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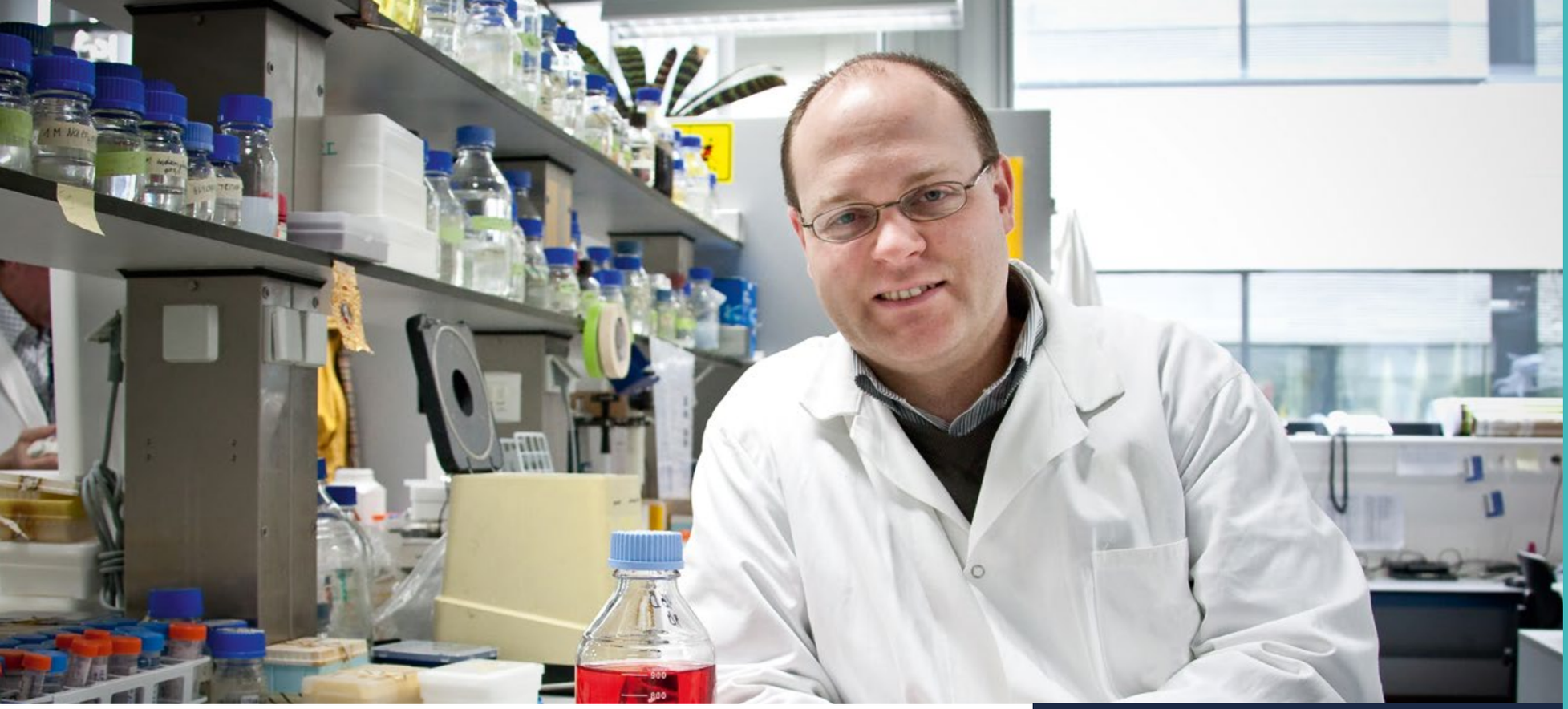
VIB

Technologies at VIB

Technology suites for better science

Alumni in the picture: Paul Van Hummelen

CRISPR/Cas



Nico Callewaert
Department Director at the VIB Medical Biotechnology Center, UGent

Technology: the tools and methods to observe and to intervene in Nature

In molecular life sciences, the incredible ingenuity of scientists and engineers such as those at VIB leads to increasingly accurate analytical methods. These are used to study the structure of the molecules that make up living matter, and to elucidate how these molecules interact in the self-propagating far-from-equilibrium steady state that essentially constitutes Life. Importantly, these methods are also those used to detect the molecular alterations that occur in diseases of plants, humans and other animals, and are the basis for the diagnostics that will progressively change medicine (and agriculture) as we know it.

Similarly, scientists are constructing increasingly sophisticated tools to intervene in Nature. This remains essential to counter the threats to our existence as the otherwise rather unremarkable primates that we are. In life sciences, methods are developed to manipulate and perturb processes in biological systems, which enable us to gain knowledge on the workings of these systems. These very same biotechnological methods are allowing us to develop new molecules, cells and organisms that help us live our billions of lives. Agricultural methods such as breeding, use of fertilizers and pest control, and medical tools such as vaccines and antibiotics have tremendously improved the prospects of more and more humans to lead longer, healthier lives. And don't forget the fermentation technology that has given us beer, wine, bread, chocolate and cheese to make those long lives more enjoyable!

Modern biotechnology is merely speeding up these long-standing human endeavors, by allowing for a much more specific, targeted approach to agriculture and medicine, most often not opposed to but synergistic with the methods of the past.

In summary, for its survival and development, humanity has had and continues to have a need to invent ways to analyze and manipulate our world (technology). Possibly because of this, humans have evolved a remarkable curiosity about how the world works. This curiosity has so far culminated in the systematic form of inquiry known as modern science. Humankind's needs inspire scientific inquiry. Scientific results inspire new technology, which allows for new scientific inquiry. The two are aspects of one and the same deeply human cultural endeavor, to which we at VIB and its partner universities are proud to contribute.

TECHNOLOGIES AT VIB

All members of VIB's Core Facilities

TECH WATCH TEAM
Complementary to Core Facilities

Since 2008, VIB's Technology Watch Team is continually analyzing the potential of new, emerging technologies. Over the years, the team has gathered an enormous amount of information about disruptive technologies that could be valuable to VIB scientists. With the help of Technology Watch funds and by expanding the network of technology suppliers, purchasing licenses and negotiating partnerships, groundbreaking technologies are constantly finding their way into VIB labs.

A CLOSER LOOK AT VIB'S 'TECHNOLOGY SUITES FOR BETTER SCIENCE'

As modern life sciences become ever more dependent on technology, scientists not only need state-of-the-art equipment at their disposal, they also require high-quality servicing in a wide range of domains. This is exactly what VIB's Core Facilities aim to offer: leading-edge platforms that enable scientists to exploit the latest technologies to the fullest, supported by the best techno-scientific expertise. Geert Van Minnebruggen, Head of Core Facilities, tells us more about the institutional value of VIB's so-called 'technology suites for better science'.

Order your copy of the new 'VIB Core Facilities' brochure via corefacilities.vib.be

First of all, why have life sciences and technology become so inextricably intertwined?
"Technology has always played a major part in scientific breakthroughs, but in life sciences, one particular milestone is crucial. When the Human Genome Project was completed in 2003, new generation sequencing methods started evolving at an unprecedented pace.
New technologies used to have a lifespan of about three to five years, but today, a brand-new technique will probably be outdated in six months' time.
For research groups, it has become impossible to keep track of all these rapid technological innovations without losing sight of their own research questions. Acquiring the expensive equipment and developing all the necessary techno-scientific expertise within a single research group is simply too time-consuming and costly."

"The Core Facilities program at VIB empowers not only internal scientists but also researchers in Flanders, Europe and the world by giving them access to state-of-the-art equipment and consultation." – *Chris Guérin (BIC Ghent)*

So, this new technology wave encouraged VIB to open up the Core Facilities to the scientific community?
"Absolutely. New technology has enabled life scientists to discover and connect biological building blocks and networks within their specific domains. These, in turn, were often useful in charting interactions on other levels. That's why we believe in an integrated approach of the so-called 'omics' domains: decoding genomes, but also studying the structures and spatio-temporal functions of proteins, expression levels of RNA transcripts and / or even the fate of metabolites during various development and disease states. It's clear that a lot is happening at the intersection of disciplines nowadays: combining primarily distant domains leads to new insights into the molecular blueprint of many development and disease processes."

In what ways can VIB's Core Facilities provide a competitive advantage?
"First of all, we ensure that our scientists have continuous access to a wide range of state-of-the-art technologies and matching expertise. The most recent example is the acquisition of a new state-of-the-art Transmission Electron Microscope in March 2016 (see page 15). This new device allows researchers to outsource parts of their microscopic-driven projects to imaging experts who decipher the structural details of the (sub) organelle of interest and provide high-resolution images to the

"We see bioinformatics training, scientific software provisioning, software development and bio-IT community-building as essential cornerstones that enable biologists to tackle data challenges in an increasingly data-intense research environment."

– Alex Botzki (BITS)

researcher of use for publications. Secondly, the Core Facilities are an excellent platform for building networks and integrating expertise. This generates a competitive advantage not just for all of the scientists in our institute, but for the research community as a whole. And thirdly, cutting-edge technology helps VIB to attract talented, (technology-driven) scientists." The Core Facilities are a strong asset to attract young PIs!

How have the Core Facilities evolved in the past few years?
"Since 2008, we have significantly professionalized the existing VIB Core Facilities and integrated them in a program format. In addition to the classical service tracks, the CFs started to develop cross-platform workflows and novel applications that open up new research opportunities for scientists. In close cooperation with our Technology Watch Team (see box on page 5), we have taken the effort to scout, evaluate (i.e. beta-test) and eventually put a set of emerging ground-breaking techniques in service mode. The results are self-explanatory: an increase in the number of VIB-affiliated high-impact papers, and a premium score for the Core Facility Program by an international advisory council. This puts us among the most renowned Core Facility programs in Europe."

"The VIB Core Facilities Program makes your research work. The chance of failure is lower when experienced people take care of the experiments that are not your daily business. In this way, the CFs take you from ideas to results much faster."

– Steve Schoonooghe (NSF)

"At PEC, we discover novel modifications and protein interaction partners on a daily basis, even for proteins that have been studied for decades." *– Francis Impens (PEC)*

Remaining at the forefront of fast-evolving technologies must be challenging.
"It is. Ensuring the competitive advantage of our Core Facilities bears a number of challenges. Thanks to the Technology Watch Team, we stay abreast of emerging technologies, but there are managerial challenges as well: managing the needs of stakeholders, hiring and retaining the right expertise and acquiring the necessary funding for investments are only some of them. In order to deal with this complexity, maintaining a dialogue with peers is necessary. That's why VIB became founding partner of 'Core for Life', an alliance of some of the finest life science core facilities in Europe. Its mission is to bundle expertise and resources across institutes and countries."

Who can use VIB's Core Facilities?
"Our Core Facilities provide their high-tech equipment and expertise to our own researchers, but also to scientists from other organizations and even industrial customers. VIB researchers will be prioritized of course, but for-profit players can definitely benefit from our services as well. In 2015, we launched a new Core Facilities website where potential customers can find detailed info about the program as a whole as well as about the individual Core Facilities (see box)."

In a nutshell, what are the plans for the coming years?
"In collaboration with the Core Facility managers, who all follow the latest trends in their fields, we have prepared a strategic plan for the next five-year cycle. An important initiative is the set-up of a fund for Core Facility-specific infrastructure investments, which will allow us to roll out a long-term investment strategy. This fund will prove to be essential to keep our facilities state-of-the-art. I also feel it's my daily responsibility to secure the close cross-talk with the individual VIB research centers as all the activities we undertake are in support of their high-level science stories.

In the years to come, we will also further develop the Core Facility program to bring the expertise of different Core Facility units together. Another aim is to boost cooperation between the tech watch and tech transfer teams. In the end, we're all pursuing the same goals: to conduct frontline research and translate scientific breakthroughs into tangible benefits for society."

"By combining its well-organized service activities with evaluation and development of new technologies in the field, PSF acts as a center of excellence that offers consultation to the institute and external clients alike."

– Jurgen Haustraete (PSF)

VIB DISCOVERY SCIENCES
Intense collaboration with Core Facilities

In order to increase the success rate of translational research, VIB has endorsed a new strategic initiative called 'VIB Discovery Sciences'. Its mission is to translate basic life science research data into drug and agro-biotech innovations. Intense collaboration with VIB Core Facilities is an essential component of this effort.

