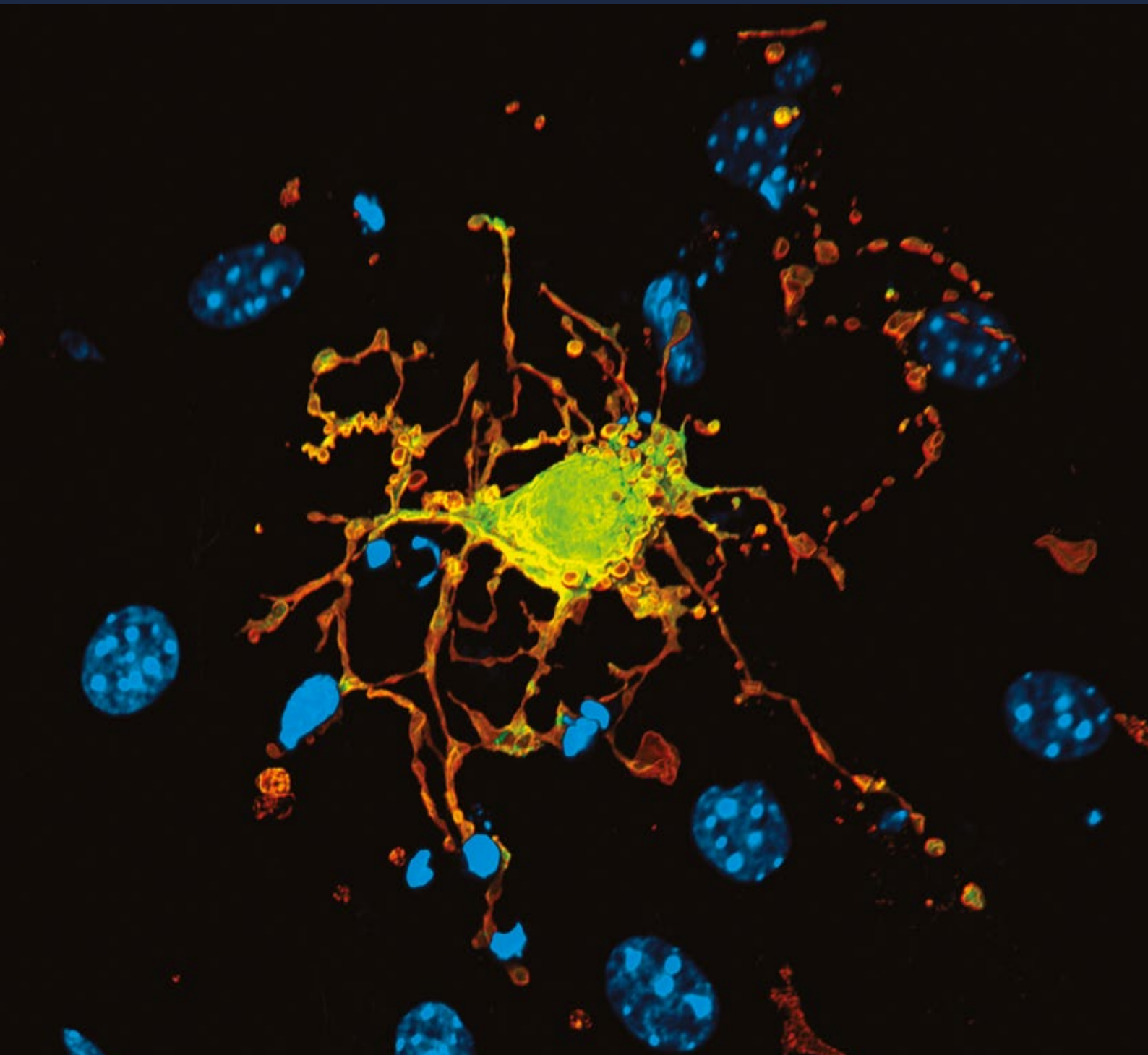
VIB TIMES
QUARTERLY NEWSLETTER OF VIB.
SEPTEMBER 2018



SINGLE CELL AT VIB

ACCELERATING PROMISING TECHNOLOGY

DAWN OF THE SINGLE-CELL ERA

Novel technologies allow the genetic profiling of every single cell within a tissue sample, whole organ or even complete organism. This is quickly revolutionizing our knowledge of biological systems across distinct research fields. No wonder many VIB groups have moved to using single cell techniques which have several advantages over earlier methods.

We ourselves recently experienced that using single cell sequencing rather than previous bulk sequencing methods, was crucial to correctly identify the critical role of ZEB2 in macrophages (page 7). Having originally performed bulk analysis for this project, we learnt our lesson about the benefits of single cell technologies, even when homogeneity is assumed. This strengthens our conviction to focus efforts on these technologies going forward. A conviction shared with many VIB colleagues.

VIB groups are actively contributing to the single-cell revolution. In this edition of VIBnews you can find a tour de force from the Stein Aerts lab who provided the first single-cell atlas of the entire fly brain during aging (page 10), from Diether Lambrechts and Bernard Thienpont who sequenced 52,698 single cells from 5 different lung tumors generating a catalogue of more than 50 cell subtypes (page 7), from the group of Jean-Christophe Marine who investigated the presence of drug-tolerant malignant cells responsible for disease relapse during anti-cancer therapies (page 12) and from the Jan Cools group whose research led to a better understanding of oncogene cooperation (page 7). Don't forget how lucky we are to have great bio-informaticians within the VIB Bioinformatics Core, but also in the teams of Yvan Saeys and Stein Aerts, who are developing algorithms to analyze and mine these fascinating datasets.

The expertise in single cell technologies at VIB is attracting significant interest from international consortia and private companies, such as the LifeTime FET Flagship consortium and the Human Cell Atlas Consortium (page 14). And there is of course the Single Cell Accelerator program at VIB (pages 4 till 9), headed by the VIB Tech Watch team with many VIB PI's involved and with Janssen Pharmaceutica as the first company to plug into this initiative (page 16). Collaboration within VIB will be key to develop the strongest protocols to be used by many different teams to solve their unique biological questions.

Thanks to all these research efforts and initiatives, VIB will definitely remain at the forefront of single cell research with access to state-of-the-art technologies for all VIB groups. Clearly, this is just the beginning and exciting times lie ahead for VIB and single cell technologies!

Charlotte Scott & Martin Guilliams, VIB-UGent Center for Inflammation Research

Charlotte Scott and Martin Guilliams

INTERESTED IN RECEIVING VIBTIMES ELECTRONICALLY? PLEASE REGISTER AT WWW.VIB.BE/VIBTIMES

SINGLE-CELL TECHNOLOGY AT VIB

The Single Cell Accelerator drives VIB to the forefront of single-cell research 4
The Single Cell Accelerator team 6
Single Cell Accelerator projects in the Technology Innovation Lab 8
Creating the world's first complete fruit fly 'cell atlas' 10
Zeroing in on drug-tolerant cancer cells 12
LifeTime FET Flagship 14
VIB leads by example in single-cell research 15
Janssen first industrial partner to plug into Single Cell Accelerator 16
Our Single Cell Research in the spotlights at SuperNova 17

SCIENCE MEETS SCIENCE

VIB Grand Challenges Program 18
Quickscan 19
New insights in cell death in plants might generate new leads for weed control 22
New weapon against chemotherapy-resistant cancer cells discovered 24
New research reveals central role of the hippocampus in instructing the neocortex in spatial navigation and memory 26
Towards robust and reliable artificial intelligence 28
VIB scientists map the Belgian beer landscape in a new book 29

SCIENCE MEETS BUSINESS

Revolutionary molecular diagnostic cancer test 30

SCIENCE MEETS PEOPLE

Awards 32
Reporter on the road: From cellfies to sciencegram 34
Puzzling together plant evolution through art 36
VIB alumnus and MSF scientist Rafael Van den Bergh bridges the implementation gap 38
Who will take home the next Alumni award? 40

EVENTS

CTLS2018: highlighting the fundamental role of life sciences technologies 42
Mark your calendar 44

On the cover: 3D rendering of a pluripotent stem cell differentiated into an oligodendrocyte. © VIB Bioimaging Core

THE SINGLE CELL ACCELERATOR DRIVES VIB TO THE FOREFRONT OF SINGLE-CELL RESEARCH

VIB was one of the earliest adopters of disruptive single-cell technologies, boosting research in this ground-breaking field. In April 2018, the VIB 'Single Cell Accelerator' program was launched to aid access to multiple innovative single cell platforms and to foster technology development tools. This new program will run through VIB's Tech Watch initiative and will inject additional funding and technological support into emerging single-cell technologies.

Single-Cell Technology at VIB

SINGLE-CELL TECHNOLOGIES ARE CHANGING LIFE SCIENCES RESEARCH

There has been a huge rise in the development and use of emerging single-cell technologies across the globe. These technologies have rapidly enhanced the molecular understanding of functional cell states underlying diseases such as cancer and inflammatory and neurodegenerative illnesses, which encompass the focal areas of about 50 research groups at VIB.

In 2016, the VIB Tech Watch team invested in one of the first 10X Genomics Chromium platforms in Europe, enabling single-cell RNA sequencing. Since then, VIB has been working at the cutting edge of the single-cell field by testing emerging applications and developing complementary technologies and downstream data analysis tools in house. As a result, single-cell analysis is now considered an essential and routine tool used to address fundamental research questions in about 50 research groups at VIB.

Diether Lambrechts (VIB-KU Leuven Center for Cancer Biology), one of the early adopters of the 10X Genomics Chromium platform, agrees that his research has benefited enormously from this platform: "Large-scale single-cell data allowed us to generate a catalog of the tumor microenvironment transcriptome at single-cell resolution, enabling us to identify multiple discrete cell populations for the first time."

VIB SINGLE CELL ACCELERATOR

A new initiative, the 'VIB Single Cell Accelerator' (SCA), was launched at the VIB seminar in April 2018. Through this initiative, VIB scientists will have access to significant additional funding in 2018-2019 to evaluate, develop and integrate emerging breakthrough single-cell technologies at VIB. The SCA will initially run for two years, and VIB groups can apply for SCA funding through the Tech Watch application process. Technology platforms will be placed in the Technology Innovation Lab (physically embedded in a host lab space, a PI's lab or a core facility), and these projects will be managed by trained technology specialists. These experts will troubleshoot to optimize the technologies and subsequently train VIB scientists in the labs to disseminate their expertise.

Halina Novak, Technology Innovation Manager at VIB, says: "By combining disruptive single-cell platforms, technology development projects, specialized data analysis and modeling tools to process omics data, and coupling this expertise with respective research themes, this program enables VIB to excel rapidly in the single-cell field." Areas of great interest to VIB in the SCA include spatial omics for the validation of single-cell sequencing data to localize distinct cellular subsets *in situ*, single-cell manipulation technologies for immune profiling, isolation, culturing, pharmacogenetics, cellular extraction/cell building and single-cell genomics.

"This program enables VIB to excel rapidly in the single-cell field."

- Halina Novak

SINGLE-CELL TECHNOLOGY EVALUATION, IMPLEMENTATION AND DEVELOPMENT

Martin Guilliams and Charlotte Scott from the VIB-UGent Center for Inflammation Research will use the SCA initiative to investigate spatial and multi-omics technologies that will contribute to their participation in the 'Human Cell Atlas' (HCA) program. This international initiative seeks to characterize all cell types in the human body at the single-cell level, which will serve as a basis to understand human health and disease. By profiling healthy and diseased liver samples at the single-cell level, they will contribute significantly to this program.

"Ongoing single-cell sequencing efforts and subsequent spatial omics technologies will no doubt rewrite scientific textbooks over the next decade," Martin Guilliams asserts. "Through the HCA, we will collectively investigate individual cell subsets in all major tissues for the most prominent diseases. This will be determined for humans as well as major model systems, revolutionizing biomedical research and ultimately bringing new cures to the clinic."

Toon Swings, Life Sciences Technology Specialist and until recently part of the Jan Michiels Lab at the VIB-KU Leuven Center for Microbiology is particularly excited about the evolution in single-cell culturing, isolation and manipulation technologies in the field of microbiology. "This will enable scientists to study the human microbiome in unmatched detail in relation to human health conditions," he explains.

"This will enable scientists to study the human microbiome in unmatched detail in relation to human health conditions."

- Toon Swings

INSPIRING NOVEL IN-HOUSE ANALYTICS AND MODELING TECHNIQUES

Yvan Saeys (VIB-UGent Center of Inflammation Research), and Stein Aerts (VIB-KU Leuven Center for Brain & Disease Research) note that the wealth of data generated by single-cell platforms presents unprecedented opportunities for bioinformatics and data analysis. This resulted in the in-house development of bioinformatics pipelines, including gene regulatory network analysis (SCENIC, Aerts lab), lightning-fast single-cell visualization tools (SCope, Aerts lab), and automated flow analysis (FlowSOM, Saeys lab).

The latter has recently shown to be one of the best-performing methods for automated cell type identification for flow and mass cytometry data. More recently, the group of Yvan Saeys began work on novel tools to gain a better understanding of cell developmental dynamics using single-cell data. Their large-scale benchmarking study comparing such algorithms attracted a lot of attention at the most recent Human Cell Atlas meeting in Hinxton.

