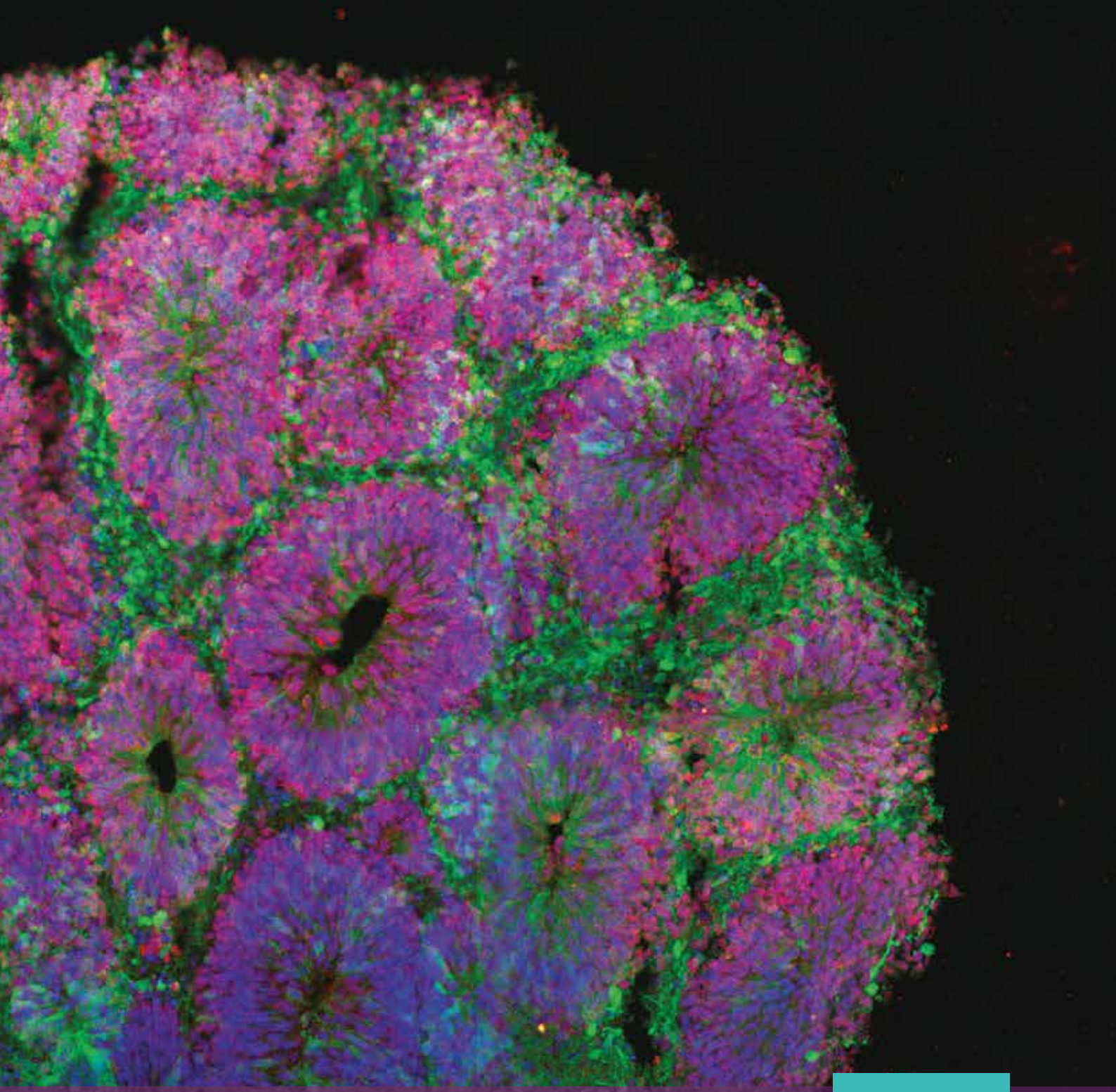
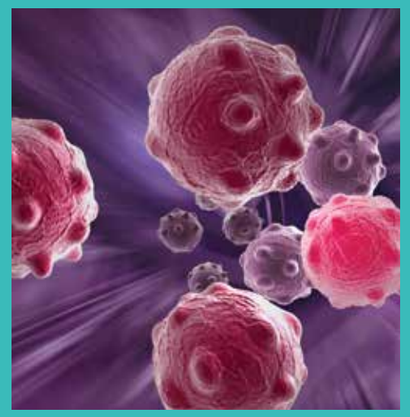
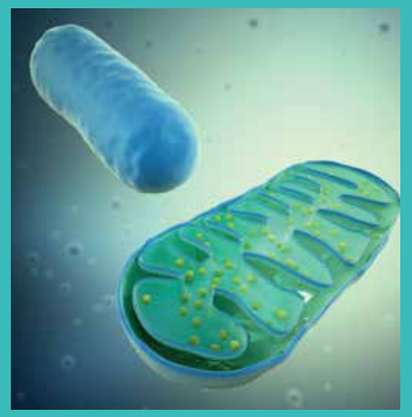


ANNUAL REPORT 2022

VIB








Contents

Advancing the future of life sciences research and innovation

Letter from the **chairman**

To stay at the forefront of life sciences research, it's essential for VIB to explore bold ideas, take intelligent risks, and pursue scientific breakthroughs that can transform the field.

VIB's researchers are the driving force of our institute as they conduct the scientific investigations that are at the heart of our mission. They explore new ideas and push the boundaries of scientific knowledge. VIB research is inspired by societal challenges such as healthy living and enhancing sustainable food production. VIB scientists develop new treatments and diagnostic tools to improve human health, and they address climate-related issues by gaining new insights into plant growth and development.

In 2022, the research findings of VIB scientists were widely published. Examples of such research papers include the publication of the Fly Cell Atlas, which constitutes a valuable resource for the research community as a reference for gene function studies at single-cell resolution. Another study produced the first comprehensive liver atlas, mapping the potential cellular crosstalk between different liver cell types and their spatial location within the liver. Discover the many scientific highlights in the 'Science with impact' section.

On the technology front, the continued investments in VIB Technologies ensure that their offering reflects the changing life sciences landscape. Including the Core Facility program and Tech Watch, VIB Technologies provides the research community with cutting-edge technologies, such as single cell omics, that unite researchers across disciplines.

Despite the difficult investment climate, the Innovation & Business team was able to accomplish an impressive outcome with one new startup, Bar.on, a new investment fund, Biotope Ventures, and significant R&D collaborations and licensing agreements with companies such as iTeos Therapeutics and Springworks Therapeutics.

The Grand Challenges program (GCP) continued its trajectory of the previous years and launched its fourth project call in June. As before, outreach activities were an important part of the GCP. The GCP project teams launched several initiatives, such as reverse science cafés in which stakeholders (patients, farmers) engage in dialogue with experts (clinicians, scientists), citizen science events, and patient activities.

One of the milestones in 2022 was undoubtedly that Jo Bury passed the torch to Christine Durinx after more than 25 years at the helm of VIB. The appointment of Christine as Co-Managing Director, the former Joint Executive Director of the SIB, Swiss Institute for Bioinformatics, strengthens VIB's commitment to focus on the burgeoning fields of data science and personalized health.

The future of life sciences research and technology transfer holds great promise. I firmly believe that VIB has the people, capabilities, and expertise to stay at the forefront of life sciences research and continue to impact society at large.

Ajit Shetty
Chairman of the Board of Directors

VIB's *raison d'être*

From excellent science to societal impact

VIB is an independent, entrepreneurial research institute in life sciences.

The mission of VIB is to make a positive impact on society through scientific progress and real-world applications.

At VIB, some 1,800 top scientists from Belgium and abroad conduct groundbreaking basic research into the molecular underpinning of life. 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.

VIB's technology transfer activities translate these insights into concrete applications that benefit society, such as new treatments and diagnostics tools for human health and new methods to adapt crops to rapidly changing climate conditions.

Collaboration is vital to achieving our mission. VIB operates in close partnership with the five universities in Flanders – Ghent University, KU Leuven, University of Antwerp, Vrije Universiteit Brussel, and Hasselt University. Young start-ups often develop applications from VIB or other companies working with VIB. As such, VIB contributes to a vibrant life sciences ecosystem surrounding us.

Core values

Curiosity & creativity

VIB promotes curiosity-driven science and creativity.

Unity across boundaries

Teamwork and commitment are crucial to success.

Inclusion & collaboration

VIB values people more than scientific competition. The focus on innovative science makes smooth collaboration essential.

Integrity & Responsibility

VIB aims to balance innovation, sustainability, and societal impact. It makes its research results available for additional development.

Respect & transparency

Transparency and trust throughout the institute are highly valued, as is respect for everyone in the organization, regardless of their place in the hierarchy.

763 PUBLICATIONS

97 PHD GRADUATIONS

SCIENCE

265 PUBLICATIONS IN TIER 5 JOURNALS

CORE FACILITIES 11

TECHNOLOGIES

TECH WATCH PROJECT APPLICATIONS APPROVED 22

5 PARTNER UNIVERSITIES → 93 RESEARCH GROUPS

1 INSTITUTE

77 NATIONALITIES ← 1,649 COLLABORATORS (FTES)

TOTAL INCOME

152.8M € OF WHICH

%53 FROM FLEMISH GOVERNMENT

TECH TRANSFER

27.3M € TOTAL INDUSTRIAL INCOME

4 NEW STARTUPS

Science *with impact*

VIB research is based on rigorous scientific methods to ensure accuracy and reproducibility so that other researchers can build on these findings and help accelerate progress in various scientific disciplines.

This annual report showcases some exciting discoveries in the various fields studied at VIB. We hope these stories will spark your curiosity and inspire you to learn more about the remarkable work of VIB's researchers. If you want to learn more, please visit our website vib.be.

Collaboration, teamwork & working across disciplines are essential for impactful research.

Unraveling *the fundamentals*

Alzheimer's study finds **42 more genes** linked to a higher risk of disease

Kristel Sleegers and Fahri Küçükali (VIB-UAntwerp Center for Molecular Neurology) contributed to the largest genetic study of Alzheimer's to date that provided compelling evidence linking the disease to disruption in the brain's immune system. The study, using the genomes of 100,000 people with Alzheimer's and 600,000 healthy people, identified 75 genes linked to an increased risk of the disease, including 42 new ones. The findings suggest that aggressive activity in the brain's immune cells, the microglia, could spur degeneration in the brains of dementia patients. The study allowed scientists to develop a genetic risk score that could predict which patients with cognitive impairment would develop Alzheimer's within three years of first showing symptoms. Their research provides a valuable framework for future developments in the treatment of Alzheimer's disease.

Bellenguez C. *et al.*, New insights into the genetic etiology of Alzheimers disease and related dementias, Nature Genetics

Shared **brain signatures** in FTLD patients

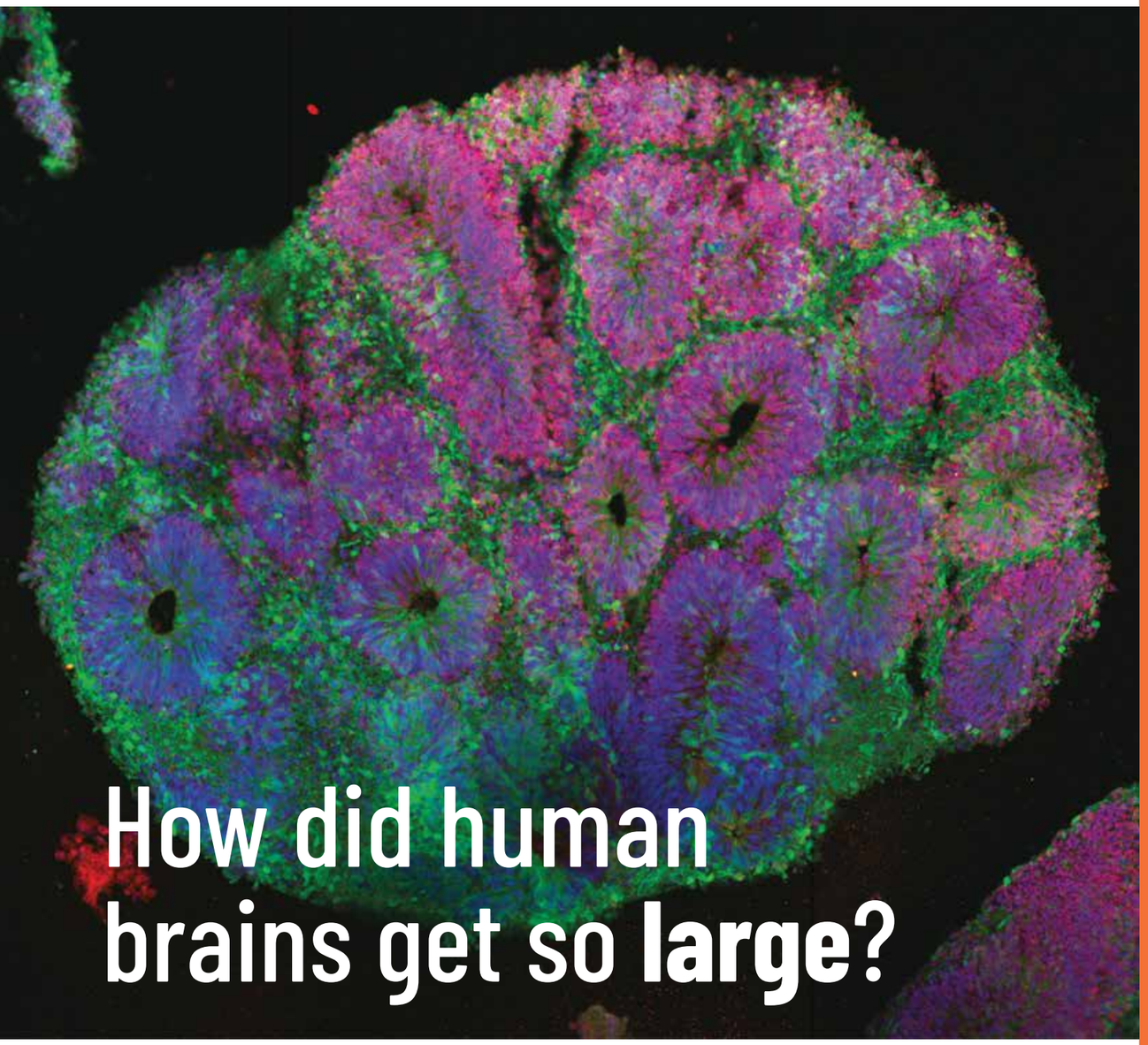
Frontotemporal lobar degeneration (FTLD) is a group of brain disorders that affect the regions of the brain responsible for controlling language, behavior, and personality. Genetic factors can cause FTLD, a well-known example being mutations in the granulin precursor (GRN) gene. The GRN gene provides instructions for making a protein called progranulin, which is involved in many cellular processes. These mutations always lead to a specific type of FTLD called FTLD-TDP-A. Rosa Rademakers (VIB-UAntwerp Center for Molecular Neurology) and her team studied gene expression in patients' brain tissue and surprisingly found that patients with and without the GRN mutation had similar gene expression patterns, with alterations to the immune response, brain cell communication, and other processes. This suggests that GRN dysfunction may also contribute to patients without a mutation, which is an important finding as this may allow a larger group of FTLD-TDP patients to benefit from the GRN-based therapies that are currently in development.

Pottier C. *et al.*, Shared brain transcriptomic signature in TDP-43 type A FTLD patients with or without GRN mutations, Brain

Blueprint of visual information

When navigating the world around us, it is vital that we can correctly process visual information. Yet, researchers still have a limited view of how the visual processing streams in our brains help us accomplish this amazing feat. A research team led by Vincent Bonin (NERF) has assessed more than 30,000 nerve cells in the mouse brain to learn more about how they specialize in processing visual information. By combining functional imaging, tracing, and manipulation of neural circuits, the researchers provide fine-grained insights into how the brain is able to see what our eyes perceive.

Han X. *et al.*, Diversity of spatiotemporal coding reveals specialized visual processing streams in the mouse cortex, Nature Communications



How did human brains get so large?

Pierre Vanderhaeghen and his team (VIB-KU Leuven Center for Brain & Disease Research) discovered a gene that may have been essential for the expansion of human brain size during evolution. The CROCCP2 gene, previously thought to be inactive, is actually highly expressed in the human fetal brain and could be responsible for the diversity of cells in the brain. The scientists linked CROCCP2 to the mTOR pathway, which is uniquely increased in the human brain stem cells and tightly linked to autism spectrum disorders and specific brain tumors that mostly strike our species. The work contributes to a better understanding of what makes the human brain distinct from other species. It also shows how our brains developed a sensitivity to certain diseases by becoming larger and more complex.

Van Heurck R. *et al.*, CROCCP2 acts as a human-specific modifier of cilia dynamics and mTOR signaling to promote expansion of cortical progenitors, Neuron

The fruit fly: mapping the tiny research hero

The single cell revolution is revealing more and more fine-grained insights into the biology of living organisms. This has enabled researchers to create the Fly Cell Atlas, covering hundreds of cell types of the adult fruit fly. A research team led by Stein Aerts (VIB-KU Leuven Center for Brain & Disease Research) has significantly contributed to this atlas. Digging deeper into the nucleus led to discoveries of how genes are regulated in the fruit fly brain. The research effort provides an important stepping stone for a better understanding of human gene regulation and can aid in multiple biological and medical research areas.