For example, the VIB Compound Screening Facility (CSF) will play a vital role as the base unit for the agro-chemical unit of VIB Discovery Sciences, while the BioImaging Core (BIC) team will be an important asset for high-resolution/high-content screening. For the biologics discovery unit of VIB Discovery Sciences, the Nanobody Core Facility (NC) and the Protein Service Facility (PSF) will be key partners.

A BIRD'S-EYE VIEW OF VIB'S CORE FACILITIES

BIO IMAGING CORE
Image experiment design
Image acquisition
Image analysis

PROTEIN SERVICE FACILITY
Recombinant protein expression
Protein production
Protein conjugation

NUCLEOMICS CORE
AACTGC
Personalized NGS services
Advanced experimental design
State-of-the-art bioinformatics support

COMPOUND SCREENING FACILITY
Assay development
High-throughput screening
Hit validation

BIOINFORMATICS TRAINING AND SERVICE CENTER
Bioinformatics training
Software management
Research informatics services

PROTEOMICS EXPERTISE CENTER
MS-based quantitative proteomics
Protein discovery and characterization
Data analysis and support

GENOMIC SERVICE FACILITY
Sanger sequencing
Genotyping service

NUCLEAR MAGNETIC RESONANCE CENTER
Epitope mapping
Protein dynamics
Biomolecular interactions

NANOBODY SERVICE FACILITY
Nanobody generation
Nanobody characterization
Nanobody engineering

More info on corefacilities.vib.be

HOW ORBITRAP

HELPS VIB RESEARCHERS EXPAND THE FRONTIERS OF SCIENCE

Since its introduction in 2005, the Orbitrap mass spectrometer has quickly become a star in the research firmament. It has contributed to numerous significant breakthroughs in life sciences, especially in the fields of proteomics (the study of proteins and their functions) and metabolomics (the study of the intermediates and products of metabolism). First developed by the Russian physicist Alexander Makarov, a wide variety of Orbitrap mass spectrometers exist today, each with their own specifications. They all enable the quantification and profiling of small ionized particles using electrical fields. What makes Orbitrap such an important technology, and how does it help VIB researchers? We asked these questions to three researchers in separate VIB labs.

STUART MAUDSLEY

Associate Department Director at the VIB Department of Molecular Genetics, University of Antwerp

"My laboratory purchased the Orbitrap Q Exactive Plus MS to investigate complex neurodegenerative diseases such as Alzheimer's disease and frontotemporal dementia (FTD). Our Q Exactive Plus platform allows us to rapidly identify complex patterns of protein expression alteration that are involved in these disorders. We also purchased a highly-specialized and ultra-sensitive Orbitrap Tribrid Fusion MS platform – the only one of its kind in Belgium. This machine allows us to investigate so-called 'micro-proteomes', which further refines our ability to identify the signaling factors that underpin the development of neurodegenerative diseases. We call these the 'molecular signatures' of the disease. My lab believes that by identifying these molecular signatures, we will be able to better design therapeutic interventions."

BART GHESQUIERE

Expert Technologist at the VIB Vesalius Research Center, KU Leuven

"We use an Orbitrap (Thermo Scientific Q Exactive) for the analysis of metabolites, the intermediates or end products that result from a complex network of intracellular biochemical reactions. Our research center is specialized in the analysis of biochemical processes by tracking the passage of isotopes through a certain reaction or metabolic pathway. This gives researchers a deeper understanding of the exact biochemical reactions that are involved in diseases such as cancer, inflammation disorders and neurodegenerative diseases. Some cancer cells, for example, are capable of surviving various chemotherapies. The resistance of these cells is often caused by unique biochemical adaptations. Understanding and identifying these biochemical reactions – thanks to technologies likes Orbitrap – may help researchers develop improved treatment strategies or therapies."

FRANCIS IMPENS

Expert Technologist at the VIB Medical Biotechnology Center, UGent

"Our lab uses the Orbitrap Q Exactive HF, one of the most powerful mass spectrometers for proteomics currently on the market. It allows us to identify thousands of proteins in a single run. Furthermore, the high resolution spectra allow the precise mapping of protein modifications. With demand for proteome analyses increasing both within the VIB scientific community and beyond, these features make the Q Exactive HF an ideal instrument to expand the MS capacity of the Proteomics Expertise Center (PEC). Thanks to a specific setup that was developed at the Max Planck Institute in Germany, we can also efficiently separate peptides in front of the mass spectrometer. This ultraperformant setup makes our Q Exactive HF instrument ideally suited for large-scale shotgun proteomics experiments, bringing the measurement of the near complete proteome of a cell or tissue within reach. With this new machine installed, PEC's other mass spectrometers can be used more efficiently to measure samples that are less complex."

VIB SCIENTISTS DEVELOP BEST METHODS FOR

AUTOMATED FLOW CYTOMETRY ANALYSIS

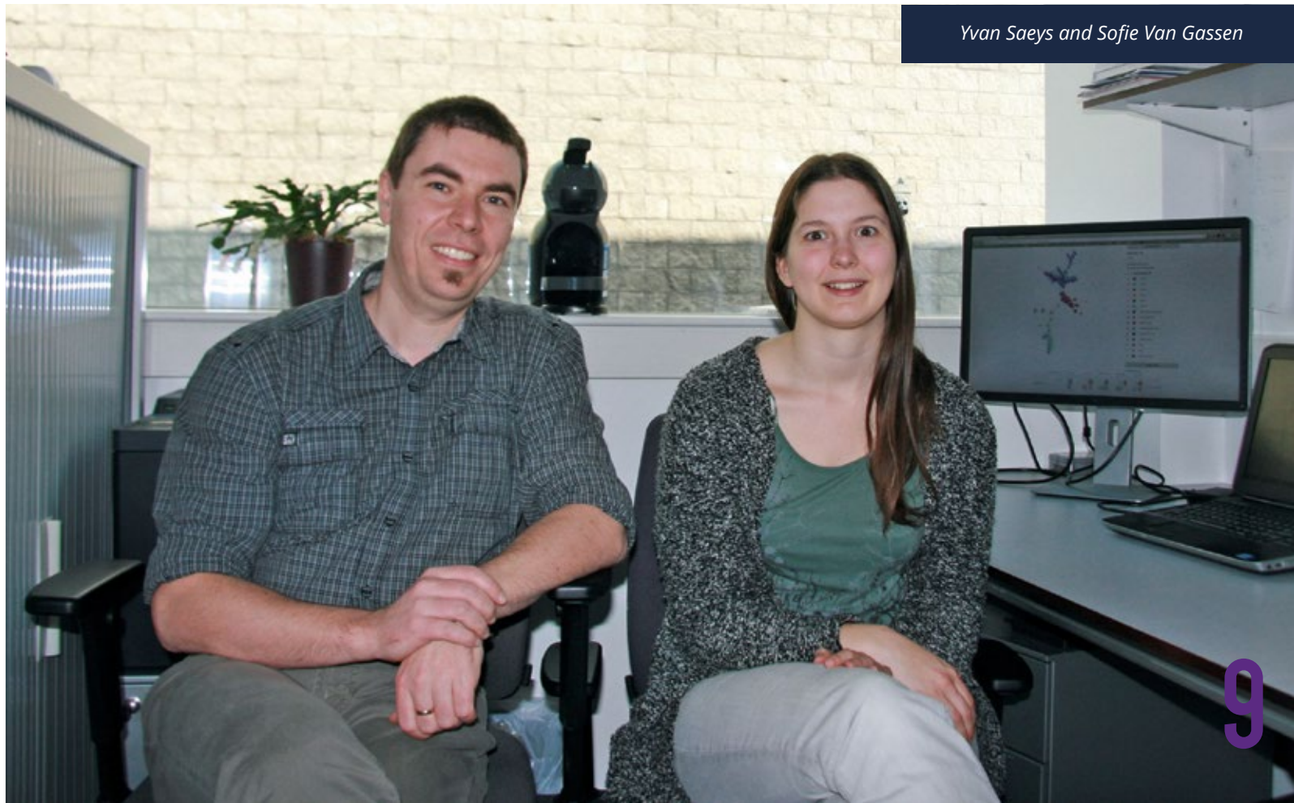
Flow cytometry has been widely used by immunologists and cancer biologists for more than 30 years as a biomedical research tool to distinguish different cell types in mixed populations based on the expression of cellular markers. It has also become a widely used diagnostic tool for clinicians to identify abnormal cell populations associated with disease. VIB scientists from the team of Yvan Saeys (VIB Inflammation Research Center, UGent) have developed novel computational tools to automate the analysis of flow cytometry data. Using their algorithm they were able to obtain the best performance in the FlowCAP IV challenge, an important benchmark in the recent field of flow cytometry bioinformatics.

The Flow Cytometry Critical Assessment of Population Identification Methods (FlowCAP) challenges were established to compare the performance of computational methods for identifying cell populations in multidimensional flow cytometry data. The most recent challenge takes these goals one step further and combines automated population identification with statistical methods to predict clinical phenotypes. The methods developed in the Saeys Lab proved to obtain the best results when predicting HIV to AIDS progression.

Van Gassen et al. Cytometry Part A, 2016

Aghaeepour et al. Cytometry Part A, 2016

"Our methods also revealed unexpected cell types that correlate well with progression to AIDS, leading to novel cell subsets potentially important in HIV to AIDS progression." *- Yvan Saeys*



Yvan Saeys and Sofie Van Gassen

NOVEL COMPONENT IN PIN RECYCLING STEERS

AUXIN-MEDIATED DEVELOPMENT

At the VIB Department of Plant Systems Biology, UGent, Michael Karampelias and Pia Neyt together with Mieke Van Lijsebettens, and in collaboration with Geert De Jaeger and Jiri Friml, identified the ROTUNDA3 protein as a regulator of the protein phosphatase 2A-driven PIN-FORMED (PIN) recycling and revealed its importance in auxin transport-related plant developmental programs. The polarity of PIN localization at the cell membrane is regulated by protein complexes, implying temporary internalization in the cell through vesicles and changes in the activity state. PIN proteins actively transport the plant hormone auxin, of which the directionality, referred to as polarity, steers developmental processes throughout the plant's life cycle.

> Mechanistic insight into the function of the RON3 protein was obtained by combining and integrating a number of up-to-date technologies in map-based cloning, genetics, cell biology, protein purification, in addition to extensive phenotyping over the entire lifecycle of the plant and in response to hormonal and gravitropic stimuli.
>
> *Karampelias et al., PNAS 2016*

TECHNOLOGICAL EVOLUTIONS IN

PLANT TRANSFORMATION

Transformation is an essential tool for functional analysis of genes in model organisms, such as Arabidopsis *and maize, and thus essential in the VIB Department of Plant Systems Biology, UGent.*

ARABIDOPSIS TRANSFORMATION SERVICE (CARINA BRAECKMAN)

Agrobacterium-mediated floral dip of *Arabidopsis* plants at early flowering stage generates seed stocks for around a thousand constructs per year in six weeks. Upon germination in tissue culture at high density by the user, T0 transgenic seedlings are selected that produce transgenic T1 seeds in the growth room in fourteen weeks. Requests for *Arabidopsis* transformation are made through an electronic website, flexibility in ecotype/genotype is provided. Throughput is further optimized by improving standard growth conditions of supply plants for dipping.

MAIZE TRANSFORMATION PLATFORM (STIJN AESAERT AND GRIET COUSSENS)

Agrobacterium co-cultivation of inbred maize immature embryos and subsequent tissue culture generates transgenic shoots that are grown in the greenhouse and backcrossed to wild type yielding with an average of ten T1 transgenic seed events per construct; the entire procedure takes eight months. Requests for maize transformation are submitted to a committee for approval. Currently, fifty constructs per year are transformed into maize. Maize transformation is further optimized to reduce the tissue culture timeline, to enhance tissue competence for *Agrobacterium* infection, to increase somatic embryogenesis and plantlet regeneration capacity.

Mieke Van Lijsebettens coordinates both the *Arabidopsis* Transformation Service and the Maize Transformation Platform.

