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BIG DATA

Big data

These days, “big data” is all over the news, and the news is not always good. We read about privacy loss as only 50-odd ‘likes’ on Facebook allow data miners to create an accurate portrait of your psychology, we experience that a website visit results in targeted advertisements everywhere we surf, and we are confronted with large-scale data collection by security services across the world. No wonder big data is sometimes treated with suspicion.

Fortunately, this isn’t the case in life sciences, which have evolved into a big data field almost overnight. Gone are the days when carefully collected specimens needed to travel half the known world on slow and capricious ships, or when the careful work of decades would unravel only a single gene sequence or protein structure. Today, we have sleek machines that wink at us with a few brightly colored LEDs while plowing through samples day and night, humming all the while like bizarre data factories from the future. As a result, the potential for data-gathering in life sciences has started to rival that of the world’s social networks or top security services, as we continue to eavesdrop on the private lives of genes, proteins and metabolites.

In life sciences, too, it has therefore become indispensable to have access to advanced artificial intelligence algorithms and hardware to process the plethora of heterogeneous and noisy data that we extract from living systems. In fact, for many researchers, this is a constant stress factor; it is now so trivial to acquire vast quantities of biological data that the inability to cope with this data is often the key research bottleneck.

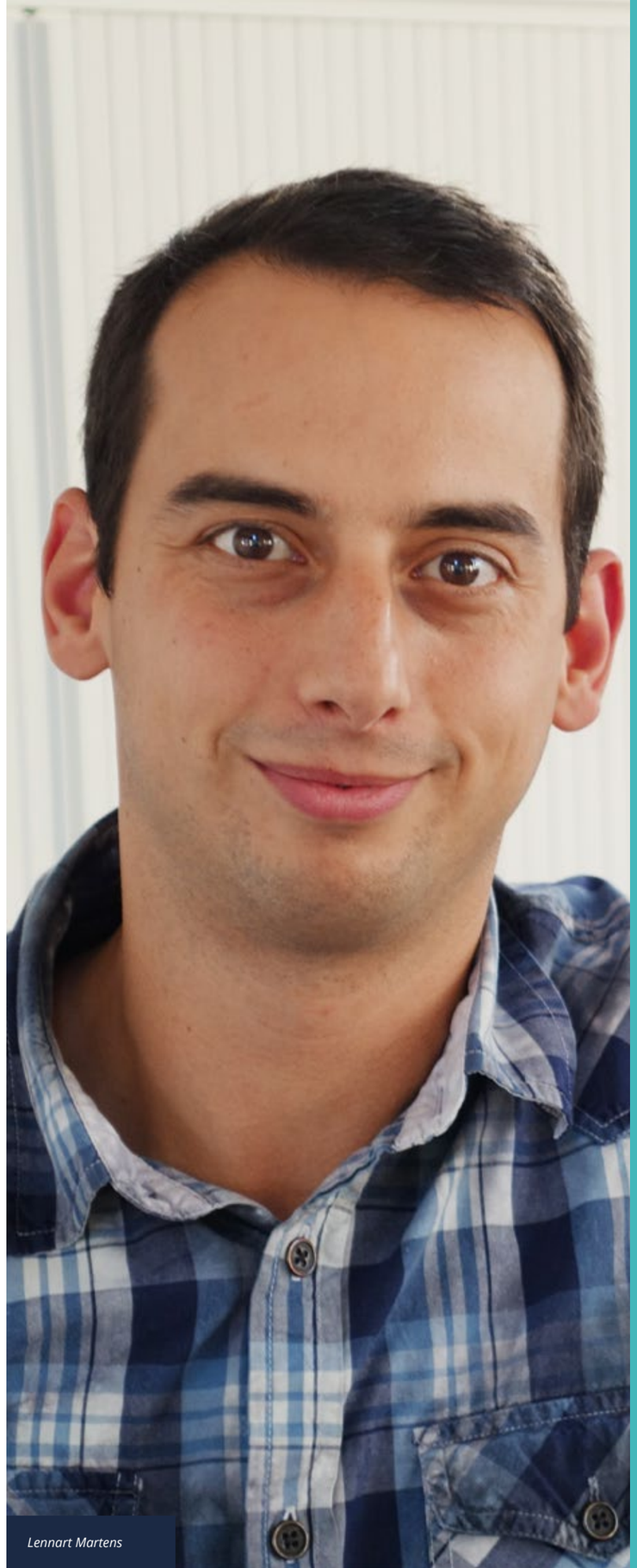
At the same time, our struggle to manage this data tsunami also means that we are typically unable to fully analyze our data, leaving large amounts of information locked inside our datasets. And so, while data generators will have extracted the relevant results for their research, the leftover, untouched information in published datasets can be a true treasure trove for computational scientists with a penchant for (orthogonal) reprocessing of other people’s data.

Perhaps the most remarkable aspect of the big data cloud that surrounds our collective online presence is the uncanny ability of data miners to connect seemingly disparate and innocent tidbits of personal information into a strongly connected and reasonably accurate representation of one’s life. Because such integrative big data analytics could provide a real boon for biological research, these approaches should be very much on every forward-looking computational biologist’s radar.

Regardless of the challenges yet before us, however, big data in life sciences is surely here to stay. And given the progress achieved so far, big data analytics will certainly play a key role in the biology of the not-too-distant future.

Clearly, it’s high time we dedicated an issue of VIBnews to the topic. Enjoy!

Lennart Martens, VIB-UGent Center for Medical Biotechnology



Lennart Martens

BIG DATA

Alexander Botzki of the VIB Bioinformatics Core about VIB’s big plans in big data 4

ELIXIR: an international brew for smarter big data management and beyond 7

Big data in life sciences: hype or hope? 9

VIB groups and big data 11

SCIENCE MEETS SCIENCE

Winning at basic science: collaboration is critical 13

A-maize-ing new molecular discovery for agronomy 15

A new unexpected key player in melanoma development identified 17

Specialized blood vessels enhance tumor-fighting immunotherapy 19

Protein responsible for allergic diseases exposed 21

Quickscan 23

SCIENCE MEETS TECHNOLOGY

Lipidomics paves the way to groundbreaking scientific discoveries 26

SCIENCE MEETS BUSINESS

VIB pushes the boundaries of science to develop new diagnostic tools 28

VIB spin-off AgroSavfe ready to conquer the world of biopesticides 30

SCIENCE MEETS PEOPLE

Alumni interview - Peter van Loo 32

Reporter on the road: Keep the conversation going 34

Awards and grants 36

EVENTS

Science meets society 38

Conferences 39

GOAL OF THE VIB BIOINFORMATICS CORE: EMPOWERING OUR PEOPLE TO EMBRACE NEW BIG DATA TECHNOLOGIES IN THEIR RESEARCH

The least you could say about the research data generated by our VIB colleagues is that it involves complex information which requires specialized data applications. However, more and more scientists are combining this complexity with large volumes at the same time. The result is big data, and that is where our VIB Bioinformatics Core (formerly BITS), led by Alexander Botzki, comes in.

Because of the heterogeneous structure of bioinformatics at VIB, data analysis is handled mainly in our bioinformatics labs or by embedded bioinformatics facilities at the various VIB centers. The goal of Alex and his team is to set up a more integrated bioinformatics community, together with Lennart Martens of the VIB-UGent Center for Medical Biotechnology, to better help VIB wet and dry lab scientists to convert data into insightful biological knowledge.

Alex, where is the VIB Bioinformatics Core now in terms of big data?
Alex: “As a core facility, our main focus is to deliver high-quality services to support our scientists. It goes without saying that we have to continuously adapt our training program and other services. Big data is a relative newcomer here, but we have already taken important steps towards our objective in this field. For example, we have launched a number of training courses to encourage our people to feel confident embracing new big data technologies in their research.”

Could you give some examples of these training courses?
Alex: “In the last three years, we have introduced several courses. For example, in next generation sequencing, we debuted RNA-Seq for differential expression and NGS analysis as well as DESeq2, EdgeR, and GATK. To facilitate the life of our trainees, our goal is to provide a walkthrough example of an RNA-Seq differential expression workflow on a web-based platform like GenePattern.

Such a tool provides VIB scientists with powerful computing resources and the ease of a graphical interface at the same time. This bulk RNA-Seq pipeline developed by Guy Bottu from our core will be complemented with pipelines for single cell transcriptome analyses in the very near future. In collaboration with the Stein Aerts (VIB-KU Leuven Center for Brain and Disease Research) and Yvan Saeys (VIB-UGent Center for Inflammation Research) labs, representative datasets to develop this workflow have been created on the 10x Genomics® Chromium™ instrument introduced by our Tech Watch team. We are also planning a 5-day summer school in 2018 to cover this rapidly developing research area.”

In 3D electron microscopy, big data is a real issue. What steps has VIB already taken in this field?
Alex: “Nowadays, electron microscopy datasets of around 500 gigabytes are the norm. Traditional software can’t really handle this volume of data, so the analysis is slow. That is why Frank Vernaillen from our team is developing user-friendly and efficient software tailored to processing 3D SEM data, such as image registration, image denoising and segmentation. This improves (semi-)automatic segmentation accuracy, and leads to cleaner images for morphological analysis. We rolled out the tool as an analysis plugin within the popular Fiji/ImageJ tool. In collaboration with the VIB Bioimaging Core, the Yvan Saeys lab and the IPI lab from UGent, version 1 has just been released, and we’re now putting new projects together into which we can incorporate the new tool.”

Alexander Botzki

‘Omics’-based research lines are generating massive data as well. What are VIB’s plans in this respect?
Alex: “The main challenge when it comes to the floods of multi-omics data has clearly shifted from data acquisition to analysis. Currently, we are still lacking one of the foundations of the data ecosystem: the ability to annotate experimental raw data with consistent and sufficient metadata. As a result, integrative analyses remain difficult. The first step has already been taken: together with Lennart Martens, we propose a common format to store metadata. Next, we will need to coordinate guidelines, best practices and provide tools and training to implement this consistently across VIB’s Core Facilities and relevant research groups.”

To which extent will this boost VIB’s already strong position in the omics field?
Alex: “The integration and analysis of pooled omics datasets is not only interesting from a purely scientific point of view; it also comes with clear valorization potential. Unlocking this wealth of information and converting it into knowledge will set the scene for new start-ups in the bioinformatics area. I’m convinced that VIB will play a strategic role in this evolution: our current bioinformatics groups already boast highly complementary, world-class expertise in each of the relevant omics fields.”

Big data evolutions will also force scientists to hone specific skills. Are there any programs being set up to help us develop new competencies?
Alex: “Staying up-to-date is indeed crucial. That is why we are in the process of building the Bioinformatics and Computational Biology Community (CBBI). And because data science and analytics skills will probably become more important in the long run, we have been pre-selected for an international project called ‘HELIS Academy’ alongside other research institutes. Together with the Dutch Techcentre for Life Sciences and the Eindhoven University of Technology, we plan to co-develop a data science and analysis curriculum. If we are successful in the second round, a 15 day-course will be set up which allows scientists and bioinformaticians from VIB and beyond to obtain the appropriate skill sets for big data in life science. And secondly, this curriculum should allow interns in the biotech sector to enter the job market more easily.”