"Even more exciting times are ahead," states Yvan Saeys. "Multi-omics technologies are able to capture more and more complementary types of information from the same cell. The spatial resolution that is already offered by some technologies will lead to novel modeling tools that will allow us to better study cell dynamics and intercellular communication, and I think this is one of the most appealing prospects offered by these new technologies."

"Multi-omics technologies are able to capture more and more complementary types of information from the same cell."

- Yvan Saeys

VIB TAKES THE LEAD IN DEVELOPING NEW SINGLE-CELL TECHNOLOGIES

Pioneering VIB groups are also investing significantly in the development of single-cell technologies, such as the Stein Aerts Lab, which is now focusing on single-cell epigenomics. The Aerts Lab is also developing new approaches to capture single cells in nanoliter droplets using microfluidic devices, allowing the flexible analysis of RNA or chromatin from tens of thousands of single cells in parallel.

THE SINGLE CELL ACCELERATOR TEAM

Joining together the expertises from researchers within the different VIB Centers and the VIB Techwatch Team, VIB can rely on a strong SCA team. We are proud to introduce them to you:

- Bob Asselbergh, Staff Employee at the VIB-UAntwerp Center for Molecular Neurology
- Yvan Saeys, Group Leader at the VIB-UGent Center for Inflammation Research
- Martin Guilliams, Group Leader at the VIB-UGent Center for Inflammation Research
- Diether Lambrechts, Science Director at the VIB-KU Leuven Center for Cancer Biology
- Jean-Christophe Marine, Science Director at the VIB-KU Leuven Center for Cancer Biology
- Stein Aerts, Group Leader at the VIB-KU Leuven Center for Brain & Disease Research
- Suresh Kumar Poovathingal, Staff Scientist at the VIB-KU Leuven Center for Brain & Disease Research
- Geert Van Minnebruggen, Head of Core Facilities at VIB Headquarters
- Halina Novak, Technology Innovation Manager at VIB Headquarters
- Silvie Van den Hoecke, Life Science Technology Specialist at VIB Headquarters
- Toon Swings, Life Sciences Technology Specialist at VIB Headquarters
- Wai Long Tam, Life Science Technology Specialist at VIB Headquarters

QUICKSCAN

#Leukemia #Oncogenes #Sequencing #Progenitor cells #Single Cell Technology

Acute lymphoblastic leukemia (ALL) is the most common childhood cancer that is characterized by the accumulation of 10 to 20 protein-altering mutations. To better understand in which order these mutations are acquired and in which progenitor cells this is initiated, the Jan Cools lab (VIB-KU Leuven Center for Cancer Biology) used single-cell sequencing of total bone marrow cells and CD34+CD38- multipotent progenitor cells for four T-cell ALL cases. Hierarchical clustering detected a dominant leukemia cluster at diagnosis, accompanied by a few smaller clusters harboring only a fraction of the mutations. Analysis of the order of mutations showed that loss of 9p21 (CDKN2A/B) and acquisition of fusion genes were rather early events, while NOTCH1 mutations were typically late events. Analysis of progenitor cells revealed that the first mutations can be acquired in either multipotent progenitors or in lymphoid progenitors. The team is currently continuing this study to determine how chemotherapy treatment has an effect on the clonal evolution in ALL.

De Bie *et al.,* Leukemia 2018

2

#ZEB2 #Macrophages #Transcription Factor #Single Cell Technology

The team of Martin Guilliams, Charlotte Scott and Wouter T'Jonck (VIB-UGent Center for Inflammation Research) demonstrates that the transcription factor ZEB2 is crucial for the maintenance of the specific identities of tissue-resident macrophages. Using the 10X genomics platform (via the SCA), the researchers sequenced RNA from liver, lung, spleen, colon and brain macrophages from mice either expressing or lacking ZEB2. Analysis of this data in collaboration with the team of Yvan Saeys (VIB-UGent Center for Inflammation Research) led to multiple discoveries which would have been missed with bulk sequencing. Firstly, not all the macrophages in the conditional KO mice efficiently eliminated ZEB2, with a proportion of macrophages in each tissue (except brain) maintaining one copy of this gene. Discriminating between these different cells was crucial in understanding the function of ZEB2 in macrophages. Secondly, the team were able to redefine the genes which contribute to the tissue-specific identities of the different macrophages, without including genes arising from contaminating cells that were present in previous bulk sequencing data. Having redefined the identities of the different macrophages, it was clear that loss of ZEB2 dramatically altered these profiles in a tissue-specific way, rendering the macrophages unfit for their specific environment and leading to their loss from their tissue of residence.

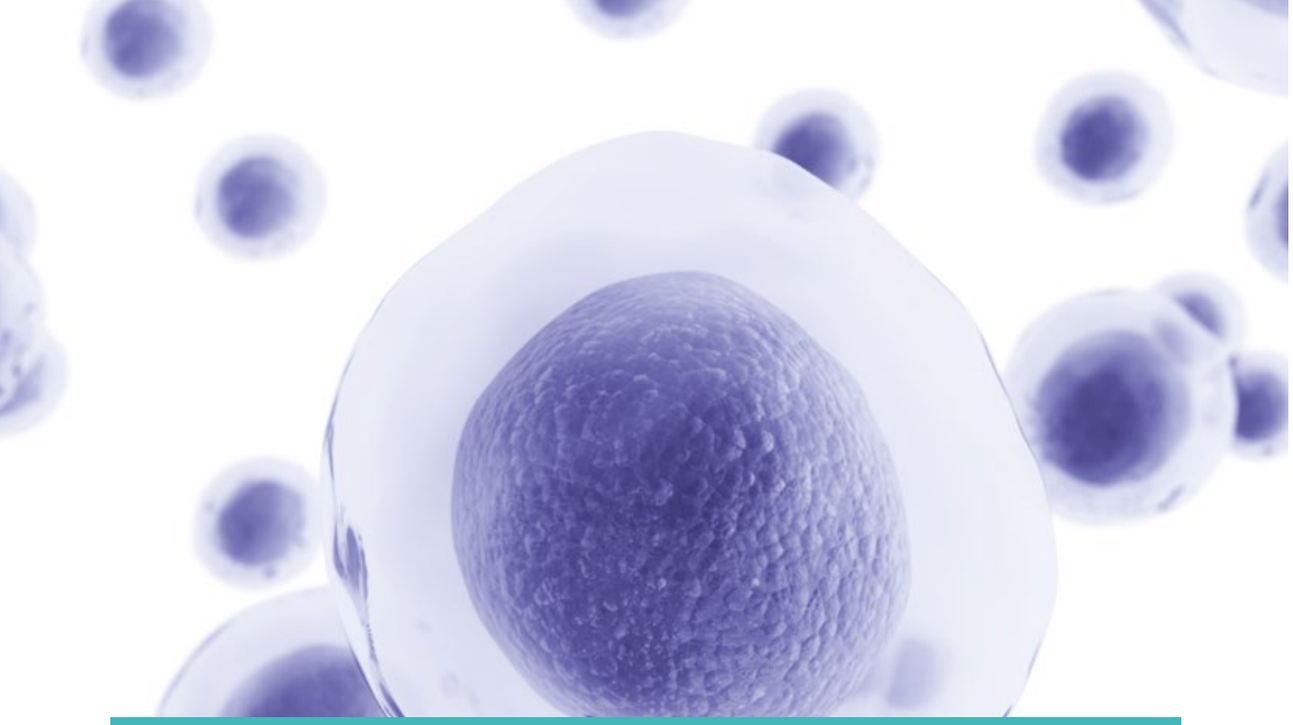
Scott, T'Jonck *et al.,* Immunity 2018

3

#Lung tumor #Atlas #Single Cell Technology

The lab of Diether Lambrechts (VIB-KU Leuven Center for Cancer Biology) together with the Bernard Thienpont Lab at KU Leuven and Els Wauters at UZ Leuven created a first complete atlas of all the cells in lung tumors. For this goal they studied almost 100,000 single cells individually and focused on the non-cancer cells in tumors (blood vessels, immune cells, fibrous cells). This led to the discovery that there are actually many more different cell types in lung tumors: 52 different types of cells were identified, versus the dozen cell types known to be present. Tumors are thus much more complex than hitherto appreciated. The research teams also analyzed cells from the lung outside the tumor and checked for each cell type how it is changed by the tumor. This revealed new ways in which tumors can be targeted. The demonstration that presence of some of these cells is associated with a worse survival of patients, further emphasizes the clinical importance of these findings.

Lambrechts *et al.,* Nature Medicine 2018



SINGLE CELL ACCELERATOR PROJECTS IN THE TECHNOLOGY INNOVATION LAB

Despite being launched just a few short months ago, there are several collaborative projects already in progress with the potential to revolutionize scientific understanding of biological and pathological processes by offering brand-new, high-resolution insights.

AKOYA BIOSCIENCES GIVES NEW POWERS TO TRADITIONAL TECH

Akoya Biosciences (US) has developed an innovative technology to enable spatially-resolved quantitative tissue phenotyping at the cellular and subcellular level. The CODEX™ technology (CO-Detection by indexing) transforms traditional fluorescent microscopes into powerful high-dimensional tissue imaging stations that can analyze tissue architecture and heterogeneity through multiplex staining. Characterizing the interaction of single cells and their corresponding microenvironments is of major interest to VIB and is also one of the key goals of the Single Cell Accelerator program.

IMPACTING RESEARCH IN VIB'S KEY DOMAINS

"This platform is clearly the next step in single cell research," confirms Martin Guilliams (VIB-UGent Inflammation Research Center). "The ability to accurately map distinct subsets of single cells in tissues such as the liver will certainly drive the Human Cell Atlas forward!" The possibility of detecting up to 50 protein markers in a single tissue section opens new research avenues.

"The Akoya system is an impressive platform that enables my group to evaluate up to 30 different cell types simultaneously in tumor niches." *- Gabriele Bergers*

Gabriele Bergers (VIB-KU Leuven Center for Cancer Biology): "The Akoya system is an impressive platform that enables my group to evaluate up to 30 different cell types simultaneously in tumor niches. In addition, it validates our spatial transcriptomics analysis and pins down protein expression to the single-cell level."

Wai Long Tam (life science technology specialist at the Technology Innovation Lab and Akoya project leader), is working alongside multiple VIB groups in both Ghent and Leuven. "Characterizing the interactions of single cells and their corresponding microenvironments is one of the key goals of the SCA," he affirms, "and the CODEX platform has quickly brought novel insights into both normal biological and disease processes."

"Together with the Technology Innovation Lab, and research groups that are willing to invest in early stages of technology-testing, we can explore future applications in the imaging field." *- Saskia Lippens*

For this project, Wai is collaborating closely with Saskia Lippens, Manager Bio-Imaging Core, adding that "Together with the Technology Innovation Lab, and research groups that are willing to invest in early stages of technology-testing, we can explore future applications in the imaging field. This allows us to get acquainted with new emerging techniques, test these and adapt them to the needs of the VIB research questions. Multiplex staining combined with spatial information is very powerful and through the Technology Innovation Lab initiative we can evaluate whether the CODEX technique is suited to become part of our future portfolio."

MISSION BIO REVOLUTIONIZES SNV IDENTIFICATION AND STREAMLINES GENOME EDITING

The Tapestri platform from Mission Bio (US) uses microfluidics to identify approximately 300 single-nucleotide variants (SNVs) and indels at the DNA level, in up to 10,000 cells per run. In this technology, single cells are encapsulated with proteases in droplets, resulting in the release of DNA. Barcoded beads with PCR reagents mix are subsequently added, and the amplicons of interest amplified by PCR. The generated sequencing libraries are then pooled and sequenced by NGS, allowing SNP profiling at the single-cell level.

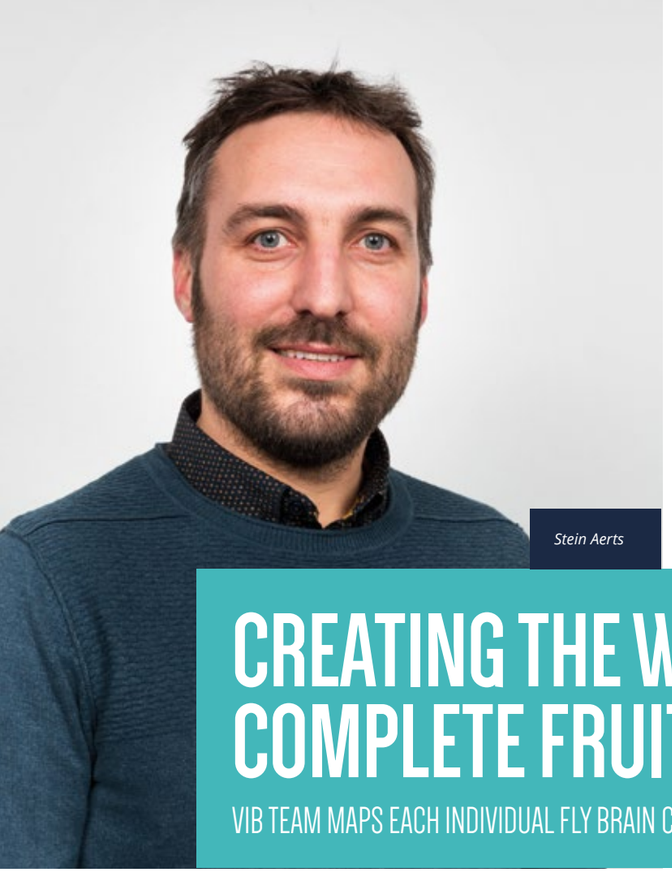
VIB will be one of the first European institutes to have the Tapestri platform, which will be placed in the Technology Innovation Lab in the VIB-KU Leuven Center for Cancer Biology. Pre-made and custom panels will be evaluated for the selected projects. Next to its importance in multiple precision medicine applications, the Tapestri system will also be highly useful in performing quality control of CRISPR genome editing of on-target and off-target events.