A SMALL BUT POWERFUL CREATURE

For over a century, fruit flies *(Drosophila sp.)* have been the go-to model organism for biomedical research. They are easy and inexpensive to culture, have a short life span, and can be genetically modified straightforwardly. Despite their small size, they have even contributed to the development of treatments for various diseases, such as cancer, immune diseases, and diabetes. This is because fruit flies are more similar to humans than their appearance suggests. Most fundamental biochemical mechanisms and pathways are conserved across flies and humans, and 75% of the genes that cause human disease can be found in the fruit fly.

THE SINGLE CELL REVOLUTION

With the advent of single cell genomic technology, scientists have been able to study tissues at unprecedented resolution, looking at the expression of all genes simultaneously in thousands of individual cells. Such fine-grained insights can help to decipher which genes and genetic programs underlie the identity of animal cell types. In the Fly Cell Atlas, an international consortium now mapped all expressed genes in each cell type. For the brain, the most complex organ in the fly, the Aerts lab added a second single cell technique to also measure the activity of the ~150,000 genomic elements that control gene expression. By profiling these control regions across 250,000 cells during fly brain development at larval, pupal, and adult stages and by training an AI model called DeepFlyBrain, they discovered how brain cell types are 'encoded' in the genome sequence.

FROM FLIES TO HUMANS

Thanks to a massive collaborative effort involving researchers from around the world, the Fly Cell Atlas was completed. This resulted in a dataset that contains over 580,000 cells, identifying more than 250 unique cell types, many of which had not been previously characterized and many of which have evolutionary similarities with cell types in the human body.

The consortium made all its data freely available online, making it a valuable resource for the research community across the globe. This will be helpful for anyone studying biological processes in flies and modeling human diseases at a whole-organism level with cell-type resolution. The Fly Cell Atlas and the DeepFlyBrain model can help advance many aspects of biological and medical research, ranging from personal genome interpretation to synthetic biology and gene therapy.

Janssens J. *et al.*, Decoding gene regulation in the fly brain, Nature, 2022.

Li H. *et al.*, Fly Cell Atlas: A single-nucleus transcriptomic atlas of the adult fruit fly, Science, 2022.

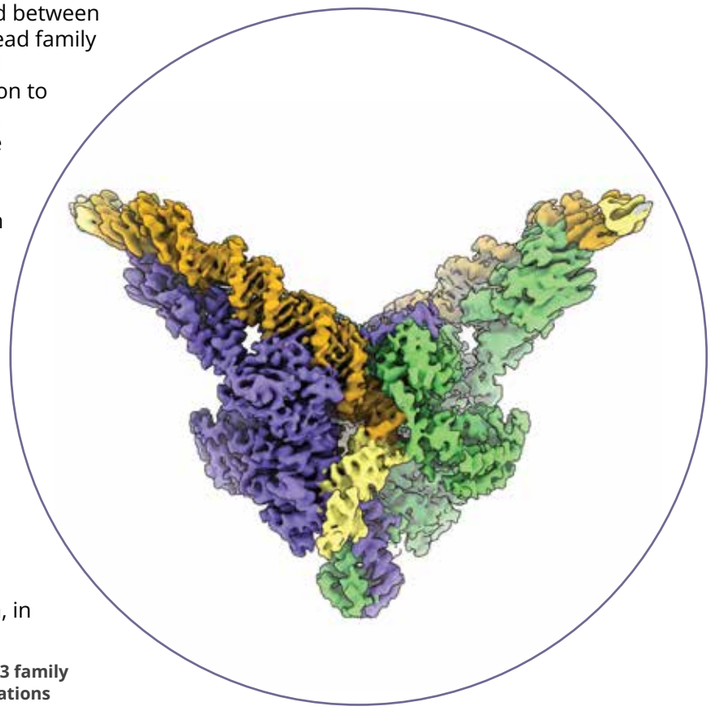
Gut bacteria across generations

Understanding how the human gut microbiota develops and changes over time is crucial for applying microbiome research to medical treatment in the future. Now, Jeroen Raes (VIB-KU Leuven Center for Microbiology) and his team investigated the transmission and persistence of gut microbiota within families over multiple generations. The study found that the composition of gut microorganisms is linked to familial relationships, with seven genera of microorganisms displaying familial distribution patterns. The analysis of microbial genotype distribution and transmission estimates indicated that cohabitation is a key factor in the transmission of bacterial strains. The highest potential transmission rates were observed between sisters and mother-daughter pairs, with rates decreasing as the daughter's age increased. Overall, the study confirmed the existence of family-bound microbiome community profiles and highlights the importance of cohabitation in the transmission and acquisition of bacterial strains.

Valles-Colomer M. *et al.*, Variation and transmission of the human gut microbiota across multiple familial generations, Nature Microbiology

Unveiling the mechanism behind gene-jumping proteins

Genomes, the collection of all the DNA in living cells, are far from static. Transposons are mobile elements in genomes that jump around between genomes all the time. Tn3 is a widespread family and among the first identified bacterial transposons famed for their contribution to antibiotic resistance. Such transposons can rearrange DNA sequences or move genes from one bacterium to another and can, in doing so, generate new genetic variations. The team of Rouslan Efremov (VIB-VUB Center for Structural Biology) used Cryo-EM microscopy to show that the transposon Tn4430, a member of the Tn3 family, has an unusual structure that brings together multiple regions of DNA to allow integration of the transposon into the target genome and its replication, furthering our understanding of how transposases work. (Transposases are enzymes capable of binding to the end of a transposon and catalyzing its movement to another part of a genome, typically by a cut-and-paste mechanism or a replicative mechanism, in a process known as transposition.)



Shkumatov A. *et al.*, Structural insight into Tn3 family transposition mechanism, Nature Communications

Developing *sustainable* crops

Speeding up gene discovery with BREEDIT

Agriculture faces significant challenges – reducing yield losses during extended periods of heat and drought, to name one. We must adapt our crops to rapidly changing climate conditions to sustain food production. But conventional breeding programs are labor-intensive and time-consuming. Scientists at the VIB-UGent Center for Plant Systems Biology and ILVO developed a fast gene discovery pipeline in maize to advance breeding programs to benefit humanity and the environment. This BREEDIT pipeline will advance the basic understanding of complex molecular networks regulating plant growth and support breeding programs in climate-resilient agriculture.

Lorenzo C. *et al.*, BREEDIT: a multiplex genome editing strategy to improve complex quantitative traits in maize, Plant Cell

Switching off inbreeding

Self-incompatibility prevents plants from inbreeding through the rejection of 'self' pollen. In doing so, self-incompatibility encourages plants to fertilize each other, which promotes genetic variation. Researchers at the VIB-UGent Center for Plant Systems Biology used engineered lines of Arabidopsis thaliana to identify crucial genes in regulating self-incompatibility. They identified the gene HLD1/AtPGAP1 as a key regulator in self-incompatibility, with a critical role in incompatible pollen recognition or rejection.

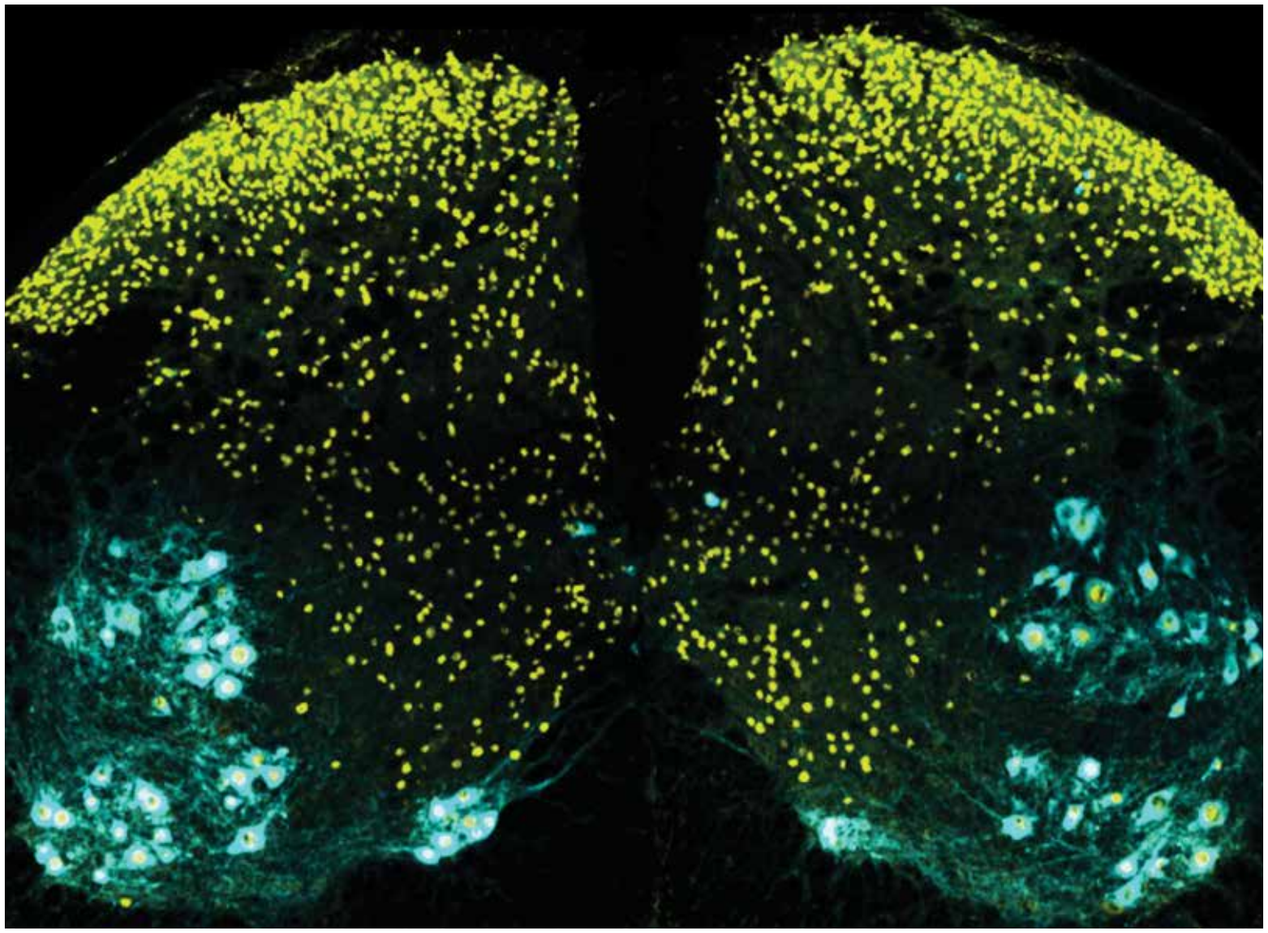
Lin Z. *et al.*, Self-incompatibility requires GPI anchor remodeling by the poppy PGAP1 ortholog HLD1, Current Biology

Mechanical cues for root growth

Plants are great regenerators, which allows them to survive severe stresses, from being partially eaten to facing harsh weather conditions. ERF114 and ERF115 are genes that regulate the regenerative capacity of plants. New work by scientists at the VIB-UGent Center for Plant Systems Biology shows that these genes are also involved in root growth. Increased activation of these genes results in a higher auxin sensitivity – auxin is a hormone promoting plant growth. The researchers also show that mechanical cues contribute to ERF114 and ERF115 expression. Together, these findings provide a framework in which cell wall signals and mechanical strains regulate plant organ development and regenerative responses.

Canher B. *et al.*, The regeneration factors ERF114 and ERF115 regulate auxin-mediated lateral root development in response to mechanical cues, Molecular Plant

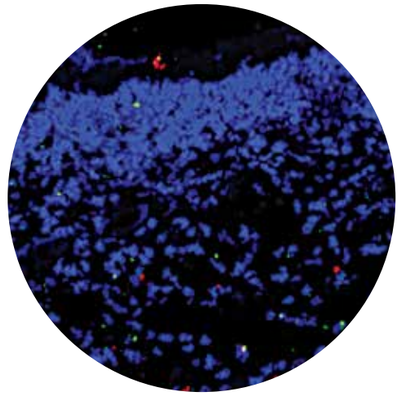
Improving *diagnostics* & *therapies*



Clearing obstacles on the road to recovery

Severe spinal cord injury in adults leads to irreversible paralysis below the lesion, while the same lesion occurring just after birth does not impair locomotion. How the spinal cord achieves such remarkable plasticity is still a mystery. A research team led by Aya Takeoka (NERF) has uncovered that specific types of nerve cells in the spinal cord undergo a switch after injury. This switch turns off communication with motor neurons that stimulate muscles and, therefore, movement. Importantly, research in mice suggests that reversing this switch can dramatically improve functional recovery, especially in combination with physical training. The findings offer important insights into rehabilitation strategies for paraplegic patients.

Bertels H. *et al.*, Neurotransmitter phenotype switching by spinal excitatory interneurons regulates locomotor recovery after spinal cord injury, Nature Neuroscience



Speeding up diabetic wound healing

The skin is the largest organ of the human body. It helps us sense the environment through touch, heat, and cold and acts as a protective barrier against dehydration and pathogens. When injured, cells of our immune system remove the dead cells and restore the skin. Delay of this healing increases the risk of wound infection and severe inflammation. This is a concern, especially for diabetics, since high blood sugar levels slow wound healing. Researchers from the VIB-UGent Center for Inflammation Research found that the protein SLC7A11 negatively regulates the removal of dying cells. As the removal of cell debris from wounds is crucial to avoid infection and promote tissue repair, deciphering the regulatory mechanisms behind healing is a key step toward better wound care.

Maschalidi S. *et al.*, Targeting SLC7A11 improves efferocytosis by dendritic cells and wound healing in diabetes, Nature

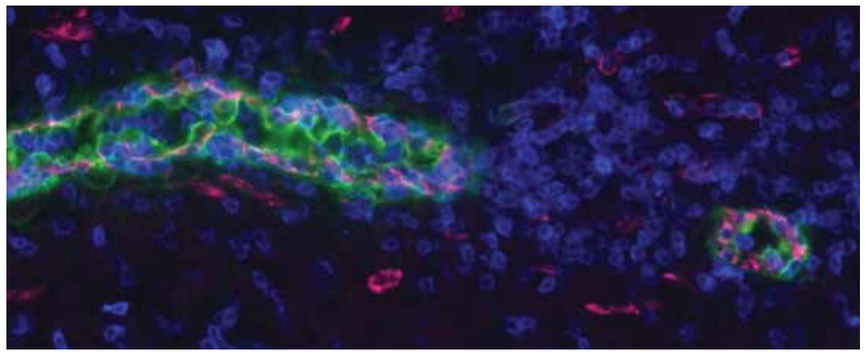
SCIENCE WITH IMPACT

Identifying a new way of supporting and sensitizing **immunotherapy** in cancer patients

Gerlanda Vella, Gabriele Bergers and Yichao Hua

Immunotherapy, specifically in the form of immune checkpoint blockade (ICB), has shown unprecedented benefits in treating cancer patients. ICB treatments work by blocking so-called "immune checkpoint proteins" from binding with their target proteins and helping the body recognize and attack cancer cells. To date, however, a majority of patients do not respond to ICB treatments, which highlights the need for new ways to support ICB treatments.

Lymphocytes, the immune cells responsible for fending off cancer cells, often cannot infiltrate the tumor well enough due to the immunosuppressive microenvironment of tumors. More specifically, blood vessels formed in the context of tumor growth form a barrier making it almost impossible for lymphocytes to get in range of the cancer cells.



THE ROLE OF HEVS

Using single-cell transcriptomics, endothelial fate mapping, and functional multiplex immune profiling, the research team led by Gabriele Bergers (VIB-KU Leuven Center for Cancer Biology) has discovered a way to increase lymphocyte infiltration in the tumor microenvironment. By inducing High-Endothelial Venules (HEVs, blood vessels especially adapted for lymphocyte trafficking), the team was able to transform the protective barrier formed by the tumor vasculature and bypass its defenses against immune cells.

The discovery offers new perspectives for immunotherapy treatments relying on Immune Checkpoint Blockers and other immunomodulating therapies. In combination with therapeutically-induced HEVs, the patient response to such treatments could potentially be increased, leading to a new way of supporting and sensitizing immunotherapy in patients.

> *We were delighted to find out that therapeutically inducing HEVs in the tumor vasculature not only facilitated better lymphocyte infiltration in the tumor environment, it also resulted in the creation of niches that expand the immune cells needed to attack the tumor! In a way, you could say that we have identified the Achilles heel of the tumor: the one spot in the tumor vasculature that we can exploit to start taking down cancer cells.*
>
> *Gabriele Bergers*

Predicting better endogenous targets

Exogenous glucocorticoids are widely used in the clinic for the treatment of inflammatory disorders and auto-immune diseases. Their use is however hampered by detrimental side effects and therapy resistance. In an effort to find more selective glucocorticoid receptor (GR) ligands, the lab of Karolien De Bosscher (VIB-UGent Center for Medical Biotechnology) characterized a set of functionally diverse GR ligands in A549 cells (A549 cells are lung carcinoma epithelial cells that constitute a cell line commonly used for a wide range of research applications).

The researchers found that luciferase reporters evaluating GR-driven gene activation and gene repression were not always reliable predictors for effects on endogenous GR target genes. Remarkably, the integration of a novel assay monitoring phosphorylation of GR Ser211 proved to be a more reliable predictor for compound effects on these endogenous GR targets. Integration of this assay in existing screening platforms running both in academia and industry potentially boosts the chances of finding novel GR ligands with an actual improved therapeutic benefit.