On a European scale, ELIXIR (see page 7) was recently launched. How does our Bioinformatics Core fit into that initiative?
Alex: “It’s definitely closely intertwined. As the ELIXIR Training Coordinator, I’m working together with our VIB Bioinformatics trainers Janick Mathys and Christof De Bo, and ELIXIR Belgium to build a Belgian bioinformatics training community. We are also organizing training courses related to ELIXIR focus areas. For example, we’re developing an introductory course on computational skills needed for data management and analysis. We have also included the training materials and events of our Belgian ELIXIR partners in the online ELIXIR TeSS platform.”

To conclude, how can life sciences harness the power of big data and focus their investments on high-impact returns?
Alex: “It’s a big leap from real-world evidence to life science data, because diverse data sets must be combined in a well-integrated data and analytics ecosystem. Our scientific frontrunners play an essential role in this story, as they are the ones who help define the possibilities of big data. As a research institute, we will have to position ourselves like life science businesses. This means embracing the opportunities of big data as a key differentiator to solve fundamental scientific questions to the benefit of society.”

Discover TeSS, ELIXIR’s online training platform on bioinformatics via www.bits.vib.be/elixir

From left to right: Lieven Sterck, Frederik Coppens, Kim De Ruyck, Yves Van de Peer and Alexander Botzki

ELIXIR: AN INTERNATIONAL BREW FOR SMARTER BIG DATA MANAGEMENT AND BEYOND

In our labs and beyond, massive and ever-increasing amounts of data are being generated. We have our own VIB Bioinformatics Core (see page 4) to help us tackle complex analyses, but the hyper-fast evolution of big data has pushed life science professionals to look at the issue – and possible solutions – on a larger scale. That’s where the European initiative ELIXIR comes in, boasting an ambitious goal: making the life of biologists and bioinformaticians easier.

Across the world, we’re all in it together – and we’re all experiencing firsthand that data management is anything but a walk in the park. As a result, the 2014 creation of a data infrastructure at the supranational level was a logical next step. Pooling together resources from across Europe – including databases, software tools, training materials, cloud storage and supercomputers – ELIXIR was launched as an intergovernmental organization. It has grown to 21 member states, currently the largest initiative of the European Strategy Forum on Research Infrastructures (ESFRI).

HOUSEKEEPING VS. THE REAL DEAL

Headquartered in the UK, ELIXIR is comprised of ‘nodes’, or networks of organizations located within each member state. Here in Belgium, our VIB-UGent Center for Plant Systems Biology is coordinating ELIXIR Belgium. Partners are VIB, Ghent University, KU Leuven, University of Antwerp, Vrije Universiteit Brussel, Université Libre de Bruxelles, University of Hasselt and University of Liège.

The mission in Belgium is to coordinate these universities and unite them into an interconnected infrastructure. This will make it easier for scientists to find and share data, merge expertise and agree on best practices. Ultimately, it will help us gain new insights into how living organisms work. Frederik Coppens is responsible for this task,

he's a staff scientist at the VIB-UGent Center for Plant Systems Biology.

Frederik: "I have noticed several times in the course of my work that many of our colleagues are not familiar with data analysis because they have not been trained in it. However, the fact that they have to assess whether research results are reliable and relevant makes it a vital skill. At the same time, computers are struggling to interpret external data as well. There is truth in the saying that bioinformaticians spend 80% of their time converting between different data formats. Rather than building scripts for 'housekeeping', we'd all like more time to spend on the really interesting stuff. That is exactly what ELIXIR is aiming for."

Interested in our monthly newsletter? www.elixir-belgium.org

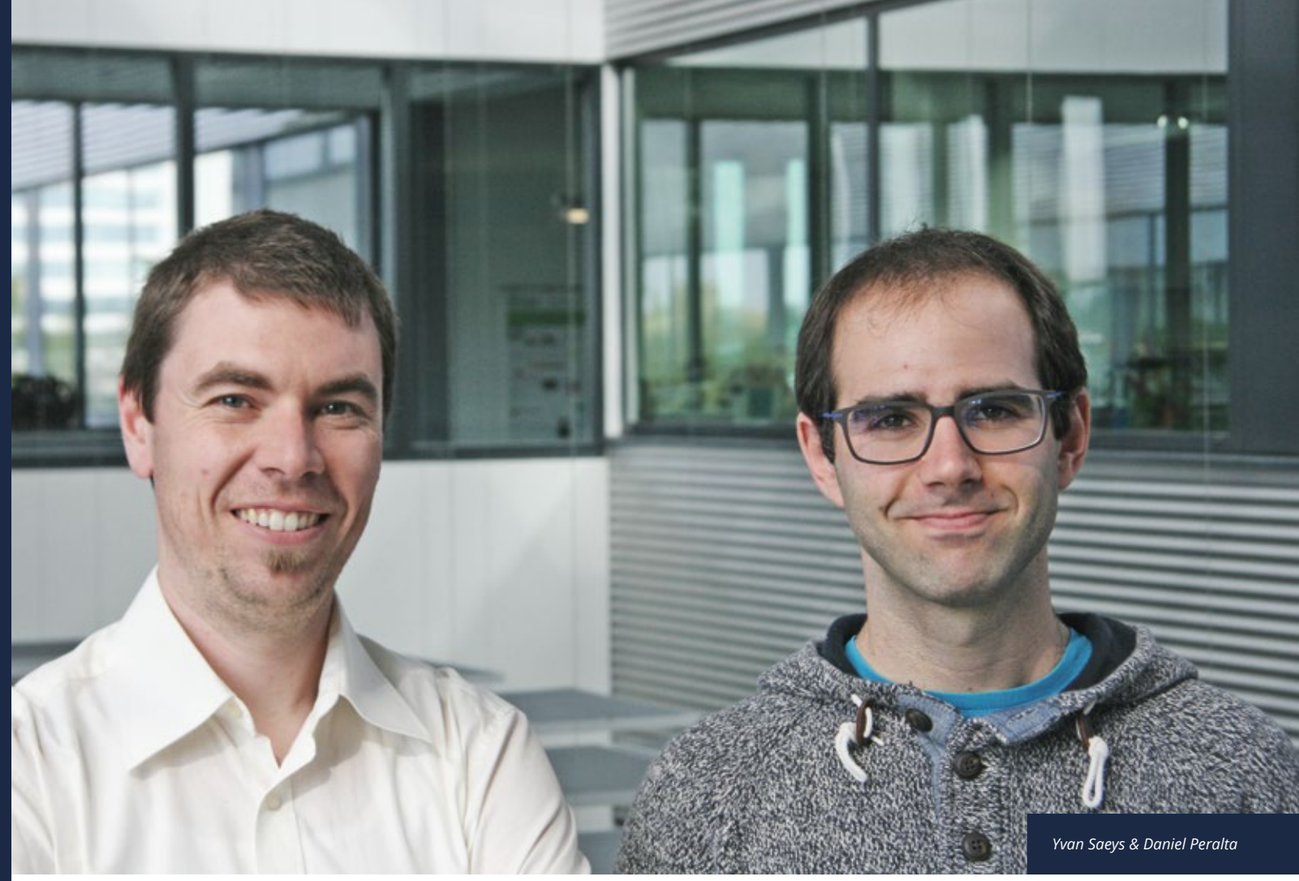
KIM DE RUYCK ON ELIXIR BELGIUM: "BUILDING A NETWORK OF BIOINFORMATICIANS"

The ELIXIR Belgium lead team includes Yves Van de Peer, Frederik Coppens, Lieven Sterck and Kim De Ruyck from the VIB-UGent Center for Plant Systems Biology, and Alexander Botzki from the VIB Bioinformatics Core. Kim is responsible for coordinating ELIXIR Belgium's activities across the country.

Kim, can you give a couple of examples of projects at VIB that have been carried out under the umbrella of ELIXIR?
Kim: "Last year, we organized the ELIXIR Belgium training meeting, with 20 participants of 13 universities and research centers, to kick off the activities of the training platform of the Belgian ELIXIR node. There, we organized a nationwide bioinformatics training network. In the meantime, four ELIXIR trainings are planned for this year. And last February, the ELIXIR Belgium launch event took place in Ghent, where we invited researchers, policy makers and funders. ELIXIR Belgium also contributed to ELIXIR's training portal TeSS. This platform allows to disseminate, discover and package training resources, training materials and events. All trainings organized by the VIB Bioinformatics Core are available in TeSS."

How are we exactly pooling together resources in Belgium?
Kim: "A good example of pooling and sharing data is our involvement in the Beacons Project. Beacons allow researchers to query individual datasets to determine whether they contain a specific genetic variant of interest. For example, they can ask Beacons simple questions like 'Do your data resources have genomes with a specific allele at a certain position?' The ELIXIR Belgium Beacon, also known as NGS-Logistics, provides access to exome variant frequencies from patients with rare genetic disorders. But, most importantly, we're also building a network of bioinformaticians in Belgium. This allows us to address common challenges."

What are the next steps for ELIXIR Belgium?
Kim: "Well, we just got started and currently I am the only person working full-time for ELIXIR Belgium. But thanks to recent Flemish funding, we are able to expand our team with two software developers, and we are in the process of hiring an ELIXIR Belgium trainer. He or she will help in organizing and providing 'train the trainer', 'train the developer' and 'train the researcher' trainings and workshops. We also aim to expand the involvement of our partners and to increase the portfolio of services offered by the Belgian ELIXIR node. And to link with the industry, we are organizing an ELIXIR Innovation and SME forum on Food and Nutrition Data targeting the microbiome."



Yvan Saeys & Daniel Peralta

BIG DATA IN LIFE SCIENCES: HYPE OR HOPE?

In science, business and society, the term big data has been on the rise for quite some time now. The last decade, however, the concept has evolved from an all-round label to tangible applications that affect our lives in numerous ways. In life sciences as well, big data technology is helping us cope with a seemingly endless tsunami of biological information. And considering the rapid pace of progress in our sector, we're just seeing the tip of the iceberg.

Big data and technology are usually mentioned in the same breath. Due to the data's immense volume, speed and complexity (see text box 'Understanding big data: the 5V mnemonic'), new high-performance tools are vital. Both hardware (infrastructure for data acquisition, storage and computing) and software (mining, analytics, visualization, database querying, etc.) are needed to leverage the power of big data. In all these areas, we have seen significant progress over the last decades, including cloud-based solutions for data storage and analysis, and novel computing paradigms for fault-tolerant, scalable and distributed data analysis (e.g. the Map-Reduce paradigm).