RNASEQ ENHANCED BY SINGLE-CELL SURFACE PROTEIN PROFILING

Multiple high-impact papers have been released in the last few months that demonstrate the importance of single cell RNA-seq in a wide range of medical applications. Correlation with protein levels at a similar resolution was previously lacking. Three different groups recently developed a breakthrough technology in parallel using oligo-tagged antibodies, which enable surface protein profiling and RNA-seq at the single cell level (Shahi *et al.*, Scientific Reports 2017 – Stoeckius *et al.*, Nature Methods 2017 – Peterson *et al.*, Nature Biotechnology 2017).

In this method, single-cell suspensions are incubated with antibodies conjugated to a barcoded, poly-adenylated oligo tag. Unbound antibodies are subsequently washed away, after which the cells are prepared for a single-cell RNA-seq experiment. Since the antibodies are barcoded, the downstream NGS results provide epitope profiles alongside single-cell RNA-seq data. Multiple VIB groups across different centers have expressed their interest in this extremely powerful technology.

Over the coming months, VIB will work towards setting up established protocols for this technology. "We really want to boost the uptake of this technology at VIB. For this, we will collaborate closely with BioLegend on their commercialized conjugated antibodies, while we will also explore different in-house routes of oligo-tagging of antibodies and other affinity reagents," says Silvie Van den Hoecke, life science technology specialist at Tech Watch.



Stein Aerts

CREATING THE WORLD'S FIRST COMPLETE FRUIT FLY 'CELL ATLAS'

VIB TEAM MAPS EACH INDIVIDUAL FLY BRAIN CELL THROUGHOUT THE AGING PROCESS

Stein Aerts (VIB-KU Leuven Center for Brain & Disease Research) and his team have accomplished a world first: a gene expression map of every cell within the brain of an aging fly. While fly brains are comparatively simple, consisting of only 100,000 different cells, they are still complex networks that aptly serve as models for the human brain. Thus, the atlas is a key step toward a better understanding of human disease development.

"Truly understanding an organ – the brain of a fly, in this case – means taking a look at every individual cell that composes it," Stein asserts. "These cells collaborate to accomplish specific functions, and each expresses a different set of genes, around 15,000 genes in the case of the fruit fly." To study cell-cell interactions and how they change over time, Stein and his team relied on two cutting-edge technologies, single-sell sequencing and artificial intelligence. These tools enabled the team to examine each cell in detail and process the huge quantities of data needed to understand the activity and function of each cell.

"Sequencing the transcriptomes of 100,000 cells also leads to exciting predictions about the functions of neurons, such as their metabolic activity. The Patrik Verstreken Lab played a crucial role in the *in vivo* validation of our findings, illustrating the importance of collaborations in these large-scale multidisciplinary projects."

"Truly understanding an organ – the brain of a fly, in this case – means taking a look at every individual cell that composes it."
- Stein Aerts

Stein, your lab is a VIB pioneer in the use of single-cell technologies. Where did your fascination start?
Stein: "We really got interested when two specific papers were published in the same issue of *Cell* in 2015, which described the use of droplet microfluidics to sequence the RNA of tens of thousands of individual cells in parallel – and more cheaply than ever. We were so excited that we called Jeroen Lammertyn, from the KU Leuven bioengineering faculty, who taught our PhD student Kristofer Davie how to design and fabricate our own microfluidic devices. Our first successful experiment came a few months later – it was a great moment to see cells cluster together as anticipated."

What do you expect from this technology in your research?
Stein: "Almost all of our research projects, which zoom in on cellular identity at various genetic levels, rely on single-cell resolution. In terms of epigenetics, new technologies will become available at the end of 2018, and we are anticipating an important evolution of single-cell sequencing for those tests as well. Even more, not too far in the future, we're expecting to see droplet-based single-cell multi-omics technologies – a mouthful of words to describe the enormous power of determining the genome, epigenome, transcriptome and subsets of the proteome from a single cell. This technique will pose challenges for machine-learning techniques, as scientists seek to integrate these multiple layers of information."

"Not too far in the future, we're expecting to see droplet-based single-cell multi-omics technologies – enabling scientists to determine the genome, epigenome, transcriptome and subsets of the proteome from a single cell." *- Stein Aerts*

You launched the Fly Cell Atlas (FCA) alongside international colleagues Bart De Plancke, EPFL, and Robert Zinzen, Max Delbruck Center. Has the wider community shown a lot of interest, and how will the platform boost *Drosophila* research?
Stein: "The FCA platform makes our detailed fly brain data freely available. It's an online space where scientists can analyze and contribute their data. The community has shown a lot of interest in the FCA, and the wider *Drosophila* field is keenly focused on developing single-cell atlases, resulting in widespread feedback and collaboration proposals. By mapping all the cells of the fly, we will have a much more thorough understanding of processes occurring during disease development.

"We organized the first FCA meeting in Leuven on December 8, 2017, and we're currently planning the second, to be held at HHMI Janelia Farm in Washington."

Tell us a little bit more about your new single-cell sequencing data visualization tool. What was the role of the VIB Bioinformatics Core in developing this tool?
Stein: "Maxime De Waegeneer and Kristofer Davie from our lab had developed a prototype of a rapid single-cell visualization app, SCope. Łukasz Kreft from the VIB Bioinformatics Core took interest in the prototype, they co-developed it further and added dozens of new features to make it even more user-friendly. As a result, we developed SCope in just two months – even collaborating between Leuven and Ghent!"

"By mapping all the cells of the fly, we will have a much more thorough understanding of processes occurring during disease development." *- Stein Aerts*

"In the meantime, several other single-cell sequencing projects within VIB have used SCope to visualize their single-cell atlases, such as the lung cancer cell atlas developed by the Diether Lambrechts Lab (VIB-KU Leuven Center for Cancer Biology)."

http://flycellatlas.org alongside
http://scope.aertslab.org

BLENDING COMPUTATIONAL MASTERY WITH LIFE SCIENCES EXPERTISE

Łukasz, as a member of the tools development team at our Bioinformatics Core, how does your facility contribute to excellent research results like those driving the FCA?

Łukasz Kreft (VIB Bioinformatics Core): "Our core facility provides bioinformatics software development resources to VIB scientists. Twice a year, the VIB bioinformatics community submits proposals for high-impact software projects. Our team, made up of myself, Alison Horne and Frank Vernaillen, closely collaborates with VIB research groups on these projects. We combine each lab's domain expertise in biological data and data processing with our knowledge of advanced data visualization, latest software development trends, as well as bioimage informatics. This dynamic mix of computational expertise and biological mastery enables us to successfully translate the biological research questions of VIB groups into computational solutions."

BIOINFORMATICS TRAINING AND SERVICE CENTER

ZEROING IN ON DRUG-TOLERANT CANCER CELLS

SINGLE-CELL SEQUENCING HELPS VIB SCIENTISTS TO IDENTIFY A RARE POPULATION OF STEM CELL-LIKE MELANOMA CELLS

Identifying new ways to treat cancer is all in a day's work for Jean-Christophe Marine and his team at the VIB-KU Center for Cancer Biology. In collaboration with research centers in Switzerland and the US, his lab's most recent research study relied on the power of single-cell sequencing technologies to reveal human melanoma cell behaviors at an unprecedented resolution. The results? Greater insight into dangerous, diverse, melanoma 'persister' cells.

Cutaneous melanoma arises from pigment-producing cells (melanocytes) in the skin. When detected early, melanoma can be treated effectively with surgery. More advanced cases of cutaneous melanoma, where cancer cells have spread to other sites in the body, may require treatments such as targeted and immune therapies.

Targeted therapy uses drugs that block specific molecules that are involved in melanoma growth. A new generation of tablet drugs, called BRAF and MEK inhibitors, have resulted in major improvements in the treatment of patients with advanced melanoma. However, after an impressive initial response, clinical relapse occurs in most patients due to the existence of residual drug-tolerant cell populations.

To better understand how this occurs, the team has focused attention on these residual drug-tolerant cells. They demonstrated that a fraction of cells adapt to the treatment by adopting distinctive features that enables these cells to 'persist' despite the presence of the drugs. Specifically targeting these 'persister' cells may open new avenues to improve existing treatments.

Group leader Jean-Christophe Marine, postdoc researcher Florian Rambow and PhD student Aljosja Rogiers further explain their research results and highlight the essential role single-cell RNA sequencing played in the identification of these cell populations.

What was the main goal of the project and what new information did it reveal?
Jean-Christophe: "High relapse rates in melanoma indicate that there is something going on that enables a fraction of melanoma cells to survive a treatment that is lethal to most melanoma cells. The goal of our study was to gain a deeper understanding of the biology of these 'persister' cells."

Florian: "The ability of melanoma cells to adapt to the changing environment created by targeted therapy is remarkable and the observation that, within one given melanoma lesion, distinct drug-tolerant cell populations co-emerge upon treatment with targeted therapy, would not have been possible without the power of single-cell RNA sequencing".

Can these insights potentially be used to target these 'persister' cells?
Aljosja: "We have to take into account the immense complexity within and diversity between residual melanoma lesions: "one size fits all" is never going to work. Our attention was drawn to a drug-tolerant cell subpopulation that, in terms of gene expression, displayed stem cell-like features. We could, by specifically targeting this particular cell population, improve the efficacy of a standard treatment in a mouse model. However, one needs to emphasize that much more research is required to enable the translation of these findings into a viable therapeutic approach. Moreover, only targeting that particular cell population may not be sufficient."

Your team was one of VIB's early adopters of single-sell sequencing technology. When did the fascination begin?
Jean-Christophe: "We started using scRNAseq back in 2015, initially endorsed by the lab of Thierry Voet at the KU Leuven center for human genetics. The Tech Watch team was also a big help in getting us early access to 10x Genomics, and our collaboration with the Stein Aerts lab (VIB-KU Leuven Center for Brain & Disease Research) was also instrumental in giving us access to top-notch bioinformatics pipelines.

Jean-Christophe Marine

"The fact that my lab is part of the LifeTime FET Flagship initiative – a visionary project supporting the use of cutting-edge technology in disease research – is a direct result of our early interest and adoption. Our researchers regularly use single-cell technology and it will absolutely play a central role in our future work."

What did you expect from this technology in the context of this study?
Jean-Christophe: "Single-cell sequencing allows us to study intra-tumor heterogeneity at a high resolution and will be instrumental in overcoming therapy resistance mechanisms by continuing to identify crucial cell populations – the very populations that would go undetected if it was not for single-cell RNA sequencing."

Rambow *et al.*, Cell 2018

LIFETIME FET FLAGSHIP

The FET-Flag LifeTime project is an unprecedented European scientific endeavor launched by a consortium of 60 scientists from all across the continent. Their goal is to track, understand and predict how the molecular make-up of cells changes in human diseases, and ultimately, how to intervene. Stein Aerts and Jean-Christophe Marine are two Belgian partners in this very ambitious project.

NEW TECHNIQUES

The success of the project relies heavily on technology development. The scientists need new ways to extract DNA, RNA, and proteins from individual cells, at high-throughput scale. Recording the spatial location and all biological parameters of each individual cell within a tissue will generate a gigantic amount of multidimensional data.

Stein Aerts: "We are keen on inventing new bioinformatics and machine learning algorithms to analyze and model which genes are active in individual cells. A variety of genome-wide information layers or "omics" data will be generated for millions, perhaps even billions of single cells. We'll need smart ways of making sense of this data if we want to use it to make valuable predictions for patients, including disease outcome, therapy choice, or prognosis."

NEW INSIGHTS

This is where cancer experts such as Jean-Christophe Marine come in. His team will exploit the single-cell methods to profile large amounts of single cells from healthy tissues and tumors. Applications extend to many other diseases besides cancer and both researchers underscore the importance of teamwork in this large endeavor. Jean-Christophe Marine: "Single-cell biology is a new field that combines multiple disciplines. This is why being part of this consortium, together with experts in technology development, bioinformatics and systems biology, is so critical and exciting for us."

Follow on Twitter: @LifeTimeFET
More information: lifetime-fetflagship.eu

Matthew Holt

VIB LEADS BY EXAMPLE IN SINGLE-CELL RESEARCH

VIB, VERGE GENOMICS AND UC SAN DIEGO UNITE AGAINST PARKINSON'S DISEASE

Verge Genomics, a drug discovery company utilizing machine learning to develop new therapeutics, launched an initiative to study gene expression in the brains of Parkinson's patients at single-cell resolution, generating the first dataset of its kind in the field. To do this, the company joins forces with VIB and the University of California San Diego.