Van Moortel L. *et al.*, Novel assays monitoring direct glucocorticoid receptor protein activity exhibit high predictive power for ligand activity on endogenous gene targets, Biomedicine & Pharmacotherapy

Fighting listeria with mRNA vaccines

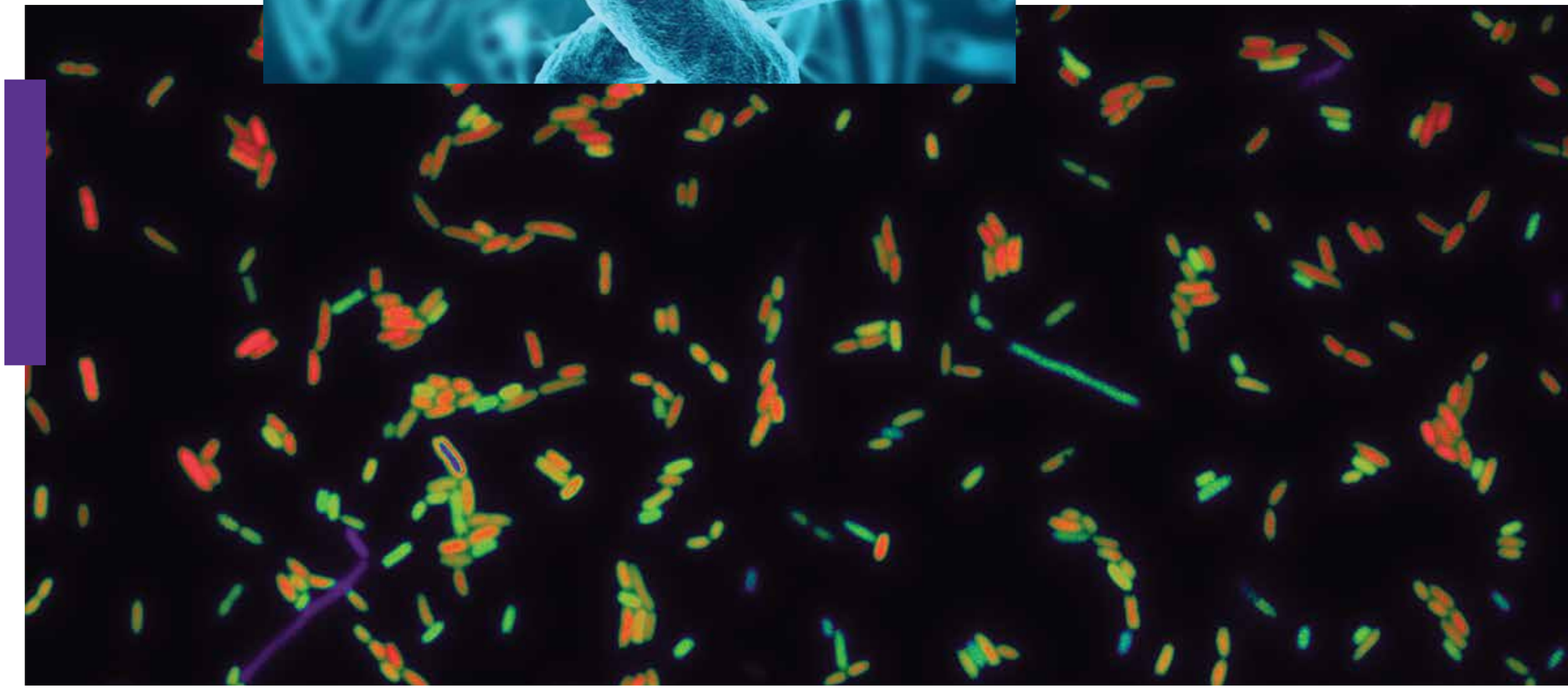
Listeria monocytogenes is a foodborne intracellular bacterial pathogen leading to human listeriosis. Despite a high mortality rate and increasing antibiotic resistance no clinically approved vaccine against Listeria is available. Francis Impens (VIB-UGent Center for Inflammation Research) and his team, together with colleagues from Ghent University and the CRIG have taken an important step towards a listeria vaccine. By combining innovative antigen discovery and mRNA vaccine technologies, the research group was able to encode antigens in an mRNA vaccine which evoked an immune response in mice and induced protection against listeriosis. Intracellular pathogens are super-difficult targets for vaccines. So, this proof-of-concept model paves the way to develop much-needed vaccines against other intracellular bacteria.

Mayer R. *et al.*, Immunopeptidomics-based design of mRNA vaccine formulations against Listeria monocytogenes, Nature Communications

Going sour to survive

Jan Michiels (VIB-KU Leuven Center for Microbiology) and his lab discovered an important aspect of antibiotic tolerance. Successive rounds of antibiotic treatment in the lab led to the development of mutant bacteria that became highly tolerant towards antibiotics. These bacteria had a malfunctioning power plant, which resulted in lower energy levels and significant acidification of the bacterial cell. They found out that this acidification shuts down the main target of antibiotics, which is the protein production machinery. Although acidification typically indicates an imbalance of metabolism and causes a stress response, in bacteria it can lead to antibiotic survival. These findings could lead to new treatments that target the acidification process, making antibiotics more effective against highly tolerant bacteria.

Van den Bergh B. *et al.*, Mutations in respiratory complex I promote antibiotic persistence through alterations in intracellular acidity and protein synthesis, Nature Communications

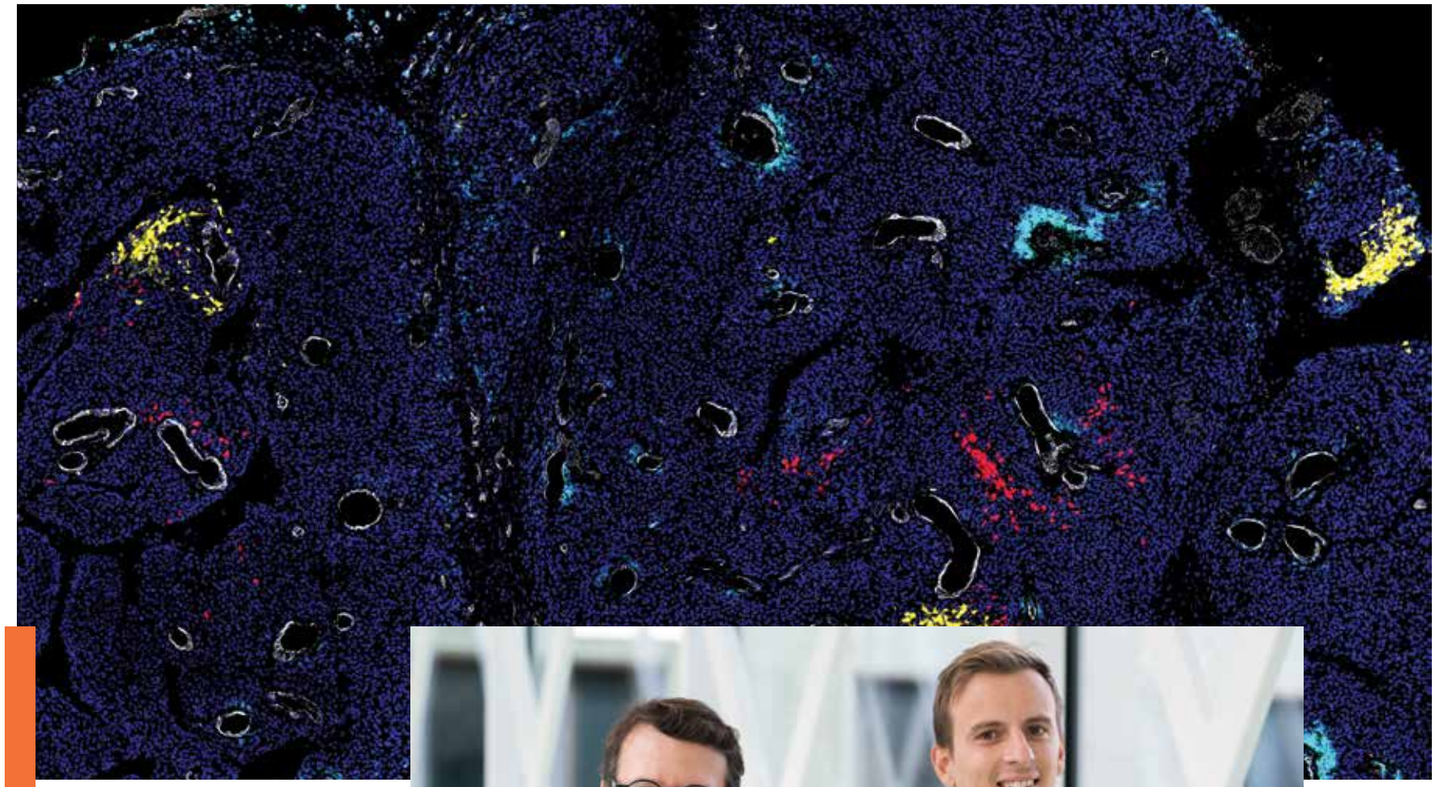


Identifying which cancer cell subpopulations cause **tumor growth and metastasis**

While cancer research has come a long way over the past years and patient survival has improved dramatically thanks to novel therapeutic options such as immune therapy, radiotherapy and improved surgery, there remain many challenges in the fight against cancer. Specifically in the case of melanoma, one of the most aggressive forms of skin cancer, early detection is essential for treatment. With more than 150,000 diagnoses accounting for 4% of all new cancer cases in 2020, it is the sixth most common cancer in Europe and is becoming more prevalent each year. Thanks to researchers from the VIB-KU Leuven Center for Cancer Biology, however, new methods for early detection and treatment might be on the horizon.

A research group led by Jean-Christophe Marine and Panagiotis Karras at the VIB-KU Leuven Center for Cancer Biology discovered which cancer subpopulations are responsible for the growth of tumors and subsequent metastasis in melanoma using cutting-edge technology at single cell resolution. The team shows for the first time that the proximity of endothelial cells acts as a catalyst for cancer cells in their ability to stimulate tumor growth. Moreover, using spatial imaging technologies, the team was able to identify a rare type of cancer cell which is the basis for metastatic dissemination, providing new targets for the prevention of metastasis.

> *Using transformative technologies, we were able to dissect the composition of tumors at an unprecedented level of resolution. This has enabled us to identify a wide variety of distinct cancer cell populations as well as normal cell types infiltrating these tumors. Importantly, we found that the proximity to endothelial cells causes cancer cells to acquire the capacity to fuel tumors. A stunning discovery, because it suggests that blocking communication between these two cell types could prove to be an attractive avenue to prevent tumor growth at an early stage.*
>
> *Jean-Christophe Marine,*
> *Center for Cancer Biology*



Jean-Christophe Marine and Panagiotis Karras

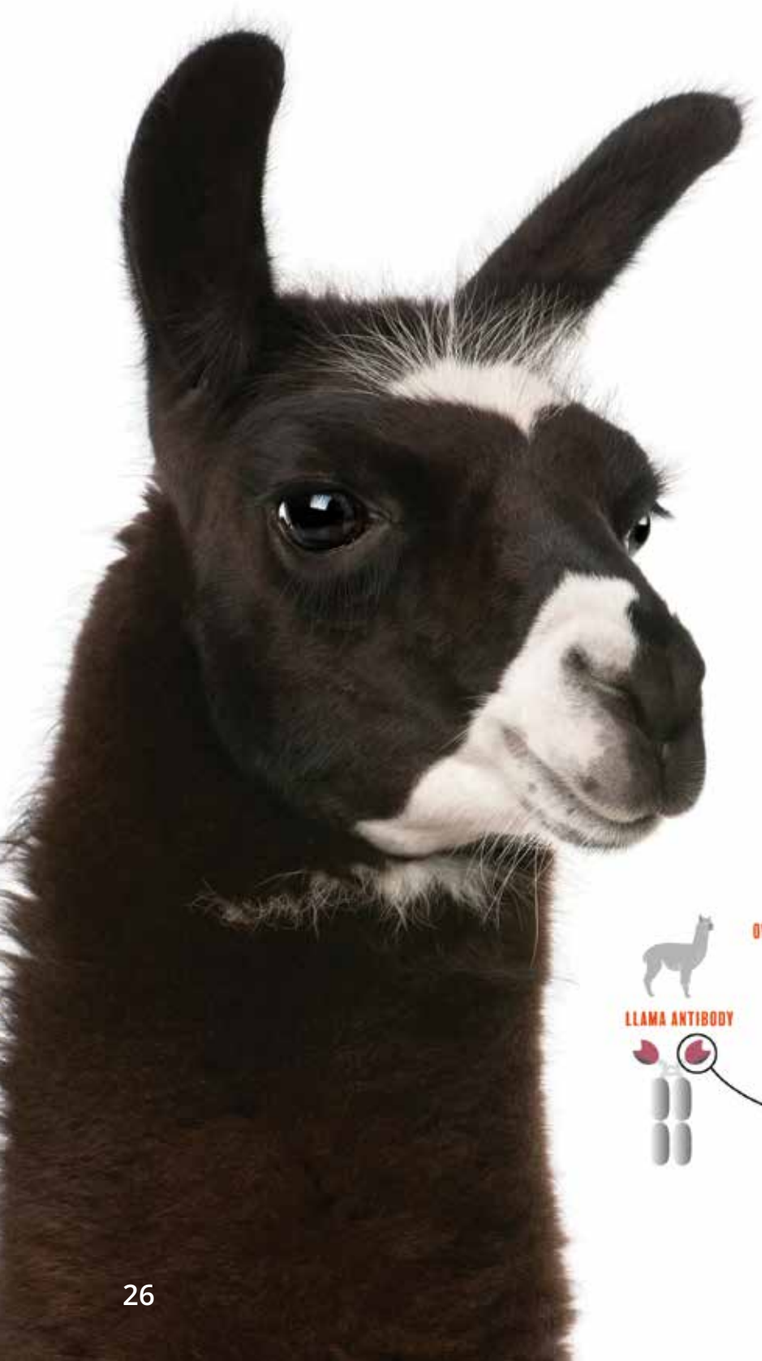
TRACKING CANCER CELLS

By generating new sophisticated mouse models to trace melanoma cells, dubbed Met-Track, the team was able to unravel the identity and spatial distribution of each cell within a given melanoma tumor.

Jean-Christophe Marine: “Once we started tracking specific melanoma cell types in our refined mouse model, we found that only a small fraction of cells, which exhibited invasive characteristics and were localized deep in the tumor tissue, was alone responsible for the seeding of all metastatic lesions in distant organs. Once these cells colonize distant organs such as the lungs or liver, they switch identities and start proliferating in their newfound locations, a process that severely compromises patient survival. These data are important as they show that the presence of such cells in primary melanoma lesions is a key indicator to predict if there is a risk of metastasis.”

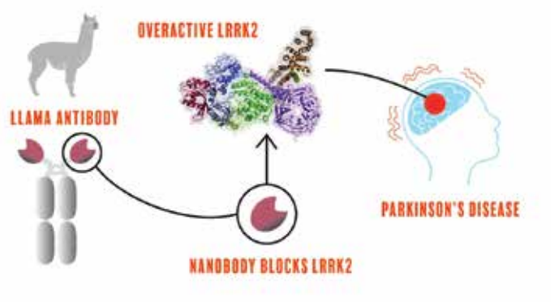
The recent discoveries of the Marine Lab further establish the important role of the tumor microenvironment in shaping tumor evolution and offer a platform for the identification of targetable vulnerabilities in the tumor. Additionally, these findings could help in predicting the aggressiveness of a tumor early on, potentially leading to new strategies that can help delay or even prevent tumor growth.

Will llama antibodies help treat *Parkinson's disease?*



Parkinson's disease is the second most common neurodegenerative disorder, affecting more than 10 million people worldwide. This number is likely to increase as the population ages, and unfortunately, there is no cure to date. The team of Wim Versées (VIB-VUB Center for Structural Biology) worked with researchers in Germany, the Netherlands and the US to explore a completely novel approach to inhibit the activity of LRRK2, a protein linked to the onset of Parkinson's disease. They found that modified llama antibodies were able to bind to LRRK2 and block its activity. What's more, in human cell cultures, the antibodies were able to block LRRK2 activity, laying out a promising foundation for potential future therapies.

Singh R. *et al.*, Nanobodies as allosteric modulators of Parkinson's disease-associated LRRK2, PNAS



Rethinking organ growth

All animals need organs of the proper size to be healthy. For a long time, a series of chemical signals known as the Hippo pathway was thought to be crucial for ensuring that organs grow to their intended size. New research at the VIB-KULeuven Center for Cancer Biology, the VIB-KU Leuven Center for Brain & Disease Research, VUB, and international collaborators now shows that this is not the case. This discovery – published in Science – rewrites the textbook on organ development.

ABOUT THE STUDY

As we grow, our organs have to grow along. But what signals does our body use to tell our organs to stop growing? After all, an organ that grows too large can malfunction and impair the function of other organs and tissues. We haven't yet fully deciphered how our body signals that an organ has become large enough and can stop growing, but previous research suggested that the Hippo signaling pathway is an important component of the message that controls organ growth.

Mutations in genes that are involved in the Hippo pathway often lead to excessive organ growth. So, it makes sense to think of this pathway as a master regulator of organ growth.

