GREAT SCIENCE HAS MANY SUPPORTERS
To progress successfully in biomedical research, patients and researchers often need to collaborate actively. To guarantee a constructive relationship between all parties requires mutual respect and a delicate balance between the expectations of all involved parties.

Patients expect both information and scientific results from the scientists who study their disease/condition. Their first strong desire is to know the cause of their disease. Is there a specific DNA or metabolic defect responsible for their conditions? Can a clear diagnosis be made based on the results of research? A second important expectation is: can research into the biological mechanisms (the pathogenesis) of the disease be translated into progress towards a cure or an improved management of the illness?

The researchers who dedicate themselves to answering these questions, however, have their own expectations. To unravel disease mechanisms, they often need access to biological samples; they have to obtain blood or tissue samples with the consent of the patient or his legal representative. Also, in order to progress from results obtained on cell cultures and animal models to a treatment on humans, they will have to organize clinical trials for which they will need patients.

It is clear that both scientists and patients bring their own invaluable experience to the quest of understanding and treating disease. The contribution of both parties should be recognized and built into a partnership which can lead to a modification of the way in which the research will be performed.

That is why ‘Kom op tegen Kanker’, for the evaluation of research projects with practical clinical applications, has set up a separate committee composed of patients and family members. The advice they give is rooted in their experience in having been treated for cancer and highlights practical consequences of the treatments to be developed or tested of which the scientists may not always be fully aware. Together with the scientific committee, an overall advice is formulated in which the patient committee contributes about 30% of the final score of the projects.
This two-committee approach has already proven its value and receives full support from the members of the scientific committee. FWO has decided to use the same approach for the projects pertaining to clinical aspects of treatment in cancer.

Research on diseases, including cancer, requires in many cases a constructive contribution of both scientists and patients. A close partnership between these two parties is essential and creates substantial added value for the quality of the research. Balancing expectations and acknowledging the value of each other’s experience and contribution is essential to develop good science aimed at keeping or making people healthy.

Jean-Jacques Cassiman, Chair of the Board of Kom Op Tegen Kanker, Chair of the Fund Rare Disease and Orphan drugs of the King Baudouin Foundation, emeritus professor Center for Human Genetics of KU Leuven.

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On the cover: the VIB-KU Leuven Center for Cancer Biology team cycling for 1000 km Kom op Tegen Kanker.
Back row from left to right: Jermaine Goveia, Joris Souffreau and Sander Willox.
Front row from left to right: Dries Verdegem, Laure-Anne Teuwen Ann Bouché, Roel Kroes and Lawrence van Helleputte.
FUNDING BASIC RESEARCH – POWERING BREAKTHROUGHS

Science is expensive. New medical treatments or improved therapies are often derived from novel insights in fundamental scientific research. Such research requires state-of-the-art equipment, talented personnel, specialized reagents and, potentially, rigorous safety testing. None of these things is cheap. Researchers therefore depend on external funding to finance their research programs and research team to tackle some of the greatest challenges we face.

Fortunately, many funding agencies, patient organizations, and investor groups recognize this reality and generously support scientists working on issues close to the societal challenges they are focusing on. Scientific breakthroughs in medicine, agriculture, and many other fields are often the direct result of the investment of external funders and donors in excellent research teams.

Funding research, or funding researchers?
The scientific ecosystem is complex. Add to that that, from time to time, major new insights arise through serendipity, and it’s easy to see that funding decisions are no walk in the park. Individual researchers can work on different projects simultaneously, research programs of different group leaders can intersect, and unexpected discoveries can shift the direction of entire fields.
So, who, or what, should be funded in order to yield maximum benefits? This is a question organizations and funding agencies must answer each time they decide to invest in scientific research. And the answer is elusive and ever-changing.

Grants are often tied to specific research projects or individual researchers, but scientists tend to work on different aspects of a topic, or on several topics at once. Furthermore, modern science thrives through collaboration, with each of the collaborators possibly funded by another source. Similarly, research programs can investigate different facets of a research avenue and involve various investigators. As such, exactly pinpointing where the money will go is a fool's errand. Perhaps the best option is to build flexibility into the financing programs with regards to the expenditure as long as the original goal remains the envisioned outcome.