BIG DATA IN THE LIFE SCIENCES

Applications in life sciences have been a driving force behind many big data projects. The European Bioinformatics Institute (EBI) – one of the world's largest biological data repositories – currently stores 20 petabytes (1015 bytes) of data and backups concerning genes, proteins and small molecules. Genomic data accounts for 2 petabytes,

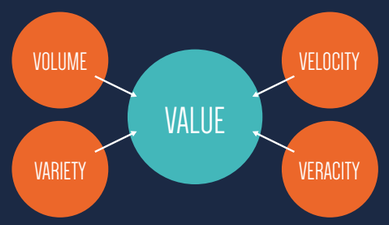
a number that more than doubles every year. Novel advances in genomics such as metagenomics and single-cell genomics will provide a multiple of that volume in data, with several types of “omics” information at the level of individual cells per patient, including different cell types and tissues. This could mean a huge asset for life scientists in the future: ideally, they have all that information at their fingertips, thanks to scalable and intelligent data integration engines.

ARTIFICIAL INTELLIGENCE AT VIB

At the VIB-UGent Center for Inflammation Research, Yvan Saeys and his team are currently developing and applying machine learning techniques to leverage these big biological data sets, with the aim of building intelligent data models. For example, the group is working on novel techniques for visualization and analysis of high-throughput single-cell data, scaling to billions of cells and up to thousands of measurements per cell. These methods can be used in a variety of contexts, including single-cell cancer studies, high-dimensional immunophenotyping and high-throughput compound screening.
Another example of this machine learning approach are the so-called deep neural networks, systems with multiple hidden layers between the (complex) input and output layers. In the field of 3D electron microscopy, they enable us to automatically annotate and mine large-scale imaging data sets.

BIG DATA SCIENCE AS A VITAL SKILL

Based on the ever-increasing scale of the generated data, it is clear we need additional knowhow and experience to use big data to our advantage and enable better hypotheses and interpretations of research results. To this end, young life scientists will need to be educated in big data science, in addition to their own fields of expertise. As for more senior scientists, they know better than anyone that lifelong learning is vital to stay at the forefront of research. Getting acquainted with the essentials and opportunities of big data will certainly be part of that picture.



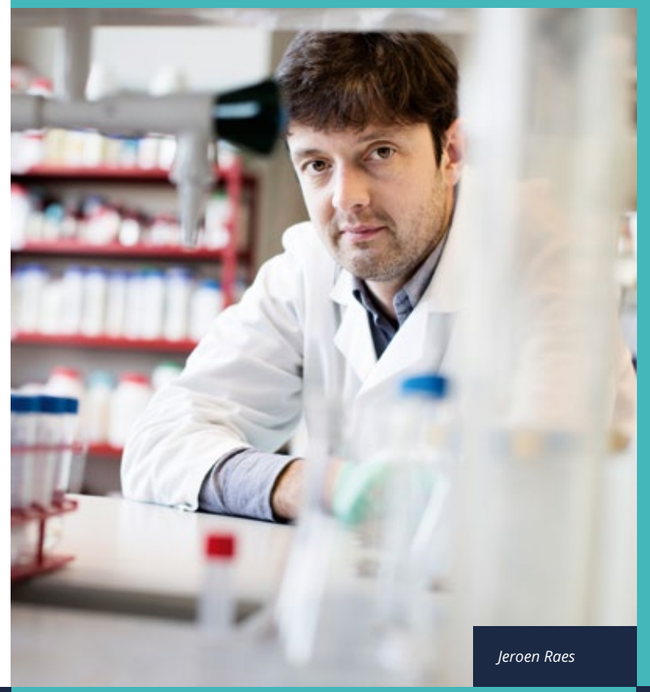
UNDERSTANDING BIG DATA: THE 5V MNEMONIC

The ‘big’ in big data refers to the information’s volume, diversity and complexity, which requires new technologies, algorithms and analyses to extract valuable knowledge from a dataset. In big data, traditional data mining applications are no longer sufficient to obtain timely, cost-effective or high-quality answers.

In other (and easy to remember) words, big data is characterized by these five key aspects:

- **Volume:** in various applications, vast amounts of data are being generated.
- **Velocity:** data is not only generated at high speed, but fast analysis is necessary as well.
- **Variety:** there are many different data types to be integrated, both structured (numbers that fit into tables or databases) and unstructured (documents, images, videos, etc.).
- **Veracity:** data quality and accuracy are often less controllable in a big data setting, leading to uncertainty about the veracity of data.
- **Value:** the ultimate goal is to obtain novel insights or patterns through the analysis of the data, leading in turn to new opportunities for research and industry.

VIB GROUPS AND BIG DATA



Jeroen Raes

How big is big data for you, and are you interested in getting even more data to analyze?

Jeroen Raes (VIB-KU Leuven Center for Microbiology): “The microbiome field is still in the development phase, so the datasets aren’t as big as they are, for example, in genetics GWAS studies. This being said, in our Flemish Gut Flora Project, there are about 3,500 individuals for which we have microbiome and genetics data, and will be generating metabolomics in the future. In addition to all the clinical and questionnaire data, this is becoming quite an impressive dataset, I’d say – and the multi-omics integration won’t be straightforward. Things will become even bigger in the future – for the trials we are currently planning, we will be collecting between 15,000 and 20,000 samples. The biggest challenge there is not the data analysis, but the logistics! ! Yet, it’s still not enough –in our recent *Science* paper, we estimated that at least 40,000 individuals need to be sampled to have a complete view of gut biodiversity in the healthy population. So, we still have quite some work ahead of us!”

Do you combine big datasets for better insights, or do you work the other way around – by slicing up big data into smaller portions for easier analysis – or perhaps both?

Diether Lambrechts (VIB-KU Leuven Center for Cancer Biology): “We reduce data size from bulk, noisy data (FASTQ/BAM files) to small, high-information datasets (VCF files). In general, we never slice, because data has cost us money and we don’t want to lose information. What we do is different from, for example, analyzing mouse clicks on a website. We combine data for better insights; vertically with other cohorts (e.g. compare/combine our results with TCGA) and horizontally with other data types (e.g. a new HRD predictor based on Alexandrov mutational signatures and SNParray profiles). Also, we should be careful in claiming that we use ‘big data’. Facebook and Google do, they use MapReduce algorithms on large databases that scale out horizontally on multiple servers. We mostly work with data that fits on RAM memory. The books and the hype around ‘big data’ really refer to the first scale of data.”

Diether Lambrechts

Stuart Maudsley

Do you need big software to analyze big data?

Stuart Maudsley (VIB-UAntwerp Center for Molecular Neurology): "There are currently three levels of accessible big data analytics – the giant level of Google BigQuery and IBM Watson (now interestingly being offered directly to public users), the intermediate level of data-specific organizations such as Envision, Neural Designer and Quire, and then finally the laboratory-based efforts that generate in-house analytical platforms both for internal and minimal-level consumer use. Profound insights, using big data analytics at the 'low' lab level can still compete effectively at the top end, especially when one considers the potential 'clarity' of the empirical data used at the lab level end compared to the indiscriminate mass-level (and often 'greying-out') data corpi used by the mega-scale players. So, to conclude, for the present time (Watson is coming however), intelligent, focused small-scale platforms can still beat giant corporations – it's still always down to the input data quality, and this is best curated in-house, near the end of your specific high-dimensionality pipeline."

In which fields are most of the big data sets produced in life sciences?

Lieven Sterck (VIB-UGent Center for Plant Systems Biology): "Nowadays, due to the ease and fast pace of generating data, big data is present in all fields of life sciences. Whether it is DNA/RNA sequencing, proteomics, metabolomics, patient (meta-)information, microbiomics, generating data is becoming cheaper and more feasible, which eventually leads to big data in every domain. Not surprisingly, most of the (really) big data can probably still be found in the medical and pharmacology fields, mainly due to the availability of both academic and industrial funding to create those data sets as well as the nature of those research fields. Nonetheless, in the plant field, data is becoming more and more accessible. A nice example of this is in plant breeding. We are currently experiencing a vastly increasing supply of information in related areas from plant genomes, water management, soil composition, fertilization, climate and automated phenotyping via drone technology to crop protection systems. The expanding ways and advances in technologies by which we can get and make use of this data is paving the way for big data to make its introduction both into farming practices as well as crop genetics. However, regardless of the field, it is clear that big data itself is useless unless we are able to turn it into knowledge."

Lieven Sterck

WINNING AT BASIC SCIENCE: COLLABORATION IS CRITICAL

A research team with Ludo Van Den Bosch (VIB-KU Leuven Center for Brain and Disease Research) at its helm has identified a new process that leads to the neurodegenerative brain diseases amyotrophic lateral sclerosis (ALS) and frontotemporal lobar degeneration (FTLD). The research uncovered important intra-cellular processes that lead to protein clumping in patients with defects in their C9orf72 genes. These key insights could lead to new treatments that prevent proteins from solidifying. This ground-breaking science would have never been possible, however, without close collaboration across VIB labs, core centers and national boundaries. We asked these VIB researchers to tell us more about the collaboration.

Scientists have known that clumps of proteins – called stress granules – form naturally in neurons, demixing from the watery cytoplasm within cells, and do not lead to disease in normal cells. In this study, VIB's Steven Boeynaems, Ludo Van Den Bosch, Peter Tompa and colleagues from Belgium and the US, observed that a mutation in the C9orf72 gene causes neurons to produce toxic peptides which bind together spontaneously and change stress granule processes. This causes stress granules to become more like solids than liquids.

Ludo, can you tell us more about the importance of this key observation?
Ludo: "The finding gives us molecular insight into the formation of protein clumps in these diseases. We believe that this process is an important step that happens just before the irreversible aggregation of these clumps into solids. After they stick together, the damage is permanent and the neuron will not function properly. It's a pivotal molecular 'moment' in the development of the disease."

A large number of players contributed to the project. Can you give us more details?
Steven: "Scientists from the VIB-KU Leuven Center for Brain and Disease Research, VIB-VUB Center for Structural Biology, VIB-UGent Center for Medical Biotechnology and several Belgian universities collaborated on the project with scientists from the Howard Hughes Medical Institute, Brown University and Harvard Medical School in the US. Even more, the capabilities of the VIB mass spectrometry, proteomics and bioimaging core facilities were essential to identify the proteins that react to the toxic peptides."

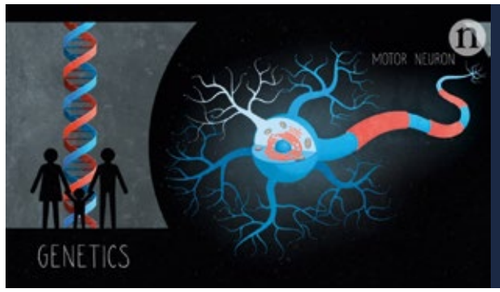
Steven, you recently presented a TEDx talk on this very basic research. Was it difficult to find the right tone to bring this story to a non-scientific audience?
Steven: "Biophysics can indeed be a challenging subject to present clearly to a lay public. Even so, the phase separation of these ALS-related proteins can easily be compared to processes that we see every day. For example, the demixing of oil and water in your salad vinaigrette is an

easily-understood paradigm that demonstrates how two liquids can coexist in a separated state."