But a new study forces us to rethink the role of Hippo in normal organ growth. Researchers from the labs of Georg Halder (VIB-KU Leuven Center for Cancer Biology), Stein Aerts (VIB-KULeuven Center for Brain & Disease Research), VUB, the University of Texas MD Anderson Cancer Center, the Sam Houston University in the USA, and the Universidad de las Americas in Ecuador found that the Hippo pathway is not necessary for normal organ growth.

By looking at the eyes of flies and the livers of mice, the scientists found that problems in the Hippo pathway lead to organs that grow too large. However, shutting down the Hippo pathway did not stop organs from growing normally. In other words, having a functional Hippo pathway can help prevent problems, but it is not necessary for organs to grow normally.

Georg Halder: "Our findings correct a long-standing misconception that states that the Hippo pathway is a master regulator of organ growth. Our new model for how Hippo signaling affects organ growth in turn reveals the need to re-evaluate our understanding of the Hippo pathway in cancer and healing responses."

FURTHERING OUR UNDERSTANDING OF CANCER CELL PROMOTION

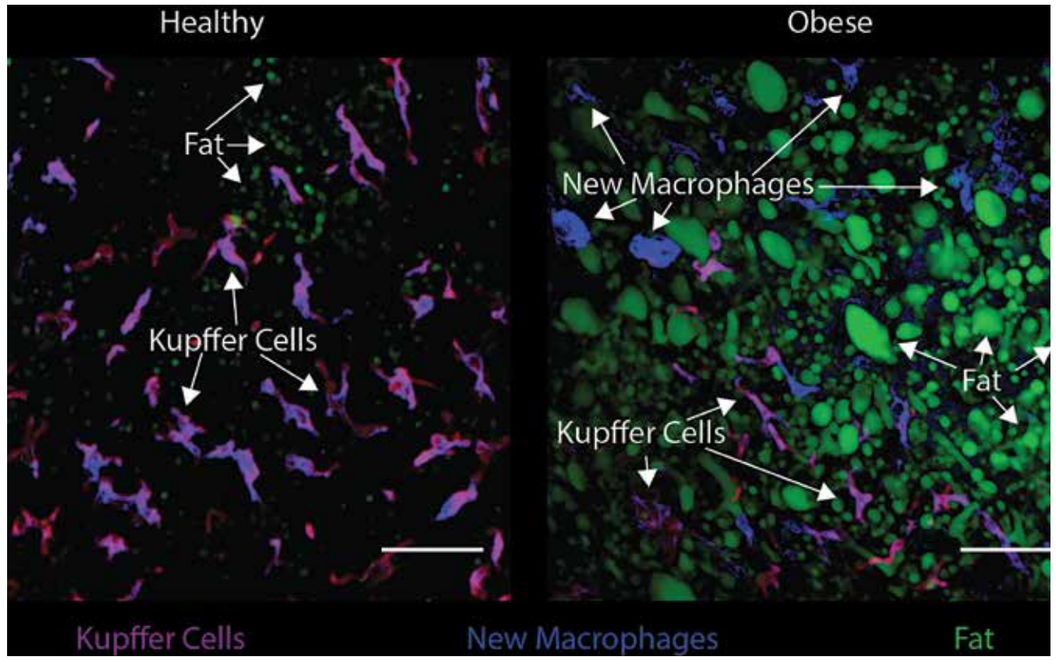
The new model detailed in the study shows how Hippo signaling affects organ growth and how this plays a role in oncogenes and in regeneration. Further research in this field could eventually lead to the identification of new mechanisms that promote cancer cell phenotypes and initiate regenerative responses.

Mapping *the liver*

Charlotte Scott and Martin Guilliams

BUILDING THE LIVER ATLAS

Advances in single-cell transcriptomics provide a better understanding of the cellular makeup of various organs across species. Despite this progress, there is still much to learn about how cells are organized within their microenvironmental niches and the cell-cell interactions that determine cellular identity within tissues. This is particularly true for the human liver, in which the precise localization and identity of most cells remains unknown. Mapping the liver can help us to address conditions such as cirrhosis and liver cancer.



Work by the teams of Martin Guilliams and Charlotte Scott at the VIB-UGent Center for Inflammation Research presents a spatial proteogenomic atlas of the healthy and obese human and murine liver, which combines single-cell CITE-seq, single-nuclei sequencing, spatial transcriptomics, and spatial proteomics. In this project, science and technology are intertwined in a clear demonstration of how research labs, VIB Core Facilities (Bioimaging Core, Flow Core, and Single-cell Core), and early access to technologies through VIB-TechWatch can push science and technology forward. Indeed, half of the techniques utilized in this project were set up in collaboration between the research teams and the Core Facilities, and with initial support from TechWatch to test these technologies.

With proteogenomic techniques, they managed to identify all cells and their specific locations within the liver, including a novel population of lipid-associated macrophages (LAMs) located at the bile ducts. They also identified the conserved program of bona fide Kupffer cells and LAMs, their respective spatially resolved cellular niches, and the microenvironmental circuits driving their unique transcriptomic identities.

The result? A Google Maps-like website (www.livercellatlas.org) with the precise location and proteogenomic identity of all the cells in the healthy and fatty liver, for both mice and humans. Scientists all over the world have found their way to the website, with over 1000 visits each week since the study was published in Cell in January 2022.

NEXT UP: DETAILED MAPS OF DISEASE

This work highlights the potential of this approach for generating a practical cellular atlas of any human tissue and unraveling the cell-cell circuits essential for the identities of cells inhabiting that tissue. By identifying the evolutionarily conserved and spatially restricted signals that drive the distinct hepatic macrophage phenotypes, the implications of this breakthrough research for understanding liver diseases such as cirrhosis and hepatocellular carcinoma are hard to overstate. Finally, this work provides a framework for further atlas studies in other tissues.

Guilliams M. *et al.*, Spatial proteogenomics reveals distinct and evolutionary conserved hepatic macrophage niches, Cell 2022

Grand Challenges Program

VIB established the Grand Challenges program (GCP) to bridge the gap between basic research and translation into practical applications. By promoting transdisciplinary collaborations, developing new diagnostics and treatments, enhancing crop productivity and quality, and promoting sustainable agriculture, the GCP plays a crucial role in addressing unmet needs. The selected projects are transdisciplinary and extend beyond the VIB research community. The Grand Challenges program is aligned with four of the UN's sustainable development goals: Zero Hunger, Good Health and Well-Being, Climate Action, and Partnerships.

Three projects are nearing completion and have led to tangible results.

In the 'Liver' project, the team has established a comprehensive collection of different liver disease samples and a reference library for healthy versus diseased liver tissue, for which downstream multi-omics analysis will be concluded in the coming months. This has resulted in a liver atlas, enabling the identification and validation of novel biomarkers for the hepatology practice to guide cost-effective use of the pharmacological and surgical treatments in the field, from non-alcoholic steatohepatitis over hepatocellular carcinomas to liver transplantation.

The research team validated the patented 'Glycocirrhosis test' for liver cancer risk classification in an independent retrospective cohort of patients, potentially contributing to the improved detection of clinically-significant disease indicators in the liver in the future.

In 2022, the GCP team continued and reinforced its efforts toward co-creation and multistakeholder dialogue to strengthen the program's objective of creating value and impact.

Personalizing immunotherapy to benefit cancer patients

The VIB Grand Challenges Pointillism project aims to understand why some patients or cancer types respond well to immunotherapy, specifically immune-checkpoint blockade (ICB) therapy, while others do not. Additionally, a thorough understanding of the biology underlying this response will guide the search for biomarkers to predict which patient will respond and new ways of treating non-responders. To achieve this goal, the project team, which includes scientists from VIB, KU Leuven, and UZ Leuven, initiated four clinical trials that involved patients treated with ICB therapy. Tumor biopsies from patients were collected before and during treatment, as well as during disease progression. These samples are used to create dynamic maps of the entire tumor ecosystem, the tumor, and its micro-environment consisting of immune and other cells, using innovative single cell profiling methods.

The project uses these innovative technologies, particularly single cell multi-omics profiling, for the first time in the context of clinical trials. This approach provides extremely rich and fine-grained data at the highest resolution possible and enables the investigation of the changes imposed by ICB therapy in the different cells of the tumor. During the pointillism project, the team established structural translational collaborations with clinicians to boost the critical mass aimed for, such as sampling, and catalyze the reverse translation from the clinic, taking the research from bench to bedside and back.

The resulting data, including biomaterials collected during the project, were collected into an extensive database and bank to facilitate future research. The project team has discovered a potential surrogate biomarker for assessing the response of breast and skin cancer patients to immunotherapy. This breakthrough has resulted in ongoing patent applications and collaborations with both academic and industrial partners. To further validate this potential biomarker, a follow-up trial called ExpandiT has been initiated, which offers breast cancer patients early access to a distinctive combination of therapies. Furthermore, a potential therapeutic target for skin cancer has also been identified.

Finally, the project team also organized a mini-symposium with clinicians and scientists to catalyze more follow-on initiatives and future collaborations.

Collectively, these accomplishments showcase the potential value of this research for patients.

Improved detection of primary immune deficiencies

WHAT ARE PRIMARY IMMUNE DEFICIENCIES?

Primary immune deficiency (PID) refers to a group of inherited disorders that affect the immune system. This means that people with PID are more susceptible to infections, autoimmune diseases, and sometimes certain cancers. The infections are often severe, recurrent, or affect unusual parts of the body. Although symptoms typically appear in childhood, they may also develop later in life.

PID is classified as a rare (or orphan) disease and affects over 10 million people worldwide. In Belgium, PID occurs in 1 in 500 to 1,000 people. Yet, PID is believed to be more common than we think, with over half of Belgian PID cases suspected to be undiagnosed.

UNDERSTANDING PRIMARY IMMUNE DEFICIENCIES

Research into PID is essential to improve our understanding of the immune system, develop new treatments, and improve patient outcomes.

The interdisciplinary VIB-GCP PID consortium wants to improve the detection and treatment of PIDs. By developing new diagnostic tools and improving immunoprofiling of specific PIDs, the consortium aims to develop a diagnostic pipeline for genetic variants related to different PIDs directly in the hospital. This research will improve the lives of affected patients but also advance our scientific understanding of PID through 'reverse translational research'.

To begin, suspected PID patients will be screened using conventional tests at the hospital. If no common PID-related gene variants are identified, the patient's genome will be thoroughly characterized through a combination of methods to detect rare or new forms of PID. The knowledge gained by characterizing the genetic underpinnings of different PIDs will be used to expand the therapeutic options available for patients.

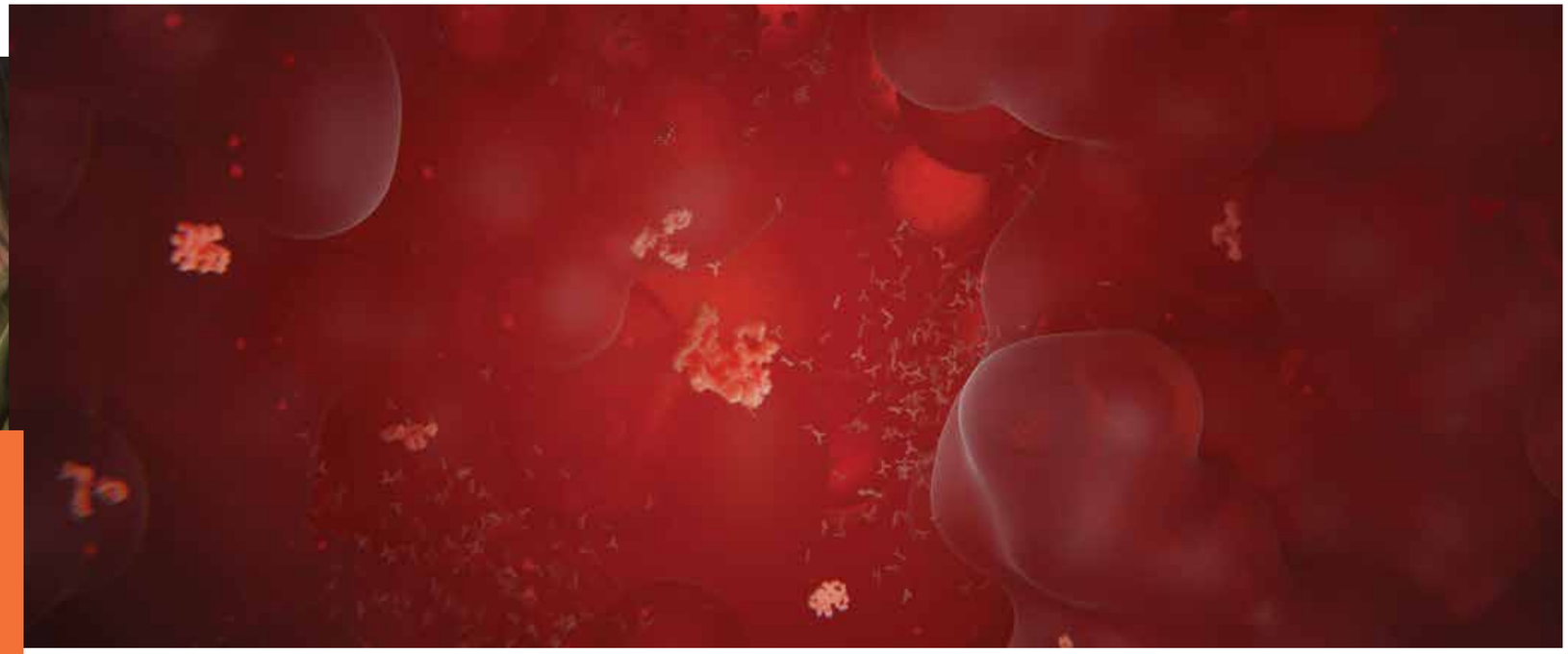
IMPACTING PATIENTS' LIVES

The PID consortium has prioritized a specific form of PID, namely SCID, for approval by the Flemish Government for inclusion in neonatal screening.

Researchers also identified two PID families, characterizing their genetic background and proposing personalized treatment options. Additionally, reimbursement for this treatment was put in place. The project team is also developing a pipeline to analyze genetic variants as part of the routine screening at UZ Gent. As a result, the PID consortium is now established as a solid substrate for further research and clinical implementation at the forefront of PID research.

Finally, the project team, in dialogue with a patient organization, explored the unmet needs of people with PID during an interactive round-table discussion with patients and their families. This dialogue resulted in an outreach effort to raise awareness of the burden of PID patients. The awareness documentary was launched during 'World PID week' and was nominated for the Edelweiss award by the Belgian patient organization RaDiOrg.

Additionally, this project was showcased during a visit of the founders of the Jeffrey Modell Foundation and was highlighted during the patient engagement session of the European Biobank Week 2021.



SCIENTIFIC IMPACT 2022

498 PUBLICATIONS IN TIER 25% JOURNALS

265 PUBLICATIONS IN TIER 5% JOURNALS

97
PhD GRADUATIONS

A SELECTION OF INTERNATIONAL RECOGNITIONS

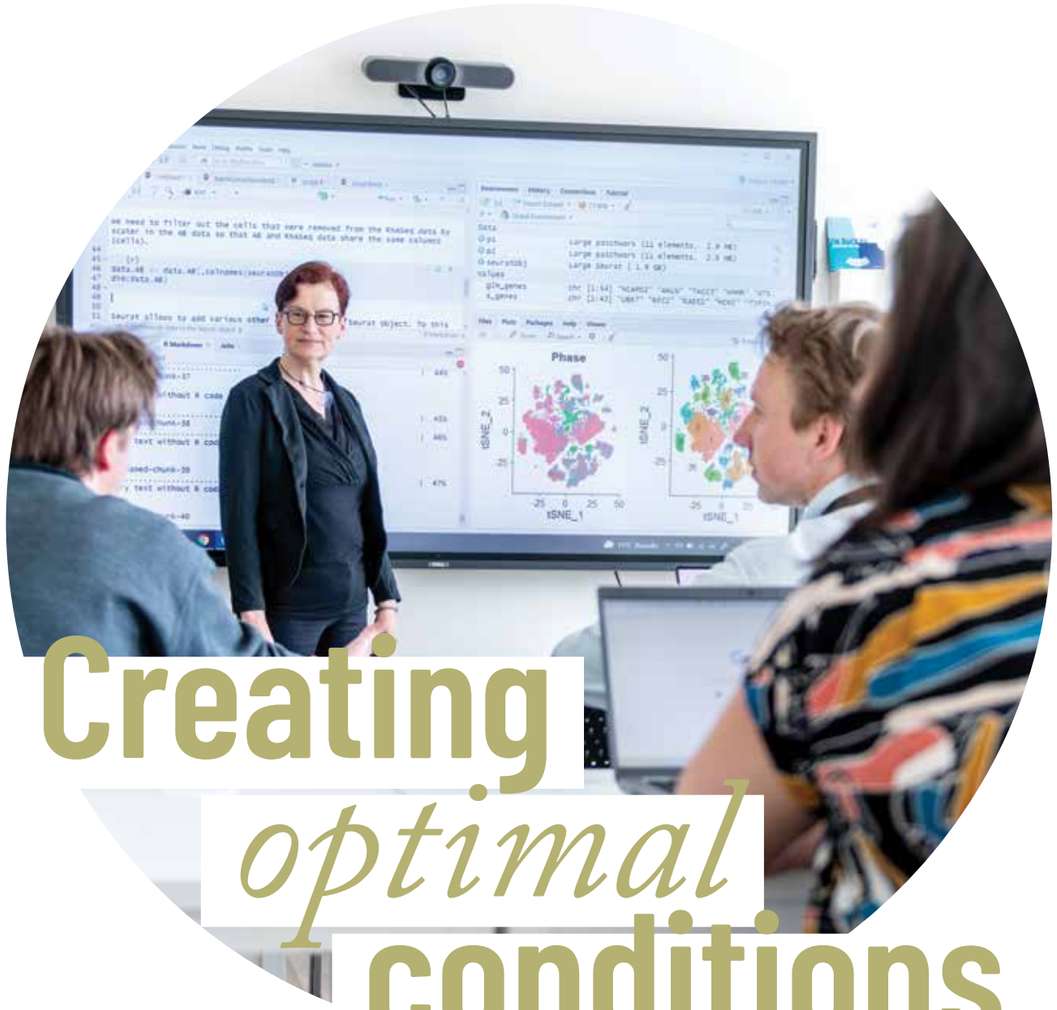
- THE GABBAY AWARD IN BIOTECHNOLOGY FOR **JAN STEYAERT**
- PRIZE ANTOINE FAES FOR BIOMEDICAL SCIENCES FOR **JEROEN RAES LAB**
- WORLD AGRICULTURE PRIZE FOR **MARC VAN MONTAGU**