Credit where credit is due
The funders are not the only ones facing a daunting question of impressive complexity. The funded scientists themselves must deal with a difficult question of their own: when and how to acknowledge the generosity that made their work possible?

In large collaborations, must every collaborator mention his or her funding sources, even when none of the funding was used in this particular project? What if the project followed from earlier work that was supported by a specific grant, but that specific grant was not used in the current project? What if a PhD student contributes to a project that is not officially part of her or his PhD (as is often the case in scientific research)? Mention the PhD funding source? Or the source of the project's funding? Or both? And what if the success of a research program depends not only on many collaborators, but also on many funding sources? Which one should be acknowledged first? Should all of them be acknowledged all the time, even though perhaps some funding is used for only part of the overarching program?

It is, as is hopefully clear by now, a path to be trod carefully.

Of course, funders should be acknowledged. That much is certain and obvious. It is the how and the when that is not obvious. Can a broader view be useful?

Funding science and progress
Science does not progress linearly. It is a large undertaking. Seemingly obvious routes ahead can hit invisible roadblocks and negative results can open up new paths forward.

Funding, at its best, facilitates breakthroughs by allowing top talent and cutting-edge technology to meet. The results of such encounters are what powers breakthroughs and generates impact. Maybe, then, the potential outcome ought to be the most relevant aspect of funding decisions rather than the details of how, when, and on whom the money is spent?

Given the enormous complexity of the current scientific endeavor, taking a step back to discern a broader picture can be beneficial to funders, scientists, and other stakeholders. Funders and donors should engage with the researcher in a culture of trust rather than in a culture dominated by accountancy, resting assured that their generous gifts are well-spent, even more so since many research institutes – VIB included – invest heavily in evaluation, research management processes and HR in order to attract the most talented and driven individuals.

It is understandable that funding agencies and organizations want to invest in specific topics that are most of interest to them. But, as any life scientist will tell you, in biology there are no clear-cut, perfectly defined research questions and answers. Many things are connected at both microscopic and macroscopic scales and will change throughout the course of the research, with the only goal: to reach the envisaged results and beyond.

Scientists can define a general direction they would like to pursue but can – and perhaps should? – forego overly strict adherence to specific, narrow research plans if this would cause them to neglect fruitful opportunities to push the boundaries of knowledge. The key to a mutually beneficial funding arrangement is sharing a vision where scientific progress positively impacts society and lessens the burden of disease, hunger, and poverty. When both funders and scientists work towards this vision, every cent will be well-spent.
Yamina Krossa, a hero of many
Yamina Krossa donated the remaining amount of money of her non-profit organization Benetiet vzw to the breast cancer research of Damya Laoui (VIB Center for Inflammation Research, VUB) who is working on a possible cancer vaccination to prevent relapse. The VUB Foundation and the VUB Vice-rector of Innovation and Valorization Hugo Thienpont were moved by Yamina’s story and proposed to set up a Fund named after her. The first beneficiary of this Fund would be Damya and her team.

Yamina, proud and grateful, considers it a privilege to be able to contribute to the groundbreaking research of Laoui: “Damya once told me how expensive it was to run her lab and that on top of that, she spends up to half of her time on searching for funds and grants. I then took on the challenge to raise funds to support her research.”

Big players – Chan Zuckerberg Initiative and Michael J. Fox Foundation
The Chan Zuckerberg Initiative (CZI), the philanthropic endeavor led by Facebook’s Mark Zuckerberg and his partner Priscilla Chan, is an initiative that seeks to fund innovative scientific projects across the world via thematic calls. VIB is one of the institutes that managed to attract its attention.

One of the supported projects brings together scientists with broad and complementary expertise to generate a comprehensive cell atlas of the human thymus across development and aging, with Yvan Saeyes (VIB-UGent Center for Inflammation Research) and Tom Taghon (Ghent University) as major contributors.