Peter, where does this study fit into the broader spectrum of basic biophysics research?
Peter: "The demixing of proteins that is a hallmark of ALS, called liquid-liquid phase separation, exemplifies similar actions in a great number of physiological and pathological processes, including the formation of stress granules. Our research contributes biophysical and structural experiments to understand these special protein states, potentially contributing to the emerging cell biology paradigm of membraneless organelles."

Thinking back on the collaboration, were there specific findings that were completely unexpected?
Steven: "Researchers considered the toxic C9orf72 proteins to be aggregation-prone, but we found that, in a test tube setting, they didn't form solid protein clumps. However, when we added them to cell lysate – a preparation made of destroyed cells – they actually caused the clumping of other proteins. We were very surprised to discover that C9orf72 proteins aren't aggregation-prone themselves, but instead induce other proteins to aggregate."

Boeynaems et al., Molecular Cell 2017



Nature Reviews Disease Primers made a great animation based on input of the group of Ludo Van Den Bosch and Wim Robberecht (VIB-KU Leuven).
Check it out on nature.com/animations/ALS17

A-MAIZE-ING NEW MOLECULAR DISCOVERY FOR AGRONOMY

Front row from left to right: Jolien De Block, Kirin Demuynck and Tom Van Hautegem.
Back row from left to right: Hilde Nelissen and Dirk Inzé

In March 2017 senior staff scientist Hilde Nelissen, lab technicians Jolien De Block, Kirin Demuynck and postdoc Tom Van Hautegem of the Dirk Inzé lab at the VIB-UGent Center for Plant Systems Biology unveiled a discovery critical to crop science – a gene called PLA1 that boosts plant growth and seed yield in maize. With the advent of rapidly changing weather conditions and a greater incidence of extreme weather events around the world, scientific insights into crop growth and yield are vital to the agriculture of tomorrow. We asked the research team to tell us more about the trials and tribulations of their PLA1 research.

Maize is the most cultivated crop on the planet, and is used as food for humans and animals as well as a source of biofuel. Focusing on the leaf growth of maize – which can be used as a blueprint for the whole plant's growth processes – the team is currently investigating the molecular mechanisms that drive crop yield. Through lab and field tests in Belgium and the US, the researchers could show maize yield was boosted by 15% percent by promoting the expression of the plant's PLA1 gene.

Why is the PLA1 research so crucial to your group?
Dirk: "This study is a nice illustration of the complete pipeline from gene identification to validation in field trials. In parallel, we also studied the mode of action of the PLA1 gene at the cellular and molecular levels. Because

PLA1's mechanism was so successful and may even play a role in adapting plant growth to adverse conditions, PLA1 is still a major focal point of our current and future research."

Tom: "On my side, it was really exciting to be involved in the detailed mode of action of lab research, and at the same time being confronted with the positive phenotypes of the plants growing in the field. In this way, we actually got to experience, hands on, the agronomic benefits of the mechanism we were trying to untangle in the lab. The fact that research in the lab and in the field go hand-in-hand is really cool – and it adds value to our research while offering the perfect team-building activity."

What were the most important experiences for you during this project?
Jolien: "It was interesting to see the effects of different genetic promoters on PLA1 to stimulate growth, but it took some tweaking to finally achieve plants with real agronomic benefits."

Kirin: "For me, the most important experience during this project were the field trials. After observing the PLA1 phenotypes in the greenhouse, the logical next step was to take them to the field. Working outdoors in the field instead of in the fully controlled, precise setting of a laboratory was a big challenge – but our success at obtaining and repeating the lab results in the field was a huge boost. Even more, the field trials gave us new insights and the practical experience we needed for future trials."

How are field trials conducted in the US, and did you have the opportunity to go there yourself?
Hilde: "We'd already gained experience in the management and execution of field trials through our collaboration with ILVO – that's Flanders' research center for agriculture, fisheries and food. However, the field trials conducted in the US were definitely on a whole different scale. The field trial of one of our collaborators that I visited in Iowa was so extensive that it required meticulous planning up front. They used a field log book and followed the general rule of never doubting the 'air-conditioned decisions' when out in the field. By being part of their field team for a couple of days, I learned several little tips and tricks that we're now applying in our own research here in Belgium."

Inzé, Nelissen et al., Nature Communications 2017

AGRONOMY 101

- **What:** a branch of agriculture concerning the management of crops and soils to optimize land use and produce needed commodities (food, fiber, fuel) that maintains – or even boosts – the quality of the environment.
- **Why:** to give agriculture and other uses of land a sustainable future that can adapt to – and even mitigate negative effects of – changes in environmental conditions and demands.
- **How:** by investigating the most fundamental mechanisms at the molecular and cellular levels at work in soils and plants, scientists work to understand and improve crop genetics, develop computer models for environmental change and soil chemistry, create new solutions to fight crop pests and harmful environmental conditions … to give just a few examples!

From left to right: Jean-Christophe Marine, Michael Olvedy and Diether Lambrechts

A NEW UNEXPECTED KEY PLAYER IN MELANOMA DEVELOPMENT IDENTIFIED

Identification and functional validation of proteins involved in tumorigenesis are essential steps toward advancing cancer precision medicine. In The Journal of Clinical Investigation researchers from the VIB-KU Leuven Center for Cancer Biology together with colleagues from INSERM (France) now report the important role for FES in the initiation and progression of melanoma, a malignant type of skin cancer, that is notoriously quick to metastasize and that responds poorly to existing cancer treatments. Unexpectedly the expression of FES, which encodes a kind of protein better known for their ability to promote cancer development-, is lost in a large fraction of human melanoma. The researchers also identified a pharmacological way through which FES expression can be restored in human melanoma. This can be the first step in a novel therapeutic strategy against melanoma.

Human melanoma is a very aggressive skin cancer, but very little is known about the mechanisms that cause the disease to progress. The fact that melanoma often exhibits UV-induced genetic alterations makes it, among other features, a very complex disease to study. Jean-Christophe Marine and others developed mouse models recapitulating some of the key histopathological features of the human disease. Importantly, the mouse melanoma lesions are far less complex than their human counterparts. Taking advantage of these 'simplified' versions of melanoma, the researchers identified a dozen of new genes that are likely to play key roles in the initiation and/or progression of human melanoma. To further validate their findings, they studied the role of one of the genes, namely FES, and established its important contribution to the development of both mouse and human melanoma.

AN ONCOGENE THAT SUPPRESSES MELANOMA TUMOR GROWTH VIA A KEY CANCER PATHWAY

Previous research identified FES as an 'oncogene' – a gene that is able to transform a normal cell into a cancer cell under certain conditions – in leukemia, for example. However, its role in melanoma appears very different.

Jean-Christophe: "To our surprise we obtained clear evidence that FES strongly suppresses melanoma growth and viability. Its expression is silenced in more than 30% of human melanoma lesions. Importantly, we showed that FES deletion in mice accelerated the growth of melanoma tumors." The team also showed that FES modulates the WNT signaling pathway. This key cancer pathway is activated in virtually all melanoma, but the mechanisms that contribute to this activation remain largely unclear. So this study provides one route through which this pathway is activated in about 30% of the cases.

PHARMACOLOGICAL IMPLICATIONS OF FES

The researchers also identified a pharmacological way of restoring the expression of FES in human melanoma. The approach involved the use of epigenetic drugs that promote DNA demethylation; some of which are currently tested in clinical trials for melanoma. It will be interesting to assess whether the efficacy of these drugs can be linked, at least partly, to restoration of FES expression.

Jean-Christophe: "We will definitely further explore this new putative therapeutic strategy. Importantly, in the same time our data raise concerns about ongoing clinical trials with broad spectrum tyrosine kinase inhibitors. Some of these inhibitors inactivate FES and therefore may lead to undesired effects."

A TRI-PARTITE COLLABORATION

This study is the result of a fruitful collaboration between the VIB labs of Jean-Christophe Marine and Diether Lambrechts and the lab of Paulo De Sepulveda of the French National Institute of Health and Medical Research (INSERM).

Jean-Christophe: "This project was spearheaded by Michael Olvedy, who worked under the supervision of myself (promotor) and Diether Lambrechts (co-promoter) within the frame of the VIB international PhD program. The high-throughput DNA sequencing capabilities of the Diether Lambrechts lab was critical to the discovery of altered genes in mouse melanomas. And finally, Paulo Sepulveda was a key collaborator that assisted us in investigating the role of FES in tumor formation in vitro. Without combining these diverse pools of expertise, we would have never achieved our valuable insights."

Olvedy *et al. Journal of Clinical Investigation 2017*

Elizabeth Allen and Gabriele Bergers

SPECIALIZED BLOOD VESSELS ENHANCE TUMOR-FIGHTING IMMUNOTHERAPY

Scientists from the VIB-KU Leuven Center for Cancer Biology, together with colleagues from the University of California and the Swiss Institute for Experimental Cancer Research have demonstrated that anti-angiogenic therapy can improve immune boosting treatments. The successful combination of these two therapies results in the growth of specialized vessels that deliver cancer-fighting immune cells to the tumor, potentially leading to more effective treatments and longer survival periods. The results of the study are published in the peer-reviewed academic journal Science Translational Medicine.

Sustained angiogenesis, the growth of new blood vessels, and the suppression of the immune system are hallmarks of cancer, with an increasing amount of evidence demonstrating that these two activities are interrelated. Therapies that prevent tumor blood vessel growth are often used in clinics to fight cancer – but they are only effective in a particular subset of patients. Similarly, the recent successes to directly stimulate the immune system with inhibitors of negative immune checkpoint regulators - such as antibodies against programmed cell death protein 1 (PD-1) or its ligand PDL-1 - has led to many clinical trials. However, only a minority of treated patients have responded to these immunotherapies, emphasizing the need to identify strategies that will increase response rates in patients. Elizabeth Allen and colleagues from the group of Gabriele Bergers at the VIB-KU Leuven Center for Cancer Biology provide evidence that anti-PD-L1 therapy can sensitize and prolong efficacy of anti-angiogenic therapy, and conversely, anti-angiogenic therapy can improve anti-PD-L1 treatment specifically when intra-tumoral HEVs are generated that facilitate enhanced whire cell infiltration, activity and tumor cell destruction.

BLOOD VESSELS HELP REGULATE IMMUNITY

To avoid being targeted by their hosts' immune systems, tumors maintain an immunosuppressive environment by manipulating the characteristics of the immune and vascular system. Increased blood supply and decreased immune activity are necessary for malignant cells to multiply.