26 RUNNING ERC GRANTS

- **5** STARTING GRANTS
- **9** CONSOLIDATOR GRANTS
- **8** ADVANCED GRANTS
- **4** PROOF OF CONCEPT

RUNNING MSCA GRANTS

- **18** POSTDOCTORAL FELLOWSHIPS
- **6** DOCTORAL NETWORKS



Creating *optimal* conditions

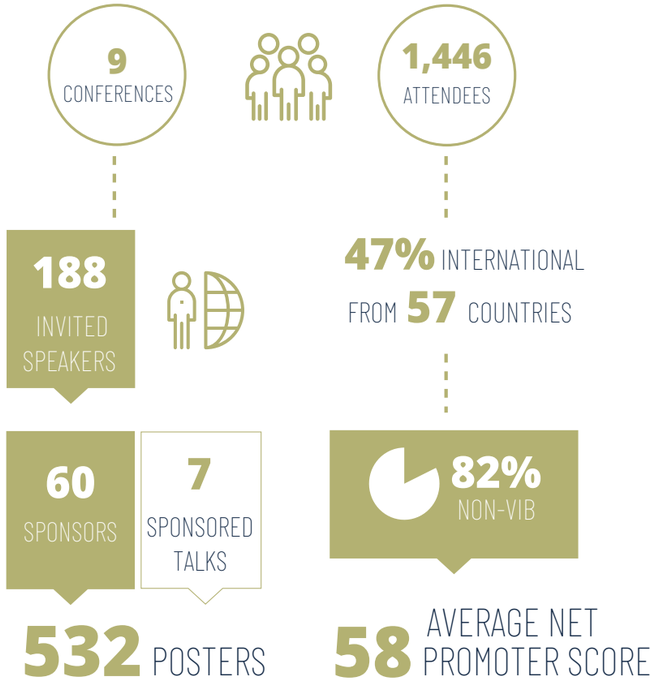
Over the years, VIB has established numerous initiatives aimed at cultivating an environment that supports pioneering research. These initiatives have laid the foundation for a dynamic and stimulating atmosphere, encouraging the pursuit of world-leading scientific breakthroughs.

Exchanging knowledge

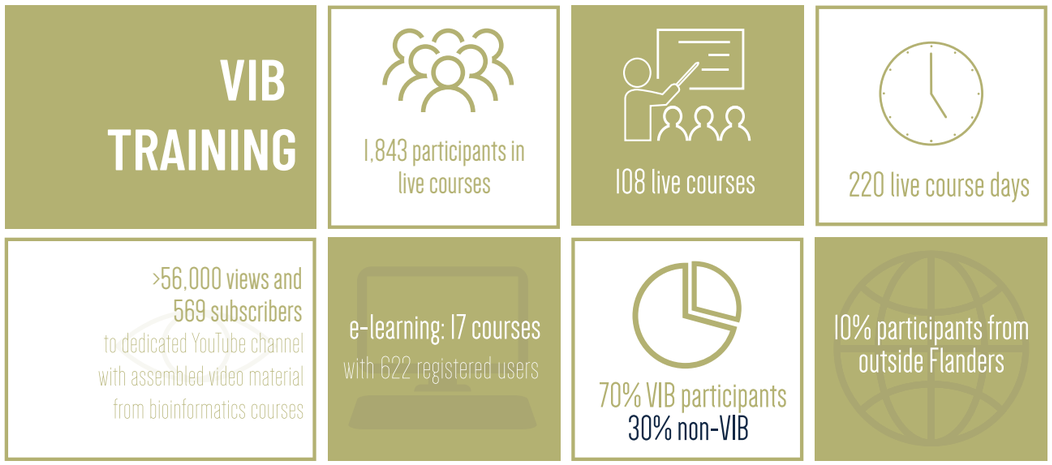
The VIB Conferences Series was established to unite scientists in a specific field from all over the world to share their work and to spark collaborations. The objective of the Conferences Series is that leading scientists showcase their cutting-edge research and technological solutions in the life sciences fields. Junior researchers are invited to present their work during poster sessions and learn from the world's experts during 'Meet the Expert' sessions.

In 2022, the program offered several conferences and science events with a total of 1,446 participants from over 57 countries.

VIB CONFERENCE SERIES 2022



The VIB Training program facilitates knowledge exchange and skills development. Its goal is to provide comprehensive training, workshops, and individual coaching to all VIB collaborators. In 2022, VIB further developed its e-learning program to make its trainings more accessible. Certain courses are also available on YouTube, with over 56,000 views.



Cultivating a positive work environment

VIB values the well-being of its employees, and it is continuously working on creating a positive culture in which its people thrive.

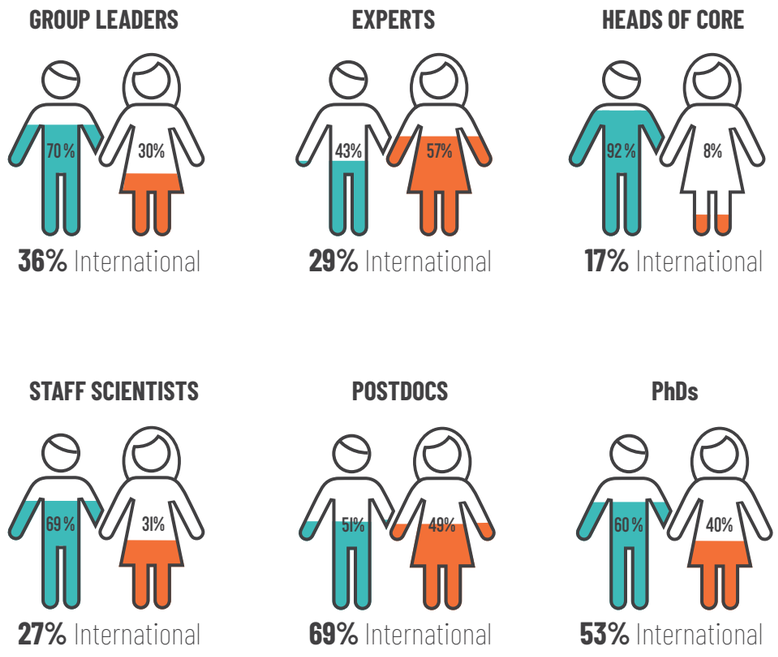
With 41% of its staff coming from other countries, VIB wants to make sure that the working environment is inclusive. At group leader level there is still an important diversity gap. To address these issues, VIB has taken several concrete measures to improve diversity and inclusion.

Life sciences research is a very competitive environment. In addition, the COVID crisis has changed the way people live and work, sometimes leading to insecurity. To this end, VIB has initiated awareness sessions on how to manage stress and prevent burnout, and online tools that help people to build resilience are provided.

Respect being one of the core values, VIB does not tolerate any form of inappropriate behavior. The HR team has developed a policy on inappropriate behavior and has implemented an online tool which can be used by employees to report any form of inappropriate behavior. Furthermore, the team organized 'active bystander' trainings that teach people how to react when they witness inappropriate behavior.

The HR team also introduced the role of 'well-being antennas" in 2022, thus creating a network of people in the research centers. These well-being antennas have been trained to provide first-line care to colleagues who are dealing with psychosocial issues. This network of well-being antennas complements the existing channels and if necessary, they can refer people in need to the appropriate persons or authorities.

Internationalization and gender balance



Creating grant & award opportunities

Obtaining national and international funding is crucial for researchers. The team at the VIB Grants Office collaborates with grant experts in each research center to offer comprehensive support throughout the grant application and the management of running grants. The team proactively searches for funding opportunities, provides guidance on writing strong grant applications, and assists researchers in navigating the sometimes complex administrative processes to ensure successful outcomes.

In 2022, the grants team actively participated in Emerald, a Europe-wide PhD program for medical doctors. VIB will welcome four medical doctors and provide them with state-of-the-art biomedicine training and thus help bridge the gap between laboratory research and clinical practice.

The grant office also provides coaching to researchers in the preparation of ERC applications. In 2022, 12 ERC candidates were supported with brainstorming sessions and mock interviews. This coaching program definitely pays off. In 2022, no less than nine VIB group leaders were awarded an ERC grant, bringing the total number of running grants to 22.

The grant office team actively identifies potential prizes and awards relevant to VIB researchers. In 2022, 34 award nomination files were submitted by the grants office. Some awards worth mentioning are the Gabbay award in biotechnology for Jan Steyaert, ERS mid-career gold medal in Asthma for Hamida Hammad, Prize Antoine Faes for biomedical sciences for Jeroen Raes, Gwen Falony and Sara Vieira, and the World Agriculture Prize for Marc Van Montagu. Ralf Gabriëls, a junior VIB scientist, received the EuPA bioinformatics for mass spectrometry award.

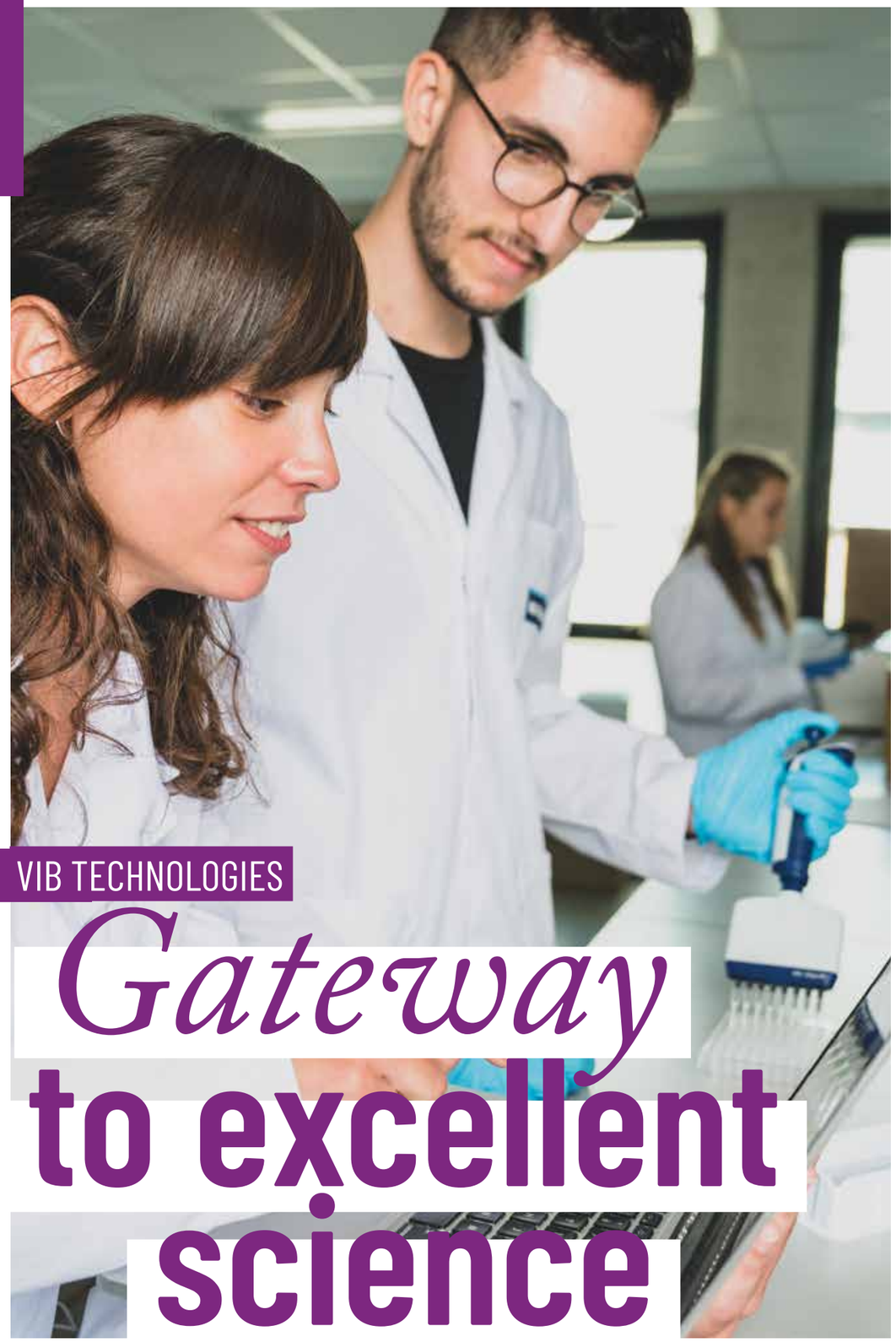
Providing cutting-edge facilities

Access to state-of-the-art infrastructure allows scientists to stay at the forefront of their field.

Since the start, VIB has invested in advanced lab facilities for the VIB community and beyond. VIB also invests in bio-incubators and accelerators to accommodate young biotech companies.

In 2022, the Agro-incubator was refurbished with renewed offices and meeting rooms while the greenhouse has been equipped with a plant phenotyping system and a robotized precision sprinkler.

In partnership with PMV, VIB is currently constructing a new incubator and headquarters at the Techlane Ghent Research Park Campus Eiland in Zwijnaarde. Commissioning of the new building is scheduled for December 2023.



VIB TECHNOLOGIES

Gateway to excellent science

VIB Technologies is a professional program with core facilities embedded throughout most of VIB's research centers and comprising over 100 technology-minded scientists. It provides cutting-edge technologies and expertise to researchers from various disciplines.

Science today is characterized by a multidisciplinary approach. It's not just a matter of applying different technologies to address biological questions, but a real evolution towards integration of different technology fields. For example, with multi-omics and single cell approaches and the strength of bioinformatics, scientists can go much further. It allows them to really peer into and through the cell and even unravel its most fundamental building blocks. The team of VIB Technologies saw these domain synergies emerge firsthand and resolutely moved to work across platforms, both within the Technology program and also with the VIB group leaders, because at this creative intersection is where the truly groundbreaking ideas come to life.

Building *better* base editors

THE CRISPR REVOLUTION

CRISPR gene editing is a powerful biotechnology tool that has revolutionized the biological sciences. It utilizes the DNA-cutting protein Cas9 to make specific changes to DNA sequences, which has numerous applications across different fields. For example, the judicious use of CRISPR has the potential to improve the crops we rely on by making them more resistant to disease and extreme weather conditions. In medicine, it has been used to treat sickle cell disease and clinical trials for many other conditions are underway. The Nobel Prize awarded in 2020 for the development of CRISPR gene-editing tools using the DNA-cutting protein Cas9 is a testament to its significance in the scientific world.

> *When we started the project, there were a few problems with the existing CRISPR base editors. The first was that they didn't work that well. Only a quarter of our targets were edited. The second was that, by then, there was a large number of different CRISPR parts. Using our existing methods to test and evaluate all of the different combinations to find the best one would take too much time. So, we developed ITER.*

FINETUNING AND EXPANDING

The development of CRISPR base editors changed the game. Base editors have the unique ability to replace one specific DNA base (a DNA 'letter') with another, allowing for more precise changes in the DNA sequence. This development was a significant breakthrough, and researchers have continued to refine and improve base editing technology ever since.

Researchers from the team of Thomas Jacobs at the VIB-UGent Center for Plant Systems Biology, BASF Innovation Center Gent, and colleagues from the VIB Screening Core and VIB Flow Core have developed a new method, called ITER, to optimize the performance of CRISPR base editors. ITER, or Iterative Testing of Editing Reagents, is a sensitive, versatile, and high-throughput method to test and quantify gene editing in plant cells. One significant challenge they faced was the sheer number of different parts available to build a functional CRISPR system, making it impossible to evaluate and test all the combinations quickly. To overcome this, they developed ITER, which allowed them to simultaneously test many potential base editors in many cells. With each iteration taking only a few weeks to complete, the researchers could optimize the performance of base editors rapidly.

LOOKING AHEAD

The potential of CRISPR technology is vast, and with the development of ITER, the potential for its application in the biological sciences continues to grow. By using ITER to optimize different types of genome editing tools in various plant species, the team is paving the way for more effective and efficient plant breeding.

Designing *nanobodies* to fight inflammation

GOING OVERBOARD

Sepsis is a potentially life-threatening condition that can lead to septic shock, organ failure and death. Sepsis is a major health concern worldwide and is a leading cause of death in intensive care units.