Yvan: “For this specific call, large consortia are definitely the best option, with a clear focus on complementarity and proven expertise of the different partners. These are big projects and no lab would be able to do it on his own. CZI focusses on interdisciplinary projects to increase the impact of the supported work.”

Tom: “One of the great things of CZI grants is that you get exposed to a lot of excellent scientists from different disciplines because networking and sharing of resources is really stimulated by CZI. As a scientist, it provides lots of inspiration for novel ideas and opportunities to use novel technologies for your own research.”

Patrik Verstreken (VIB-KU Leuven Center for Brain & Disease Research) leads another CZI project, alongside clinical expert Wim Vandenbergh (UZ Leuven) and neuro-engineer Dries Braeken (imec). The team plans to create a new chip to study the mechanisms of Parkinson’s disease.

Patrik: “Of course I was pleased to receive the email that confirmed we got the grant. But at that moment I didn’t have an idea of the impact CZI has, besides the financial value of the grant. The Chan-Zuckerberg Initiative is well known and, since the number of grantees is much more

SNAPSHOT OF OUR FOUNDATIONAL FUNDING
Funding for scientific research is not easy to come by. At the same time, many foundations generously pledge significant amounts to scientists and research programs they believe can further their cause. Below is a snapshot of foundational funding for VIB research.
limited than that of let us say ERC grantees, it gives you extra exposure. This grant really opens doors, we have been quite successful in raising funds in the US, not evident for a European research team.”

VIB’s Wim Versées (VIB-VUB Center for Structural Biology) received several grants from The Michael J. Fox Foundation for Parkinson’s Research (MJFF) to use Nanobodies® to characterize potential drug targets for the disease.

Wim: “I was of course delighted when I received the news. Funding by MJFF implies more than just the financial support that allows you to conduct the research you love. It is also a recognition that your research is relevant for society and for patients. MJFF’s support is key for the further translation of our findings into potential novel therapies for Parkinson’s.”

**Generous patrons – Opening the Future and Mission Lucidity**

KU Leuven started Opening the Future in 2013 as a campaign to gather patrons seeking to support research into neurodegenerative diseases. Unique in Flanders, it gathered around 40 generous families whose support, vision, and trust solidified the initiative.

After this auspicious beginning, Opening the Future has built a unique community of patrons of science with outstanding local and international results. An example of this is Mission Lucidity, a collaboration between VIB, UZ Leuven, KU Leuven, and imec that seeks to decode dementia.

Through Opening the Future, scientists and patrons join each other in a journey towards an improved quality of life for everyone through societally impactful projects. The campaign will continue to support research into neurodegenerative conditions while branching out to oncological research. Opening the Future already supported VIB-KU Leuven researchers Bart De Strooper, Patrik Verstreken, Ludo Van Den Bosch, Philip Van Damme and Peter Carmeliet. With the new campaign others may follow in the future.

**The Dutch Lung Foundation**

As a Dutch health organization, medical research charity and patients’ association, the Dutch Lung Foundation (Longfonds) is focused on finding solutions for chronic lung diseases, especially for COPD (Chronic obstructive pulmonary disease) and asthma. To accelerate a medical breakthrough in lung research, Longfonds launched an international collaboration of top scientists under the name of LONGFONDS | Accelerate. (for more information: longfonds.accelerate.nl)

The Dutch Lung Foundation consulted experts in the field of lung research and asked which pioneers should be involved. This led to the launch of the consortium on Asthma Prevention, involving Bart Lambrecht and Hamida Hammad (VIB-Ugent Center for Inflammation Research), and groups from the United Kingdom, Germany, the Netherlands and Australia.

**Together against Dystonia**

At the turn of the century, fashion designer Lieve Van Gorp and art director Greet Ruelens were managing a successful fashion label out of their hometowns Antwerp (Belgium) and Paris (France). When Greet learned she had dystonia after a 4-year long search for a diagnosis, the designer duo established the Foundation for Dystonia Research (FDR) in 2009. The aim of the Foundation is to promote scientific research into the biological mechanisms driving dystonia. “After all, fundamental research is the starting point in our endeavor to find a better treatment and, hopefully, a cure”, says Greet Ruelens, who is still seeking an optimal treatment to improve her quality of life.