Gabriele Bergers: "The network of blood vessels itself is an important regulator of immunity because it controls white blood cell trafficking. By preventing the infiltration of white blood cells, the cancer is able to evade the host's immune system."

Interestingly, the team showed that combining anti-angiogenic and immune-stimulating therapies in the treatment of tumors in mouse models resulted in better therapeutic outcomes by providing white blood cell gates through which they can infiltrate cancers.

Elizabeth Allen: "It was interesting to observe that this combination of immune system-activating and anti-angiogenic antibodies causes a positive feedback loop. The result is the growth of specific blood vessels that deliver cancer-fighting immune cells into the tumor. These high endothelial venules (HEVs) are normally found in lymphoid organs such as lymph nodes, where they help transport white blood cells. For the first time, we showed that the growth of HEVs can be therapeutically induced in tumors."

DESCRIBING THE PROCESS

The results of the study indicate that the two therapies stimulated significant growth of HEVs in pancreatic and mammary tumors, leading to malignant cell death and tumor shrinkage. The next step in this research involves investigating how intratumoral HEVs are formed and maintained.

Gabriele Bergers: "Understanding the underlying mechanisms of the process will contribute to the overarching goal of developing new therapeutic approaches to boosting the immune system in tumors."

Allen, Jabouille et al., Science Translational Medicine 2017

From left to right: Rudi Beyaert, Savvas Savvides and Kenneth Verstraete

PROTEIN RESPONSIBLE FOR ALLERGIC DISEASES EXPOSED

Scientists at the VIB-UGent Center for Inflammation Research have managed to unravel the functioning of what is thought to be the 'master protein' that drives a range of widespread allergic diseases, such as asthma and eczema. On a molecular level, the team described how a protein called TSLP assembles with its molecular partners at the surface of cells. This is the cornerstone of TSLP's bioactivity. These insights, published in the leading scientific journal Nature Communications, also enabled the team to develop a new molecule that can block TSLP's activity. Due to the molecule's promise in terms of the development of new therapies for widespread allergic conditions, the researchers are currently planning follow-up studies and seeking industrial partnerships.

Millions of people worldwide suffer from common allergies – ranging from light asthmatic symptoms to severe atopic dermatitis, a frequent form of eczema. Such diseases cause a heavy burden in the quality of life of people suffering from them, and at the same impose a gigantic socioeconomic and healthcare footprint. The exact causes of such diseases are not known yet, although the answer probably lies in a combination of genetic, molecular, and environmental factors. While some treatments may reduce the severity and frequency of symptoms, a comprehensive cure has yet to be found.

FUNDAMENTAL SCIENCE PAVES THE WAY TO NEW THERAPEUTICS AGAINST ALLERGIC DISEASES

To tackle the complex issue of studying diseases at the molecular level, Savvas Savvides coordinated a multidisciplinary team spearheaded by his postdoc Kenneth Verstraete. This team united expertise from three VIB-UGent research centers, Ghent University, the University of Antwerp, The Pontifical Catholic University of Peru, and the University of Toulouse in France. The researchers focused on understanding the molecular and structural mechanism of how TSLP interacts with its two molecular receptors at the cell surface. A key undertaking has been the elucidation of the three dimensional structure of the molecular assembly mediated by TSLP. In parallel, the team developed and characterized a novel protein-based inhibitor of TSLP that can efficiently capture TSLP to prevent its association with its natural receptors on the cell surface. In this way, the bioactivity of TSLP can be blocked. The study has been supported by funding from national and international sources, as well as research infrastructure at the European level.

Savvas: “For the first time, we have obtained detailed snapshots of TSLP’s function. More specifically we unraveled how it mediates the protein assembly at the cell surface responsible for several atopic diseases, including asthma and atopic dermatitis. TSLP has been the focus of many prominent academic laboratories worldwide, as well as major pharmaceutical companies. This knowledge offers them a new tool for therapeutic intervention. Our study proves that basic research at the molecular level is the pillar for developing new therapeutic strategies.”

FUTURE DEVELOPMENTS

Savvas’ team is currently working closely with the partner team led by Rudi Beyaert and with VIB’s Technology Transfer department towards follow-up studies, with a twofold goal: to optimize the TSLP inhibitor on one hand, and to test the molecule in appropriate animal models for a range of allergic conditions on the other.

Rudi: “The detailed structural and biochemical insights are a key source of information for understanding and optimizing the potency of our inhibitory molecule against TSLP. We are very excited about the implications and promise of this work.”

Savvas: “We strongly believe in our discovery’s potential in the development of new therapies against allergic diseases. At the same time, we hope that the insights and tools we have generated in this study will catalyze further developments in the field. The TSLP story is far from done, as recent reports have added intriguing new twists to TSLP’s function. We will take advantage of our pole position in the field to continue to contribute to our understanding of this fascinating protein. Nonetheless, our priority now is to identify possible industrial partnerships to actually develop a novel therapeutic tool.”

Verstraete et al., Nature Communications 2017

QUICKSCAN

1

#SPION #Nanoparticles #Subcellular localization

The Wim Annaert Lab (VIB-KU Leuven Center for Brain and Disease Research) engineered superparamagnetic iron oxide nanoparticles (SPIONs) targeting distinct subcellular compartments. They used different types of SPIONs to compare the biomolecular compositions of lysosomes and plasma membranes isolated from wild-type and Niemann-Pick disease type C1 (NPC1) deficient cells, and found disease-related alterations that were location-specific. These findings demonstrate how SPIONs can be used to fingerprint subcellular compartments and identify pathological changes at a much better resolution than in whole cells or tissues.

Tharkeshwar et al., Science Reports 2017

2

Simon Tavernier, Sophie Janssens, Bart Lambrecht

#IRE1 #Dendritic cell survival

Previous research elucidated a role for the unfolded protein response (UPR) sensor, IRE1, in the functional specialization of splenic type 1 dendritic cells (DCs). These DCs activate CD8 T cells, crucial effectors of the immune response against viral infections and malignant cells, and this process is critically dependent on the proper activation of the IRE1 endonuclease. By further investigating the role of IRE1, Simon Tavernier and Fabiola Osorio from the team of Bart Lambrecht and Sophie Janssens (VIB-UGent Center for Inflammation Research) have discovered additional functions of this protein in DC biology. The IRE1/XBP1 pathway maintains DC viability at the mucosal borders in an IRE1 endonuclease-dependent manner. The endonuclease activity is differentially fine-tuned in DCs across different organs and might be associated with their tissue-specific functions.

Tavernier et al., Nature Cell Biology 2017

3

#Parkinson #SYNI #Autophagy

The Patrik Verstreken Lab (VIB-KU Leuven Center for Brain and Disease Research) has characterized a mutation in synaptojanin 1 (SYN1) that was recently linked to early onset Parkinson’s disease. Using fly models and patient-derived iPS cells, they demonstrated that mutant SYN1 is active exclusively at the synapse. The mutation induces defects in autophagic mechanisms, affecting stress coping mechanisms at the synapse. Last year, the Verstreken lab uncovered that mutations in LRRK2, another Parkinson-related gene, cause exactly the same problems, putting the synapse at center stage in the disease’s pathology.

Vanhauwaert et al., The EMBO journal 2017

4

#Asthma #Dendritic Cells #Skin

The skin is recognized as the route of allergic sensitization to house dust mite (HDM), and this often precedes the development of allergic asthma. How allergy develops via the skin was not well-understood. Julie Deckers from the Hamida Hammad Lab (VIB-UGent Center for Inflammation Research) identified skin IRF4-dependent dendritic cells, and not Langerhans cells, as crucial players in Th2 sensitization to HDM. These findings will help understand how alterations in skin-expressed proteins in patients at risk for developing asthma could interfere with this basic mechanism of DC-driven type 2 immunity.

Deckers et al., J Allergy Clin Immunol 2017

5

Doris Vandeputte

#Gut microbiome #Prebiotics

A new study by the Raes Lab (VIB-KU Leuven Center for Microbiology), in collaboration with Kristin Verbeke (KU Leuven) with the support of BENEO, assessed the impact and specificity of inulin prebiotics on gut microbiota. The results showed that inulin selectively affected only three bacterial genera, settling a long-term debate about the breadth of inulin impact. Bifidobacteria and *Anaerostipes*, known for multiple beneficial effects, were increased, in line with previous work. Next to this, *Bilophila* levels went down, linked with both less constipation and improved quality of life measures, pointing at *Bilophila* as an interesting novel target in this area.

Doris Vandeputte (VIB-KU Leuven Center for Microbiology): "This is the first time that a direct link has been established between the consumption of inulin, a selective change in microbiota composition and an improvement in quality of life – something that is very important for support of such products and for translational microbiomics as a whole."

Vandeputte et al., Gut 2017

6

#Plant growth #F-box protein

The network of genes that determines final leaf size is complex and not completely unraveled up to now. The Dirk Inzé Lab (VIB-UGent Center for Plant Systems Biology) discovered an additional player in this network. The F-box protein FBX92 acts as a repressor of leaf growth in Arabidopsis, as indicated by the effect on leaf size when altering AtFBX92 expression levels, by affecting cell division rates and expression levels of cell cycle genes. Identification of the substrates of this F-box protein offers the potential to further reveal growth regulatory networks.

Baute et al., Plant and Cell Physiology 2017

7

#Flowering time #Photoperiod #Transcriptional regulation

Seasonal responses are adjusted in plants by the coordinated action of circadian and photoperiodic rhythms. Recently, the Alain Goossens Lab (VIB-UGent Center for Plant Systems Biology) discovered two regulators of these processes in *Arabidopsis thaliana*, namely FAR1 RELATED SEQUENCE 7 (FRS7) and FRS12. These proteins form a complex that accumulates particularly in short day conditions to repress key regulators of flowering time and diurnal growth. Thereby, this study offers a better insight into how plants adapt to seasonal changes.

Ritter et al., Nat Commun 2017

8

#Charcot-Marie-Tooth #SGPL1

Charcot-Marie-Tooth disease (CMT) is a genetically heterogeneous inherited peripheral neuropathy. The Albena Jordanova Lab (VIB-UAntwerp Center for Molecular Neurology) is the first to identify recessive mutations in *SGPL1* causing an axonal form of CMT with acute onset and peculiar clinical course. *SGPL1* defects resulted in a partial deficiency of the encoded sphingosine 1-phosphate lyase, catalyzing the final step of the sphingolipid catabolism. The neuron-specific knockdown of the *Drosophila* orthologue impaired the neuromuscular junction and caused progressive neuronal degeneration. The results underline the importance of sphingolipid metabolism on the neuronal function.