The inflammatory response to infection, which is initiated by activated myeloid cells, plays a crucial role in the development of sepsis. In sepsis, the overproduction of proinflammatory cytokines, such as macrophage migration inhibitory factor (MIF), can cause significant damage to the body's tissues and organs. Identifying ways to inhibit the action of MIF has become a focus of research in the field of sepsis treatment.

BIOLOGICAL DESIGN AT THE NANOSCALE

Small-molecule inhibitors and monoclonal antibodies against MIF or DNA-based MIF vaccination strategies attenuate inflammation in animal models of sepsis. However, these approaches require either repetitive dosing because of the rapid clearance of the molecules or large amounts of humanized antibodies, which could generate undesirable local and systemic side reactions.

Recent work by the team of Jo Van Ginderachter at the VIB-VUB Center for Inflammation Research describes the isolation and characterization of tailorable, small, affinity-matured nanobodies (Nbs) directed against MIF that binds both human and mouse MIFs. Nbs have several valuable properties that make them promising candidates for the development of biologics with improved potencies and specificities.

The researchers identified 11 Nbs that can reduce the harmful effects of endotoxic shock-mediated lethality. They also inhibit endotoxin-induced TNF production by human monocytes and murine macrophages, suggesting that they can reduce inflammation.

SMALL SIZE, HUGE POTENTIAL

This work provides valuable information regarding the use of Nbs as an effective strategy to interfere with the action of MIF in septic shock and other conditions of inflammatory end-organ damage. More generally, the use of nanobodies as a therapeutic strategy against MIF represents a potential therapeutic option for the treatment of sepsis and other inflammatory pathologies in humans.

The customizable nature of Nbs implies they can be developed for diagnostic and therapeutic purposes in the field of cancer, inflammatory and infectious diseases, neurodegenerative diseases, and so on. The VIB Nanobody Core is continuously streamlining the generation, identification, and engineering of Nbs, as well as the development of technology platforms that make use of the molecules' unique properties.

Leveraging the trove of data

Life sciences research has been inundated with an immense amount of data due to advancements in high-throughput technologies such as next-generation sequencing and new imaging methods. Data management is increasingly crucial for life sciences researchers going forward to shape the future of the field. As an illustration, describing the entire human genome could take up to 130 printed book volumes with 3 billion letters. Today, VIB alone manages approximately 10 petabytes of data.

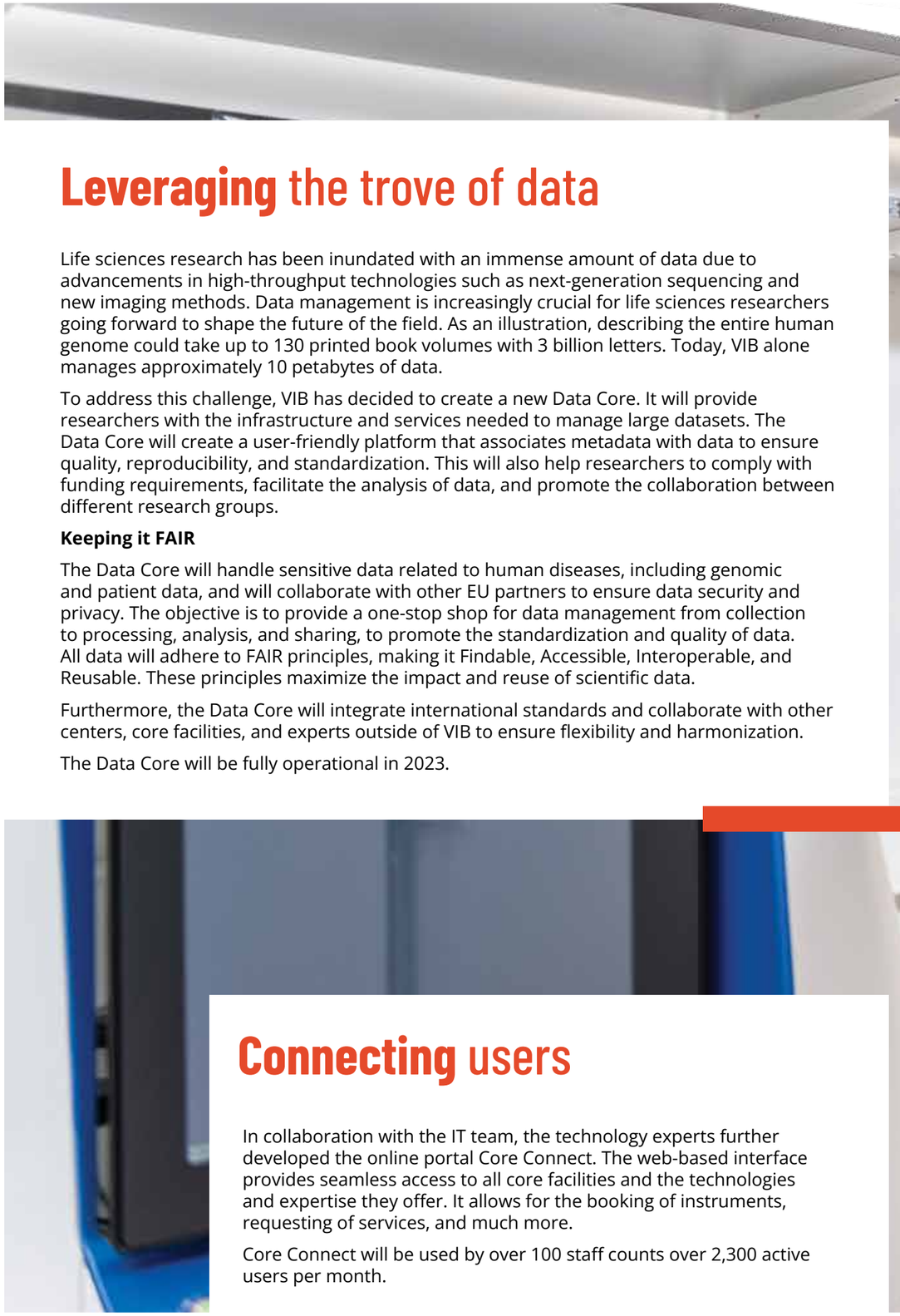
To address this challenge, VIB has decided to create a new Data Core. It will provide researchers with the infrastructure and services needed to manage large datasets. The Data Core will create a user-friendly platform that associates metadata with data to ensure quality, reproducibility, and standardization. This will also help researchers to comply with funding requirements, facilitate the analysis of data, and promote the collaboration between different research groups.

Keeping it FAIR

The Data Core will handle sensitive data related to human diseases, including genomic and patient data, and will collaborate with other EU partners to ensure data security and privacy. The objective is to provide a one-stop shop for data management from collection to processing, analysis, and sharing, to promote the standardization and quality of data. All data will adhere to FAIR principles, making it Findable, Accessible, Interoperable, and Reusable. These principles maximize the impact and reuse of scientific data.

Furthermore, the Data Core will integrate international standards and collaborate with other centers, core facilities, and experts outside of VIB to ensure flexibility and harmonization.

The Data Core will be fully operational in 2023.



Connecting users

In collaboration with the IT team, the technology experts further developed the online portal Core Connect. The web-based interface provides seamless access to all core facilities and the technologies and expertise they offer. It allows for the booking of instruments, requesting of services, and much more.

Core Connect will be used by over 100 staff counts over 2,300 active users per month.

Single Cell Core

In 2022, the Single Cell Core (SCC) was established to offer state-of-the-art services and expertise to researchers seeking to apply single-cell omics workflows into their research. The core provides an integrated approach that spans the multidisciplinary nature of single cell experiments. The expertise required ranges from experimental design to flow cytometry, sequencing, data analysis and visualization. The SCC makes sure that all this expertise from within the SCC team and other core facilities is consolidated. Among its flagship devices is the BD Rhapsody™ single cell analysis system that enables high-throughput capture of multi-omics information from single cells. This technology was already used for 28 projects to study low-input samples, micro-dissected tissue areas and challenging agrobiological samples. In addition, the SCC has invested in increasing the reproducibility of the single-cell omics pipelines through the Hamilton Microlab Vantage, an automated liquid handling platform. This robotics platform can process more samples in less time without risk of error or variability. Furthermore, the SCC team fine-tuned a diverse portfolio of assays based on the 10x Genomics technology, including single cell RNA sequencing, surfacing proteogenomics, and immune cell and epigenetic profiling.

The SSC's experienced staff provides support and coordination throughout the entire workflow to ensure seamless execution. The core will operate across multiple sites in a hub-node structure, with facilities in Leuven, Antwerp, and Ghent. The SCC team really got off to a flying start with more than 130 projects, analyzing 900 samples for 45 different labs.

Accelerating technology uptake

The Tech Watch team scouts and assesses promising life sciences tech innovations for VIB researchers and Core Facilities. For over a decade, Tech Watch has aided scientists in experimenting, adopting, and advancing new technologies. Some examples of 2022 are the MARS platform of Applied Cells adopted in collaboration with the VIB Flow Core, allowing label-free gentle cell sorting using acoustics for cell washing and concentration. To allow for the investigation of new therapeutics, the team introduced the synthetic long DNA fragments from Neochromosome with virtually no restrictions in length, repeats or GC (Guanine-Cytosine) content. VIB Tech Watch also tested and implemented Ambergen's antibody conjugation technology to extend MALDI (matrix-assisted laserdesorption ionization) imaging to intact proteins.

To further stimulate VIB scientists in adopting novel technologies in their research, a hands-on training for single-cell nuclei sequencing was set up in collaboration with the VIB Training Unit. Read more about this training on page 47.

Collaborations between the Tech Watch team and technology providers have earned VIB international recognition as a technology accelerator. VIB is often chosen as a preferred partner to test new technologies, as is illustrated by the cooperation with BGI. The VIB Tech Watch team was asked to test the Stereo-seq technology, enabling unbiased spatial transcriptomics with unprecedented field-of-view and resolution. After positive evaluation of the technology in 2021, the implementation of the Stereo-seq pipeline was set up in 2022 in close collaboration with multiple expertise units at VIB. As such, these collaborations have facilitated the adoption of breakthrough technologies in research environments.

Bringing *cutting-edge technology* to the bench

PIONEERING TECHNOLOGY

The Tech Watch Innovation Lab optimizes and benchmarks prototype platforms and protocols to strengthen the technology portfolio of VIB.

One of the technologies Tech Watch has pioneered for use within VIB is sNucSeq, or single nucleus RNA sequencing. By analyzing the RNA in the nucleus of single cells, sNucSeq has significant implications for understanding genetic heterogeneity within tissues and complex diseases such as cancer, where subpopulations of cells can have unique genetic mutations. With its ability to sequence the genome of individual cells, sNucSeq promises to unlock a new level of understanding in biological systems and accelerate the development of, for example, personalized medicine.

UPTAKE AND TRAINING

A diverse portfolio of sNucSeq assays has been finetuned. As a result, sNucSeq has become available to different VIB Cores and several group leaders have incorporated the technology into their research programs. This technology is often used in more difficult tissues as the isolation of nuclei is generally easier than the isolation of intact cells for single cell sequencing. Traditional methods in single cell sequencing often use enzymes that damage cells, which can lead to an incorrect and incomplete interpretation of the results. As a result, at VIB, sNucSeq is often applied to brain and tumor samples.

The Tech Watch team has also developed hands-on training for single cell nuclei. The course is available via VIB Training and the e-learning platform. The course has been rated as 'very good' (maximum score) by its attendees.

STAYING AT THE FOREFRONT

The rapid development and uptake of sNucSeq technology in VIB is an illustration of how Tech Watch ensures access to cutting-edge technology, an increasingly crucial component of breakthrough life sciences research.

Driving *progress* through innovation & business

The VIB Innovation & Business team ensures that groundbreaking research findings and inventions are translated into practical applications. This can take many forms, such as licensing intellectual property to industry partners, creating new spin-offs, or establishing exciting partnerships and collaborations with companies. By giving researchers the tools they need to bring their findings to the market, VIB is not only driving economic growth, but also creating new jobs, and stimulating investments in the life sciences sector.

De-risking discoveries for smoother translation

VIB's Discovery Sciences (DS) is the translational research lab within VIB's Innovation & Business unit. A dedicated team of industry-trained scientists works closely with VIB group leaders to de-risk and validate innovative targets, biomarkers, and concepts. In doing so, they establish proof-of-concept for agro and drug product pipelines and diagnostic assays. The main goal of the team is to maximize the societal and economic impact of VIB's research.

A prime example of this is the development of the HRD diagnostic test. Explore all the details on page 54.

Furthermore, in 2022 the team has been working on an antisense drug pipeline for Alzheimer's in the context of a new startup company, on small molecule programs for obesity and Parkinson's, three biologics programs in immuno-oncology, respiratory and inflammatory diseases. The team is also exploring technologies for delivering drugs to the central nervous system (CNS) across the blood-brain barrier, biomarker validation for disease risk prediction and the establishment of a soybean transformation platform to support the growing ecosystem in sustainable crops in Flanders.

New VIB startup develops technology for producing **planet-friendly beer** in seconds

Developed through a collaboration between the lab of Kevin Verstrepen and entrepreneur Dirk Standaert, Bar.on is changing the face of the beer industry by allowing consumers to create any beer they desire, in seconds, right from their own countertop. With Bar.on's molecular mixing technology, consumers can experiment with their own flavor combinations, adjusting the alcohol content and flavor profile to suit their own taste. This technology not only offers great convenience but also reduces carbon footprint and packaging waste, making it a truly planet-friendly option.

Bridging the gap between science & industry

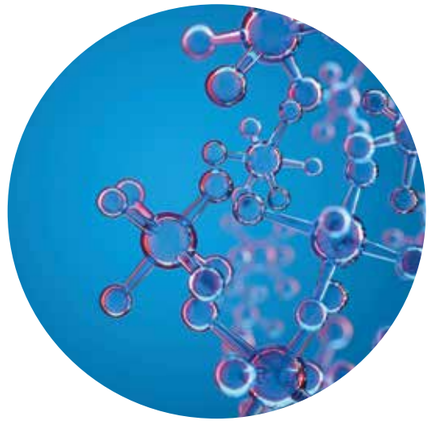
A good example of an R&D collaboration is the cooperation between the lab of Kevin Verstrepen and Chr. Hansen. Chr. Hansen is a global bioscience company headquartered in Hoersholm, Denmark, that develops and produces microbial solutions for the food and beverages, nutritional, pharmaceutical, and agricultural industries. This collaboration resulted in a commercial license on two yeast strains to produce non-alcoholic beverages.

Another striking example is the collaboration with iTeos Therapeutics, a clinical-stage biopharmaceutical company. Together with the lab of Max Mazzone they are developing molecules designating a new immuno-oncology target, paving the way for a new generation of highly differentiated immuno-oncology therapeutics for patients.

Such exciting partnerships are inspiring examples of how bridging the gap between scientific research and the industry can lead to impactful real-world applications.

And it's not only about partnerships – VIB's licensing agreement with Springworks Therapeutics has already led to an important milestone in 2022. Springworks has selected a candidate molecule for further development.

Read more about this agreement on the following page.



Reaping the first *benefits* of an industry collaboration

In 2021, VIB announced a licensing agreement with Springworks Therapeutics, based on a collaboration between the KU Leuven Center for Drug Design and Discovery (CD3), VIB Discovery Sciences, and Georg Halder (VIB-KU Leuven Center for Cancer Biology) and his team.

Nearly two decades ago, Georg Halder's research group identified the importance of the Hippo pathway in cell proliferation and organ growth. Essentially, the Hippo pathway triggers the TEAD (Transcriptional Enhanced Associate Domain) transcription factors through a sequence of molecules and signals. Since the Hippo pathway is genetically altered in approximately 10% of cancers, inhibiting TEAD activation presents an attractive therapeutic strategy.

This collaboration aims to build a portfolio of small-molecule TEAD inhibitors for the treatment of solid tumors.

In 2022, the collaboration reached the first important milestone as Springworks has selected a candidate molecule for further development (SW-682). The company now expects to file an Investigational New Drug Application (IND) for SW-682 in 2023.

This licensing agreement and collaboration serve as a prime example of how effective and persistent collaboration between VIB research groups, VIB Discovery Sciences, and strategic partners can accelerate the development of innovative therapies that create significant social and economic added value from groundbreaking fundamental research.

Helping young biotech entrepreneurs to realize their *dream*

The journey of a young biotech entrepreneur starts with an innovative idea that has the potential to grow into a profitable business. biotope by VIB was devised to help these young entrepreneurs with a new program that combines well-equipped labs, scientific support, and business know-how.

SETTING THE SCENE

biotope by VIB is a pre-seed incubator program designed to provide a dynamic ecosystem that helps young biotech entrepreneurs take flight. Initially, the program will focus on agritech and foodtech applications and later expand to other areas. Whenever possible, biotope will join forces with existing initiatives such as Leuven Mindgate and the imec.istart incubator program. The program hopes to attract international entrepreneurial teams that are developing innovative biotech solutions addressing concrete societal challenges and contributing to the local biotech ecosystem.

The biotope program offers pre-seed funding of 250 K€, milestone-bound to ensure scientific, business, and risk mitigation. In addition, biotope offers a personalized development trajectory, including mentorship and access to lab and office space. Furthermore, the selected startups can rely on the expertise and cutting-edge equipment provided by the VIB Technologies program, expertise units in the Plant Systems Biology Center, and facilities in the biotech ecosystem.