When FDR was established, Dystonia research was still non-existent in Belgium. To remedy this situation, the Foundation decided to substantially invest in a Dystonia research group together with VIB and KU Leuven. Via an international call Rose Goodchild was attracted to join the VIB-KU Leuven Center for Brain & Disease Research and pursue her Dystonia research as part of the VIB community.
"The Charcot Research Fund allows us to test the broader impact of our basic research on different autoimmune diseases, in this case MS."

Rudi Beyaert (VIB-UGent Center for Inflammation Research)

**RESOURCES VIA CHARITY AND FOUNDATIONS**

<table>
<thead>
<tr>
<th>Year</th>
<th>2014-2019</th>
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<tbody>
<tr>
<td>3%</td>
<td>INFLAMMATION, INFECTION &amp; MICROBIOLOGY</td>
</tr>
<tr>
<td>43%</td>
<td>CANCER</td>
</tr>
<tr>
<td>49%</td>
<td>NEURO</td>
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**DID YOU KNOW...**

- that the King Baudouin Foundation regularly organizes multistakeholder dialogues to set priorities for different purposes? This is a very strong tool to involve people and to identify unmet needs.
- that all parties involved - patients, scientists and companies - are striving for evidence-based medicine? Because this is the only way we can really defeat diseases.
- that investing from the start in basic research often leads to tangible results? It may take a while, though, and funding is scarce to build the bridge from such research to validated assets in which industry can invest. The Fournier-Majoie Foundation has invested to help build such a bridge from a research project of Nico Callewaert (VIB-UGent Center for Medical Bio technology), that has resulted in a diagnostic kit for liver diseases. More on page 39.
- that mentioning your funders when communicating about your research can have a lot of effect? By doing so you express your gratitude and show the community who helped in making your research possible. It can be very simple, for instance by tagging your funders in a social media post.

Great science has many supporters
LOCAL PLAYERS ARE GREAT SUPPORTERS

While big international funding initiatives might be the most eye-catching science funding sources, local foundations often play an equally pivotal role. They are often more in touch with the local scientific landscape and patients. VIB research would not be where it is now without their support. Here you can find a small sample of generous givers and their interactions with VIB researchers.

**Stichting Alzheimer Onderzoek**
*(Foundation Alzheimer’s Research)*

For World Alzheimer’s day (September 21st), SAO organizes an annual cupcake sale during the entire month of September. Since 2016, the VIB-KU Leuven Center for Brain & Disease Research actively participates in the sale (and consumption) of cupcakes. With the money, raised in the most delicious way, *Stichting Alzheimer Onderzoek* can support Alzheimer research throughout Belgium by awarding grants to promising researchers.

**1000 km Kom op Tegen Kanker**

For the past three years, VIB has been represented by several teams in the 1000 kilometers of Kom op Tegen Kanker. This annual 1000 km cycling challenge for teams of volunteers is organized to raise funds for cancer research. Each year, the VIB cyclists and their colleagues have set up various fundraising actions to sponsor their trip. The most remarkable one was organized by the VIB-KU Leuven Center for Cancer Biology: a charity concert with the winner of the International Queen Elisabeth Piano Competition 2016, Lukáš Vondráček. Jean-Jacques Cassiman, professor of human genetics and chairman of ‘Kom op Tegen Kanker’ hosted the evening. Members of the center also participate in the annual flower sale to support the charity. In addition to the fundraising activities, Kom op Tegen Kanker organizes lab visits.

**Stichting tegen Kanker**
*(The Belgian Foundation against Cancer)*

*Stichting tegen Kanker* is an important national funder for cancer research. Its donors often visit the labs whose research their donations support. Many of the donors are (former) patients. Their visits allow the scientists to show them the latest research, while the donors can talk to the scientists about the realities of living, or having lived with, cancer.