Arabidopsis

Maize

SFINX: COOL ACRONYM, MORE ACCURATE PROTEIN ANALYSIS

The labs of Jan Tavernier, Kris Gevaert and Sven Eyckerman from the VIB Medical Biotechnology Center, UGent tackle some of the most fundamental life sciences questions in their research into the detection and analysis of protein-protein interaction. This kind of analysis helps scientists come up with new hypotheses for the functions of proteins. Unfortunately, good data analysis in this area is tricky. Until now: Jan, Kris and Sven developed SFINX, a powerful online tool that does away with the hassle.

Sven: "High-end mass spectrometry instruments are incredibly sensitive. Since they are capable of identifying huge numbers of proteins, finding the relevant ones is quite an analytical challenge. PhD student Kevin Titeca developed an intuitive and powerful tool to filter out the relevant proteins that can be applied to a number of different approaches and techniques. In collaboration with Lennart Martens from our department and researchers from the University of Antwerp, he developed the Straightforward Filtering INdeX, or simply SFINX."

HARDER, BETTER, FASTER, STRONGER

There are already software solutions that separate false from true positives in these protein-protein interaction datasets, but none of them combine accuracy, speed and user-friendliness without the need for external data.
Kevin: "SFINX outperforms other techniques. It's stronger, faster and highly intuitive. Unlike the other solutions out there, it doesn't need any external resources, which makes its results more objective and reproducible. SFINX's algorithm and web interface are user-friendly and produce immediate visual results."

Anybody can easily access SFINX via its web interface at sfinx.ugent.be.

Back row from left to right:
Jan Tavernier and Sven Eyckerman
Front row from left to right:
Kevin Titeca and Kris Gevaert

VIROTRAP

TRAPPING MAMMALIAN PROTEIN COMPLEXES IN VIRAL PARTICLES

The VIB/UGent research team led by Sven Eyckerman has developed Virotrap, a generic platform for characterizing protein complexes under native conditions. Virotrap catches a bait protein together with its associated protein partners in virus-like particles that bud from mammalian cells. In this way, cell lysis is not needed and protein complexes are preserved during purification. Virotrap is already successfully being used in collaboration with other VIB teams.

The development and application of this pioneering technique is described in a paper in Nature Communications.
Eyckerman et al., Nature Communications 2016

From left to right: Elvis Noah, Daria Gawron, Kris Gevaert and Petra Van Damme

POSITIONAL PROTEOMICS

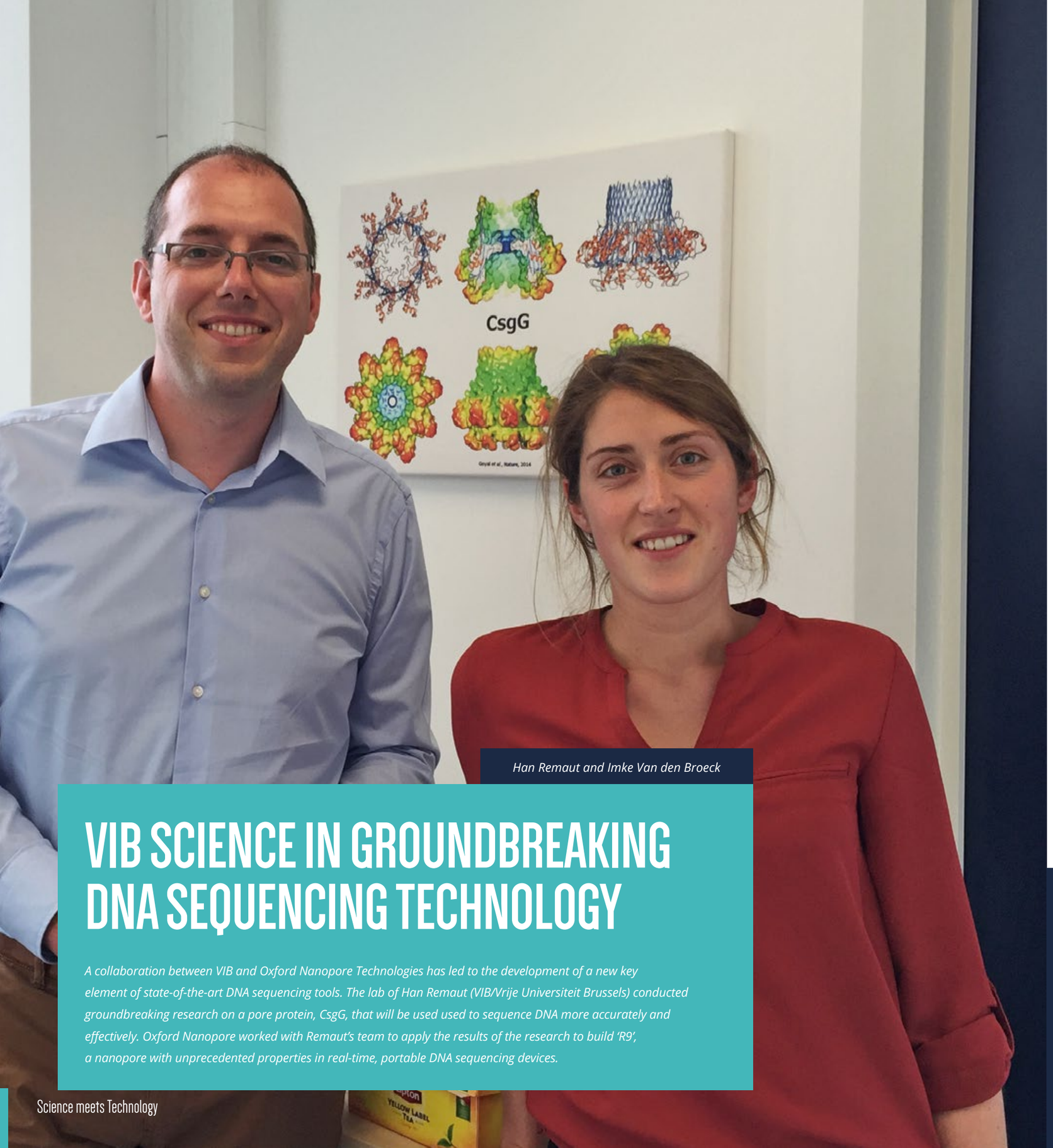
DISCOVERING MORE ABOUT PROTEINS CREATED BY GENES

Even though the human genome was sequenced a decade ago, figuring out which DNA regions create which proteins remains a challenge. Recent research suggests that current knowledge of protein creation sites on genes is incomplete, pointing to the possibility that 10-20% are created at alternative sites. In their new project, Petra Van Damme of the of VIB Medical Biotechnology Center, UGent and her team studied newly discovered N-terminal proteoforms (protein "bits" created by a single gene). She's happy to tell us all about it.

Petra, can you tell us more about protein stability?
Petra: "Protein stability has a big impact on gene expression, which determines which types of cells our bodies make. Ours is the first large-scale study of protein stability that can see differences between multiple N-terminal protein forms that are produced by a single gene. Using the method we developed in our lab, we confirmed that N-Terminal proteoforms come from alternative start sites on the same gene, and that they can vary widely in stability."

How will these findings be put to use?
Petra: "It's important for us to expand our current understanding of proteoforms – and the human genome – by exploring alternative start sites of proteomes. Overlooked in the past, alternative proteoforms can cause problems in biomedical research because of their effects on antibodies and gene expression."

What are your plans moving forward in terms of proteomics research?
Petra: "There's a real lack of scientific literature in this area, and N-terminal proteoforms are still poorly-understood. Our future goals center around identifying where and why certain proteoforms are generated within genes. We also want to expand scientific awareness of the processes that drive alternative translation events, and increase our understanding of translation regulation and the creation of these protein forms."



Han Remaut and Imke Van den Broeck

VIB SCIENCE IN GROUNDBREAKING DNA SEQUENCING TECHNOLOGY

A collaboration between VIB and Oxford Nanopore Technologies has led to the development of a new key element of state-of-the-art DNA sequencing tools. The lab of Han Remaut (VIB/Vrije Universiteit Brussels) conducted groundbreaking research on a pore protein, CsgG, that will be used used to sequence DNA more accurately and effectively. Oxford Nanopore worked with Remaut's team to apply the results of the research to build 'R9', a nanopore with unprecedented properties in real-time, portable DNA sequencing devices.

Nanopore sequencing technology depends on small electrical currents that run through a narrow protein pore, or small hole – a nanopore – through which strands of DNA are guided during the sequencing process. Han's lab has discovered that CsgG pore proteins have a structural build-up that can generate superior quality data compared to other nanopore sensors. Since this discovery, Oxford Nanopore has been fine-tuning the structure of the nanopore with the end goal of integrating it into cutting-edge electronic sensing devices including MinION and PromethION. This collaboration has a positive impact on both parties, allowing VIB to expand the scope of its research and enabling Oxford Nanopore to build its offering of fast and portable sequencing solutions in labs and remote areas, which benefits the community, the economy and the world.

Han, what makes this collaboration so interesting?
Han: "It's very satisfying to see our basic research have such an impact on new technologies. CsgG-based pores give a tremendous increase in sequencing accuracy and speed compared to available nanopores. We started with a different focus when we set out to investigate the structure of the CsgG pore, which had to do with understanding its role in an unusual protein secretion process in bacteria. Strikingly, we also discovered that its structure makes it perfect for nanopore sensing applications such as DNA sequencing. Working with Oxford Nanopore will give our team the opportunity to continue to study CsgG in even more detail."

Imke, how has your work with Oxford Nanopore impacted the future research goals of the project?
Imke: "I initiated the single channel conductance experiments on CsgG to help us understand its pore properties. These experiments allowed us to form a plausible model of the protein secretion mechanism adopted by CsgG, and also hinted at the protein's potential for nanopore sensing applications. Single channel current recordings can be tedious and time-consuming to set up. The MionION device that Oxford Nanopore technologies developed for its nanopore DNA sequencing applications allows the parallel read-out of hundreds of channels at a time. Through this collaboration we can now address fundamental questions about substrate recognition and transport by CsgG that would not have been practically feasible using more classical electrophysiology setups."

Goyal et al, Nature 2014

FROM KNOWLEDGE TO REAL SOLUTIONS: TECH TRANSFER IS CRUCIAL

It's obvious that expanding our knowledge base and doing excellent basic science is an essential piece of learning and innovation. But it's only one side of the coin; a balance must be struck between pure research and the application of knowledge to develop products that solve real problems.VIB is dedicated to both performing top-notch fundamental science and translating it into tangible solutions to real world needs. Linking the power of scientific knowledge with the here and now — that's the beauty and symmetry of tech transfer.

CRISPR

BIOTECH BREAKTHROUGH, IP BATTLE AND ETHICS QUESTION OF THE CENTURY

Jennifer Doudna and Emmanuelle Charpentier's development of CRISPR/Cas, a revolutionary DNA-slicing tool that allows the precision mix-and-matching of genes, won them USD 3 million each, with a Nobel Prize likely in their future. However, it hasn't been all sunshine and flowers for the pair, who are now embroiled in a bitter battle with another researcher over the intellectual property rights of the new tool. What makes this technology so controversial?

THE SCIENCE OF SLICING AND SPLICING

Doudna and Charpentier's tool, the Clustered Regular Interspaced Short Palindromic Repeats/CRISPR associated protein 9 tool – CRISPR/Cas9 for short – has been described as a "molecular scalpel for genomes" and is touted as the biggest life sciences discovery in 100 years. A star-studded award ceremony was held in honor of its discoverers, and the prize money they won was dished out by famous tech billionaires, including Mark Zuckerberg.

But why all this fuss? Because, using CRISPR/Cas, it is possible to precisely modify, cut out, or replace a gene sequence within a genome; a.k.a. quick and easy genetic modification. It represents an unprecedented leap forward in gene-splicing technology, which has historically relied upon the slow, inefficient introduction of mutations into animal genomes by specialized labs. CRISPR/Cas is driven by specially-engineered 'guide-RNA' used to target sequences in precise locations on a genome.

Initially, Doudna and Charpentier demonstrated the successful slicing and replacement of gene sequences in bacterial cells, which are much simpler than the complex cells — or eukaryotic cells — of higher organisms. However, they later reported success in editing human genes ... in the very same month that the team of Feng Zhang of the Broad Institute, Inc and MIT separately achieved the same success with the technology. Cue the patent battle!