SIX COMPANIES IN THE STARTING BLOCKS

Since its inception in March 2022, the biotope team has launched two calls. In total, 61 applicants from 41 countries submitted project applications. An external advisory committee selected the ten most promising startup teams which were invited to participate in the biotope basecamp, a three-week hybrid program that provides accelerated learning and thorough due diligence on biotech, IP, market preparedness, and team competence. An investment committee of external specialists has selected six startups with the greatest potential to join the extensive biotope incubator program. From dealing with excessive manure, non-dairy cheeses, and plastics made of seaweed to microbial solutions for food, feed, and surfactants, these are the companies biotope by VIB will be supporting over the next year: N-Fix (Be), Bolder Foods (Be), Amphistar (Be), Elogium (LV), Probitat (FI) and B'Zeos (NO). The companies have moved into the VIB Agro-Incubator where they have access to labs, office space, and greenhouses. They have embarked on their tailored one-year journey to become a seed-stage company.

FINANCIAL SUPPORT

In conjunction with the scientific and business guidance, VIB also secured vital financial support by establishing the Biotope Ventures fund, with a first close of 4.5 million euros. Through this separate legal entity, the startups receive 250 K€ in cash in the form of a convertible loan which serves as a kickstart investment to give them the time to derisk the underlying technology, prepare the necessary data, and create a solid business plan to attract professional early-stage investment funds.

Innovative HRD test offers hope to patients with ovarian cancer

Ovarian cancer ranks as the eighth leading cause of cancer-related deaths among women.

TOWARD PERSONALIZED TREATMENT

In Belgium, around 800 women are diagnosed with ovarian cancer annually. The disease carries a very high risk of relapse and poor long-term survival. Currently, surgery and conventional chemotherapy are the primary treatment options. Unfortunately, resistance to chemotherapy drastically reduces the chances of a good outcome for patients.

New targeted therapies, such as Poly (ADP-Ribose) Polymerase Inhibitors (PARPi), offer a more personalized approach that deviates from the 'one-chemo-fits-all' route. Clinical studies have already confirmed the positive effect of these treatments, indicating a long-term response and improved quality of life. To date, however, little is known about the optimal timing for treatment strategies in individual patients and which patients may benefit the most.

In this collaborative project between Diether Lambrechts' team at the VIB-KU Leuven Laboratory for Translational Genetics and Professors Toon Van Gorp and Ignace Vergote of the Department of Gynaecological Oncology at UZ Leuven, a clinically available and ready-to-use biomarker was developed to determine the most suitable therapy for each patient at the optimal time in the treatment process. This project has the potential to significantly impact the lives of individual ovarian cancer patients in Belgium and beyond.

PROMISING RESULTS

Using a targeted Next Generation Sequencing (NGS) approach to detect defective DNA repair mechanisms, they could predict the response to therapy or early disease relapse. This is a prime example of how comprehensive and innovative genomic profiling can revolutionize traditional treatment practices.

The results demonstrated that the VIB-Leuven HRD test has an equivalent predictive power toward therapy response and that the test can be performed significantly faster and more cost-effectively compared to the reference test. The VIB-Leuven HRD test is currently being transferred to the Centre for Human Heredity (CME) at UZ Leuven but it will be made widely available to patients in Belgium and Europe. In parallel, discussions with potential commercial partners for the development of the test in an *in vitro* diagnostic (IVD) format are ongoing.

Securing capital for **sustained innovation**

The VIB spin-offs are constantly looking for creative solutions to the challenging financing environment, from financing rounds to mergers and partnerships.

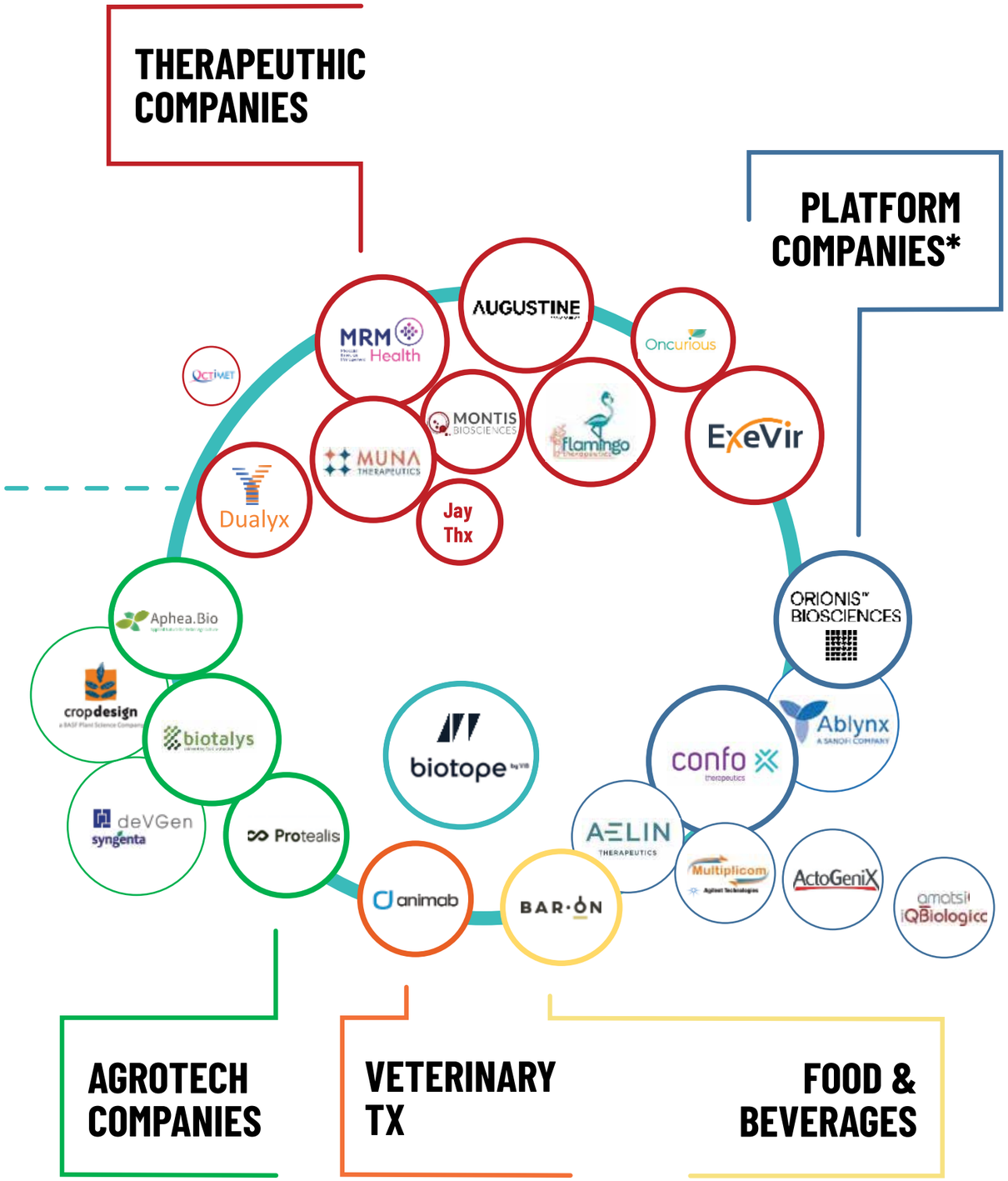
In November 2022, Animab concluded a Series A round of just under 10 M€. These additional funds will allow them to bring their new category of orally administered antibodies for veterinary medicine to market and add new antibody products for animal health to their portfolio.

Another exciting development is the merger between VIB spin-off Flamingo Therapeutics and Dynacure, resulting in a new company focused on developing RNA therapies in oncology under the name Flamingo Therapeutics. The company's current investors, Kurma Partners and PMV, have increased their investments in the company.

Confo Therapeutics also announced a landmark licensing deal with Eli Lilly for its peripheral pain candidate, resulting in an astonishing 630 M$ upfront and milestone payments with the possibility of gaining an additional 590 M$ in milestone payments if the company proceeds with a second product candidate.

And let's not forget Orionis Biosciences, which secured 55 M$ financing to advance its lead cancer immunotherapy programs into clinical trials and cemented a drug discovery deal with Novartis.

Total number of VIB startups: 36
1.72 B€ capital investment (cumulative)
More than 950 employees in total



* companies based on differentiated technologies for discovering new applications

ECONOMIC IMPACT 2022

36 STARTUPS

4 NEW SPIN-OFFS IN 2022

1.6B € CAPITAL INVESTMENT IN TOTAL

950 DIRECT EMPLOYEES

INWARD INVESTMENTS

2 INWARD INVESTMENTS IN 2022

21 INWARD INVESTMENTS IN 25 YEARS

2.6B € CAPITAL INVESTMENT IN TOTAL

+1000 DIRECT EMPLOYEES

INDUSTRIAL INCOME

157M € OVER THE LAST 5 YEARS

VIB

INTELLECTUAL PROPERTY

757 TOTAL NUMBER OF PATENT APPLICATIONS

273 TOTAL NUMBER OF ACTIVE PATENT FAMILIES

INFRASTRUCTURE

BIO-INCUBATOR GHENT

6,322 M^2

12 COMPANIES

BIO-INCUBATOR LEUVEN

15,200 M^2

31 COMPANIES

BIO-ACCELERATOR GHENT

18,000 M^2

3 COMPANIES

In the *Spotlight*

Meet the researchers and discover VIB's outreach activities

VIB owes its success to the people driving scientific research and technology transfer. Find out what inspires them and how they communicate about their work.

If you would like to read the full stories, please visit the VIB blog page (scan QR code).

How young researchers find their feet in neurosciences

To date, the human brain remains one of the most complex and fascinating organs in the known universe. No wonder that many young researchers are drawn to neuroscience and want to gain a distinctive insight into the workings of the brain and discover the thrill of pushing the boundaries and applications of cutting-edge technologies. Çagatay Aydin, who joined the Bonin lab at NERF as a PhD student after concluding his MSc in Biomedical Engineering in Turkey, now helps to develop the second generation of neuropixels. Marie Mulier took a different route. After earning an MSc in biophysics, she chose to delve into the study of pain mechanisms by joining the Voets lab at the VIB-KU Leuven Center for Brain & Disease Research. What do they have in common? Their fascination for technology and their ambition to make it as a neuroscience researcher.

A change of plan

Teun Klein Gunnewiek, who is a postdoc at both the VIB-KU Leuven Center for Brain & Disease and the VIB-UAntwerp Center for Molecular Neurology, originally had Australia in mind to conduct his research. Still, the outbreak of COVID-19 disrupted his plans. Despite the setback, Teun remained unfazed and discovered another window of opportunity much closer to his home country of the Netherlands. He saw an advertisement for a postdoc position to research microglia-synapse interactions in the labs of Joris de Wit and Renzo Mancuso and seized the moment. His research project aims to investigate whether microglia interact differently with synapses in the context of Alzheimer's disease. By working across two different labs, Teun can draw upon complementary knowledge and expertise, and take advantage of alternative research methods and approaches.

The women and science behind an incurable disease

Charcot-Marie-Tooth (CMT) is an inherited disorder that impacts the nerves, causing muscle weakness and loss of sensation. Typically, patients first experience symptoms in their limbs at a young age. CMT affects approximately 2.5 million people worldwide, with around 3,500 cases reported in Belgium alone, making it the most prevalent rare disease.

In the context of CMT awareness month, we interviewed a patient and two researchers who are investigating the disease. Hilde Uytterhoeven, who wasn't diagnosed until she was 32, frankly relates the challenges of living with the disease. Karen Libberecht, a PhD student at the VIB-KU Leuven Center for Brain & Disease Research and UHasselt and Esther Wolfs, Karen's supervisor and lecturer and group leader at UHasselt, talk about their research and how they use a model to better study Schwann cells, which are affected in CMT.

How the love of data led to a career as group leader

Wet lab or dry lab? That was the question for Katleen De Preter. While working on her Master's and PhD theses, it became apparent that she found analyzing the data resulting from experimental work the most enjoyable. Manipulating and visualizing the data gave her satisfaction and that is why she decided to specialize in R, a popular programming language and software environment used for statistical computing and graphics, and bioinformatics. At the end of 2022, Katleen joined the VIB-UGent Center for Medical Biotechnology and created the Lab of Translational Oncogenomics and Bioinformatics (TOBI) where she and her team develop analytical and bioinformatic pipelines for diagnostic, prognostic, and predictive analyses, which can lead to more accurate cancer management.

How does climate change affect our daily bread?

Bread has played a significant role in the traditional European diet for centuries, dating back to ancient civilizations. Historically, bread has been a key source of carbohydrates and other nutrients. Even today, bread remains a common daily item on the Western table. However, rising temperatures, droughts, floods and other extreme weather conditions caused by climate change can reduce crop yields, making it harder to produce enough wheat and other grains needed for bread production. In addition, political conflicts can disrupt the supply chain, causing certain ingredients to become scarce or unobtainable, complicating the production process.

In comes Ive De Smet, group leader at the VIB-UGent Center for Plant Systems Biology, who investigates the biology of how wheat and other plants react to elevated temperatures.

Alumni spreading their wings to pursue new challenges

For over 25 years, VIB has been a fertile breeding ground for PhD students and postdocs. With a backpack full of scientific knowledge, unique experiences, and the necessary skills gained during their time at VIB, over 5,000 young researchers have departed, ready to embark on successful careers. The career paths for these young people are very diverse, ranging from academic positions as researchers or professors to roles in the industry for drug discovery or product development, as well as science communication and consultancy positions.

Staying in touch with their 'alma mater' can benefit our alumni as it allows them to expand their professional network and connect with other alumni who may be in their field or industry. And they can also 'give back' to VIB by sharing their experience and inspiring other young researchers to make the right choices.

VIB has implemented various initiatives to facilitate alumni engagement. One of the newest initiatives is the VIB Alumni Series, which kicked off in 2022. These networking events held prior to major VIB Conferences, aim to foster interaction between VIB alumni and current staff members.

Why *public outreach* matters

At VIB, researchers are encouraged to participate in public outreach initiatives to share their knowledge, inform the public about their work, actively listen to people, and collaborate with communities beyond academia.

Public engagement helps to effectively communicate VIB's goals, build trust, inspire future scientists and encourage collaboration.

Growing soy in Flanders

Soybean is a vital source of plant-derived protein for food and animal feed. Its cultivation improves soil quality and reduces the need for nitrogen fertilization, thereby curbing nitrogen pollution and making it a sustainable crop. Currently, the majority of soybean cultivation takes place in South America, with Belgium importing approximately 800,000 tons of soy and soy-derived products annually, mainly for animal feed. Latin America is expanding its soybean production to meet growing global demands, with devastating consequences for local biodiversity due to deforestation. Furthermore, climate change necessitates Belgian farmers to grow alternative, subtropical crops for human consumption.

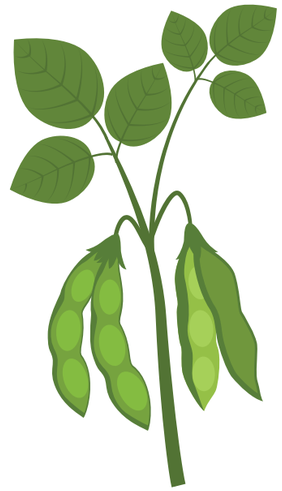
Sustainable, local soy production would reduce our dependency on imports and reduce our ecological footprint. It is currently challenging to cultivate soy in Belgium with an acceptable yield due to its need for interaction with nitrogen-fixing *Rhizobium* bacteria in their root nodules. The commercially available bacterial inoculants are not adapted to the Belgian soil and environmental conditions.

WITH THE LITTLE HELP OF SOME FRIENDS

The Soy in Flanders project promotes soy as a sustainable crop in Flanders by engaging citizens to grow soy in their own gardens. Through collaboration between the citizens and scientists, the project aims to isolate nitrogen-fixing bacteria from soy plants grown in Belgian soil, integrate data on soil type, microorganisms, and soy variety to develop optimal cultivation methods, improve public knowledge and awareness of the benefits of legumes, and produce tailored soy seeds adapted to local soil conditions.

Following an extensive media campaign by VIB, 1,200 citizens, including farmers, were successfully recruited in Flanders. Over a period of six months, the soy seeds and plants were closely monitored, and citizens reported on the growth and yield parameters.

The Soy in Flanders project was integrated into various educational and public outreach activities. In addition, an arts and science project was developed in collaboration with Bozar and Gluon, resulting in an installation on 'plant immigration' drawing public attention during several exhibitions.



Turning the tables

A SEAT AT THE TABLE

Reverse Science Cafés (RSCs) promote dialogue between experts (scientists, clinicians) and end users (patients, citizens, farmers) in an open and interactive discussion. This approach allows the identification of unmet needs and potential recommendations to remedy these.

VIB's first experience with this RSC approach already came in 2019, when a first RSC was held in the context of the Grand Challenges PID project in 2019, to consult patients and their families about the daily struggles related to their disease. The discussion resulted in a documentary that shed light on the daily lives and struggles of PID, which was nominated for the Edelweiss award by the Belgian Rare Diseases Patient Organization Radiorg.

OPENING UP THE DISCUSSION

Building on the PID experience, VIB organized reverse science café sessions as part of the Soy in Flanders project in 2022. Scientists met up with citizens and farmers to collect feedback and lessons learned about the citizen science methodology, including questionnaires, platforms, and bias towards intrinsically motivated participants. Additionally, farmers' concerns and questions about local soy cultivation, including yield stability, market security, and technical breeding difficulties, were identified. The continued development of the Soy in Flanders project will incorporate the collected feedback.