**Vlaamse Parkinson Liga**
*(Parkinson Liga)*

*Vlaamse Parkinson Liga* often receives donations which it funnels into research funding. One of the beneficiaries is VIB’s top research into neurodegenerative conditions. The interaction between patients and VIB researchers is something that is actively pursued and leads to an increased mutual understanding of living with Parkinson as well as the scientific work being done. This leads to both an enduring motivation for the researchers and hope for the patients.

**ALS Liga**

Following the success of the ‘cool’ ice bucket challenge, the *ALS Liga* organized the ‘hot’ pepper challenge last year. The Ludo Van Den Bosch group (VIB-KU Leuven Center for Brain & Disease Research) confidently took on the challenge together with several actors on the set of the soap Thuis. They made it onto national television.
Enter reversed science cafés
Reversed science cafés are a relatively new format of interaction that focuses on the discussion of societal and ethical but also potential impact aspects of the latest scientific work or novel technologies. Both the general public and expert scientists participate in these events. The dialogue begins with questions or statements the experts have prepared for their audience. The answers often provide new insights for the scientists and fertile grounds for further enquiry and research.

During these events usually a methodology is followed whereby the dialogue is executed in small rotating groups, each of which tackles a specific set of questions, as presented by the expert and supported by a moderator and reporter. The key thing is that no one is talking to someone, but that the participants are talking with each other.

Scientists can update the audience on the state of their research and what they’re currently working on, unhindered by paywall barriers or jargon-laden papers. The audience, commonly including patients or citizens if the topic at hand involves research into one or more diseases or societal challenge, can relate their experiences directly to the people working on potential treatment options or assistive technologies or solutions. Real-life testimonies are invaluable for scientists and clinicians and other experts who seek to attain maximal impact with their research. Such first-hand accounts can reveal neglected problems or areas that might warrant further attention. This way, scientists and clinicians learn new things too, even about the topic they are specialized in.

For science to have maximum societal impact, the specific knowhow and experiences from different stakeholders, including patients and citizens besides researchers, academia, clinicians, industry, funders, government, should be better valued, from research priority setting, over discerning research goals, to translating the results into potentially wide-ranging benefits for society. In other words, a multi-stakeholder dialogue reinforces impact. Still today this societal outreach is too often limited to one-way information monologues ex cathedra by researchers or academics, with limited room for interaction, let alone consultation.

Great science has many supporters
Reversed science cafés leave the general public with an improved understanding of the current state of the research into a specific topic. The participating experts are pulled away from their real or metaphorical microscopes and get a close-up of the social, ethical, and patient-related aspects of their work that may not always get the attention they deserve.

Win win.

A real-life example: VIB's Grand Challenges PID event
On March 17, 2019 researchers and clinicians involved in the PID Grand Challenge Project welcomed 115 patients and their families at the VIB-UGent FSVM Research building for an interactive morning program. The event was co-organized with Bubble ID, a PID fund from CPIG, the Centre for Primary Immunodeficiencies Ghent that wants to burst the bubble of isolation that surrounds both the condition and the patients.

Beyond scientific proceedings in PID, lab tours, and kids only workshops (got to keep them busy, no?), the event also included a reversed science café.

The participants were divided into groups of about 8 persons each, including teenager or adult PID patients, parents and grandparents. An expert clinician or researcher explained the question or statement and another researcher or patient representative acted as moderator to ensure a productive conversation. After a while the participants of the groups moved to another table with different experts. This way, many aspects of PID could be discussed. This was followed by a roundtable discussion to formulate general conclusive remarks.