The discovery that drives CRISPR/Cas is no secret, and Doudna and Charpentier have been fully credited with its development. Even so, the intellectual property rights to the technology — which have the potential to generate huge amounts of cash for their owner — are under dispute because it was used by two separate teams to achieve the same milestone: successful edits of eukaryotic cells. So, who did it first, and does it matter? We'll get to those questions in a bit.

IT'S NO SECRET, BUT IS IT SAFE?

CRISPR/Cas is a powerful gene engineering tool that could have widespread impacts upon all areas of life sciences. Even though it is well-understood by scientists, the technology isn't perfect, even when used under ideal circumstances. Although precise, the guide-RNA used in CRISPR/Cas isn't 100% accurate, potentially leading to unintended changes to the genome, called 'off-target' effects.

Off-target effects could be unnoticeable, or they could have substantial negative impacts on the organism being mutated. There are several ways to seriously limit the chance of off-target effects and avoid them, including the use of software tools to make sure that the design of the guide-RNA is as specific as possible, and the limitation and modification of the RNA and Cas9 proteins being used to identify and slice gene sequences.

With CRISPR/Cas technology you can also create efficient 'gene drives'. Gene drives can be used to push – even potentially harmful – genetic modifications into wild populations of an organism. Gene drives should be designed and used very carefully. Also avoid the creation of a gene drive by accident. When you use non-integrating Cas9 constructs or purified Cas9 proteins and sgRNA you will not create a gene drive by accident.

THE CLASH FOR CASH: INTELLECTUAL PROPERTY AND TECH TRANSFER

Despite the fact that Doudna and Charpentier applied for a patent on the basic CRISPR/Cas technology 6 months before Zhang, he was awarded the first US granted patent. How? His backers were able to get him prioritized examination under a specific US patent program. It's a close fight because of those eukaryotic cells, which Zhang targets as specific provisions of his patent, and which is also where the money is. But do these specific applications fall under the broader umbrella of Doudna and Charpentier's US patent application, which was submitted before Zhang's, but also before the 'first-inventor-to-file' system was activated in the US on 16 March 2013? It's still a heated debate.

Jan Demolder, VIB's senior IP Manager, feels that diverse players in the biotech community should have access to CRISPR technology. "It shouldn't just belong to a single party. Non-exclusive licenses should be granted to parties in a range of different disciplines — agriculture, healthcare and industrial biotechnology, for example — for maximum societal benefit," he explains. "CRISPR/Cas is one of the biggest, brightest stars in recombinant DNA tech," continues Jan. "It's generating the publication of hundreds of scientific papers. Since VIB is an academic institution, we can rely on the research exemption to use this technology as long as we stick with academic research without commercializing our findings."

When asked how this USpatent infringement situation will affect businesses, Jan replies: "With two parties squabbling over the rights, the legal situation is still up in the air for companies that want to invest in CRISPR/Cas-based applications." In other words, the longer the battle draws out, the more money the

CRISPR/CAS AT THE TRANSGENIC MOUSE CORE FACILITY (TMCF) OF IRC (VIB/UGENT)

Tino Hochepied (VIB/UGent): "The big advantage of nuclease mediated gene editing is that the mutation can be introduced directly in one-cell embryos, resulting in fully mutant founders. The components needed to introduce the mutation are very simple to generate, especially when using CRISPR/Cas. Moreover, mutations can be generated in a very efficient way. These huge advantages now makes it possible to engineer any mammalian species in a reasonably efficient way, something that researchers only could dream of some 10 years ago. The efficiency and simplicity of the CRISPR/Cas system has made this the new golden standard of genome engineering technology and has even pushed ZFN and Talen technologies into the background." The team of Tino already generated several knockout mice and one knockin mouse using CRISPR/Cas. They continuously try to improve the procedures in order to come to an efficient, standardized procedure to generate any desired mutation in the genome of mice.

Tino: "Although CRISPR/Cas technology is already widely used, there are however still a lot of parameters that need optimization and mechanisms that need to be revealed in order to fully exploit the efficiency and the possibilities of the CRISPR/Cas system, something that researchers worldwide are eagerly working on."

duelers will spend defending their cases, and the longer companies will have to wait before having legal certainty. In the meantime we see many new players developing improvements of the CRISPR-technology and also on the development of patent design around strategies.

CRISPR/CAS STIRS UP AND REVIVES SOCIETAL DEBATES

CRISPR/Cas presents a revolution in scientific research comparable to the introduction of PCR in the second half of the 1980s. But where PCR was a mere detection tool, CRISPR/Cas is an engineering tool. It's a tool that generates great enthusiasm among scientists, but it also provokes societal debate on different fronts.

CRISPR/Cas and possibilities to engineer the human genome

The possibilities created by CRISPR/Cas also once again stir up the debate on engineering of the human genome. For classical gene therapeutic approaches there is a worldwide agreement not to engage in germline gene therapy. But the ease and precision brought by CRISPR/Cas puts new pressure on the debate. Chinese researchers have already applied the technology to introduce a mutation that renders humans resistant to HIV infection into a defective embryo left over from an in vitro fertilization. Most researchers however are very careful to consider the use of CRISPR/Cas <niet splitsen> for human genome engineering. In most cases the use of CRISPR/Cas is not necessary because a certain disease causing genetic defect can be prevented from being passed on to the next generation by applying pre-implantation genetic diagnosis. There are however certain cases where pre-implantation diagnosis or classical somatic gene therapy cannot help, and there is debate at the highest level on the ethics of the use of CRISPR/Cas in such cases.

CRISPR/Cas and the creation of 'hidden GMOs'

Genetically modified organisms (GMOs) are the subject of great controversy. NGOs have been campaigning against GMOs for many years with success. For them, GMOs represent a technological evil dominated by multinational corporations that wish to take over agriculture and food production. They see CRISPR/Cas as yet another technology that is used to engineer the genetic make-up of organisms in a highly technological fashion. To them, these organisms are GMOs by definition and should be strictly regulated. Where scientists point to the precision of the technology, they point to uncertainties and possible off-target effects. The jury is still out as to whether the use of CRISPR/Cas leads to the formation of organisms subject to the requirements of GMO legislation. If the opinion of the European Commission, which is expected over the course of 2016, states that they are not, NGOs are likely to challenge this at the European Court of Justice. But whether it is to be considered a GMO or not, NGOs will in any case continue to perceive the use of CRISPR/Cas as unnatural, even though in most cases the edits generated can or do occur in nature, and cannot be distinguished technically from natural mutations.

More in 'Biosafety considerations of CRISPR/Cas gene editing' on SPOC

Following the successful VIB training day on Precision Genome Engineering (January 27, 2016 in Ghent - 150 participants), a more advanced 'CRISPR-based Genome Engineering' training will be organized on October 27, 2016 in Leuven. TRAINING AT VIB is making efforts to organize a CRISPR/Cas practical training, targeting lab technicians and starting PhD students. More info soon on www.vib.be/training

BIO IMAGING CORE OFFERS BRAND-NEW TRANSMISSION ELECTRON MICROSCOPE

In March, a new Transmission Electron Microscope (TEM) was inaugurated at the Institute for Nuclear Science (INW) in Ghent. The acquisition of this remarkable instrument was made possible by the collaborative investment of several VIB departments and academic research groups. The TEM will later be moved to the Inflammation Research Center and made available to both internal and external research groups and industry players.

TEM is a microscopy technique in which a beam of electrons is transmitted through an ultra-thin specimen. TEMs are capable of imaging at a significantly higher resolution than light microscopes, which makes them essential for frontline life science research.

USER-FRIENDLY AND EFFICIENT

"TEM expertise is the perfect addition to the technologies offered by the Bio Imaging Core", says Saskia Lippens, Expert Technologist at VIB. "It allows researchers to study cells, tissues, bacteria and viruses in great detail. The microscope – a Jeol JEM1400Plus – is a very user-friendly piece of equipment with excellent applications. It also has a digital camera, which makes the process of discussing and interpreting images a lot more efficient."

SUCCESSFUL COLLABORATION

Several VIB departments, the VIB Technology Fund and the Medical Genetics Department of Ghent University were all involved in this joint purchase.

At the inauguration, Ghent University's rector prof. Ann De Paepe stressed the importance of cooperation between academic research groups and VIB.

"This investment is a prime example of a collaboration that makes infrastructure and expertise available to the scientific community, which is essential to the advancement of modern science,"

- Rector UGent, Prof. Anne De Paepe

FULL HOUSE AT FIRST EDITION OF VIB CONFERENCE ON APPLIED BIOINFORMATICS IN LIFE SCIENCES IN LEUVEN

From March 17-18 2016, VIB organized the first edition of the conference on Applied Bioinformatics in Life Sciences (ABLS) in Leuven. With 220 attendees and representing 24 countries, the conference was sold out.

Since bioinformatics has become an integral part of biological research, this first edition focussed on recent developments in the field of bioinformatics, and highlighted the power of bioinformatics in the fields of medical, agricultural, and biotechnology research.
As a highlight in the session Modeling and Data Integration, Nuria Lopez-Bigas (University of Pompeu, ES) discussed cancer drivers, presenting their brand new Cancer Genome Interpreter (TCGI) platform which assesses the oncogenic relevance of each alteration observed in a tumor individual and their consequences for shaping anti-cancer treatment responses. In the session on Next Generation Sequencing, Thierry Voet (KU Leuven, BE) explained how his research group uses single-cell genomics to study the biology of cellular heterogeneity in health and disease. Christine Orengo (University College London, UK) presented their new tool CATH FunFHMMer used for protein functional annotations based on functional protein family assignments in the topic Protein Bioinformatics. The closing talk of this two day conference was was given by Eran Segal (Weizmann Institute, IL) who emphasized the importance of your personal microbiome for future precision medicine.

In addition to this exciting scientific program in which featured a total of 22 speakers and 77 poster presentations, the conference provided ample networking opportunities.
A Meet the Expert session was organized for junior researchers. 20 young scientists discussed career development in academia with Matthias Mann (Max Planck Institute of Biochemistry, DE).

In addition, 56 young scientists joined the workshop on 'Successful Planning of Large Data Generating Experiments' organized by TRAINING AT VIB the day before the conference. This workshop focussed on providing a proper foundation on planning large data generating experiments.

Given the very positive feedback received from the participants, the Organizing Committee is looking forward to the 2nd edition of ABLS in 2018.

FACTS AND FIGURES ABOUT NEW PLANT BREEDING TECHNOLOGIES

The brand-new VIB Fact Series issue 'From plant to crop: The past, present and future of plant breeding' is now available on the VIB website. This report outlines how the crops we know today have evolved from nature, with particular emphasis on the role humans have played. With new breeding technologies taking center stage, it becomes clear that plant breeding is continuously on the move.

Download the file at www.vib.be/factseries

From left to right: Shamil Sunyaev, Benjamin Haibe-Kains, Eran Segal, Lodewyk Wessels, Thierry Voet, Monica Nicolau, Alexander Botzki, Nuria Lopez-Bigas, Jeroen Raes, Lennart Martens, Peer Bork, Michael Lynch, Matthias Mann, Rob Kent

From left to right: Jolien Steyaert, Elke Bogaert, Steven Boeynaems, Wendy Scheveneels and Ludo Van Den Bosch

ONWARD TO NEW THERAPIES FOR NEURODEGENERATIVE DISEASES ALS AND FTD

Amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD) are fatal, adult-onset neurodegenerative disorders. The group of Ludo Van Den Bosch and Wim Robberecht (VIB/KU Leuven) has discovered profound new insights into the causes of these diseases that will drive future research and hopefully lead to more effective treatments.

Under the supervision of professors Ludo Van Den Bosch and Wim Robberecht, PhD students Steven Boeynaems and Jolien Steyaert, lab technician Wendy Scheveneels and Dr. Elke Bogaert investigated the behaviors and characteristics of the proteins that cause ALS and FTD. This work was made possible by a collaboration between a large number of VIB groups, including the groups of Kevin Verstrepen, Patrick Callaerts, Christine Van Broeckhoven and SWITCH. As a result of the project, two papers have been published in the journals *Nature Neuroscience and Scientific Reports*.