The first RSC for the Spartacus project took place in the beginning of 2023. As this project aims to improve treatment for spondylarthritis patients, the patients' view on treatment changes is essential. During the RSC, patients expressed the need for preventive measures, better communication about clinical trials and more awareness of the disease in society.

IN THE SPOTLIGHT

Inspiring the *scientists* of the future

VIB believes in the need to play an active role in promoting the significance of biotechnology through various approaches, including disseminating science-based information for diverse audiences, hosting public outreach events, and several educational projects. Our efforts are aimed at people of all ages, especially children and adolescents to inspire the next generation of scientists.

This is particularly important to increase the number of students in STEM disciplines. Although the popularity of STEM has already improved over the last years, considerable efforts are still needed to counter – among other things – the gender imbalance in professional STEM bachelors.

SCIENCE ON THE ROAD

Science on the road (better known as 'Wetenschap op Stap' in Dutch) is a program that aims to spark curiosity and interest in science among pupils who are between 10 and 12 years old. The program invites practicing scientists to visit classrooms and engage with the pupils.

Before the scientist's visit, the pupils are encouraged to do some research on the topic the scientist studies and prepare some questions so that they can interact with the researcher and make the most of the visit. In 2022, 70 VIB scientists visited approximately 2,000 children in their classrooms.

MAGIC SOYBEANS AND THE POWER OF BLOOD

'Magic soybeans and their friends' is a project focused on sustainable soy cultivation based on the Grand Challenges project, Soy in 1,000 gardens'. Pupils aged 10 to 12 plant and grow soybeans at school to learn more about the interesting challenges of growing this crop.

In 'The power of blood' project, a combination of fun presentations, simple experiments, and data analysis, lets students aged 10 to 12 explore the world of blood and learn about its importance in their lives.

Together, these two projects have reached about 80 classes or approximately 2,000 pupils for the 2022-2023 school year.

VIB also offers experimental kits for DNA separation and visualization, as well as ELISA kits for detecting antigens in the classroom. These kits are designed for older students between 14 to 18 years old, and last year, VIB reached over 2,525 with the DNA kits and over 1,000 students with the DNA and ELISA kits.

VIB also teamed up with VRT to develop a digital learning tool called Pandemics EDUbox to inform young people about pandemics, how they occur, and how we can combat them. And, for teachers looking for extra resources, VIB developed a range of materials and brochures to support science education in the classroom.

Organization & governance

Managing a research institute as diverse and complex as VIB, with multiple locations and disciplines, requires a suitable organizational framework.

General Assembly (GA)

VIB is a non-profit organization and its most senior body is the general assembly. The general assembly meets at least once a year. During this meeting, they approve the institute's annual activity report of the previous year and the next financial year's budget. The GA is also authorized to change the organization's articles of association, approve the accounts and budgets; and appoint and revoke general assembly members. The GA consists of 41 members representing the ecosystem in Flanders with representatives from the universities and other scientific institutes, the life sciences industry, employee organizations and the Flemish government.

Board of Directors (BoD)

The Board of Directors heads the association, it holds fulll authority over all management actions and represents it extrajudicially. The daily management responsibilities are assigned to the general management, but the BoD determines their authorities and evaluates their performance. The BoD meets five times a year to take decisions concerning the management and strategic direction of the institute. Additionally, the BoD has formulated the Good Governance Charter and ensures its compliance. The board comprises 13 members, including six Flemish university delegates, four business representatives and two representatives from the Flemish government.

Institutional Advisory Board

The Institutional Advisory Board (IAB) serves as an advisory body for VIB and is responsible for formulating regular recommendations to VIB on its institutional policy. Additionally, the IAB discusses policies to improve the performance and global recognition of VIB as a center for life sciences research. The IAB is composed of distinguished international scientists and managers.

General Management

Christine Durinx and Jérôme Van Biervliet (Managing Directors), ensure the institute's day to day management. They are assisted by the unit managers.

Directors' Committee

The directors of VIB's research centers serve as the institute's scientific leaders and are responsible for VIB's scientific direction. They, along with certain members of the general management from VIB HQ, form the institute's Management Committee (MC).

Group Leader Committee

The Group Leader Committee (GLC) is an advisory board and equal partner to the MC to make decisions on any issues related to principal investigators (PIs), to ensure a creative, stimulating and inclusive work community conducting impactful science at a globally competitive level. The GLC constitutes a voluntary team of VIB group leaders (GLs) from each of the VIB Centers and a representative from the VIB Core Facilities. It acts as a solution-oriented think tank and communication hub between GLs and VIB-HQ/MC, working proactively and responsibly on GL-related opportunities and challenges at VIB.

Postdoc Committee

The Postdoc Committee (PDC) enhances collaborations and connections both within and between VIB research centers and industry while providing a supportive network for postdocs to develop their soft skills and advance their careers.

VIB Technologies

Scientific Advisory Boards

Each VIB research center has a Scientific Advisory Board that consists of international experts in the field. It plays an important role in defining the strategic directions of the center, together with the science directors, and it helps to shape research programs.

Organization & governance

VIB Board of Directors

ACADEMIC REPRESENTATION

Anne De Paepe
Prorector, UGent

Luc Moens
Professor, UGent

Christel Van Geet
Vice-rector, KU Leuven

Gerard Govers
Vice-rector, KU Leuven

Ronny Blust
Vice-rector, Universiteit Antwerpen

Hugo Thienpont
Vice-rector, Vrije Universiteit Brussel

INDUSTRY REPRESENTATION

Ajit Shetty
Honorary chairman, Janssen Pharmaceutica

Staf Van Reet
Managing Director, Viziphar Biosciences

Marleen Limbourg
Founding Partner, Atoms & art

Griet Nuytinck
Managing Director, Anacura

Koen Quaghebeur
Director, Globachem

GOVERNMENT OF FLANDERS

Dieter Deforce
Professor, UGent

Bart De Moor
Professor, KU Leuven

Directors' Committee

Christine Durinx
Managing Director VIB

Jérôme Van Biervliet
Managing Director VIB

Bart Lambrecht
Science Director VIB-UGent Center for Inflammation Research

Dirk Inzé,
Science Director VIB-UGent Center for Plant Systems Biology

Nico Callewaert
Science Director VIB-UGent Center for Medical Biotechnology

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

Diether Lambrecht
Science Director VIB-KU Leuven Center for Cancer Research

Kevin Verstrepen
Science Director VIB-KU Leuven Center for Microbiology

Jan Steyaert
Science Director VIB-VUB Center for Structural Biology (spokesperson for all VIB research centers)

Rosa Rademakers
Science Director VIB-UAntwerp Center for Molecular Neurology

Rik Audenaert
CFO

Marijke Lein
HR director

Wim Goemaere
COO

Geert Van Minnebruggen
CTO

Institutional Advisory Board

Detlef Weigel
Director, Max Planck Institute for Developmental Biology, DE

Kay Davies
Director, MRC Functional Genomics Unit, Department of Physiology Anatomy & Genetics, UK

Huda Zoghbi
HHMI Investigator, Professor Baylor College, US

Peter Piot
Handa Professor of Global Health and former Director of the London School of Hygiene & Tropical Medicine

Aviv Regev
Executive Vice President, Research and Early Development, Genentech, South San Francisco, US

Daria Mochly Rosen
Professor, Chemical & Systems Biology – Stanford, Founder and co-director SPARK, US

Luc Debruyne
Strategy advisor to CEO of CEPI, Board member UZ KU Leuven, Board member Z.org KU Leuven, Board member Fund Plus, BE - Life science Board member Greenlight BioSciences, US

Susan Gasser
Director, ISREC Foundation, Lausanne, CH

Balance sheet

(€ THOUSANDS)

ASSETS	31.12.2022	31.12.2021	31.12.2020	2022-2021%
Intangible fixed assets	3 906	2 812	1 925	39%
Tangible fixed assets	34 857	33 900	33 970	3%
Financial fixed assets	53 510	53 929	46 686	-1%
Contracts in progress	11 927	10 596	14 265	13%
Amounts receivable after one year	121			
Amounts receivable within one year	15 452	21 497	19 942	-28%
Investments	116 811	100 970	90 418	16%
Cash at bank and in hand	29 878	27 797	35 373	7%
Deferred charges	4 186	3 280	2 730	28%
TOTAL ASSETS	270 648	254 781	245 309	6%

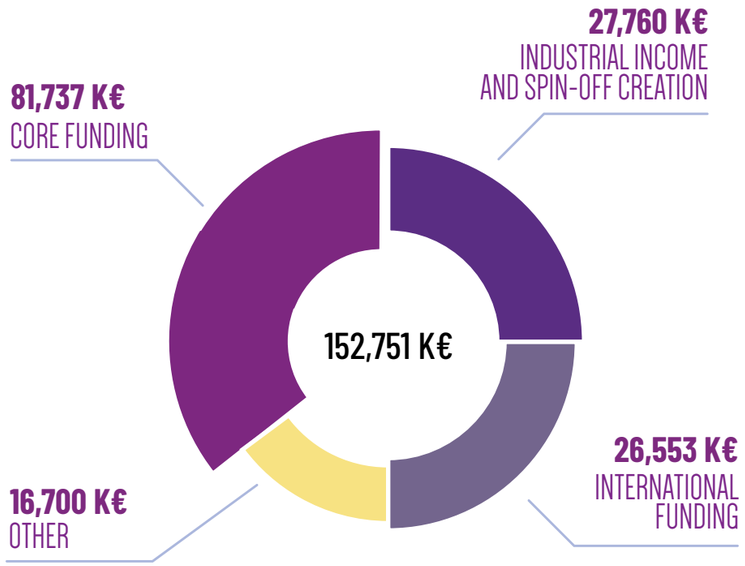
LIABILITIES				
Allocated funds	115 717	120 963	115 184	-4%
Investment grants	38 470	35 837	34 438	7%
Amounts payable after one year	13 958	16 010	15 120	-13%
Amounts payable within one year	57 862	46 286	51 918	25%
Accrued charges and deferred income	44 641	35 685	28 649	25%
TOTAL LIABILITIES	270 648	254 781	245 309	6%

Profit & loss statement

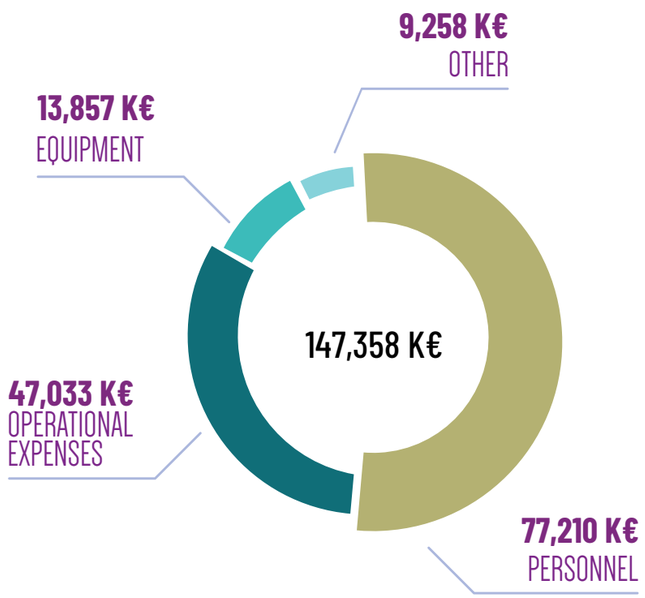
(€ THOUSANDS)

OPERATING INCOME	139 153	124 611	120 464	12%
Turnover (from contract research)	36 928	47 760	34 313	-16%
Contracts in progress (+/-)	1 331	-3 670	175	-136%
Grants and subsidies	99 978	84 436	84 248	21%
Other income	916	2 085	1 728	-56%
OPERATING EXPENSES	**-137 269**	**-120 421**	**-117 550**	**14%**
Raw materials and consumables	-13 027	-12 467	-12 160	4%
Services and other goods	-35 212	-29 987	-30 802	17%
Remuneration, social security costs and pensions	-75 568	-65 139	-63 730	16%
Depreciation	-11 843	-11 040	-9 961	7%
Other operating expenditures	-1.619	-1 788	-897	-9%
Financial income	**543**	**1 628**	**506**	**-67%**
Financial charges	**-7 397**	**-631**	**-848**	**1072%**
Extraordinary income	**748**	**92 398**	**9 796**	**-69%**
Extraordinary expenditure	**-1 024**	**-1 806**	**-5 659**	**-43%**
PROFIT/LOSS FOR THE FINANCIAL YEAR	-5 246	5 779	6 709	-191%

Revenue 2022



Expenses 2022



*ESR figures

Good governance

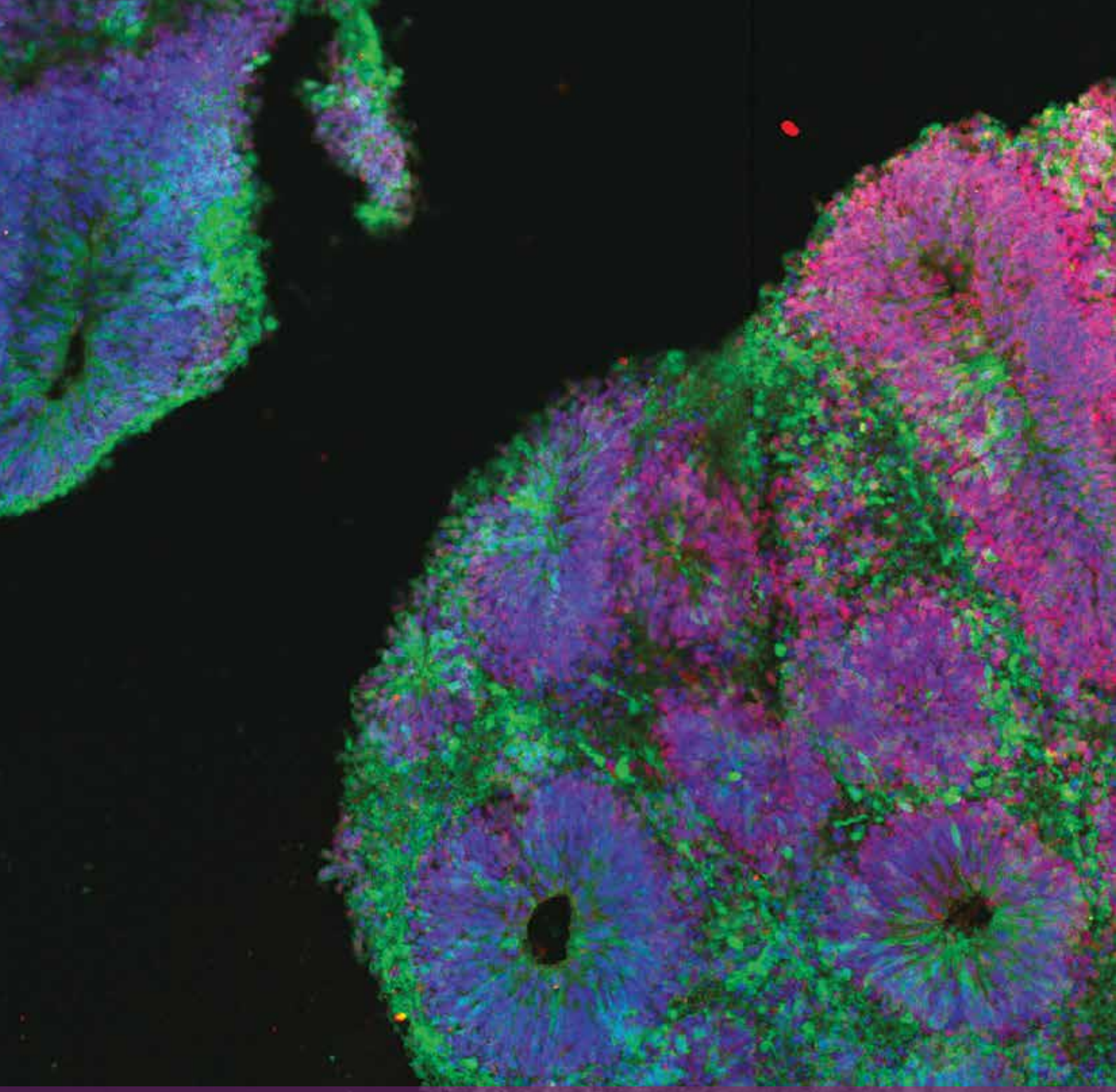
VIB has implemented a 'Good Governance Charter', which is publicly available on our website. Our principles of good governance are regularly evaluated and refined, allowing us to benefit from local and global advancements in this area and meet the expectations of all our stakeholders.

Sustainability reporting

VIB's annual report provides a comprehensive overview of the societal impact of our research.

VIB has already taken several initiatives to decrease the environmental impact of its operational activities.

The European regulatory framework on sustainability and sustainability reporting, including the CSR Directive and the ESA standards, has been implemented nationally. Although these standards are not mandatory for non-profit organizations, VIB regards sustainability and sustainability strategy as crucial and will use these regulations as guidelines. We will further develop and enhance our existing initiatives in accordance with the evolving European framework by formulating and communicating a strategy, establishing a monitoring system, and setting up reporting and validation procedures for our initiatives.



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The cover shows human brain organoids imaged with confocal microscopy.

Image: Vanderhaeghen Lab, VIB-KU Leuven Center for Brain & Disease Research

R.E. Christine Durinx, Rijvisschestraat 120, 9052 Ghent, Belgium - D/2023/12.267/1