Experience of participating in reversed science café:
“As a researcher I have been studying the underlying mechanisms of PID for years, learning from patients and their family how they ‘live’ the disease and what their needs are was most encouraging to continue and guide our research.” - Researcher

“Learning about the current R&D is most interesting to us, being consulted during the reversed science café empowers us and that is most reassuring.” - Grandparent of young PID patient

“Being able to enter into a dialogue with patients in another setting, together with basic scientists creates an atmosphere of trust, a true added value.” - Clinician
Kim Plasman, on the other side of research funding

Kim Plasman

VIB alumna Kim Plasman is scientific director at the Stichting Alzheimer Onderzoek. Between 2008 and 2015, she worked at VIB-UGent Department of Medical Protein Research (now the VIB-UGent Center for Medical Biotechnology). Under the supervision of Kris Gevaert and Petra Van Damme she studied the substrate specificities of granzymes, a class of serine proteases that induce apoptosis. She traded the academy for industry by becoming application scientist at the Ghent-based life science company Trinean. When Unchained Labs acquired Trinean, she became marketing application scientist. Since May 2018, she combines her scientific and marketing expertise at Stichting Alzheimer Onderzoek.

What kind of an organization is 'Stichting Alzheimer Onderzoek'?

Stichting Alzheimer Onderzoek is a national, Belgian non-profit organization founded in 1995. The aim of the organization is to promote scientific research into Alzheimer’s disease and related neurological disorders. We provide financial support for basic and clinical research. The focus is on the causes, possible new treatments and ways to prevent dementia. We raise funds from the general population. This can range from small amounts – just a few euros - to large donations through legacies. The Belgian Ministry of Finance has recognized our organization.

We also receive funds from organized activities. For example, in September we try to encourage as many people and companies as possible to bake and sell cupcakes and muffins for World Alzheimer’s Day (September 21). Also in the context of the ‘Warmste Week’ people organize all kinds of activities for the
benefit of Alzheimer’s research supported by Stichting Alzheimer Onderzoek. Furthermore, we have a close collaboration with the King Baudouin Foundation, which trusts that Stichting Alzheimer Onderzoek selects only the most innovative, promising research and thus KBF sponsors some of our projects through their funds.

What is the impact of the foundation?
Every year the foundation launches a call for research projects and scholarships. The ‘standard grants’ are intended for established researchers. Until last year they could apply for a grant of up to 150,000 euros for 2 years. From this year on, this will be up to 225,000 euros for 3 years.

In addition, we are convinced that we should also support promising young researchers. They can submit pilot projects of up to 75,000 euros for 2 years.

The last ten years, we are on a clear growth path. In 2018 we were able to select 20 research projects for a total amount of 2,450,000 euros. That was nearly one million more than the year before. Also for the 2019 applications, we will be able to raise our funding power. In short, over a period of 20 years, we have spent over 14 million euro on 160 research projects.

Many VIB groups have benefitted from donations to the Stichting Alzheimer Onderzoek. In the past three rounds, 13 out of 32 standard grants and 9 out of 12 pilot projects were awarded to VIB labs.

Raising and spending money is one thing, how do you select the most promising projects?
Our Scientific Advisory Board of 7 Belgian scientists, all highly experienced in Alzheimer’s research and chaired by Wim Annaert (VIB-KU Leuven Center for Brain & Disease Research), advises the Board of Directors on the applications to fund. Each application goes through a strict selection procedure based on quality and relevance, including a review by external referees. The Scientific Advisory Board makes the final ranking. Procedures like these guarantee our donors that only the best research projects are financed.

Despite your success in raising funds, how do you counter the growing skepticism about dementia research? In the late 1980’s, bright people claimed that they would crack Alzheimer’s disease before the turn of the century, 30 years later we seem to be nowhere when it comes to medicines that cure the disease. In those 30 years, we have learned a great deal about the disease, mainly thanks to research funding from many different sources. Alzheimer’s turns out to be much more complex than we thought at the time. The disease starts 15 to 20 years before the first symptoms appear. So we need to intervene much earlier, essentially in people who are still healthy. Moreover, we realize now that dementia is a multifactorial disorder. The biology of APP and tau is only one factor. Obesity, high blood pressure, depression, and social contacts are also factors that tilt the balance in our brains towards dementia. All this has come to light in recent years.

How important is it for your organization to bring donors in contact with researchers?
We are committed to reach out to our sponsors. We inform them in various ways. There is our bimonthly newsletter with a spotlight on research results. This newsletter also includes information about the risks of dementia, healthy nutrition, lifestyle, prevention, treatment etc. Besides the newsletter, we have published brochures and leaflets on how to live with dementia, we organize lectures and performances about Alzheimer’s disease and together with students from the Ritcs and the King Baudouin Foundation we produced a short film with a surprising view on dementia, through the eyes of young people.

