently partnering in two industrial projects.”

Suresh Poovathingal, Staff scientist, VIB-KU Leuven Center for Brain & Disease Research

“With these two simple messages, the Ecoteam of VIB-UGent started the biotech for nature fundraising campaign. Donations via www.hutsepotbos.be go entirely to a conservation organization and are used to conserve a local nature reserve. So far, we collected over €3,000, sufficient to protect about 700 square meters of nature.”

Arnout Bruggeman, PhD student, VIB-UGent Center for Inflammation Research

“I, as PhD student at the VIB-UGent Center for Inflammation Research and neurologist-in-training at Ghent University Hospital, have the unique possibility to be involved in a clinical trial that will investigate fecal microbiota transplantation (FMT) as a potential new treatment for Parkinson’s disease; the first of its kind in the world. Our patient recruitment went faster than expected, in no small part thanks to the ‘VIB Ik werk mee’ initiative and our participation in science communication events such as the ‘VIB biotechdag’ and ‘Dag van de wetenschap’. This translational and multidisciplinary research is only possible through intensive collaborations within VIB and with external organizations such as Ghent University and Ghent University Hospital. As the trial has been kicked off, I look forward to it further developing in the coming year and to the ultimate results.”
Backed by its research facilities and scientists, VIB offers a range of training courses in the life sciences. Both specialist and cross-disciplinary courses are available. The reason for this variety is that in this 21st century it is no longer enough to stay in the lab and stick to a specific discipline to become a top-notch scientist. Success as a scientist increasingly hinges upon the availability of broad training that allows the formation of multi-disciplinary scholars. This broad training program does not focus solely on scientific skills but includes several courses in ‘soft skills’ as well. There are numerous opportunities for interested VIB members to develop their communication or management skills, and career coaching is provided both for those who want a scientific career and those who want to explore new professional waters.

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**

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<tr>
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<tr>
<td>Intangible fixed assets</td>
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<td>TOTAL ASSETS</td>
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<td>197,074</td>
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<th>LIABILITIES</th>
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<td>Amounts payable within one year</td>
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<td>TOTAL LIABILITIES</td>
<td>226,076</td>
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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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