What is the most important finding of this research?
Ludo: "It is the first time that we see an important role for inter-cell transport in the most important genetic forms of ALS and FTD. Even more, these insights have a solid basis, since they come from four different scientific angles. It is an important next step in our understanding of these terrible diseases."

Do the findings of your research suggest new treatments for these diseases?
Wim: "Recently, two other papers were published in Nature using fruit flies with these genetic repetitions that also generated toxic proteins. The studies showed that problems in the transport system within cells is important in genetic ALS and FTD. With this in mind, changing the processes that govern this transport system could be a promising new therapy for these diseases."

Can you describe the biggest challenges you encountered during this project?
Wendy: "The time pressure on this project was high and therefore we needed to be ready to switch rapidly between different approaches and techniques. To be able to finish this study in one year was experimentally challenging, but highly rewarding."

How did you experience the dynamics within your own research group?
Jolien: "We work with fruit flies to study different genes involved in neurodegeneration. My PhD project focusses on a different gene as the one described in this paper, nevertheless both projects benefited from each other. It was an opportunity to be involved in this nice research project. The scientific discussions that we had in our team were always in an open atmosphere and very interesting."

How did all these teams get involved in this study?
Steven: During my master training in the lab of Kevin Verstrepen (VIB/KU Leuven) I learned more about "junk" DNA and yeast research. I started my PhD in Ludo's and Wim's lab on the newly discovered repeat expansions in ALS and FTD. Here the idea originated of using the genomic toolbox of yeast to get insights in human disease. We teamed up with Kevin and started generating yeast disease models which we could use for genome-wide screening. At the same time, we generated fly models for these repeat expansions with Patrick Callaerts (VIB/KU Leuven). We found out that the group of Aaron Gitler at Stanford University was pursuing similar objectives. Hence, we decided to divide the work load and focus ourselves on the fly work, whereas the Gitler group would build further on our initial yeast data. Compellingly, the modifiers that we found in yeast were nicely validated in our fly genetic screen. In the last stage of the project, we used the expertise of the SWITCH lab (VIB/KU Leuven) and the Van Broeckhoven lab (VIB/Antwerp University) to check whether our identified modifiers could be important to the human disease, which turned out to be the case.

Was it a challenge collaborating with so many people and groups?
Elke: "It has been a great experience collaborating with so many top labs. The expertise brought in by each and every collaborator was pivotal in finishing this study. We had tremendous benefits from the open research environment that VIB has created as we experienced that the approachability of the different teams was great, even for PhD students and Post Docs. The smoothness of this collaboration made it possible to complete the story from start to finish in one year. This was crucial to keep up with two competing American groups."

Yeast paper: Jovičić et al., Nat Neurosci. 2015
Drosophila paper: Boeynaems et al., Scientific Reports 2016

ABOUT ALS AND FTD

In ALS, parts of the brain and spinal cord that are involved in movement and motor control are affected, causing muscle weakness and paralysis. In FTD, neurons in the brain degenerate which leads to behavioral, personality and language disturbances. ALS and FTD are the extremes of one disease spectrum. The most important genetic cause of ALS and FTD was discovered in 2011: a mutation causing the repetition of a piece of non-coding or "junk" DNA in a gene with an unknown function, called C9orf72. Proteins encoded by this junk DNA are potentially toxic but how these proteins cause toxicity is not yet completely understood. Using genetic tools available in yeast and fruit flies, Ludo's research team confirmed that two of these proteins hijack the nucleocytoplasmic transport system, causing proteins to mislocalize within the cell.

THE FLEMISH GUT FLORA PROJECT IS FLOURISHING

Did you know that one of the world's largest gut microbiome research efforts is run by a VIB lab? Jeroen Raes and his team started a bottom-up initiative in 2012 that would soon turn out to be a huge research project involving the collection of thousands of Flemish stool samples. The goal of the Flemish Gut Flora Project? To investigate the links between the billions of gut bacteria, health and lifestyle. The project's first extensive paper was released in April and was immediately a massive hit in scientific circles – and beyond.

From left to right: Marie Joossens, Jeroen Raes, Jun Wang, Leen Rymenans, Sara Vieira-Silva, Gwen Falony and Chloë Verspecht

Published in Science, the study identified 69 factors associated with the volume and diversity of gut flora, most of which are related to stool transit time, diseases, food intake, the use of medicine, and age. However, despite the incredible efforts of the Gut Flora team and the 5,000 Flemish volunteers who participated in the project, only 7% of gut flora variation has currently been mapped out. In other words: we are only seeing the tip of the iceberg. This is why Jeroen and his team (VIB/KU Leuven) are now pushing full steam ahead to recruit new volunteers.

But who can describe the ins and outs of this great feat better than our researchers themselves?

Where did your fascination with gut flora come from?
Gwen Falony (staff scientist and co-first author): "When I was six, I fell in the septic tank of my grandparents' farm – luckily it was empty. The family legend states that in the end they found me in the tank, playing with disgusting bugs and repulsive insects. I don't remember much of the incident, but one could say my future as a gut microbiota researcher was just meant to be."

What were the biggest hurdles in this project?
Jun Wang (postdoc and co-first author): "For me, collecting all the data (online and on paper) and organizing them into forms that a statistician can work with was the real challenge. At the time, every step was new. But when the first results started to show up, we knew we'd been successful."

What is it like to do science together with and thanks to thousands of volunteers?
Sara Viera-Silva (postdoc and co-first author): "Although setting up such a large-scale project was definitely a logistic challenge, we feel very grateful for their participation and their support on social media. Moreover, our volunteers were an extra motivation to finalize this first publication and communicate our results. We hope that these will answer some of their questions, and reinforce their curiosity about gut flora."

How does it feel to publish these first results?
Marie Joossens (postdoc and co-first author): "We're very proud! Because we knew that we were competing with international groups with bigger resources, we focused on high quality data. When we could confirm our results with those of an independent Dutch cohort, we knew that all of our efforts had been worthwhile!"

Can you briefly describe the samples' journey from volunteer to the lab?
Chloë Verspecht (Lab Technician): "The initial plan was to invite participants to deposit their sample in a VIB bus that would be parked on a central square in their hometown. But that wouldn't be very practical. Based on a suggestion of a pharmacist, we set up several collection points in pharmacies. There, the fecal material was frozen, after which we collected the samples and transported them to our lab on a regular basis. Blood samples came through the primary care physicians of the participants, together with the medical questionnaires."

Leen Rymenans (Lab Technician): "So you can see the logistics of this study was very challenging – but we managed thanks to the help of all these doctors and pharmacists! After that, our hard work started: dealing with all the incoming packages, manually aliquoting thousands of samples, DNA extraction, quality control, PCRs, library prep and sequencing – and not switching a simple sample thanks to the barcoding system we put in place!"

What will the future bring?
Jeroen Raes: "There is still so much we want to do! First of all, we still have a few thousand samples to analyze that were not part of this first paper. Secondly, we realized that we probably need to include ten thousands of additional people to get the full picture. Third, we are already following up some clues from this paper in target studies. But the thing I'm really interested in is the dynamics – what will these peoples' microbiota look like in a year, two years from now? How stable is the microbiota and what is the time scale? Can we predict future health of these individuals from current samples? And a million other questions – this is really just the start!"

GUT FLORA AND LIFESTYLE: 3 REMARKABLE LINKS

Among the 69 factors associated with gut flora, we also noticed some surprising links.

1. A particular bacterial group has a preference for dark chocolate. The Belgian chocolate effect?
2. Beer consumption also impacts the gut flora composition.
3. Not only antibiotics, but also hay fever drugs and hormones (e.g. birth control pills) associate with gut flora.

TWO PROMISING NEW AVENUES TOWARD A CURE FOR MELANOMA SKIN CANCER

When it comes to finding a cure for melanoma skin cancer, major strides are being taken as we speak. One of the driving forces behind this great work is Chris Marine (VIB/KU Leuven). His team has recently achieved two important breakthroughs in melanoma research. Let's take a closer look at their remarkable endeavors.

From left to right: Michael Dewaele, Roberto Vendramin, Chris Marine, Karen Willekens and Eleonora Leucci

The first study involved an international collaboration with researchers from Singapore. Published in the leading Journal of Clinical Investigation, it suggested a new way of interfering with the mechanism by which melanoma prevent natural tumor suppressors from doing their work. Chris and his PhD student Karen Willekens elaborate on their findings.

Why is this study so important, Chris?
Chris: "As everybody knows, the ultimate goal of cancer cells is to multiply. But there is a specific protein, called p53, that suppresses this multiplication. In the case of melanoma, however, cancer cells manage to inactivate p53 by overexpressing MDM4, another protein. Previous research from my lab focused on targeting the physical interaction between MDM4 and p53, which proved to be a real struggle. Instead, we have now discovered a method allowing the targeting of MDM4 abundance. It's an important finding, because this method showed great therapeutic potential in mouse models and, importantly, is amenable to the clinic."

Karen, which lesson learned will help you in future research?
Karen: "Always be prepared for the unexpected! In this case, all of our initial hypotheses turned out to be wrong. We had to accept our negative results and adapt to our unexpected findings, trust these "strange" results and keep moving forward, following logic reasoning. It all made sense in the end, but it was still a surprising and exciting result."

Chris, the paper described a SAMMSON 'addiction'. Can you explain?
Chris: "Expressed in more than 90% of malignant – and not in benign – human melanomas, this lncRNA is paramount to the survival of melanoma cells. In both in vitro and pre-clinical studies in mice, the reduction of SAMMSON through targeted antisense molecules makes cancer cells rapidly and massively die off. We also discovered that this lncRNA is recruited to mitochondria, an organelle that provides energy to the cancer cells. By promoting the degradation of SAMMSON, these antisense molecules disrupt vital mitochondrial activity, which stops the tumor's growth."
Dewaele et al., Journal of Clinical Investigation 2015

Non-coding RNAs – long considered 'junk DNA' – are emerging as potentially important molecules in various biological processes and diseases. Together with post-doctoral scientist Eleonora Leucci and researchers from the University of Ghent, Chris discovered a new long non-coding RNA (lncRNA) gene called SAMMSON, which is crucial for melanoma survival. The importance of this discovery to the development of both diagnostic and therapeutic tools was illustrated in the March issue of Nature.

Eleonora, congratulations with the Nature publication! Did you celebrate it?
Eleonora: "A Nature paper is such an intense experience that the only appropriate celebration would be one month off on a tropical island. But I'm already working on the next study, so no special celebrations for me. We did have a few drinks with our colleagues, however."

How did the publication affect your next steps in this research?
Eleonora: "SAMMSON increased the visibility of our laboratory in the non-coding RNA and melanoma field, leading to new and interesting collaborations with top scientists in the future. I see the paper as an essential starting point, but there are still many scientific questions to be answered. Moreover I already received enthusiastic messages from patients and their relatives, encouraging us to proceed with our studies. Perhaps after the publication I feel more responsible towards these people and motivated to bring SAMMSON to the next level."

Are you already teaming up with industrial partners?
Eleonora: "We are currently looking for partners who want to invest in our project. In the meantime, we are also collaborating with companies to develop more potent SAMMSON inhibitors and to perform toxicological studies. When all this work is done, we will finally be able to contact clinicians to start a trial. All these steps require communication and persuasion skills, which are not obvious for a scientist! But luckily, we are not alone in this venture: VIB has an excellent tech transfer team."
Leucci et al., Nature 2016

CAUGHT ON TAPE: BEHIND THE SCREENS OF OUR LAB

A while ago, a camera crew recorded the exceptional work of our melanoma team. You can discover the lab work from up close on Vimeo (Melanoma research at VIB)

James Dooley and Adrian Liston

THREE MAJOR BREAKTHROUGHS IN THE IMMUNOLOGY FIELD

Early 2016 seems like publishing time for the Adrian Liston Group (VIB/KU Leuven). Between February and March, three completely different stories got published. We had a talk with Adrian and James Dooley (Principal Staff Employee), co-first author on the Nature Immunology and Nature Genetics papers and also an author on the Science Translational Medicine paper.