AN UNPRECEDENTED GLIMPSE INTO DISEASE PROGRESSION

Growing evidence shows that neurodegenerative diseases like Parkinson's result from multiple interacting cell types, each contributing in their unique way. But datasets that capture gene expression changes across individual cell types in patients and healthy people don't exist yet.

That's what the consortium wants to change: using the latest single-cell sequencing technologies, the team will analyze gene expression in individual cells of brain tissue from people with and without Parkinson's disease, making it possible to assess how gene activity changes in the disease across multiple cell types.

"We hope this project will accelerate the development of effective treatments for this incurable disease."
- Matthew Holt

A STRONG PARTNERSHIP

The secret to the project is the unique combination of expertise and resources in the consortium. With the VIB Single Cell Accelerator's cutting-edge single-nucleus RNA sequencing technology, UC San Diego's outstanding collection of tissue from patients and their families, and Verge's machine-learning platform to generate and analyze new types of patient data at a resolution only recently made possible, the team is armed for battle.

Matthew Holt, group leader at the VIB-KU Leuven Center for Brain & Disease Research, is excited to be part of the initiative: "Single-cell technology is advancing rapidly, opening up new opportunities for us to understand how the healthy brain functions and what goes wrong in disease. Our collaboration with Verge and UC San Diego places us at the forefront of this field and will allow us to understand the molecular mechanisms underlying Parkinson's disease at an unprecedented level.

"Currently, the only approved treatments for Parkinson's disease address its symptoms, but do not prevent the illness or halt its progression. We hope this project will accelerate the development of effective treatments for this incurable disease."

JANSSEN FIRST INDUSTRIAL PARTNER TO PLUG INTO SINGLE CELL ACCELERATOR

VIB's expertise in the single-cell field is also of great value for Biotech and Pharma, and long-term collaborations are being established in the Single Cell Accelerator (SCA). Janssen Pharmaceutica NV, part of the Janssen Pharmaceutical Companies of Johnson & Johnson, is the first pharma partner in the SCA. Both VIB and Janssen Pharmaceutica are looking forward to this exciting collaboration.

Johan Cardoen and Stef Heylen (COO Janssen R&D and Managing Director Janssen Pharmaceutica)

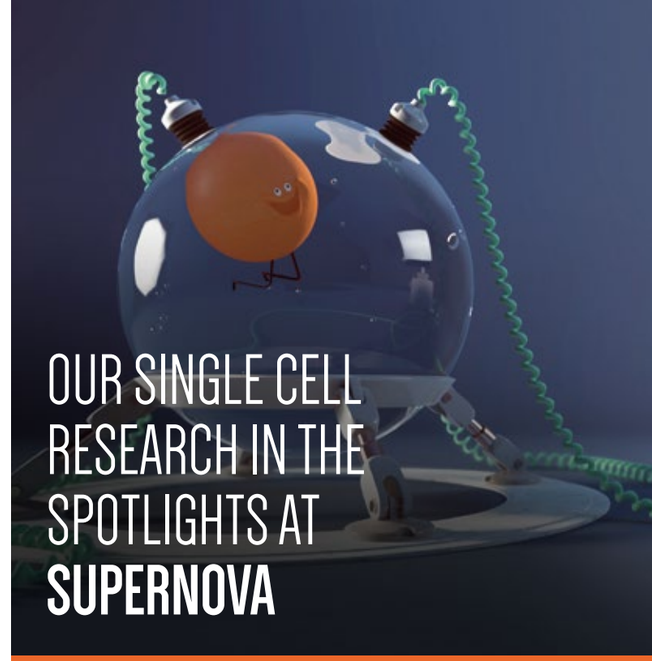
Jérôme Van Biervliet, Head of Business Development VIB: "We have had a long-standing relationship of intense collaboration, strategic partnerships and scientific exchange with Janssen. The current collaboration now extends this tradition to another legacy of VIB – namely accessing emerging research technologies through our Tech Watch program. The Single Cell Accelerator will also accelerate industry-academia collaborations and leverage the expertise on both sides."

SENIOR LEADERSHIP TEAM OF JANSSEN R&D VISITS VIB

The signing took place during a visit of the Senior Leadership Team of Janssen R&D to VIB last June. Senior Leaders from different research domains within Janssen R&D had the opportunity to meet with and get introduced into the research of Bart Lambrecht, Dirk Elewaut and Martin Guilliams from the VIB-UGent Center for Inflammation Research, Diether Lambrechts, Jan Cools and Gabriele Berger from the VIB-KU Leuven Center for Cancer Biology and Bart De Strooper from the VIB-KU Leuven Center for Brain & Disease Research, including existing collaborations with Frederik Stevenaert and Dieder Moechars from the Janssen campus in Beerse. A very inspiring meeting for all attendees.

Pieter Peeters, Sr Director, Computational Biology of Janssen Pharmaceutica: "The enthusiasm and passion for science is what made, and will continue to make, the collaborations between VIB and Janssen a success. I believe that the interaction between VIB PI's and senior leaders at Janssen R&D has planted the seeds for more systematic interactions in the near future. We are very excited about our partnership with VIB's Single Cell Accelerator and the opportunity it will provide us to enhance our ability to understand disease and mechanism of action of novel therapeutics".

This new collaboration will help VIB and Janssen Pharmaceutica to combine forces to develop and evaluate emerging single-cell technologies, which will allow both parties to excel rapidly in the single-cell field. The newly developed methodologies will also be disseminated across the VIB centers to make an institute wide impact.



OUR SINGLE CELL RESEARCH IN THE SPOTLIGHTS AT **SUPERNOVA**

The SuperNova festival is a one-of-a-kind immersive experience, occupying "Het Eilandje" in Antwerp. The public festival takes place on September 29-30, 2018 and features the free Expedition, Tech Fair and TalentBuzz zones. Feed your curiosity and discover the new ideas and technologies of tomorrow!

In the Expedition zone, visitors can explore VIB's single cell research through an interactive installation. Inspired by the recent breakthrough of Stein Aerts and his team of the VIB-KU Leuven Center for Brain & Disease Research (see pages 8-9), who mapped all cells in the fly brain, a giant brain "puzzle" will bring the concept of single-cell technology closer to people.

Alongside 90 other game-changing companies and organizations, VIB will showcase its scientific highlights at the Tech Fair. A captivating exhibition is designed to offer a fresh view of VIB's groundbreaking research and the Innovation & Business team's realizations. Giving you a glimpse of tomorrow's solutions, the SuperNova Tech Fair is the perfect place to discover new and innovative products, platforms and solutions.

You can also visit the TalentBuzz zone, a dynamic talent marketplace. Through this AI-driven platform, potential employees can easily connect with their future employers in the science and tech sector.

Find out more about this not-to miss event at www.supernovafest.eu.

3 PROJECTS SELECTED IN VIB GRAND CHALLENGES PROGRAM

The VIB Grand Challenges Program is a translational research program with which we aim to significantly increase the societal impact of VIB. We are convinced that this can be done by teaming up with experts outside VIB who have complementary expertise (clinic, agriculture, engineering …). Together we can exploit our knowledge, expertise and toolbox to generate new, otherwise untapped avenues to create added value for society. Three projects were selected and will receive funding up to 2.5 M€. We look forward to the outcome of these collaborations!

1 OVERCOMING THE MAIN CURRENT DIAGNOSTIC CHALLENGES IN HEPATOLOGY PRACTICES

- Identify and validate novel biomarkers for hepatology practice to guide cost-effective use of the pharmacological and surgical treatments in the field
- VIB groups: Nico Callewaert, Kris Gevaert, Francis Impens & Lennart Martens from the VIB-UGent Center for Medical Biotechnology, and Bart Ghesquière from the VIB Metabolomics Expertise Center at the VIB-KU Leuven Center for Cancer Biology
- Non-VIB PI's: Jo Vandesompele (UGent), Hans Van Vlierberghe (UGent/UZ Gent), David Cassiman and Ina Jochmans (KU Leuven/UZ Leuven) and Sven Francque (Antwerp University/UZ Antwerp)

2 TRANSLATIONAL SCIENCE INITIATIVE ON PRIMARY IMMUNE DEFICIENCIES

- Identify novel biomarkers for rare or novel primary immune deficiency diseases (PIDs), a heterogeneous group of life-threatening genetic disorders of the innate and adaptive immune system
- VIB PI's: Bart Lambrecht, Rudi Beyaert, Yvan Saeys & Martin Guilliams from the VIB-UGent Center for Inflammation Research and Adrian Liston from the VIB-KU Leuven Center for Brain & Disease Research
- Non-VIB PI's: Isabelle Meyts, Rik Schrijvers & Xavier Bossuyt From KU Leuven/UZ Leuven and Jan Philippé, Elfride de Baere & Filomeen Haerynck from UGent/UZ Gent

3 POINTILLISM, IMPROVING IMMUNE CHECKPOINT INHIBITOR RESPONSE BY SINGLE CELL INTEGRATIVE MULTI-OMICS OF THE TUMOR ECOSYSTEMS

- Identify novel biomarkers that predict the response to immune checkpoint blockade and guide the clinical implementation of effective treatment combinations
- VIB PI's: Jean-Christophe Marine, Diether Lambrechts, Gabriele Bergers & Massimiliano Mazzone from the VIB-KU Leuven Center for Cancer Biology
- Non-VIB PI's: Thierry Voet (KU Leuven) and Ignace Vergote, Sabine Tejpar, Hans Wildiers, Paul Clement & Olivier Bechter from KU Leuven/UZ Leuven

Via new calls VIB strives to obtain a maximal impact. Last August a next call was launched for additional research projects that could be financed as from 2019.

QUICKSCAN

1 #Wheat #Phosphoproteomics #High temperature

Wheat is one of the most important human food sources, but this crop is very sensitive to temperature changes. While this has been investigated on various levels to some extent, very little is known about early signaling events associated with an increase in temperature. Here, Lam Dai Vu, Tingting Zhu and colleagues in the Ive De Smet group (VIB-UGent Center for Plant Systems Biology) and the Kris Gevaert group (VIB-UGent Center for Medical Biotechnology) present the impact of a short-term and mild increase in temperature on the phosphoproteome, allowing us to capture phosphorylation-mediated signaling mechanisms.

Vu, Zhu *et al.*, Journal of Experimental Botany 2018

2 #RNF41 #Interactome

RNF41 is an E3 ubiquitin ligase involved in a diverse set of cellular processes including signaling of various receptors, intracellular trafficking and apoptosis. The Jan Tavernier and Sven Eyckerman Labs (VIB-UGent Center for Medical Biotechnology) jointly established a high-confidence interactome map of RNF41 thereby providing a unique tool for further elucidation of the role of RNF41. This first RNF41 interactome was generated by using three MS-based orthogonal assays, Virotrap, BioID and AP-MS, combined with datasets from previously performed microarray MAPPIT and Y2H screens.

Masschaele *et al.*, Journal of Proteome Research 2018

3 #Microglia #A20

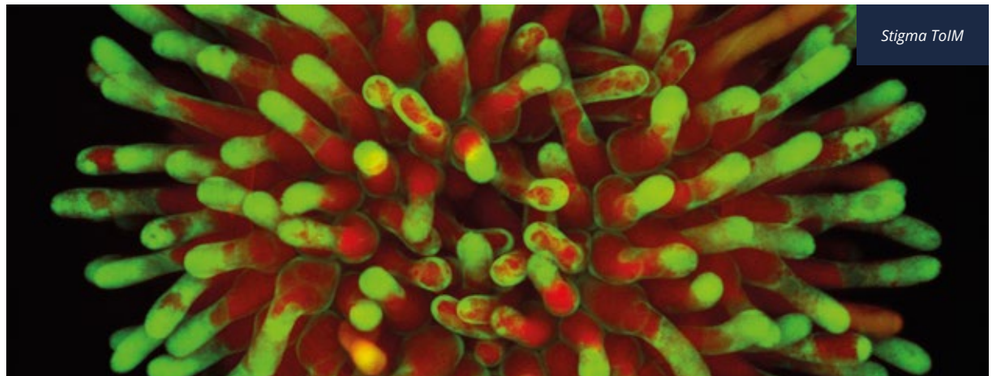
Microglial cells are the resident mononuclear phagocytes of the CNS and have a functional role in both immune defense and CNS maintenance. These cells may however also acquire a detrimental pro-inflammatory phenotype that actively contributes to the chronicity of inflammatory brain diseases, including the neuroinflammatory disease multiple sclerosis (MS). Sofie Voet of the Geert van Loo Lab (VIB-UGent Center for Inflammation Research) showed that the anti-inflammatory protein A20 plays a critical role in the control of microglia activation in CNS homeostasis, but also in MS-like disease by regulating inflammasome activation and Interleukin-1b secretion.

Voet *et al.*, Nature Communications 2018

4 #Programmed cell death #Senescence #Flower

The transience of flowers is proverbial. Flower life span is tightly regulated and defines the time frame in which flowers can be pollinated to produce fruit and seed. Zhen Gao and colleagues from the Moritz Nowack lab (VIB-UGent Center for Plant Systems Biology) show that age-induced programmed cell death in the pollen-receiving floral stigma contributes to the termination of floral receptivity in *Arabidopsis*. This knowledge might provide new leads to modulate flower longevity as a means to stabilize seed set and fruit yield in crops.