Atkinson et al., Neurology 2017

9

#Frontotemporal dementia # TANK-binding kinase I #TBKI

Julie van der Zee of the Christine Van Broeckhoven Lab (VIB-UAntwerp Center for Molecular Neurology), in collaboration with the European Early-Onset Dementia Consortium, has performed a large-scale mutation screening of the TANK-binding kinase 1 (TBK1) gene in European patients with frontotemporal dementia and/or amyotrophic lateral sclerosis. Using both *in vivo* and *in vitro* methods, they explored the full mutation spectrum of TBK1 and demonstrated that loss of TBK1 function leading to disease can result from different mechanisms, including loss of transcript, loss of protein, as well as various degrees of loss of protein function.

van der Zee et al., Human Mutation 2017

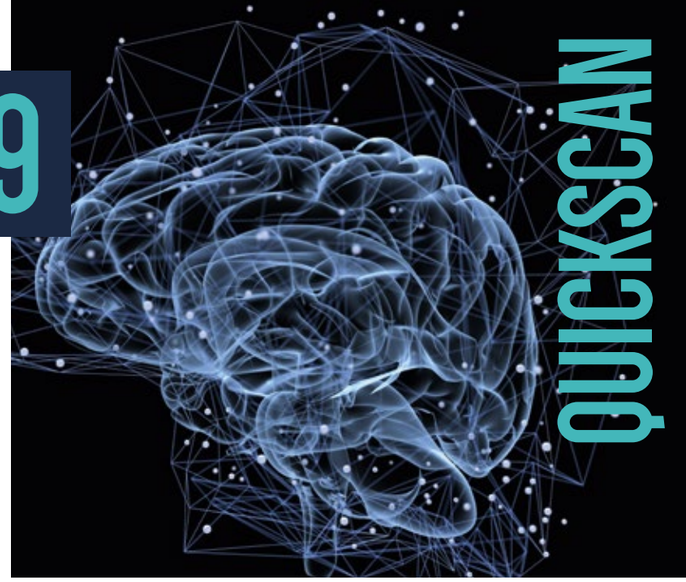
11

Xavier Saelens

#RSV #Nanobodies®

In a joint effort, the Xavier Saelens Lab (VIB-UGent Center for Medical Biotechnology), researchers from the Geisel School of Medicine at Dartmouth and several other collaborators developed a new antiviral strategy against human respiratory syncytial virus (RSV). The approach hinges on the use of single-domain antibodies, also known as Nanobodies®, which target and inactivate a vital protein of RSV, rendering it unable to enter lung cells. The study elucidates how these Nanobodies® interact with and neutralize the virus and demonstrates their ability to successfully protect mice from RSV infection and related inflammation.

Rossey et al., Nat Comm 2017



#Daucane esters #Glucocorticoid receptor #SEGRMs

In the search for novel Selective Glucocorticoid Receptor Modulators (SEGRMs), a class of naturally occurring daucane esters was found to efficiently suppress NF-κB- and AP-1-dependent pro-inflammatory pathways. Concomitantly, the most active entities inhibited pro-inflammatory gene expression and protein production. Although the most active compounds competitively repressed GR-driven GRE-dependent reporter gene activities, the GRE-mediated anti-inflammatory gene GILZ, but not DUSP1, was found to be upregulated. This research, This research, led by Karolien De Bosscher from the Jan Tavernier Lab (VIB-UGent Center for Medical Biotechnology) may be relevant in combination strategies attempting to circumvent side effects of glucocorticoids upon long-term anti-inflammatory treatments.

Popović et al., Phytomedicine 2017

10

Karolien De Bosscher

LIPIDOMICS PAVES THE WAY TO GROUNDBREAKING SCIENTIFIC DISCOVERIES

Patrik Verstreken

Wim Annaert

Rose Goodchild

Mark Veugelers

VIB's Technology Watch team has been active for almost a decade, continuously analyzing the potential of emerging technologies and mediating researchers' access to them. By expanding VIB's network of technology suppliers, purchasing licenses and negotiating business partnerships, the Tech Watch team enables VIB scientists to have privileged access to cutting-edge scientific innovations. One example comes in the form of a powerful lipidomics research tool made available to VIB scientists through a collaboration with Lipotype, a Max-Planck spin-off and key service provider. Since 2015, Lipotype technology has been a crucial factor in several major breakthroughs in multiple life sciences domains.

THE BENEFITS OF A DEDICATED LIPIDOMICS COLLABORATOR

Lipidomics, or the analysis, identification and quantification of lipids, has important applications in basic and clinical research, as well as in the nutrition, cosmetics and personalized healthcare industries. Using Lipotype's Shotgun Lipidomics Technology, researchers can rapidly analyze large samples at reasonable prices, benefiting from the ultra-broad coverage and absolute quantification of lipids enabled by this technology.

Mark Veugelers (VIB Tech Watch):
"In close collaboration with VIB group leaders we are constantly on the lookout for new technologies that can have a major impact on VIB research. The Lipidomics services offered by Lipotype is a good example. But identification of a novel technology with potential isn't enough to produce breakthrough results. Key in the process is the hands-on experience of VIB scientists when evaluating the potential of these novel technology opportunities."

Oliver Uecke (Lipotype):
"Tech Watch at VIB is a win-win situation for all parties involved: VIB researchers get access to innovative technologies early on, while technology providers have the Tech Watch team as single entry point to address the VIB collective of researchers. VIB profits from providing their researchers with means to generate cutting edge research results and with an improved basis for licensing and spin-off creation."

BETTER TECH INTEGRATION, IMPACTFUL RESULTS

After just two years of collaboration, VIB scientists at the VIB-KU Leuven Center for Brain and Disease Research working with Lipotype have published three papers in high-impact academic journals. This demonstrates the integration of new innovations into VIB research leads to more and faster discoveries.

Wim Annaert:
"Lipotype's Shotgun technology was critical to our recent paper on a new approach to analyzing subcellular dysfunction. Our next challenge is now to integrate lipidomics with proteomics data to better understand what goes on at the level of a single subcellular compartment for instance in a disease context."
(relevant publication: Tharkeshwar et al., Scientific Reports 2017)

Patrik Verstreken:
"My team recently made groundbreaking discoveries related to mitochondrial defects in Parkinson's Disease. Tech Watch – and access to Lipotype tech in particular – were essential to these findings."
(relevant publication: Vos et al., J Cell Biol 2017)

Rose Goodchild:
"Tech Watch funding significantly boosted our confidence in collaborating with Lipotype for our work on cellular lipid metabolism. Lipidomics is a key emerging technology that we don't have in-house, and our access to it – especially when it comes to molecular and cellular research – adds huge value to our projects."
(relevant publication: Gonzalez et al., Developmental Cell 2016)

VIB PUSHES THE BOUNDARIES OF SCIENCE TO DEVELOP NEW DIAGNOSTIC TOOLS

Greater knowledge of molecular mechanisms and novel bio-analytical methods lead to more efficient and accurate diagnostics. With their world-leading strengths in molecular research and biotechnology, various VIB labs are paving the way for novel diagnostic tools that will ultimately reduce disease burden and save lives by making disease diagnosis better, faster and more flexible. The proof is in the partnership: three recent collaborations between VIB, university hospitals and diagnostics industry leaders highlight just how critical molecular science at VIB is to the development of cutting-edge diagnostic technology.

Jan Staelens, VIB Business Development Manager: "It is very fulfilling to see how the perseverance of our researchers makes it possible to translate a conceptually novel test to clinical utility. This endeavor also requires persistent support and advice from external partners, and funding from agencies like ERC, the UGent Industrial Research Council, VLAIO and others. But also private initiatives such as the Fournier-Majoie Foundation (FMF) and its founder, Mr. Bernard Majoie were essential for their funding and long-term support. We are grateful for all these efforts in bringing new diagnostics to the clinic that can reduce the disease burden of cancer."

INTELLIGENT LIVER DISEASE DIAGNOSIS AND MONITORING

In cooperation with VIB, Helena Biosciences – a UK-based medical diagnostics firm – is currently right on track toward commercializing a comprehensive blood test for chronic liver disease. The new test, called the Glyco Liver Profile, enables medical professionals to non-invasively diagnose and monitor liver diseases. In particular, it can detect liver cirrhosis at an early stage and can predict a liver cirrhosis patient's likelihood of developing liver cancer within five years – a first for the market. This will enable cost-effective intensive monitoring for early stages of liver cancer in the group at high risk, at which stage effective treatment options are available. In patients with fatty liver disease, Glyco Liver Profile allows to detect chronic inflammation, which is the main hallmark of NASH (nonalcoholic steatohepatitis), the more advanced stage of the disease that requires intensive therapy.

The technology behind the tool was first developed in 2004 by Nico Callewaert of the VIB-UGent Center for Medical Biotechnology and Roland Contreras (VIB-UGent). They collaborated with Hans Van Vlierberghe and Joris Delanghe at UZ Gent for further validation of the technology. The test is the first one that is based on direct analysis of the glycome (mix of sugar modifications) of serum proteins, which are mainly produced by the liver. "Wouter Laroy, Dieter Vanderschaeghe and Wim Nerinckx in our labs, with help of many others, had to design and produce all critical reagents and develop it to the point that the test could be run on an existing clinical diagnostic instrument like the one of Helena. This now leads to a test that fills important gaps in diagnostic capabilities in chronic liver disease. Thanks to our collaboration with Helena, it will bring substantial benefits to patients and medical centers in the form of accuracy and personalization of patient follow-up and treatment," Nico explains.

Callewaert et al., Nature Medicine 2004
Blomme et al., Dig. Liver. Dis. 2012
Verhelst et al., Clinical Cancer Research 2016

COLON CANCER SCREENING DREAM TEAM

Another key example of how VIB research has enabled the innovation of critical new diagnostic tools in human healthcare is in the form of a collaboration with DNAlytics to develop a non-invasive colorectal cancer screening test. If detected at an early stage, colorectal cancer responds very well to treatment, making early detection a huge priority. However, current tests fall short at delivering quick, comprehensive and accurate results.

Using insights gained through the research of Massimiliano Mazzone from the VIB-KU Leuven Center for Cancer Biology on the identification of cancer bio-markers using a specific type of white blood cell, the tool – called the ColonoKit – meets the demand for a diagnostic suitable for any kind of patient. It offers greater certainty and the ability to detect bowel cancer very early on, potentially eliminating half of non-urgent or unnecessary colonoscopies. It also offers the unique possibility of following previously treated colorectal cancer patients over time in order to quickly detect relapses and improve cure success. "I've been working on the role of the immune system in cancer for more than 10 years now," says Massimiliano. "It's a puzzling field with a lot of potential for clinical application, and it's great that our work is the basis of a novel diagnostic kit with clear advantages for the patients."

DNAlytics, a specialized data analytics firm, is currently in the process of developing an evolving online platform to complement the ColonoKit. Underlining the importance of this research even more, Massimiliano was awarded a Proof of Concept grant by the European Research Council to further develop the kit alongside his cancer and immunity research colleague Hans Prenen at UZ Leuven.