GENETIC PREDISPOSITION FOR BETA CELL FRAGILITY UNDERLIES TYPE I AND TYPE 2 DIABETES

Despite being labeled a "lifestyle disease", diabetes has a strong genetic basis. James Dooley and colleagues in the Adrian Liston group discovered that a common genetic defect in beta cells may underlie both forms of diabetes.

Adrian: "The Nature Genetics paper is really a baby of mine. I started the work 14 years ago when I was a PhD student in Australia. I had seen diabetes in the insHEL male mice, an odd result on what should have been a negative control. My PhD supervisor was not keen on following it up, thinking that it might be an epiphenomenon. I put the project on the back-burner for 3 years during my post-doc, but it was the first thing I started at VIB after moving to Belgium. The paper was actually submitted two years ago; it really took a heroic effort to get through all the experiments suggested by reviewers."

James: "The project started when we first began in Belgium in 2009. This has been a strong focus of the lab with almost everyone (both past and present) contributing in some way or another. This also involved a strong collaboration with labs in Leuven and Australia. This is the first paper that demonstrates strong linkage between T1D and T2D showing that beta fitness is pivotal to both."

Dooley et al (2016) Nature Genetics

THE CELLULAR COMPOSITION OF THE HUMAN IMMUNE SYSTEM IS SHAPED BY AGE AND COHABITATION.

The research took a detailed look at the immune systems of 670 people to understand more about what drives variation in our immune systems between individuals. From an assessment of the effects of a range of factors, including age, gender and obesity, one of the most potent factors that altered an individual's immune system was whether they co-parented a child.

James: "Extreme care was taken during this project to optimize all aspects of the protocols. We needed to understand the effects of time, temperature and limitations that were in place. To do this we needed to use a single individual, as there is substantial variation from person to person, and to evaluate the effect of temperature as the clinic and lab space are substantially variable depending on the time of year. We also had limitations as to when and how long it would take for the blood to get from the clinic to the lab so we needed to evaluate and develop criteria that could be applied to all samples to minimize variation between individuals. Finally, developing a robust multi-parameter flow cytometry based platform required testing of many different antibodies in various combinations.

Adrian: "When I say that James made the study happen through his blood, sweat and tears, I mean that rather literally. To set up the study, James was bled every few hours to look at how different processing protocols would alter the results. Then during the four years of the study, James was bled dozens of times to give a standard control. We even had him bled for the TV, so that VTM could get some good visuals."

Carr & Dooley et al. (2016) Nature Immunology

FAMILIAL AUTOINFLAMMATION WITH NEUTRO-PHILIC DERMATOSIS REVEALS A REGULATORY MECHANISM OF PYRIN ACTIVATION

A mysterious inflammatory disease has been afflicting a Flemish family for three generations, causing severe skin lesions, fevers, pain and exhaustion. Research by Adrian Liston and colleagues has found the genetic mutation and also identified an effective treatment.

Adrian: "We have been working on a lot of different patients with inflammatory disease. Quite often we end up with new biological understandings from assessing these patients, but it is relatively rare that we can immediately use this information to redesign a treatment. It is quite odd for a biomed scientist actually. Normally we are so used to thinking "maybe in 10 years someone will use this information to make a new drug, which will take another 10 years to come out", so having an actual immediate impact on people's lives is humbling."

James: "Working previously in the emergency room I had missed seeing the immediate results of my efforts. Although we are working on many patients, every case where we are able to find something that can help a patient is truly motivating and keeps us striving to solve each case. This work is the result of a strong collaboration with many people involved. In this case it was not only possible to discover the cause of the disease but a cure too. Anytime that you are able to do this, it is something remarkable."

Masters et al. (2016) Science Translational Medicine

IN 2016 EPPENDORF AG, THE HAMBURG LIFE SCIENCE COMPANY AWARDED ADRIAN LISTON ITS HIGHLY PRESTIGIOUS RESEARCH PRIZE.

The Jury: "Adrian Liston's experiments have paved the way for understanding key steps in controlling regulatory T-cells that are critical for balancing between autoimmunity and immunosuppression. His work opens up the way for new therapeutic approaches towards diseases resulting from a dysregulated immune homeostasis."

Adrian Liston: "I am thrilled to learn that I am to be awarded the 2016 Eppendorf Award. A great recognition of the work done by all of the amazing people in my lab!"

QUICKSCAN

1

#angiogenesis #lumen #blebbing

The Holger Gerhardt Lab (VIB/KU Leuven and MDC Berlin) has discovered that endothelial cells expand lumens in vivo by a previously undescribed mechanism of inverse membrane blebbing. Using high resolution imaging in live zebrafish embryos, they followed membrane and cytoskeleton dynamics and showed that endothelial cells actively control inverse bleb retraction through actomyosin contraction: a process required for lumen expansion.

Gebala et al., Nat Cell Biol 2016

2

#persistence #structural biology

Bacterial persistence is mediated by a plethora of so-called toxin-antitoxin modules that slow down or halt basic cellular metabolism, often through cleavage of mRNAs. The Remy Loris lab (VIB/Vrije Universiteit Brussel) determined the crystal structures of the archetypic *E. coli* MazF toxin in its active state in complex with a substrate analog and in its inhibited state in complex with a segment of the antitoxin MazE. These structures point towards a conserved mechanism for substrate recognition and an unusual catalytic mechanism and provide an evolutionary link with a family of gyrase poisons.

Zorzini et al., J. Biol. Chem. 2016

3

#lateral root development #visualized protocol

Lateral roots contribute significantly to the root system architecture, and hence are crucial for plant growth. Different aspects of lateral root initiation and development have been revealed using the Lateral Root Inducible System developed in the lab of Tom Beeckman (VIB/UGent). Because of the great interest of the community in this system, the lab decided to produce a professional visualization of the protocol to make the system as accessible as possible for future research.

Crombez et al., JoVE 2016

4

#MyD88 #MAPPIT

MyD88 is an essential adapter in Toll-like receptor and IL-1 signaling. Laurens Vyncke and Frank Peelman (VIB/UGent) used the mammalian two-hybrid system MAPPIT to show how MyD88 TIR domains homo-oligomerize into a left-handed helix and interact with Mal and TLR4. It is shown how this MyD88 helical assembly is promoted by Mal, by phosphorylation and by an oncogenic MyD88 mutation.

Vyncke et al., Structure 2016

5

#hospital acquired infection #Staphylococcus aureus cell wall

A major problem in hospitals is the occurrence of microbial biofilms on medical implants. The Patrick Van Dijck lab (VIB/KU Leuven), in collaboration with the Yves Dufrêne lab (UCL) showed that the *Staphylococcus aureus* matrix protein PIA (polycatyonic polysaccharide intercellular adhesion) is required for bacteria-bacteria interactions by binding to the electronegative teichoic acids in the cell wall. This finding is important as it may open up novel avenues to prevent biofilm formation by this type of hospital-acquired bacteria

Formosa-Dague et al., ACS Nano 2016

6

#mirna #variant effect prediction

MicroRNAs are important regulators of gene expression. Genetic variants in miRNA genes can have profound effects on miRNA expression and targeting. The Christine Van Broeckhoven lab (VIB/Antwerp University) developed miRVas, a tool to predict this effect based on the location of the variant in the gene and its influence on the structure. A test set of genetic variants and their experimentally validated impact on miRNA expression was used to show the usefulness of the software.

Cammaerts et al., Nucleic Acids Res 2016

7

#homozygosity mapping #whole exome sequencing #HOMWES

Homozygosity mapping is a method used to identify identical-by-descent genomic DNA stretches harboring recessive traits in consanguineous families. To facilitate this analysis, the Albena Jordanova Lab (VIB/Antwerp University) has developed a tool to detect homozygous regions starting from whole exome sequencing data. This tool (HOMWES) outperformed other available algorithms and allowed identification of novel mutations in known Charcot-Marie-Tooth and hereditary spastic paraplegia genes.

Kancheva, Atkinson et al. Genet Med 2015

8

#tomato #steroidal alkaloids

The Alain Goossens lab (VIB/UGent) has identified a transcription factor, GAME9, which controls the biosynthesis of steroidal glycoalkaloids (SGAs), cholesterol-derived molecules produced by *Solanaceous* species and often toxic to humans. Accumulation of SGAs and the upstream cholesterol intermediate is modified in plants with altered GAME9 expression. These findings provide means for modulating SGA levels in crops such as tomato and potato.

Cárdenaset al., Nat. Commun 2016

9

#enzymes #protein therapeutics #protein engineering

Natural selection results in proteins that are soluble to the level required to carry out physiological function. At the much higher concentrations required for biotechnological applications proteins often aggregate. The SWITCH lab (VIB/KU Leuven) has shown that mutations at specific positions within a protein that can be computationally predicted can produce large improvements in solubility and expression level by suppressing aggregation. Big pharma and enzymes companies are already using this method to select safer protein sequences that are easier to produce.

Ganesan, Siekierska et al., Nature Communications 2016

MACROPHAGES: ONE OF THE OLDEST IMMUNE CELLS REVEALS ITS HIDDEN BEAUTY AFTER A CENTURY

We are in 2016, an important year for macrophages (and macrophage researchers). It has been 100 years since the death of Elie Metchnikoff who discovered macrophages: the ideal opportunity to focus on macrophage research within VIB. We had a chat with Martin Guilliams (VIB/UGent), Jo Van Ginderachter (VIB/Vrije Universiteit Brussel) and Max Mazzone (VIB/KU Leuven).

Picture of red and green labeled macrophages, which are put together under fusing conditions. This results in the yellow multinucleated giant cell (courtesy of Jan Van den Bosssche).

How did macrophages get on the scientific stage?
Martin: Different scientists had witnessed that some cells, later to be identified as macrophages, could internalize bacteria. At the time Robert Koch* postulated that these cells functioned as hiding places for bacteria, so they could multiply and spread within the body. Elie Metchnikoff* was the first to propose that the macrophages actively 'eat' foreign particles and microbes to eliminate them. This launched the whole concept of cellular immunity.

Max: This discovery followed a landmark experiment in 1883 (see frame). Metchnikoff challenged starfish larvae (Hydra) with thorns to stimulate their immune cells to attack the foreign insult. He named the cells 'phagocytes' (from the Greek 'phago' - 'to devour' -, and 'cytos' - 'cell') and the process 'phagocytosis'. What makes this story even more interesting is the fact that a zoologist has contributed to medicine with an intuitive concept. Being an Italian, I also like the fact this discovery was made in Messina (Sicily).

Metchnikoff - 25 years after the famous Messina experiment:
"One day when the whole family had gone to a circus to see some extraordinary performing apes, I remained alone with my microscope, observing the life in the mobile cells of a transparent star-fish larva, when a new thought suddenly flashed across my brain. It struck me that similar cells might serve in the defense of the organism against intruders. I said to myself that, if my supposition was true, a splinter introduced into the body of a starfish larva, devoid of blood-vessels or of a nervous system, should soon be surrounded by mobile cells as is to be observed in a man who runs a splinter into his finger. Very early the next morning I ascertained that it had fully succeeded. That experiment formed the basis of the phagocyte theory, to the development of which I devoted the next twenty-five years of my life."

Metchnikoff, O., "Life of Elie Metchnikoff." Constable, London, 1921. pp. 116- 117

This September, CELL organizes a meeting on 100 years of phagocytes in Sicily to acknowledge the Sicilian roots of this discovery - www.cell-symposia-phagocytes.com
The VIB Conference on 'ER stress, autophagy and immune system' takes place in Bruges in January 2017 - www.vibconferences.be

Was the relevance of macrophages clear at once?
Max: No, I do not think the importance of this discovery was immediately clear to Metchnikoff. But when confronted and aligned to other discoveries by Paul Ehrlich* on humoral immunity and antibodies, it became clear how our immune system protects us against harmful events via innate and adaptive immunity. For this breakthrough research Metchnikoff and Ehrlich received the Nobel Prize in 1908.

Jo: Also the interaction with Louis Pasteur* was crucial to Metchnikoff. As a matter of fact, Pasteur offered lab space to Metchnikoff in 1888, so Metchnikoff's earlier findings must have made an impression. In those years, the first fundamental principles of current immunology and vaccinology were established.