Gao *et al.*, Nature Plants 2018



Stigma ToIM

5

#OxidativeStress #RedoxRegulation

The Joris Messens Lab (VIB-VUB Center for Structural Biology), in collaboration with the Frank Van Breusegem Lab (VIB-UGent Center for Plant Systems Biology) and the Kris Gevaert Lab (VIB-UGent Center for Medical Biotechnology), identified the proteome of oxidized methionines in *Arabidopsis thaliana* leaves exposed to high light stress. To understand the influence of the post-translational modifications on protein function, glutathione transferase Tau23 and Phi9, which detoxify herbicides, were structurally and kinetically characterized. Our findings showed that under oxidizing conditions, both enzymes maintain functionality using different compensatory mechanisms. In addition, redox regulatory systems restore the activity of both enzymes. These studies provide insights on how enzymes remain functional under oxidizing conditions and help plants survive oxidative stress.

Tossounian *et al.,* BBA General subjects 2017
Tossounian *et al.,* Protein Science 2018

6

#PromethION #Visualization

The Christine Van Broeckhoven Lab (VIB-UAntwerp Center for Molecular Neurology) is employing the long-read sequencing platforms MinION and PromethION from Oxford Nanopore Technologies, which provide invaluable additions to the toolbox of genetic research. However, software tailored to the dominant short read technologies is not always appropriate for these long reads. To address this issue, we developed NanoPack, a set of tools for processing, creating statistical summaries and visualizing long-read sequencing data. Our software enables in-depth quality control and comparison across datasets.

De Coster *et al.*, Bioinformatics 2018

7

#Glucocorticoids #Compound A #Lymphoid malignancies

Glucocorticoids (GCs) are a cornerstone in the treatment of lymphoid malignancies, but prolonged GC treatment is hampered by deleterious side effects and GC resistance. To tackle and overcome these GC-related problems, Dorien Clarisse and Karolien De Bosscher (VIB-UGent Center for Medical Biotechnology), assessed the combination of classical GCs with a plant-derived anti-inflammatory, Compound A, as a treatment for lymphoid malignancies. Yet, this combination neither enhances GC-induced apoptosis, nor prolongs GC responsiveness of lymphoid malignant cells.

Clarisse *et al.,* PLoS One 2018

8

#Glucocorticoid Receptor #STAT1 #TNF-induced inflammation

Researchers from the Claude Libert Lab (VIB-UGent Center for Inflammation Research) found that the Glucocorticoid Receptor (GR), as a homodimer, controls the expression of another transcription factor, STAT1. When this control fails in the intestinal epithelium, an interferon response develops spontaneously because of permanent stimulation by the microbes. This response sensitizes the epithelium to cell death, and the whole organism to sepsis. This data reveals a new level of interplay between microbiota and gene expression control in the intestinal epithelium.

Ballegeer, Van Looveren *et al.,* Journal of Clinical Investigation 2018

9

#Alzheimer's disease #ABCA7

ABCA7 is one of the most compelling new risk genes for Alzheimer's disease (AD), but previously identified loss-of-function mutations in ABCA7 could not account for the observed genome-wide association. The lab of Kristel Sleegers, part of the Neurodegenerative Brain Diseases Group (VIB-UAntwerp Center for Molecular Neurology), discovered that this association is explained by tandem repeat expansions in ABCA7. These expansions alter ABCA7 alternative splicing and AD biomarkers in cerebrospinal fluid and strongly increase the risk of disease.

De Roeck *et al.,* Acta Neuropathy 2018

10

#Superior colliculus #Visual processing

The superior colliculus plays an important role in the orienting responses of the eye, head and body. The team of Karl Farrow (NERF, VIB-KU Leuven-imec) used two-photon calcium imaging to record the activity of collicular neurons in mice and determine whether their receptive field properties show any systematic organization around the monocular-binocular border, where information from the two eyes meets. Nasal and temporal motion selectivity were found to be separated in retinotopic space, illustrating the important coherence between the spatial organization of inputs and response properties within the visual system.

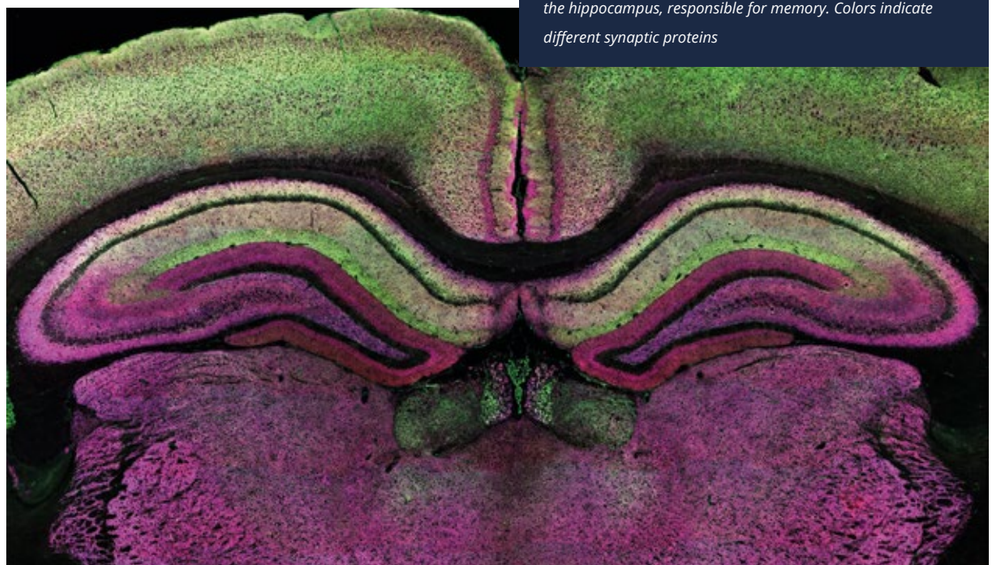
de Malmazet *et al.,* Current Biology 2018

11

#Synaptic identity #LRR proteins

The group of Joris de Wit (VIB-KU Leuven Center for Brain & Disease Research) showed that hippocampal pyramidal neurons express multiple Leucine-rich repeat adhesion molecules with specific synaptic distributions. FLRT2, LRRTM1 and Slitrk1 have different effects on synaptic architecture and function, and act in input-specific combinations and in a context-dependent manner to specify synaptic properties. These findings help to unravel the regulation of neuronal connectivity and may lead to a better understanding of how mutations related to autism and schizophrenia affect circuit connectivity and brain function.

Schroeder *et al.,* Neuron 2018



Cross section of a rat brain, showing folded structure is the hippocampus, responsible for memory. Colors indicate different synaptic proteins

Moritz Nowack

NEW INSIGHTS IN CELL DEATH IN PLANTS MIGHT GENERATE NEW LEADS FOR WEED CONTROL

Some plants like the giant sequoia trees can grow into the "Largest Living Things on Earth". Ironically, most of a tree's biomass is actually not alive, but is formed by persistent cell corpses that are collectively called wood. Wood development is terminated by a tightly controlled cell death process of the individual cell types. The formation of wood is only one of the many programmed cell death processes that are important for plant growth and development.

The lab of Moritz Nowack (VIB-UGent Center for Plant Systems Biology) investigates the regulation of these plant cell death processes in the model plant *Arabidopsis*.

Marlies Huysmans, first author of this study: "To study plant cell death, we are using the plant's root cap as a model system. The root cap is situated at the tip of the growing root, guiding and protecting the delicate root tip as it pushes through the soil. Individual root cap cells are constantly regenerated and have a short life span that ends in programmed cell death."

In this project, the researchers aimed at discovering new genes that control the cell death process in plants. To this end, they studied transcription factors, which regulate gene expression as the starting point of protein production. The regulated production of proteins is an important first step to ensure the orderly execution of cell death.

Marlies: "To identify regulators of cell death, we compared which transcription factors are produced both in wood cells and in root cap cells. As both cell types undergo programmed cell death, we hoped to identify important regulators of this process. We found a number of common transcription factors and analyzed two of them, ANAC087 and ANAC046, in detail."

In mutants that abnormally produced these factors outside the root cap, the team of Moritz found that many cells died within 24 hours, leading to growth arrest and seedling death. Conversely, when analyzing mutants that were unable to produce ANAC087 and ANAC046, they found that root cap cells lived much longer than in regular *Arabidopsis* plants.

Moritz: "These results show that both transcription factors are important regulators of programmed cell death in *Arabidopsis*. Surprisingly, our results also revealed that root cap cells that are detached from the roots and reside in the rhizosphere have a genetically determined life span."

Identifying transcription factors controlling the cell death program is but a first step. To find the proteins that do the actual killing job, target genes controlled by ANAC087 and ANAC046 need to be analyzed.

Moritz: "Ultimately, we strive to understand the complex network of proteins that is necessary to execute cell death in plants. This knowledge might generate new leads on how to control cell death in weeds and crop plants. Inducing naturally occurring cell death in weeds would be an environment-friendly way for weed control, while optimizing cell death processes in crop plants could contribute to stabilization of plant yield under adverse environmental conditions."

Huysmans *et al.*, Plant Cell 2018

NEW WEAPON AGAINST CHEMOTHERAPY-RESISTANT CANCER CELLS DISCOVERED

Neuroblastoma, one of the most common aggressive forms of cancer in many young children, exhibits an increased resistance to the current generation of chemotherapy. To be able to treat these sorts of tumors, a new type of therapy is required. Research from VIB, Ghent University and the University of Antwerp, led by the brothers Tom and Wim Vanden Berghe, has led to the discovery of a new molecular mechanism that can kill cancer cells in mice. Withaferin A, an active substance from a medicinal plant extract (Ashwagandha) from traditional medicine in India, plays an important role in this.

Tom (VIB-UGent Center for Inflammation Research): "The clarification of the working mechanism of Withaferin opens perspectives for new strategies to treat these aggressive tumors. These first results in mice are very promising and have come to light thanks to the support of Stichting tegen Kanker [Foundation against Cancer], but there is still a long way to go before we can use this as real treatment in practice."

DIFFICULT-TO-HANDLE CANCER IN CHILDREN

Neuroblastoma typically occurs in young children; over half of patients are under 2 years old. This aggressive form of cancer is coupled with an elevated resistance to chemotherapy. This sort of resistance often emerges through defects in the molecular mechanisms that in normal circumstances lead to the destruction of cancer cells (cell death). The challenge is to find alternative molecular pathways to kill the cancer cells. Researchers in the team of Tom Vanden Berghe and Peter Vandenabeele, in collaboration with the team of Wim Vanden Berghe of the University of Antwerp, have discovered how Withaferin A, which comes from a medicinal plant, kills aggressive neuroblastoma cancer cells.

Peter Vandenabeel, Behrouz Hassannia, Wim Vanden Berghe and Tom Vanden Berghe

Wim: "The roots and leaves of the *Withania somnifera*, commonly known as Indian ginseng or Ashwagandha, have been used for thousands of years in traditional medicine in India (Ayurvedi) to treat ulcers and cancer. Extracts from plants, but also from fungi and marine organisms, are important sources to identify chemical structures that can be used as medicines. Traditional medicine is often based on centuries-old practices that can potentially lead to new types of medicines."

FERROPTOSIS: A NEWLY DISCOVERED TYPE OF CELL DEATH

Researchers with years of experience in cell death have been able to demonstrate that Withaferin A triggers a sort of biological rusting in mice called ferroptosis. The term ferroptosis refers to an iron-driven oxidation reaction of the membranes of cancer cells, which quickly kills off the cells.

As part of his doctoral research, Behrouz Hassannia was successful in showing the superior efficacy of Withaferin A in comparison to current chemotherapies in mice, after administering locally. In most mice, no relapse was observed. Behrouz: "We successfully administered Withaferin A intravenously by locking it inside nano-particles. These accumulate in the tumor, leading to efficient killing of the tumor cells and reduced side effects. This offers important prospects for an improved neuroblastoma treatment but also for other chemo-resistant cancers."

Tom: "These crucial new insights into how we can initiate ferroptosis (or biological rusting) in chemotherapy-resistant tumors was only possible thanks to the collective efforts of an international team of researchers with extremely diverse expertise, ranging from neuroblastoma cancer, nanotechnology, pharmacology, molecular biology and epigenetics to advanced technologies like oxidative lipidomics."

Hassannia *et al.*,
Journal of Clinical Investigation 2018

NEW RESEARCH REVEALS CENTRAL ROLE OF THE HIPPOCAMPUS IN INSTRUCTING THE NEOCORTEX IN SPATIAL NAVIGATION AND MEMORY

A research collaboration between the Bruce McNaughton group at the Canadian Centre for Behavioural Neuroscience at the University of Lethbridge and the Vincent Bonin group at the Neuro-Electronics Research Flanders (NERF, VIB-KU Leuven-imec) has provided new insight into how the brain learns about the environment and why the hippocampus, a key part of the brain, is so important in this process.

"This is quite a major breakthrough in understanding and supporting a long-standing theory for which there was virtually no neurophysiological evidence, mostly just behavioural evidence and conjecture," says Bruce McNaughton.