Hamm, Prenen, Van Delm et al., Gut 2015
Wenes et al., Cell Metabolism 2016

AUTOMATING MSI TESTING TO PREDICT RESPONSE TO CANCER IMMUNOTHERAPY

Characterization of genetic alterations accumulating in solid tumors is a key research area of Diether Lambrechts' lab at the VIB-KU Leuven Center for Cancer Biology. Microsatellite instability (MSI) is a particular type of tumor characterized by mutations that arise during DNA replication and that are not corrected by the DNA repair machinery. MSI is most often found in colorectal or endometrial cancer patients, where it predicts response to chemotherapy in stage 2 or 3 patients or tailors patients with a metastatic colorectal tumor to cancer immunotherapy. Until now, MSI testing technologies have been complex and time-consuming to perform, which makes MSI often underdiagnosed in the clinical setting.

After receiving a grant of EUR 750,000 from the Flanders' Organization for Innovation and Entrepreneurship (VLAIO) in March 2017, Belgian medical diagnostics company Biocartis is working alongside the VIB scientists to develop a fully automated, highly accurate MSI test for colorectal cancer integrated with Biocartis' Idylla™ platform. A set of unique MSI biomarkers, identified by Diether's lab, were licensed to Biocartis in 2013.

"MSI testing can offer high clinical value to oncology treatments," Diether asserts. "The biomarkers that we identified, in combination with the advantages of Biocartis' Idylla™ platform, will allow us to significantly lower the barriers to MSI diagnostics. We're excited to extend our collaboration with Biocartis into the immunotherapy space."

Zhao et al., Elife 2014
Claes et al., J Clin Oncol 2015

VIB SPIN-OFF AGROSAVFE READY TO CONQUER THE WORLD OF BIOPESTICIDES

This spring VIB spin-off AgroSavfe welcomed seasoned manager and life sciences expert Luc Maertens as CEO. The company also extended its financing round, attracting a total of EUR 11 million with a major investment from Sofinnova Partners, a reputed international life sciences investment fund. With an expanded management team and fresh funding, the agro-biotech start-up is gearing up to become a world player in bio-pesticides.

Established in 2013, AgroSavfe creates next-generation bio-pesticides for the control of pests and diseases of crops and harvested products. The basis of these bio-pesticides are Agrobodies®: small proteins designed and formulated to specifically bind to essential target molecules of crop pests and diseases. The really good news? They are safe and environmentally friendly, and can be produced cost-effectively. At its R&D center in the Technologiepark in Ghent, AgroSavfe has now generated Agrobodies® with anti-fungal activity, which are being developed into a new class of bio-fungicides.

STRENGTHENED MANAGEMENT TEAM

In view of the transition of the company from its research into its product development phase, the management team was recently expanded. Luc Maertens, who packs 20 years of experience in strategy development and implementation in the agro-industry, was appointed CEO and joined the AgroSavfe board. Marnix Peferoen, who has led AgroSavfe since its inception and led the team that created the Agrobody® technology platform, was appointed as Chief Technology Officer.

“I’m delighted to have the opportunity to lead the company in its next growth phase,” Luc said in an official statement. “We will work together with the team and all stakeholders to develop and introduce the next generation biological control agents to make agriculture and horticulture more productive and sustainable.” The Agrobody® technology platform is in place, and has delivered a first generation of bio-fungicides.

FRESH FUNDING

In March 2017, AgroSavfe added another chapter to its ongoing success story when its latest financing round reached EUR 11 million. The biggest investor was Sofinnova Partners, a leading European venture capital firm specialized in life sciences. Earlier investors in AgroSavfe include Agri Investment Fund, Biovest, Gimv, Globachem, Madeli Participaties, PMV, Qbic, some private investors and VIB itself.

Sofinnova Partners, which focuses on paradigm-shifting technologies, was clearly impressed with the potential of the Agrobody® technology. “Agro chemicals, and in particular fungicides and insecticides, are huge markets that biologicals can address if they can be scaled up and produced at competitive cost compared to chemical compounds,” said Denis Lucquin, Sofinnova’s managing partner, who also joined AgroSavfe’s board.

WORLD DOMINATION

With this latest capital injection, AgroSavfe can further accelerate the development of Agrobodies® as a new class of bio-pesticides and roll out the international registration process.

ABOUT AGROBODIES® AND NANOBODIES®

The Agrobodies® AgroSavfe uses for its highly inventive bio-pesticides are essentially Nanobodies® that are used in agricultural applications. These Nanobodies® originate from the work in the VIB-VUB Center for Structural Biology and were the basis of different start-ups: Ablynx, Confo Therapeutics and AgroSavfe.

Due to their unique structural and functional properties, Nanobodies® are the ideal building blocks for next-generation biological drugs, as well as – in the case of AgroSavfe – bio-pesticides.

GLYCODELETE START-UP PROJECT: MOST PROMISING AND INNOVATIVE CATALYZER PROJECT AT THE BIOVISION LIFE SCIENCES FORUM

Carla Snoeck, Manager New Ventures at VIB, pitched the GlycoDelete start-up project at the 2017 edition of the international Biovision life sciences forum in Lyon. This event is a springboard for innovative health projects and start-ups. An expert committee of investors and industry partners awarded GlycoDelete as the most promising and innovative project.

GlycoDelete is a novel glyco-engineering technology platform for the design and development of next-generation biopharmaceuticals. This glyco-engineering technology was developed in the lab of Nico Callewaert (VIB-UGent Center for Medical Biotechnology) and is now further incubating within VIB. This incubation period will be used to build a convincing business case to attract VC funding.

Carla: “The Biovision forum offers an excellent opportunity to put VIB’s start-up projects in the spotlight of the French investor community. This award generates lots of visibility for both the GlycoDelete project and VIB’s start-up approach. This holds promise for the future and gives us an extra boost to start a company founded on years of world class basic research in glyco-engineering by Nico and his team.”

Meuris et al., Nature Biotechnology 2014

Piron et al., Nature Biotechnology 2015

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

PIONEERING WORK IN LONDON BY BELGIAN ‘CANCER ARCHEOLOGIST’

Cancer researcher Peter Van Loo recently visited Belgium to accept the 2017 VIB Alumni Award. From his base at the prestigious Francis Crick Institute in London, Van Loo is mapping the history of tumors using mathematical algorithms and computers. “Pure, fundamental research with few concrete applications,” is how he describes it. This is actually false modesty: dozens of labs all around the world use his computer programs, and he has already turned the cancer research world upside-down a few times as a molecular archeologist.

“Changes to DNA are the key elements in the origin and development of cancer. New technologies have been available for the last ten years, including next-generation sequencing, to track these changes,” says Peter Van Loo, “it’s because they produce such an unbelievable tsunami of fragmented data that you need computers and mathematics to assemble and interpret this data.”

ENGINEER-ENGINEER

This was right up Peter Van Loo’s alley, who combined studies in civil engineering and bioengineering at the University of Leuven. He did his PhD in the group of Peter Marynen (VIB-KU Leuven), at the interphase between biomedicine and bioinformatics. “The period at Peter Marynen’s lab has shaped me as a researcher. It has giving me a critical way of thinking that has been invaluable throughout my career,” Peter says. During a short postdoctoral period at the Institute for Cancer Research in Oslo in 2008, he developed a mathematical application - ASCAT. Today, this is used by hundreds of researchers around the world, and it was crucial in the discovery of countless genes that, in mutated form, drive the formation and growth of tumors.

VIB ALUMNI AWARD

“I HAVE VERY FOND MEMORIES OF THE TIME I SPENT AT VIB”.

HISTORY OF CANCER GENOMES

From Oslo, he returned briefly to the Peter Marynen group and, in 2010, headed to the Wellcome Trust Sanger Institute in Cambridge (UK), the European DNA-sequencing Mecca. It was here that he specialized in cancer archeology, initially of breast-cancer tumors and later prostate tumors and other cancers.

“There is a significant variation in mutations between cells in the same tumor,” says Van Loo. “This variability carries the mutation and growth history of the tumor. By reconstructing that history, you obtain a dynamic picture of the tumor evolution and the molecular mechanisms that drive tumor growth.”

PROSTATE TUMORS

“It seems that in patients with so-called multifocal prostate tumors, multiple tumors develop independently of each other. How that happens is still a mystery. Does the patient have a particular genetic makeup that stimulates this effect? Is it an epigenetic effect? Are there environmental factors that have had impacts? At the moment, we do not know.”

These findings have immediate implications for the treatment of multifocal prostate cancers: as the genetic background of the tumors is varied, it does not make sense to treat the patient with a ‘personalized’ therapy targeting just one of these tumors.

PROSTATE METASTASES

In a second study, he investigated the origins of lethal prostate metastases. He made a surprising discovery here as well: “Some metastases have originated from at least two different metastatic tumor cells. The hypothesis until then was that metastases were formed by a single splitting. It is now apparent that cells from various tumors can be located in the same place. They may work together and obtain an evolutionary growth advantage from this. But it could also be that this location in the body forms an attractive environment for tumor cells and that multiple tumors have developed here for opportunistic reasons.”

“What will the future bring? Mapping the mutated genome of single tumor cells is a first technological innovation,” says Van Loo. “This will provide us with much more detailed results than the ‘bulk’ sequencing of tumors we have been performing until now.” In a second phase, Van Loo wants to look at how genomic changes can eventually result in changes to the transcriptome, epigenome, proteome, and interactome, because the final basis of cancer will eventually be found in these changes. The genomic studies are only the first step in unraveling cancer.

Source: Artsenkrant

REPORTER ON THE ROAD: KEEP THE CONVERSATION GOING

Liesbeth Aerts

After completing her PhD at VIB, Liesbeth set out to explore new horizons and ended up at UNSW Australia. She writes about her scientific adventures on the other side of the world. Follow Liesbeth on Twitter @Liesbeth_Aerts

NO COMMUNICATION, NO IMPACT

Impact—the magic buzzword we sprinkle all over our grant applications to highlight just how great our science is. The fact that there are one hundred ways of measuring it illustrates that impact is about so much more than which journal you publish in. You may be developing a new technology, paving the way for a new product or treatment, or influencing policy on all kinds of levels. It is also possible you are making a difference on a much smaller scale in the lives of students or patients.

Whichever way you look at it, you always need some form of communication if you hope to make any impact. And as scientists, we communicate every day. Aside from writing papers and presenting data, we talk to our peers, supervisors and students, but also to our friends and families. We apologetically explain to our partners why we need to be in the lab this weekend (again!) and if our paper finally gets accepted, we celebrate it with both the scientists and nonscientists in our life. In other words, we all are science communicators already.

WHAT IS HOLDING YOU BACK?