How did the perception of macrophages change over the years?
Jo: Macrophages were quite popular cells until Ralph Steinman* discovered dendritic cells in 1973. All of a sudden, everybody became interested in these "new" cells that had the capacity to activate resting T-lymphocytes. For the next 30 years macrophages were considered the less interesting sister cell. They only regained popularity about 10 years ago. The initial trigger was the discovery of very distinct activation states thanks to the pioneering work by Siamon Gordon. The past two to three years have seen a revolution in the ontogeny of these cells, with the realization that we are born with a pool of macrophages in our tissues which are maintained throughout life thanks to stem cell-like behavior.

Martin: In my view, another thing that induced a revival of the macrophage field, is the discovery of the astonishing diversity of macrophages, revealed by gene expression profiles of macrophages from different tissues. This is an indication that macrophages perform tissue specific functions.

How did you start working on macrophages?
Max: During my postdoc when studying the tumor vasculature, I realized that it was unavoidable to investigate the role of macrophages. I have now been studying their role in governing the formation of a vascular network in pathologies such as cancer and ischemia for ten years.

Jo: The lab of Patrick De Baetselier at VIB-VUB has a long-standing tradition in macrophage research, with early work already in the 1980s on the interaction between cancer cells and macrophages. During my PhD in Patrick's lab studying the interaction between tumors and the immune system, the macrophage has always been in the picture.

Martin: I also obtained my PhD in the lab of Patrick De Baetselier and like Jo, got infected with a chronic passion for macrophages by working with Patrick. By the end of my PhD I developed a growing interest for liver-resident macrophages (called Kupffer cells). During my post-doc in the lab of Bernard Malissen I acquired the technology necessary to generate knock-in mice and in collaboration with Alain Beschin at VIB-VUB we generated the first Kupffer cell-specific mice which now make it possible to study these cells *in vivo*. Kupffer cells not only seem to play a role in the elimination of Listeria bacteria (ongoing work by Alain Beschin), but also in the elimination of metastatic cancer cells (ongoing work by Jo) and in lipid metabolism (ongoing work by Charlotte Scott in my team).

What other exciting findings have there been recently?
Max: From my point of view, the most exciting aspect is the central role of these cells in cancer immune evasion. In the days of immunotherapies, it is impossible to talk about immune checkpoints without

considering that tumor-associated macrophages (TAMs; and this acronym was also founded in Italy by Alberto Mantovani) are so key in defining immunosuppressive pathways.

Jo: Along with Max (and often in collaboration) we contribute to the understanding that macrophages are important regulators of tumor growth and metastasis. This is very important, since cancer therapies currently available still focus on targeting the cancer cells, without touching the tumor-supporting cells such as macrophages. We aim to bring this "forgotten half of the tumor" to the foreground.
With Martin we investigate the contribution to tissue homeostasis and various pathologies of tissue-resident macrophages on the one hand and tissue-recruited macrophages on the other hand. We generated very innovative genome-engineered mice which allow us to answer this question for the first time for the liver and soon hopefully also for the brain.

Martin: In the last couple of years we have witnessed a conceptual revolution in the macrophage field. It is becoming clear that these cells do much more than just 'eat' pathogens. They also seem to play essential functions for their tissue of residence: brain macrophages regulate synapse formation, influencing memory generation, lung macrophages protect against a disease called Pulmonary Alveolar Proteinosis (PAP), Kupffer cells seem to be involved in lipid and iron metabolism in the liver, etc. This suggests that the tissues have 'outsourced' some functions to the macrophages throughout evolution.

Are there already therapeutic applications coming out of macrophage research?
Max: Nothing that is used in clinical practice already, but anti-CSF1R antibodies show a lot of promise in clinical trials. They are supposed to deplete the 'bad' macrophages, the ones that are angiogenic, prometastatic and immunosuppressive sparing the anti-tumoral macrophages.

Martin: The fact that macrophages have the unique capacity to self-maintain indefinitely in tissues also renders these cells ideal for cellular therapy.

MACROPHAGE RESEARCH IN THE VIB LABS

Hypoxia induces inflammation and inflammation leads to hypoxia... Coming from the hypoxia field, Max Mazzone and his group investigate how the lack of oxygen is dictating the macrophage phenotype.

The Jo Van Ginderachter Lab uses the heterogeneity of macrophages as an in vivo sensor to track inflammatory responses and as a target for therapeutic intervention. In this regard, they developed three main research lines: tumor myeloid cell immunology, hepatic myeloid cell immunology and brain myeloid cell immunology.

Within the Bart Lambrecht lab, Martin Guilliams and his group study the cellular origin, development and functional specialization of liver-resident macrophages (Kupffer cells) and lung-resident macrophages (Alveolar Macrophages).

NOBEL PRIZE WINNERS IN THIS PIECE

* Robert Koch: Nobel Prize in Physiology or Medicine in 1905 for his research on tuberculosis
* Élie Metchnikoff and Paul Ehrlich: Nobel Prize in Physiology or Medicine in 1908 for their work on immunity
* Ralph Steinman: Nobel Prize in Medicine in 2011 for his discovery of the dendritic cell and its role in adaptive immunity
* Louis Pasteur: no Nobel Prize, but immensely important for his discoveries of the principles of vaccination, microbial fermentation and pasteurization

TECHNOLOGY WATCH FOR SYNTHETIC BIOLOGY: TOWARDS THE $1,000 SYNTHETIC GENOME

VIB's Tech Watch has boosted many projects by enabling access to cheap synthetic DNA and in this text we highlight some examples showing how VIB scientists have adopted these technologies.

Novel, emerging DNA synthesis technologies allow very cheap synthesis of DNA molecules, enabling new applications in gene function discovery. Some companies are even claiming that DNA synthesis will become so cheap that cloning will end. Many VIB scientists are already using synthetic DNA to replace time-consuming DNA cloning. In addition to replacing cumbersome cloning steps, synthetic DNA technology also allows one to perform experiments which are nearly impossible using traditional cloning.
An example is Hendrik Grootaert's in the Nico Callewaert group (VIB/UGent) who screened a large library of synthetic DNA to discover novel high-value enzymes: 'Before we could even start the enzyme screening, we needed about 100 DNA sequences from a wide variety of organisms, including difficult-to-culture bacteria. Fortunately, we were aided by Tech Watch in using new DNA synthesis technology which enabled us to skip cloning altogether and directly perform recombinant protein expression and carry out the screening'.
Likewise, Tech Watch supported Lieven De Veylder's group (VIB/UGent) in ordering synthetic genes encoding diatom gene circuits. According to Lieven, 'DNA synthesis allowed us to obtain in a cost and time effective manner several complex genes that we otherwise might have never been able to isolate using the classical cloning techniques. Not only does it save us time, it also expands the possibilities of things we can do'.

In case you have a cool idea on how to use/develop SynBio tools, please contact techwatch@vib.be or call Halina Novak at VIB/HQ.

VIB IN TOP 10

OF LARGEST BELGIAN PATENT APPLICANTS

As always, VIBnews is jam-packed with information about groundbreaking research and applications that benefit society. But in order to keep our position at the forefront of biotech, we also have to protect our inventions. That's where patents come in. Remarkably, VIB ranks seventh among the largest Belgian patent applicants. Considering the fact that the top 10 list is mainly composed of larger players and big enterprises, our position is even more impressive.

Although we can definitely take pride in our ranking, good science is not about winning the inventions race. To give us a clear view of what this top 10 list actually means, our colleague Jan Demolder (Senior Intellectual Property Manager) sheds some light on the world of patents, applications and records of inventions.

Jan, how 'good' is being seventh on a chart like this?
Jan: "There's no doubt that it is a high position. Nevertheless, it doesn't really matter whether we are seventh, sixth or eighth. After all, the organizations in this list are very diverse in terms of size, scope and science domain. Just being one of the top 10 patent applicants is already quite an achievement, especially for a relatively small research institute. It clearly shows that VIB is a significant player in the Belgian innovation landscape."

In other words, we can't use this chart to compare our endeavors with other organizations?
Jan: "Exactly. If we'd want to measure this, we'd have to calculate the number of applications per employee or per R&D money invested. In addition, a single year is too narrow of a timeframe to get a complete picture, because inventions come in waves. We cannot predict when they will occur. And finally, different organizations are active in different technologies and scientific disciplines."

AN INVENTION'S JOURNEY

Our scientists may be more familiar with the term 'records of inventions'. Can you elaborate on this crucial first step?
Jan: "When a scientist has come across a new finding, he or she should alert the technology transfer team, through a record of invention. It is essential that our tech transfer team gets this record as soon as possible – definitely before the publication or public presentation of the potential invention. This means that the possibility of a patent depends to a large extent on the awareness of our researchers."

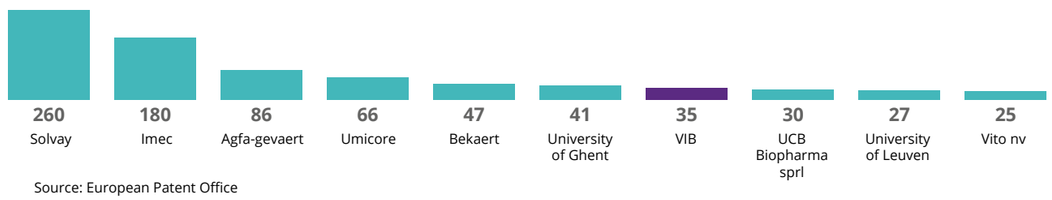
So what's next? How do we deal with these records?
Jan: "We translate about 60% of the records of inventions into patent applications. And we admit that we set the bar very high. We have no choice, because the patent-handling national authorities are becoming increasingly strict. In order to obtain a patent, a huge amount of watertight data is indispensable. Besides, having a patent is only one side of the coin. Commercializing the invention is a whole different story – and a crucial one, because patents cost a great deal of money."

How long does it take to have a granted patent?
Jan: "It is essential to differentiate between patent applications and granted patents. The national procedures to obtain a granted patent can take a while: usually between 4 and 8 years. And in some countries, like Brazil, you would have to wait even longer."

ENSURING SOCIAL VALUE

Can you describe the importance of patents for VIB?
Jan: "They are the lifeblood of both VIB and the biotech sector in general in order to translate research into tangible products. Adequate protection of intellectual property – or IP – becomes a means to ensure that biotechnology companies can reduce the likelihood of imitation by competitors. Of course, VIB does not develop products. In our case, patents have an important function to attract investors and collaborators. IP can form the basis of a research and collaboration agreement with industry and can also be licensed to obtain industrial income. And last but not least, IP is crucial for attracting capital needed to set up a new company."

THE LIST: LARGEST BELGIAN PATENT APPLICANTS IN 2015



Source: European Patent Office

VIB AND ILVO JOIN FORCES TO ACCELERATE BREAKTHROUGHS IN AGRICULTURE

VIB and the Institute for Agriculture and Fisheries Research (ILVO) signed a strategic collaboration agreement. It marks the beginning of an alliance that brings basic research and applied field knowledge together.

5 EXAMPLES OF HOW THIS COLLABORATION MAKES A DIFFERENCE

Sofie Goormachtig

SOIL ORGANISMS BENEFICIAL TO AGRICULTURAL CROPS

Sofie Goormachtig (VIB) and Tine Maes (ILVO)
Maize is one of the main crops in Flanders, but it is also very susceptible to illnesses and cold during the first weeks after planting. These problems are often avoided by sowing late and harvesting early, and by using pesticides. In order to work out a durable solution, VIB combined its expertise in crop growth with ILVO's knowledge of crop diseases and soils. In this way, the rhizosphere organisms of maize can be analyzed and bacteria at the maize root can be mapped and tested. By treating maize seeds with bacteria that positively affect endurance, the maize can be sowed earlier and becomes less susceptible to disease.

Nathalie Wuyts

IN SEARCH OF CLIMATE-RESILIENT CROPS

Nathalie Wuyts (VIB) and Peter Lootens (ILVO)
Because of climate change, crops have to be more resistant to unpredictable weather conditions. Currently, long periods of cold, heat or drought cause plant stress, which leads to slower growth and lower quality of crops. In order to gain a better understanding of these stress factors, VIB combined its profound knowledge of growth chamber stress factors with ILVO's insights into agricultural practice. VIB and ILVO aim to develop the use of automatic and semi-automatic phenotyping techniques and modelling at plant and crop level.