A 2017 study conducted by Dun Mao (PhD '17), then a graduate student working in the labs of Bruce McNaughton and Vincent Bonin, was the first to show that cells in the cerebral neocortex, specifically the retrosplenial cortex, look very much like 'place cells' in the hippocampus. Place cells are involved in navigation and learning. However, the researchers didn't know whether the retrosplenial cortex developed activity patterns on its own or relied on instructions from the hippocampus.

"Navigating and remembering rely on extensive interactions between the hippocampus and the neocortex," says Dun, now a post-doctoral fellow at Baylor College of Medicine in Houston, Texas. "This study provides the first direct evidence of the role of the hippocampus in sending a continuous, sequential code to the neocortex. I think it will inspire a new direction of research in the field."

The study, Hippocampus-dependent emergence of spatial sequence coding in retrosplenial cortex, has been published in PNAS. The idea of the study stemmed from the long-held hippocampal indexing theory. Neuroscientists have proposed the indexing theory to explain how the hippocampus interacts with the cortex. Since the brain's cortex has many cells, distant regions of the cortex don't communicate strongly with each other. However, each part of the cortex is able to store information in its own domain.

Indexing theory proposes that, each time an animal has a unique experience, the hippocampus creates a unique pattern of neural activity that it sends to the rest of the cortex. That unique pattern acts like a context code and is stored in different regions of the cortex, along with the raw data the regions are responsible for encoding, such as shapes, sounds and motion. If the hippocampus recreates that index, it will simultaneously appear in all the cortical regions involved at the time, thereby retrieving the individual parts of the experience to create an integrated memory. Although this theory was initially proposed more than 30 years ago, direct neurophysiological evidence has been lacking.

In the current study, Dun damaged very precise locations in the hippocampus in mice so that the hippocampus was no longer functional but the cortex remained intact. He then used 2-photon calcium imaging to track the activity of neurons in the cortex as the mice navigated and learned about the environment. This allowed him to witness how retrosplenial activity develops and to determine the role of the hippocampus in that learning.

"In those mice, we found that there was a loss of this place-cell like activity in the cortex, thereby strongly supporting the conclusion that the cortex gets its spatial code, or its index code, from the hippocampus itself," says Bruce.

Vincent Bonin

"Most compelling are the strength and specificity of the effects," says Vincent. "The effects are stunning. With an intact hippocampus, activity in the retrosplenial cortex is precise and orderly. In the absence of it, it's a complete mess, as if the animal had never been exposed to the environment. Having such a strong phenomenon to rely on will be helpful in basic studies but also in studies of brain disorders and neurodegeneration."

The results pave the way for further studies to determine how general the phenomenon is and determine how and if indexing activity helps the cortex retrieve stored information.

"We need to know the circuit mechanisms," says Bruce. "We need to know how those particular indexing cells are connected to the other cells in those regions of the cortex. Very detailed neuroscience needs to be done in order to get a complete picture of how this memory- or knowledge-creating system actually works at the level of the nuts and bolts of the brain."

Bruce looks forward to these future studies as new high-tech tools should be available in the next five years that will allow for deeper exploration of the brain, as well as techniques that will allow for simultaneous recording of the activity of tens of thousands of brain cells, rather than the few hundred currently possible.

Mao *et al.*, PNAS 2018

TOWARDS ROBUST AND RELIABLE ARTIFICIAL INTELLIGENCE

Jonathan Peck and Yvan Saeys

Leaps forward in artificial intelligence (AI) enable computers to solve previously unsolvable problems, such as image recognition and self-driving cars. Nowadays, it has become routine to rely on AI systems to make automated decisions in complex real-world environments.

The "adversarial patch". This small sticker can mislead almost any AI used for image recognition. © Brown et al. *2017*

Yvan Saeys (VIB-UGent Center for Inflammation Research): "While high-performing, useful and increasingly prevalent, modern AI is still surprisingly fragile and easy to mislead, as we explained in a recent article in "De Standaard"[1]. A small sticker as the one shown here causes almost any AI system for image recognition to mislabel the picture containing it. Apply it to a traffic sign, for example, and a self-driving car will think the sign is actually a toaster."

AI systems are increasingly being used in biotechnology and medicine as well, for example, to diagnose patients, integrate huge volumes of data and implement precision medicine. While hacking might not be an immediate threat in these scenarios, the underlying frailty of AI systems poses other risks, such as lack of robustness and interpretability of the models.

Jonathan Peck from the Yvan Saeys group: "Exactly why our AI systems are so fragile is poorly understood, as many AI systems are notoriously difficult to understand. They operate as 'black boxes' where you can observe the input and the result, but you cannot easily figure out why those results come from those inputs. Designing more interpretable AI will be a big step towards making our systems more robust and accountable."

Peck *et al.*, NIPS 2017

[1] "En plots herkent uw slimme auto het stopbord niet meer" De Standaard, 12 mei 2018

VIB SCIENTISTS MAP THE BELGIAN BEER LANDSCAPE IN A NEW BOOK

USING SCIENCE – AND TASTE BUDS – TO GAIN INSIGHTS INTO SOME OF THE WORLD'S MOST DELICIOUS BREWS

Miguel Roncoroni and Kevin Verstrepen (VIB-KU Leuven Center for Microbiology) put their minds – and their mouths – to work, on behalf of beer enthusiasts the world over. "As scientists, we try to understand the world through observation, experimentation and reason," Miguel explains. "With this in mind, we tackled the interesting challenge of investigating Belgian beer – using science." The result is a new book: 'Belgian Beer – Tested and Tasted'. You don't want to miss this one!

Belgium is known around the world as the origin of some of the tastiest and most celebrated beers. However, with this reputation comes a truly dazzling and enormously diverse Belgian beer landscape. To shed new light on this confusing assortment, Miguel and Kevin, our resident 'beer doctor' and 'beer professor', respectively, have put together a neutral guide that relies on scientific data and the palates of trained international beer specialists.

Kevin, what led you toward this intoxicating research topic? What was your goal with this book?
Kevin: "As far as we're aware, nobody had ever composed a dataset to serve as a fact-based atlas for beer or any other beverage. It's an introductory guide to Belgian beer, a reference for the experienced beer fan and a source of inspiration for readers – and drinkers – to explore new brews. Because we combined the analysis with advanced principle component analysis, we were able to make a 2D map of beers."

How did you develop the atlas – and which beers came out on top?
Miguel: "We analyzed 250 beers in our lab, measuring color, bitterness, alcohol content, sugars, proteins and 70 aroma compounds. Adding an element of expertise, we put together a panel of beer experts to blind-taste the beers and give their feedback on flavor and experience. The way the beers were analyzed – through blind tastings by a trained 15-person panel, and a comprehensive chemical analysis using GC, GC-MS, NIR, LC and enzyme assays – allowed us to define the aroma of each beer without missing details. It also avoided any bias that is always there if a limited number of people taste, and if they know what beer they are tasting.

We didn't give a final score to each beer – everybody has a different palate and preferences, after all. However, most of the beers we analyzed are objectively excellent, and we did label those beers that received the top scores from panel members."

A portion of the proceeds of the book will go to VIB's 'Wetenschap op Stap' science education initiative for children.

The book (in English and Dutch) will be available soon. More info via www.vib.be/belgianbeer.

Cover of the book 'Belgian Beer – Tested and Tasted'

A NEW ERA
IN MSI TESTING

IDYLLA ™ MSI ASSAY

REVOLUTIONARY MOLECULAR DIAGNOSTIC CANCER TEST

BIOCARTIS LAUNCHED A FAST, ACCURATE MSI ASSAY ON ITS IDYLLA™ PLATFORM, OFFERING THE POTENTIAL TO PREDICT EFFECTIVE CANCER TREATMENT OPTIONS

One of VIB's key missions is the translation of basic science into benefits for society. Furthering our ambition, research conducted by the Diether Lambrechts Lab forms the partial basis of the Idylla™ MSI Assay, that was launched very recently on July 17, 2018. This ground-breaking new assay was developed by molecular diagnostics company Biocartis and has the potential to provide better and faster access to personalized treatments to patients with colorectal cancer.

IDYLLA™: BRINGING NEW INSIGHTS TO COLON CANCER SCREENING

Microsatellite instability, or MSI, is caused by the body's inability to fix DNA errors, contributing to cancer development in various organs, such as the colon, stomach and the endometrium. Tumors characterized by MSI have specific mechanisms driving cancer development and progression and should receive different therapies than other tumors. For instance, MSI tumors need alternative chemotherapy approaches compared to non-MSI tumors, while in advanced cases, MSI tumors respond well to checkpoint immunotherapy. The Idylla™ MSI Assay (Research Use Only, a CE-IVD version is expected in 2019) developed by Biocartis offers a more efficient and effective MSI testing method to predict which treatments would result in better outcomes, and could also potentially be used to predict how successful immunotherapy would be for a specific patient.

Idylla™ uses a single piece of human tumor tissue to perform the MSI testing, rather than the usual two pieces of tumor tissue that currently used MSI testing methods require today. The Idylla™ MSI Assay also offers high sensitivity and accuracy, quick results and detailed automated reports. Seven novel MSI biomarkers, which were identified by the group of Diether Lambrechts (VIB-KU Leuven Center for Cancer Biology) and licensed to Biocartis in 2013, are at the core of the test.

TRIED AND TRUE TECHNOLOGY

VIB collaborated to conduct two research studies that examined the function and output of the test, which were both selected for publication at the annual meeting of the American Society of Clinical Oncology (ASCO) in Chicago (US). The results are clear: Idylla™ is as accurate as currently-used MSI testing methods, provides faster results using simpler procedures and has the potential to effectively predict the clinical outcomes of immunotherapy in MSI-high patients.

Diether Lambrechts

"These studies show the high clinical value of the MSI Biomarkers first identified in our lab and now combined by Biocartis with the advantages of the fully automated Idylla™ system," says Diether Lambrechts. "The seven biomarkers show a remarkable association with both tumor mutational burden and quantity of DNA errors. This provides us with a novel and easy-to-implement tool to predict tumor response to immunotherapy."

ASCO LAUNCH FOR MAXIMAL IMPACT

The Idylla™ MSI test was launched at the ASCO annual meeting, which is the largest oncology conference in the world. This timing illustrates just how much of an impact Biocartis expects to have with the introduction of the technology on researchers, oncologists and ultimately, colon cancer patients.

Before the official launch event, a prelaunch campaign took place, highlighting Idylla™'s features and advantages over current MSI testing methods. Over 90,000 pathologists and oncologists in Europe received e-mails from Biocartis prior to ESMO 2018, and a segmented product branding campaign was put in place via the Biocartis website, social media and conference promotion media.

Moving forward, this new, rapid and easy Idylla™ MSI technology, which will allow many more patients access to MSI testing versus today's more cumbersome MSI tests, could be adapted to offer opportunities in detecting other tumor types that are associated with high MSI levels.

The Idylla™ MSI Assay is currently labeled for 'research use only' (RUO). However, the launch of a CE-IVD version which can be used in diagnostic procedures is expected in the first half of 2019.

AWARDS

Over the last couple of months, several VIB frontrunners were awarded national and international prizes for their excellent research. Congratulations to all!

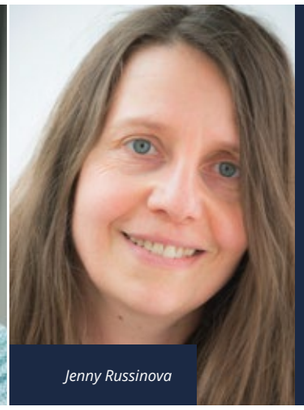
BLOOD VESSEL RESEARCH WINS BIG

Peter Carmeliet won the prestigious biannual worldwide **2018 Heineken Prize for Medicine** – worth $200,000 – for his groundbreaking research on blood vessel formation and endothelial cell metabolism in angiogenesis. He's the first Belgian scientist to win the prize, which is considered one of the most important awards in the scientific community and widely regarded as third only to the Breakthrough Prize and the Nobel Prize.

Earlier this year, Peter Carmeliet received the **46th annual ARC Foundation Leopold Griffuel Award**. Receiving these two prestigious prizes in such a short time frame highlights the impact of his research in the medical field. Peter himself couldn't be more pleased: "These awards are a great recognition of the work my group has been doing. It is an important impetus to continue to perform top-level research that can impact the lives of patients in the future."

Peter Carmeliet

Patrik Verstreken



Jenny Russinova

VIB SCIENTISTS JOIN THE EMBO

Patrik Verstreken and **Jenny Russinova** were elected as **EMBO members**. The two VIB group leaders, together with 60 additional researchers, will join a group of over 1,800 outstanding life scientists from Europe and around the world. Jo Bury, VIB Managing Director: "This membership means a great recognition of the excellence of a researcher. The election of these two group leaders fills us with great pride."

WINNING PUBLICATION ON STOOL CONSISTENCY

Doris Vandeputte took home the **Ken Heaton Award 2018** for her publication in Gut on the effect of stool consistency on gut microbiota. The winner of the Ken Heaton Award is picked based on the number of citations a paper gets. Her win was announced at Digestive Disease Week 2018, the world's most important congress in the field. "This is fantastic," says Jeroen Raes. "The prize awards the most impactful work in gastroenterology of the last two years. It's a great honor."