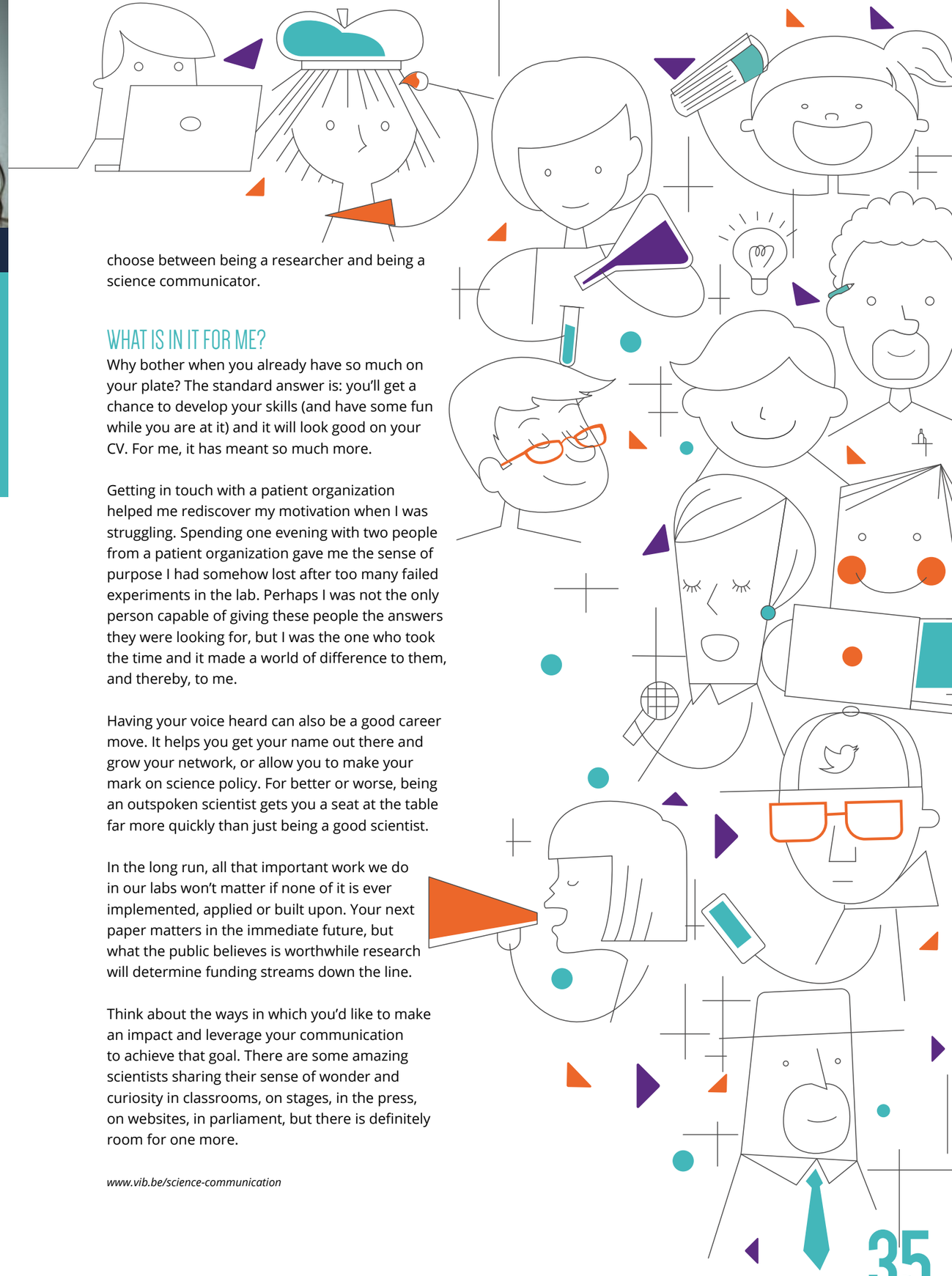
Let me get some misconceptions out of the way. You don't need to be on Twitter to be a science communicator. You don't need to be on TV or in the newspapers, or be funny or entertaining.

The list of possibilities and channels is endless and depending on your style and goal, some may be more appropriate than others.

There are, however, two skills you need: science skills and communication skills. The former are deeply embedded in our training, but the latter we often only get to practice among one particular type of audience: other researchers. To fill this gap in experience, workshops for scientists often focus on how to capture someone's imagination, tell a story, and avoid jargon… While all of this is definitely important, your science skills are equally essential to simplify without lying, to striking a balance between reaching out and overselling.

As with all things in life, you'll get better with every attempt. You can follow one of the many courses and workshops available, but sooner or later you will have to take the plunge by just trying something out. You could compete in Falling Walls, Fame Lab or the PhD cup, or participate in one of VIB's initiatives such as 'Wetenschap op Stap'. There's a long list of options and new initiatives are popping up each year.

If you are worried about what your supervisor or colleagues may think, don't be. Not everyone may be enthusiastic, but that's okay. Your credibility as a scientist is not in danger (there is actual science backing this up). Just remember you don't need to choose between being a researcher and being a science communicator.



WHAT IS IN IT FOR ME?

Why bother when you already have so much on your plate? The standard answer is: you'll get a chance to develop your skills (and have some fun while you are at it) and it will look good on your CV. For me, it has meant so much more.

Getting in touch with a patient organization helped me rediscover my motivation when I was struggling. Spending one evening with two people from a patient organization gave me the sense of purpose I had somehow lost after too many failed experiments in the lab. Perhaps I was not the only person capable of giving these people the answers they were looking for, but I was the one who took the time and it made a world of difference to them, and thereby, to me.

Having your voice heard can also be a good career move. It helps you get your name out there and grow your network, or allow you to make your mark on science policy. For better or worse, being an outspoken scientist gets you a seat at the table far more quickly than just being a good scientist.

In the long run, all that important work we do in our labs won't matter if none of it is ever implemented, applied or built upon. Your next paper matters in the immediate future, but what the public believes is worthwhile research will determine funding streams down the line.

Think about the ways in which you'd like to make an impact and leverage your communication to achieve that goal. There are some amazing scientists sharing their sense of wonder and curiosity in classrooms, on stages, in the press, on websites, in parliament, but there is definitely room for one more.

www.vib.be/science-communication

AWARDS & GRANTS

Scientists at VIB are among the world's leading researchers and are regularly recognized for their vision by renowned institutions across the globe. Following is an overview of VIB colleagues who have recently received awards and/or grants for their excellent science – congratulations to all!

Roos Vandenbroucke

Roos Vandenbroucke, staff scientist at the VIB-UGent Center for Inflammation Research, received the prestigious Grant for Medical Research 2017 for 'neurological diseases', which is provided by the Fonds Baillet Latour. Her Royal Highness Queen Mathilde of Belgium presented the prize on April 20 at the Academy Palace in Brussels.

Bert De Rybel, group leader at the VIB-UGent Center for Plant Systems Biology, is one of the Society for Experimental Biology Gothenburg 2017 President's Medalists. These annual awards go to young scientists of outstanding merit in one of four categories of biological sciences. The 2017 awards will be presented at the Annual Meeting of SEB Gothenburg, which takes place from July 3-6, 2017.

Bert De Rybel

Tony Gutschner and Lena-Christin Conradi

Lena-Christin Conradi, a postdoc in the lab of Peter Carmeliet of the VIB-KU Leuven Center for Cancer Biology, received the first annual UMG research award on January 21 in Göttingen, Germany. The prize, which is given to scientists under 35, consists of EUR 10,000 donated by the Peter Jochimsen Foundation. She shared the prize with Tony Gutschner, a junior professor in Halle, Germany, for basic research excellence in oncology.

Mark Cruts, staff scientist in the Christine Van Broeckhoven lab of the VIB-UAntwerp Center for Molecular Neurology has received a grant of EUR 120,000 from the Queen Elisabeth Medical Foundation (GKSE). The grant will contribute to further research into the genetic defects that lead to frontal lobe dementia and Alzheimer's disease.

Princess Astrid of Belgium, honorary chairman of the Queen Elisabeth Medical Foundation, visited the lab to find out about the research of the entire team.

Christine Van Broeckhoven: "Princess Astrid visiting our labs in person, underlines her support for and interest in our research. It also means a lot for the patients and families suffering from this disease."

Princess Astrid of Belgium, Archduchess of Austria-Este ©Uantwerp

Wim Versées, staff scientist at the VIB-VUB Center for Structural Biology, received a Michael J. Fox Foundation grant. The foundation provides funding for translational and clinical research supporting Parkinson's-related breakthroughs.

Wim Versées

Arne De Roeck

Arne De Roeck, PhD student at the VIB-UAntwerp Center for Molecular Neurology, has been awarded a Rotary 'Hope in head' grant for the amount of EUR 9,000 for his project 'The role of ABCA7 dosage as a cause, modifier, and cure for Alzheimer's disease', promoted by Kristel Sleegers.
Sahana Srinivasan, PhD student at the VIB-UGent Center for Inflammation Research, gave a presentation at the event about the importance of inflammasome activation and regulation in microglia in Alzheimer's disease.

SCIENCE MEETS SOCIETY

At VIB, we take science communication seriously. Facing a growing disconnect between science and society, communicating science has to be more than simply exposing the bare facts. Understanding how to engage people in their research is something that scientists must learn
to do in order to bolster trust and support.

To foster conversation and learning about effective two-way communication between scientists and the public, VIB and Ghent University organized the seminar 'Science meets society – communicating complex issues' on March 18 in Ghent.

Speakers from different backgrounds – scientists, philosophers and journalists – explored the factors that influence public support of science, methods of illustrating complex scientific topics to laypeople, and societal concerns that scientists and science communicators can take into account.

Front row from left to right: Stefaan Derveaux, Michaela Asp, Ida Höijer and Halina Novak
Back row from left to right: Diether Lambrechts and Mark Veugelers

INTERNATIONAL STARS OF NGS GATHERED IN ANTWERP

On March 20-21, 2017, the second edition of the VIB conference 'Revolutionizing Next-Generation Sequencing' took place in Antwerp. About 350 people from academia and industry - of which more than 50% came from abroad - gathered in the renovated Flanders Meeting & Convention Center located in the heart of Antwerp. Top scientists in the field of NGS discussed emerging tools and approaches for large-scale sequencing, applications for current and emerging next-generation sequencing platforms, computational genomics and data analysis and many more.

VIB was honored to welcome 44 speakers, among which were Elizabeth Reczek, CEO of SeqLL (US) - a technology company involved in developing diagnostic tools that guide cancer treatment; Amos Tanay (Weizmann Institute of Science, IL) who opened the conference with a presentation on single cell epigenomics; and Christopher Mason (Well Cornell Medicine, US) with his exciting talk on sequencing in space. Two Swedish scientists won the poster prize: Michaela Asp from Gene Tech, KTH and Ida Höijer from Uppsala University, Rudbeck lab.

www.vibconferences.be

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MARK YOUR CALENDAR

VIBes in Biosciences
September 27-29, 2017 – Ghent

Next-Generation Antibodies and Protein Analysis
October 16-17 – Ghent

Biotech Day
October 22, 2017 – Ghent

Genome Engineering and Synthetic Biology
January 25-26, 2018 – Bruges