Alain Goossens

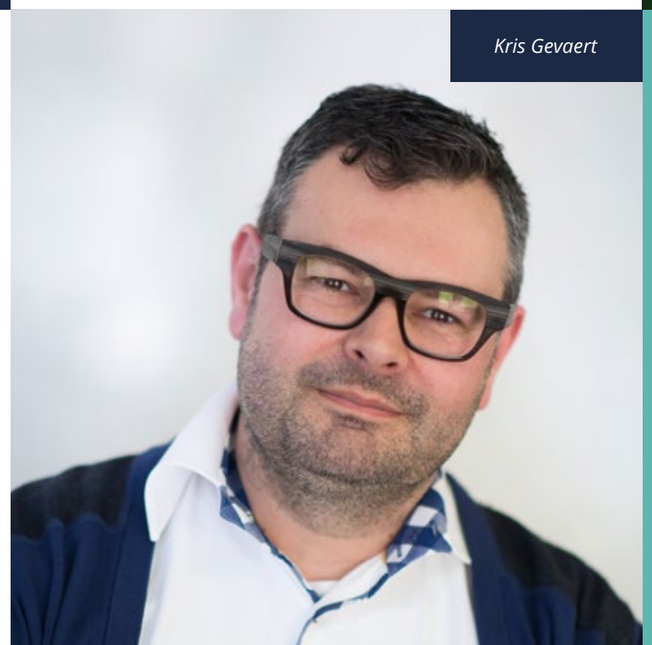
QUALITATIVE NUTRITIONAL COMPONENTS IN PLANT-BASED FOOD

Alain Goossens (VIB) and Bart van Droogenbroeck (ILVO)
One of the main challenges the future brings us, is not only to produce more food, but also to produce qualitative food. That is why VIB and ILVO investigated how to extract the nutritional components of fruit and vegetables. As a first step, VIB's expertise in bioactive components was combined with ILVO's insights into plant breeding, in order to learn how to extract bioactive components out of tomatoes and endive. This knowledge creates an important base for the development of pharmaceutical and functional food.

TWO-WAY TRAFFIC IN THE IMPROVEMENT OF CROPS

Hilde Nelissen (VIB) and Isabel Roldan & Hilde Muylle (ILVO)
In-depth knowledge of genes, phenotyping and system biology allows us to develop plant varieties with improved yield and tolerance to multiple forms of stress. In order to put this knowledge into practice, ILVO was tasked with testing the theory under realistic conditions. Knowledge generated in these realistic conditions, allows us to base future research on relevant questions and to define the appropriate pathways to investigate at a molecular and physiological level. That is how the collaboration between VIB and ILVO can create great opportunities in biological research in a quickly evolving environment.

Hilde Nelissen



Kris Gevaert

ALLERGENIC FOOD: TOWARDS MORE ACCURATE DETECTION

Kris Gevaert (VIB) and Christof Van Poucke (ILVO)
As 8% of all children and 5% of all adults suffer from severe food allergies, clear product information on packaging is of fundamental importance. Unfortunately, current allergen information does not describe the impact of processing the food, although proteins can change by cooking, freezing or mixing them. That is why the ILVO Food Pilot processed four important allergens. VIB submitted these results to HRMS in order to identify the peptides that are characteristic of the allergen and which remain stable during processing. That way, high-quality allergen tests can be achieved.

Peter Carmeliet

ANITSCHKOW PRIZE IN ATHEROSCLEROSIS RESEARCH FOR PETER CARMELIET

The European Atherosclerosis Society (EAS) was founded in 1964 with the aim of "advancing and exchanging knowledge concerning the causes, natural history, treatment and prevention of atherosclerotic disease". They awarded Peter Carmeliet (VIB/KU Leuven) with the Anitschkow Prize 2016. This prestigious prize recognizes outstanding research in the field of atherosclerosis and linked metabolic disturbances. "Peter Carmeliet receives the prize in recognition of the originality and novelty of his work and the promise for future high impact work to follow. The impact of his work is evident in many medical fields, not least within cardiovascular disease", says Prof Alberico L Catapano, EAS President.

THE BAILLET LATOUR GRANT 2016 FOR MEDICAL RESEARCH AWARDED TO MO LAMKANFI (VIB/UGENT)

Each year the Baillet Latour Fund awards a grant to a young group leader to promote medical research in Belgium. This year the grant was awarded to Mo Lamkanfi for his research project in the field of infectious diseases. These are often aggravated by inflammatory complications. Mo Lamkanfi's research aims to better understand this causal relationship in view of minimizing the destructive inflammatory process. The award was given to Mo by her Royal Highness Queen Mathilde.

Quote by Mo: "With this prestigious grant, we will be able to explore new avenues for treating life-threatening infections and inflammatory diseases that are based on modulating inflammatory cell death."

Her Royal Highness Queen Mathilde and Mo Lamkanfi

Zeinab Hefny and Patrick Van Dijck

ZEINAB HEFNY RECEIVES FACULTY FOR THE FUTURE FELLOWSHIPS

The Schlumberger Foundation is a non-profit organization that supports female students from developing countries who show a strong interest in raising the standard of education in their home country. Their most important flagship is the Faculty for the Future Program with several thousand applicants for about 100 fellowships. Zeinab Hefny, an Egyptian PhD student in the Van Dijck lab (VIB/KU Leuven) recently obtained such a fellowship.

Patrik Van Dijck: "Zeinab is a focused, dedicated and independent PhD student. In her first two years she solved a question that had been out there for more than 20 years, by identifying two enzymes in the Saccharomyces cerevisiae glycerol metabolism pathway. Her findings may have important consequences related to bioethanol production. Zeinab really wants to become a professor in Egypt and I am sure she has the right skills and attitude to achieve this. As I mentioned in my support letter for the fellowship application, she will be an ambassador for the Schlumberger foundation as well as for VIB. Once she is back in Egypt, the aim is to set up collaborative research and education programs between our labs."

ODYSSEUS GRANTS

Through the Odysseus program, FWO internationally attracts outstanding researchers to Flanders to establish their labs at one of the Flemish universities. Four of the best ranked scientists have an affiliation with VIB.

Lieve Ongena (Sr. Science Policy Manager at VIB): "Thanks to the Odysseus initiative, Flanders is able to attract outstanding researchers with a major start-up grant and a Faculty position at the host university. This is a unique type of high-level funding that enables independent research groups to be established, comparable to HHMI in the US or ERC in Europe. That four of these top-class scientists choose to start their research group at VIB affirms our reputation as an outstanding research environment."

Andrea Cerutti (Italian), currently working at the Mount Sinai School of Medicine, will start his group at IRC (VIB Inflammation Research Center, UGent) focusing on IgA response and gut immunity.

Kodi Ravichandran (American), currently working at the University of Virginia, is offered a position at IRC (VIB Inflammation Research Center, UGent). He is specialized in apoptotic cell clearance.

Olivier Van Aken (Belgian) studied the molecular mechanisms of stress in plants at the University of Western Australia. He will start his VIB research at PSB (VIB Department of Plant Systems Biology, UGent).

Markus Kleinewietfeld (German), previously selected as VIB PI in SALK, UHasselt, was recruited from TU Dresden to set up a VIB lab focusing on environmental factors leading to Multiple sclerosis. He applied for an Odysseus funding and was selected.

ILSE GIJSELINCK RECEIVED DR. KAREL-LODEWIJK AWARD

The Belgian Royal Academy of Medicine has granted the Dr. Karel-Lodewijk Verleysen award to Ilse Gijselinck, postdoc at the VIB Department of Molecular Genetics (University of Antwerp). With a prize amount of 15,000 euros, the award recognizes Ilse's groundbreaking medical research in the field of neurodegenerative brain diseases.

Frontotemporal Lobar Degeneration (FTLD) and Amyotrophic Lateral Sclerosis (ALS) are two fatal neurodegenerative diseases, often affecting people who are mid-career and raising a family (45-65 years). As there are no preventive or curative treatments available, scientific understanding of the neurodegenerative processes occurring in patients' brains is essential. With her research, Ilse aims to further expand medical science's understanding of the affected gene networks and biological processes in order to identify therapeutic targets that could delay or halt the diseases.

'A CULMINATION OF MY RESEARCH'

The Dr. Karel-Lodewijk Verleysen award consists of 5,000 euros as a personal reward and 10,000 euros for the continuation of the scientific research. "This award is a great culmination of my research", Ilse says. "Over the past 12 years, we have identified the three main genes for FTLD and ALS. I hope that the prize will help us continue and expand our research so that we can find therapies to help people with these devastating diseases."

VIB ALUMNI: PAUL VAN HUMMELEN

Paul Van Hummelen founded the VIB MicroArray Facility, now part of the VIB Nucleomics Core, in 1999. Paul is currently Associate Director at the Center for Cancer Genome Discovery (CCGD) within the renowned Dana-Farber Cancer Institute, a teaching affiliate of Harvard Medical School in Boston. The CCGD is one of the Integrated Research Centers and functions as the Research & Development unit for PROFILE, Dana-Farber's Precision Cancer Medicine effort.

VUB, Lawrence Livermore, VIB-Leuven, Rutgers University and the Dana-Farber Cancer Institute … a nice, but diverse list of places to work. Is there a common theme?
Paul: "Without a doubt, the common theme in my professional life is technology development. During my PhD at the Vrije Universiteit Brussel I was working on a genetic analysis procedure for environmental toxicity screening in tadpoles. When I moved to Lawrence Livermore National Laboratory (LLNL) in 1994, I developed multi-color FISH to study genome instability in human germ cells and introduced microarray technology to study the expressed genome in the embryo. Those were really the very early days of this technology."

So when VIB asked you to introduce that technology in Belgium, you jumped at the chance?
Paul: " Setting up the VIB MicroArray Facility was really a dream come true. I had the rare opportunity to build a new lab from scratch, hire the best people, bring in the newest high-tech instruments and have the funds to create the first industry-like service facility within Belgian biomedical academia. Within five years we became a reference lab for Affymetrix, Agilent, Molecular Dynamics and accomplished financial independence."

Was it not surprising for academic researchers to see a service facility around the corner of their lab with industrial dimensions?
Paul: " Yes and no. There was already a certain mindset at VIB that 'big data generation' would be the next big thing in bio-molecular research thanks to the human genome project. However researchers in the US were used to subcontract part of their work, but this was not customary in Europe. Convincing colleagues that they could advance their research by relying on others with technology experience was my biggest challenge in the early days. The even bigger challenge came when they realized they had to pay for that service!"

You started at the Dana-Farber Cancer Institute nearly six years ago. What is your current assignment?
Paul: " I direct a staff of 10-15 employees and manage a range of research projects to advance precision cancer medicine. We were one of the first groups to develop targeted sequencing to interrogate the Cancer Genome from clinical samples. In the meantime, every cancer patient at Dana-Farber receives a pan-cancer genome-profiling test developed by us. The test is used for making treatment decisions and enrolling patients in clinical trials.
Our biggest task for the near future is to develop tumor profiling on circulating cell-free DNA. The idea is that low levels of DNA from the tumor cells are floating around in the peripheral blood. If we can push the sensitivity of the technology we should be able to repeatedly screen the patient during and after treatment, without the need for invasive biopsies. This would be a significant breakthrough in precision cancer medicine."

Do you still have contact with VIB core facilities?
Paul: " Absolutely. Some of my good friends are still at the Nucleomics Core and it is always nice to see them. I also noticed that VIB is trying to bring its core facilities closer together in a platform type approach. That is a sensible strategy. Research is driven by asking the right question and having the latest technologies available to answer that question. The ability of solving biological questions increases tremendously when you can pool technologies. However, providing the latest technologies is ineffective without technical and scientific support by experts. Thinking along with scientists about the most efficient and cost-effective use of technologies is so important. Running a successful core facility is all about providing full service! "

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

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The Brain Mosaic: cellular heterogeneity in the CNS
September 22-23, 2016 – Leuven

VIB's 20th anniversary
October 5, 2016 - Brussels

Advances in Cell Engineering, Imaging and Screening
November 17-18, 2016, Ghent

Hallmarks of Cancer, Cell-VIB Symposium
December 11-13, 2016, Ghent