The award is named after Prof. Ken Heaton, who devoted his career to research on stool characteristics and developed the Bristol Stool Scale. "In fact, we used that very scale in our study to score our measurements," Doris says. "And now we take home the prize named after it. Quite a peculiar coincidence!"

- **Dries Vaneechoutte** and **Klaas Vandepoele**, group leader at the VIB-UGent Center for Plant Systems Biology, were awarded the 2017 **Best Paper Award Gold Prize** for their publication on genome-wide characterization of differential transcript usage in Arabidopsis thaliana. The Plant Journal recently initiated these annual awards to honor the best papers in each of the three categories it publishes.

- Out of over 100 applicants, **Federica Perrone**, PhD Student at the VIB-UAntwerp Center for Molecular Neurology, received a prestigious **Gustave Boël-Sofina scholarship**. This will allow her to join the internationally acclaimed RIKEN Center for Brain Research in Japan for five months. Guided by Prof. Takaomi Saido, Federica will dive deeper into new techniques that provide insights into the ways rare genetic variations in Alzheimer's genes contribute to dementia.

- **Fernand Lambein**, emeritus professor at Ghent University and volunteer at the International Plant Biotechnology Outreach (IPBO), was recognized for his lifelong support of research on *Lathyrus*. The award was given out by the **International Center for Agricultural Research in the Dry Areas** at their conference on May 6-8, 2018 in Morocco.

- The **International Plant Biology Outreach** (IPBO) landed a **€730,000 project**. The program focuses on climate-smart bananas: scientists in Leuven will focus on finding drought-resistant varieties, which will then be tested in Africa. The European-African partnership between the IPBO, KU Leuven, Gembloers, Spain, Kenya and Uganda falls within the context of the EU LEAP-AGRI call.

- **Charysse Vandendriessche**, PhD Student at the VIB-UGent Center for Inflammation Research, won the **Best Oral Award** at the International Society of Extracellular Vesicles Meeting in Barcelona. The conference unites over 1,000 scientists and offers 150 speakers a stage from which to share their research. Charysse is the only PhD student of the excelling three award winners.

- Continuing her glory tour is **Damya Laoui**, postdoc at the VIB Center for Inflammation Research: after being selected for the MIT Innovators Under 35 Europe last year, she has now been named **New Scientist Wetenschapstalent 2018**. The judges were particularly impressed by Damya's original approach to research: she's developing a vaccine to protect cancer patients from metastases that is based on immune cells from within the tumor.

REPORTER ON THE ROAD: FROM CELLFIES TO SCIENCEGRAM

Social media has changed our lives, for better or worse. But what about our professional lives? Can we embrace social media and use it to our professional advantage? I am by no means an expert, but I will try to share with you my own experiences with venturing out into the social media jungle, and what I learned from talking to other scientists online.

THE BASICS OF ONLINE PRESENCE

Whether you want it or not, you have an online footprint. More importantly, your online record is only one Google search away. The use of nicknames, privacy settings, etc.; it all seems very basic. However, it is never a bad idea to check this every once in a while. Google your name and see what pops up. This is what your colleagues, fellow scientists, the HR team of the university or biotech company you are interviewing with, will see. Is this the image you want them to have of you?

Okay, so you're ready to start shaping a professional online presence. LinkedIn and Google Scholar profiles require very little effort and can easily function as your basis to start from. I would argue that there is a wealth of apps and social networks out there which, while they maybe require a bit more input, yield a far greater return on investment. However, there is no one size fits all in this. Which apps do you use yourself? What do you want to get out of social media in the context of your career? The answers to these questions will likely predict what will work best for you. Below are some examples of how scientists use certain networks and apps in their professional lives.

A LITTLE BIRD ONCE TOLD ME

From Trump tweets to teens eating dishwasher soap pods, there is more nonsense being spewed on Twitter by the second. As a result, it may come as a surprise to learn that Twitter is probably the best-suited social network for scientists. Tweets are 280 characters in length, forcing you to be concise. No boring 15-minute talk, no full paper to read: science Twitter gives you the essence of every important paper in your field in just a few sentences.

The brevity, wide audience and swiftness of Twitter are its major advantages. This is especially highlighted by two examples. First is 'live-tweeting' at a conference. During the last EMBO meeting, I was tweeting the bottom line of every talk for three days straight using the hashtag of the conference (note: always consult the conference's social media policies, and respect authors' wishes to not tweet about their data). While conferences are important networking events, you can now build your online network at the same time. Numerous people that could not attend the meeting followed the conference in real time via my tweets, hereby moving the discussion from the conference room to the global stage. An important professor in my field that missed his flight came to thank me on the second day of the conference since, through my tweets, he was able to keep up with the meeting while traveling. Just 280 characters and a valuable new connection.

The second main use for Twitter is keeping up with literature. With the rise of pre-print servers, a PubMed alert no longer allows you to stay up to date with the field. Rest assured, there are currently people in your field tweeting about every interesting study that is uploaded to BioRxiv. A lab mate once emailed me a quite controversial *Cell* article that had just come out, with the question, "Did you see this?!". I told her that my Twitter buddies and I already completely turned that paper inside out three months before its publication, since someone had fished it out of BioRxiv and tweeted about it.
As pre-prints will become more and more important, their fast distribution will also be key, and given its characteristics, Twitter could be one of the most suitable platforms for this.

SHARING #CELLFIES ON #SCIENCEGRAM

Instagram. The app has a lot more to offer than just pics of people's dinner. Just as there is on Twitter, there is a large community of scientists from across the globe active on Instagram. The visual aspect of Instagram makes it ideal for outreach and science communication, and this is exactly why the app has become increasingly popular among (mostly younger) scientists. Whether it is a selfie of you in the lab or a 'cellfie' of your cells in the petri dish, by sharing such pictures you can achieve two main goals. The first is to show the world that scientists are not only old white males with beards, but a diverse group of people with different backgrounds, genders, ethnicities, etc. For example, @500queerscientists is an initiative that aims to highlight the LGBTQ community in STEM.

Secondly, pictures of your science allow you to easily communicate about your work to laypeople. @science.sam is an Instagram rock star who pioneered this use of the app to successfully explain neuroscience to a broad audience.

We all know that PhD training can be frustrating and overwhelming at times, and it is no secret that mental health issues are very common among trainees. Within this context, there is an Instagram community that seeks to break taboos surrounding this issue and tries to provide a supportive environment for fellow students. An example is @ph_d_epression, an account where PhD students share their setbacks and provide inspiring stories of how they eventually made it through those difficult moments during their PhD training.

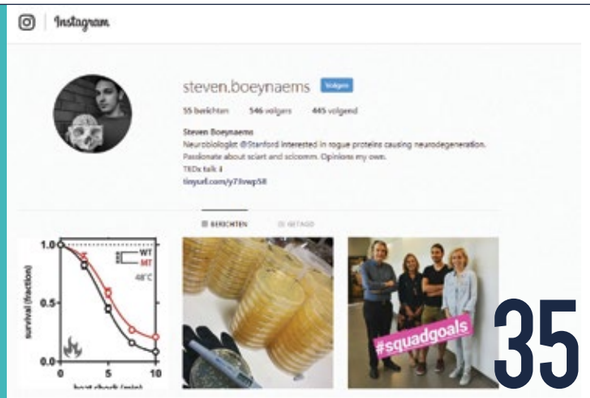
Besides Twitter and Instagram, there are many other social networks and apps that can be useful to our science. Slack is a forum-like app that is used by numerous labs and groups of scientists with similar interests. ResearchGate is a well-known online scientific community that is mostly used for sharing papers. Yet, there are many more options.

A waste of time? No way!

"Interesting points, Steven, but isn't this all a waste of your time?" While benefits won't be immediately obvious since building a network takes time, I would argue that doing so is very rewarding. I got to know other postdocs in my field through Twitter and Instagram, and this has resulted in multiple new spontaneous collaborations. I also received feedback on manuscripts and new experiments, and regularly have online brainstorming sessions with fellow scientists. Even more, no matter which conference I attend, I know I will never be alone, since my online friends will surely be there.

Steven Boeynaems is a VIB alumnus who worked at the Kevin Verstrepen Lab (VIB-KU Leuven Center for Microbiology) and the Ludo Van Den Bosch Lab (VIB-KU Leuven Center for Brain & Disease Research). Recently he traded Belgium for the Californian sun. At Stanford University he keeps pursuing his passion for science and science communication.

@steven.boeynaems | @BoeynaemsSteven



PUZZLING TOGETHER PLANT EVOLUTION THROUGH ART, AND VICE VERSA

When he's not in the lab, chances are you'll find Ive De Smet in a museum. The VIB-UGent Center for Plant Systems Biology group leader has found a peculiar link between his research work and art and turned it into a unique hobby.

It has to do with biology, but also with art… I'm confused. What exactly does your hobby entail?
Ive: "In short: I study old paintings, drawings, and other art pieces that depict plants, flowers, crops, vegetables and fruits and try to link those with biological information. By looking at the way artists presented these species many centuries ago, I hope to gain insights into their biology and how they've evolved over time. At the same time, I try to correlate what is depicted with what we already know about the molecular evolutions of certain species."

I've never heard of anyone doing this before. How did you come up with the idea?
"It all happened when my childhood friend David Vergauwen and I were visiting Saint-Petersburg. He's an art historian working for Amarant, a Ghent-based art organization. We were in a museum when he spotted some paintings with odd fruits and vegetables. We wondered: was this just bad painting, or did the species actually look that way at the time the painting was made? After a few beers in the local pub, we started fantasizing: how amazing would it be to blend my knowledge of molecular plant biology with his art history expertise? Now, three years later, our kooky idea has turned into an actual hobby."

It definitely seems like a fun pastime, but are your insights scientifically relevant at all?
"In the past few years, we've looked deeper into two species: carrots and wheat. By combining our knowledge, we've learned a lot about the domestication of these species. A summary of the results of our studies are even published in Trends in Plant Science and Current Biology. So yes, we do more than just stare at paintings – we actually gather enough material to be able to draw scientific conclusions.

"In our study on carrots, for example, we were able to connect color differences through the centuries by looking at the molecular components of carotenoid and anthocyanin accumulation in the plants. And in the wheat study, we looked at the length of the crops. Did you ever notice that in really old paintings, wheat is much taller than it is nowadays? By connecting this oddity to genetic changes, we unlocked the mystery of the height variation in art through time."

How does your art project relate to what you do at VIB?
"My group focuses on molecular changes in plants under stress, which impacts their growth and thus their yield. More specifically, we study the proteins that play a role in signaling associated with low or high temperature. If you think about it, that's very similar to what David and I do: trying to match the phenotype – shape, size, color – of a plant to its genotype."

What do you like most about your hobby?
"Our project helps bring science closer to the general public – something we always aim for at VIB as well. Through art, we put biodiversity and molecular science in the spotlight in a visually attractive way. And it works: we recently received a lot of attention on radio and TV. Apparently, people are genuinely interested in the reason some fruits look strange in paintings and are intrigued by the variety of vegetables in the supermarket. Our project tries to explain all those things.

"And, of course, it's a fun new way to look at paintings, which hasn't been done before. It gives our trips together that extra twist and stimulates David and I to go traveling more often – without our partners *(laughs)*."

What does the future look like for your fascinating project? Do you and David have any big plans?
"Our goal is to create a book and a class at art organization Amarant, where David works, by the spring of 2019. We've already laid the groundwork with our studies on carrot, wheat, melon, watermelon, cucumber, potato and strawberry. And we are starting to look into wild cabbage-derived vegetables, such as cauliflower, Brussels sprouts, and broccoli. But to take our project to the next level, we need the help of other enthusiasts. After all, we can't possibly visit every single museum."

"That's why we launched a crowdsourcing campaign. Everyone is very welcome to send us their photos of artwork containing cereal crops, fruits or vegetables. They might be of value for our research. For now, the campaign focuses on Flanders and the Netherlands, but we're definitely planning to take it worldwide!"

Vergauwen, De Smet *et al.*, Current Biology 2017
Vergauwen, De Smet *et al.*, Trends in Plant Science 2016

IVE AND DAVID NEED YOUR HELP!

Did you stumble upon a painting with an apple, radish, carrot or any other plant or fruit? All you need to do is take three pictures, one each of:

- the info plate next to the painting: painter, name and date of the work
- the complete painting
- a detail of the plant, fruit or vegetable

Send all three photos to ArtGeneticsDavidIve@gmail.com and they'll do the rest!

Tip: find Ive and David at the VIB Biotech Day on October 21 to see their project come to life!

ALL VIB ALUMNI ARE INVITED TO JOIN THE VIB ALUMNI GROUP ON LINKEDIN.

VIB ALUMNUS AND MSF SCIENTIST RAFAEL VAN DEN BERGH BRIDGES THE IMPLEMENTATION GAP

Research and innovation are often disconnected from medical practice, especially in low-resources settings and countries in crisis. As senior fellow in the Operational Research Unit of Doctors Without Borders/ Médecins Sans Frontières (MSF), VUB-VIB alumnus Rafael Van den Bergh tries to bridge the gap between scientific knowledge and daily practice in clinics, health centers, medical cabinets and community health projects worldwide. How he closes this gap? By doing more research … not fundamental or strategic basic research, but 'operational' or 'implementation' research.

Even more, if the opportunity is there, he conducts clinical trials in the field. As an epidemiologist, Rafael was one of the scientists who, together with his colleagues at MSF, WHO and other humanitarian organizations, successfully mitigated the Ebola crisis in West Africa in 2014.

The world knows Médecins Sans Frontières (MSF) as a medical aid and humanitarian organization. The research activities of MSF are much less known. What is this research about?
"MSF's operational research is designed to assess and improve practices in health programs, to help health workers to find suitable practical solutions to specific situations in crisis contexts, and to communicate what we witness on the ground. There is an immense gap between scientific and medical knowledge and the implementation of this knowledge in the field, especially in low-income countries and regions in crisis. MSF closes this gap by embedding operational research into its emergency and/or humanitarian interventions."

What is your role in these projects?
"About one week a month, I am in the field, anywhere in the world, either to provide training on how to conduct operational research in resource-poor contexts, to carry out evaluations of projects, or to help set up new research programs. When I am not abroad, I work from the MSF offices in Brussels or Luxembourg. Sometimes MSF is also directly involved in clinical trials. We were involved in three clinical trials during the 2014 Ebola crisis in West Africa. That was mainly because most patients were treated by MSF doctors – if we didn't co-organize the trials, they just wouldn't have happened. But it is rather exceptional that we conduct clinical studies ourselves."

You have (co-)authored about seventy scientific publications since you joined MSF in 2011. Is publishing a deliberate strategy of MSF?
"Publishing in peer-reviewed journals increases the impact of our research tremendously. Not only because other humanitarian organizations can learn from our experiences, but also in our advocacy work with governments and health authorities, a peer-reviewed publication is worth more than ten internal reports – it's largely a credibility issue."

You started working for MSF after finishing your PhD on the interaction between HIV and monocytes in the lab of Patrick De Baetselier (VIB-VUB). Going from VIB to MSF is a big step. What was your motivation to take this step?
"Like all PhD students, I ended up being an expert in a very narrow niche – in my case, I was probably the world expert on how the protein visfatin is involved in the interaction between HIV and monocytes. But this seemed such a narrow aspect of the whole HIV story, and so far away from any practical benefit for patients and clinicians. Such benefits might emerge in the very long term, yes, if I was very lucky.

But during my PhD, I was fortunate to be able to work with Bob Colebunders from the Institute of Tropical Medicine in Antwerp, one of the field pioneers on HIV. We started a research project in Uganda – which didn't get off the ground that easily, by the way – but through this experience, I realized that there were research opportunities other than working in a Western laboratory. What excites me at MSF is the diversity of the research projects – I'm not a world expert in anything, but I'm a dabbler in many things. And above all, I love the direct and immediate impact of our research on patients, clinicians and communities. We really make a difference, here and now."

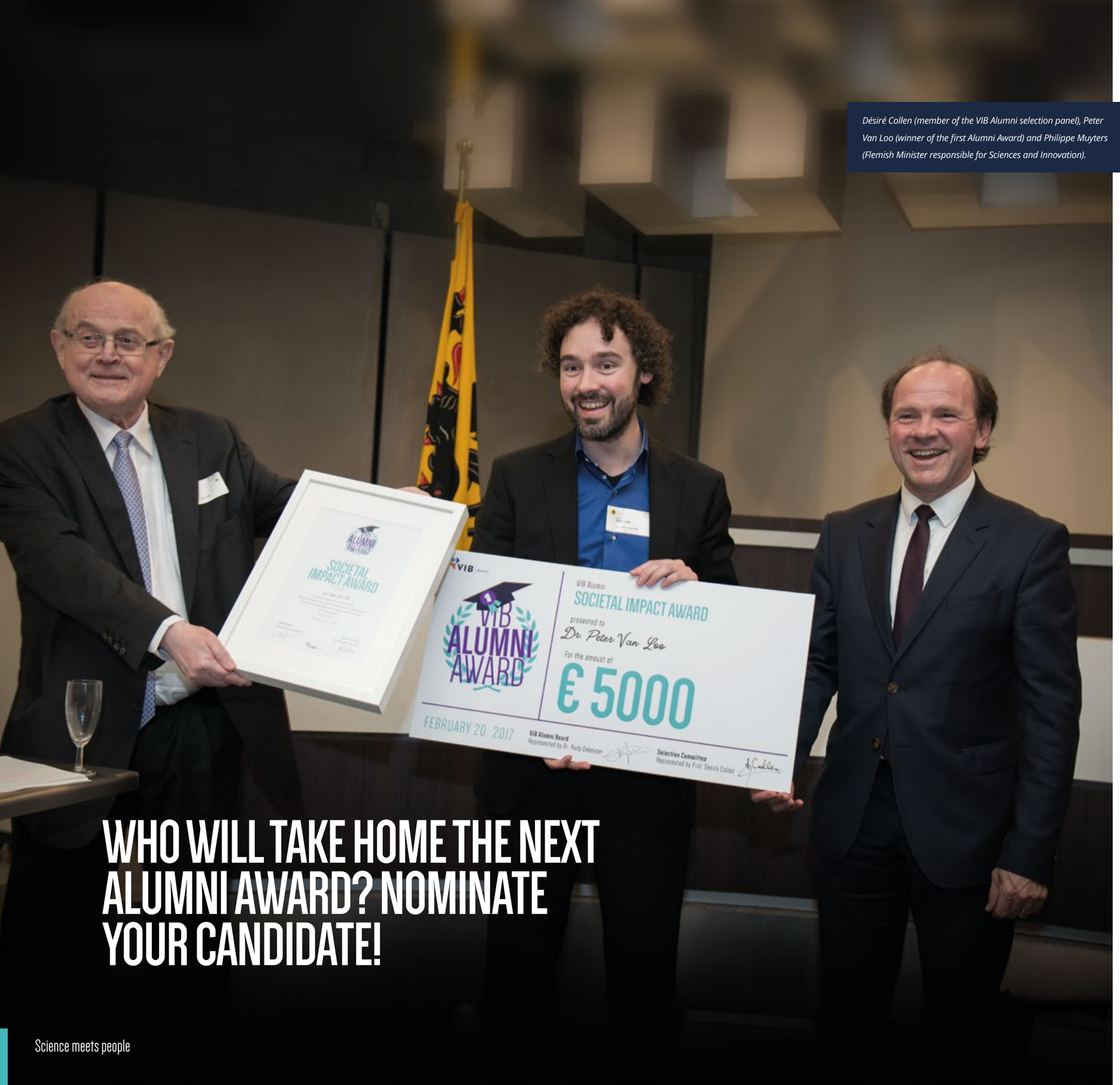
Can VIB help you in the work you are doing right now?
"There is currently one missing link in our operational research activities: the feedback loop from us back to biomedical research organizations and research funders is not closed. We should be at the negotiation table when research organizations like VIB, universities, industry and big funders (like the EU Commission or the NIH) set up their health research agendas. We at MSF have a great deal of knowledge and expertise that could inspire research. But we are – for the time being – absent in research agenda setting.

Let me give just one example where VIB could help us out: when a patient comes to a health center with an infection, it is not always immediately clear whether this is a viral or a bacterial infection. The follow up of this patient is usually not possible; therefore, the clinician has to decide on the spot. Most often, the patient will be given antibiotics, just to make sure. This is ineffective health care, but it is the way in which medicine is practiced in most parts of the world.

A simple test to rapidly distinguish viral from bacterial infections would be immensely helpful. VIB has the knowledge, capabilities and capacities to develop such a rapid test."

Rafael Van den Bergh

"You see, at first sight, the distance between VIB and MSF might seem intergalactic, but in reality, there are many avenues on which we can work together." - *Rafael Van den Bergh*



Désiré Collen (member of the VIB Alumni selection panel), Peter Van Loo (winner of the first Alumni Award) and Philippe Muyters (Flemish Minister responsible for Sciences and Innovation).

WHO WILL TAKE HOME THE NEXT ALUMNI AWARD? NOMINATE YOUR CANDIDATE!

Since its establishment in 1996, VIB has grown into a widespread international community. On top of the 1,600 people working at VIB today, another 3,000 alumni continue their careers in universities, research centers, governments and hospitals. The Alumni Board connects the two and recognizes one meritorious VIB alumnus with the Alumni Award – worth € 5.000.

THE HALL OF FAME

The first Alumni Award was presented at VIB's 20-year anniversary celebration in 2017. The winner was Peter Van Loo, who is currently working at the Francis Crick Institute. His research findings have been translated into clinical practice such as CALR mutation testing and are already being used to diagnose bone marrow diseases.

The next scientist stepping up to the winners' stand could be your (ex-)colleague. Anyone who has worked at VIB for at least six months and left at least one year ago is eligible for the prize. Self-nominations are not accepted.

PRACTICAL

Submit the application form (via SPOC) by September 28, 2018 to nominate your fellow scientist. The VIB Alumni Board will judge and rank all nominations. The winner will be picked by the VIB Alumni selection panel consisting of Désiré Collen (former Scientific Director at VIB-KU Leuven), Marc Van Montagu (former Scientific Director at VIB-UGent), Joël Vandekerckhove (former Scientific Director at VIB-UGent) and Hugo Van Heuverswyn (former Chairman of the Board of Directors).
The Award ceremony is planned at VIB's General Assembly on April 24, 2019.

CTLS2018: HIGHLIGHTING THE FUNDAMENTAL ROLE OF LIFE SCIENCES TECHNOLOGIES

From July 1-4, 2018, VIB proudly hosted the 3rd conference of the Core Technologies for Life Sciences Association in Ghent. Keynote speaker Sir Paul Nurse opened with a powerful reminder that great scientific discoveries are built on the technologies that make modern research possible. The 300 attendees, mostly core facility staff members, were already well aware of this fact. Still, it's always nice to hear it from a Nobel laureate.

This most recent event was the third biennial conference of the association. Two previous meetings set the stage for what was the best-attended and diverse conference to date.
"The 3rd biennial CTLS conference was a wonderful milestone for this young association," asserts Chris Guerin (Bio Imaging Core Ghent), CTLS council member and lead congress organizer. "It generated remarkable enthusiasm from both existing and new CTLS members to work together and improve the ways core technology facilities support cutting-edge science."

OFFERING A BROAD ARRAY OF INFORMATIVE EXPERIENCES

Over the course of four days, the participants listened to 42 speakers, browsed 60 posters and attended seven company workshops. Even more, there were four satellite symposia to wrap up the program. In addition to the meeting a social program including a beer tasting at the Great Butchers Hall, a boat tour and a dinner at the Old Fish Market gave everyone many opportunities for networking and community-building.

The presentations were diverse and addressed the scientific, administrative and technological challenges facing core facility staff. Importantly for this inclusive association, the group of speakers included as many women as men. There were plenary sessions on big data, international alliances and core interactions with users, vendors, funders and each other. Eight parallel sessions covered scientific issues such as single-cell technologies and research and development in cores, as well as administrative topics like career development and the reproducibility of core facility data. The overwhelming impression left by the meeting: core facilities are the technological engines that drive life sciences research.

"The overwhelming impression left by the meeting: core facilities are the technological engines that drive life sciences research."

TECHNICAL STAFF FORM THE FOUNDATIONS OF EXCELLENT SCIENCE

Another important take-home message came from both Paul Nurse and Kelly Vere of the UK Science Council: never underestimate the importance of technical staff. Kelly presented the UK Technician's commitment that over half of the universities in the UK have signed, which helps ensure that the contributions of technical staff are duly recognized and rewarded. Sir Paul described his early experience working in a laboratory media kitchen before beginning his university career, emphasizing the fact that the work of technical support staff should never be undervalued.

MARK YOUR CALENDAR

MARK YOUR CALENDAR

SuperNova
September 26-30, 2018 – Antwerp

Cell-Nerf symposium: Neurotechnologies
September 30 – October 2, 2018 – Ghent

Biotech Day
October 21, 2018 – Antwerp

International Meeting on Optical Biosensors
November 15-17, 2018 – Ghent

Dag van de Wetenschap
November 25, 2018 – Flanders

Metabolism in Cancer and Stromal Cells
November 26-27, 2018 – Leuven

BioBusiness Winter Retreat
December 11-13, 2018 – Ghent

Celebration 90 years FWO
December 14, 2018 – Antwerp

COLOPHON

Responsible Publisher
Jo Bury
VIB vzw
Rijvisschestraat 120
9052 GHENT
BELGIUM

Chief Editor
Sooike Stoops

Coordinator
Tiny Sterck

Photography
Lander Briels
Ine Dehandschutter
Joyce Lanssens
Conor McGuire
Eef Parthoens
Anna Schroeder

All Enquiries
VIB HQ
Rijvisschestraat 120
9052 GHENT
BELGIUM
Tiny Sterck
E-mail: tiny.sterck@vib.be
Tel.: +32 9 244 66 11
Fax: +32 9 244 66 10
www.vib.be

www.vib.be/VIBtimes
Via this link you can (un)subscribe for VIBtimes (electronically and/or hard copy)