Stichting Alzheimer Onderzoek has only funded research projects from individual research groups at Belgian universities and research centers. Is there no willingness to fund international or to focus on collaborative projects?
According to our statutes as a Belgian public utility foundation and because of the authorization to deliver tax certificates we can only fund Belgian research programs. We cannot finance foreign researchers, unless they work at a Belgian university. Therefore, the collected funds must stay in Belgium otherwise we will lose our tax redemption status. Of course, biomedical research, especially in a complex disease like dementia, is no longer a one-man or one-woman enterprise. Collaboration is key to success. Therefore, I do not exclude that we will, at some point, evolve towards sponsoring international and/or collaborative research. For that, we will have to align our efforts with funding organizations in other countries. We are establishing contacts with partner organizations abroad to pave the way for a more collaborative future.
**Understanding Charcot-Marie-Tooth Disease**

Charcot-Marie-Tooth disease (CMT) is a condition that affects the peripheral nervous system. It leads to progressive muscle weakness and loss of sensation in the lower and later on upper limbs. It is the most commonly inheritable neuromuscular disorder and, at the moment, remains incurable. CMT is very heterogeneous and the first symptoms can appear both in early childhood or during adult life. Its heterogeneity makes it a difficult condition to study and find treatment for.

Now, the Albena Jordanova group from the VIB-UAntwerp Center for Molecular Neurology has taken another stride forward in understanding the disease. The researchers used fly models of CMT to uncover new aspects of the disease. We spoke to Albena and Sven Bervoets, the first author of the paper which appeared in *Nature Communications*.

**Where did the idea for this research come from?**

Albena: “The idea dates back to 2009 and to my first PhD student here in Antwerp (Ricardo Goncalves). We began unravelling the role of aminoacyl-tRNA synthetases in neurodegeneration. At that time, we had just created the *Drosophila* model of CMT, the first ever fly model of peripheral neuropathies. Back then we were scanning all old reports about tRNA synthetases and spotted two orphan papers describing their detection in the nucleus. Unexpectedly, we were contacted by our collaborators from the Yang lab at the Scripps Research Institute who had mapped the nuclear localization sequence of tRNA synthetases and asked us whether we would be interested in studying it further. Over the years we nurtured a very fruitful collaboration that yielded ground-breaking findings.”

**Is there a specific person who encouraged or inspired you to pursue this question?**

Sven: “During my master thesis, performed at the lab of Albena, I already knew I wanted to do a PhD, but I wasn’t sure yet on the topic. The afternoon after I had defended my thesis, I was at a conference on CMT in Antwerp. Here, I met our collaborators from the Scripps research institute for the first time. We started talking about a project they were working on regarding the nuclear function of tRNA synthetases in CMT. Hearing all the preliminary data made me realize that this would be a very innovative research topic. I was hooked immediately.”

**At which moment did you realize that this work was going to be so significant?**

Sven: “Despite the promising preliminary data, the start of the project was pretty rough as we had to start from scratch and re-generate the proper fly lines. Once the phenotyping of the flies started and we noticed the prevention of the disease phenotypes, we knew we were on the right track. A second realization came once we were able to exclude the protein from the nucleus upon feeding the flies with embelin. Pharmaceutical treatment of our CMT *Drosophila* model resulted in the prevention of the disease phenotypes, which could have great implications for CMT patients.

“But the molecular mechanisms leading to the disease remain to be elucidated. As a result, no cure exists so far. First, we will have to investigate the nuclear involvement of all the remaining aminoacyl-tRNA synthetases involved in CMT. Next, while the interaction of tyrosyl-tRNA synthetase with one transcription factor has been described, it is unclear which other transcription factors are important. We have to identify all the interacting partners of these synthetases. Only when these research questions have been addressed, we can start thinking about a unified therapeutic approach.”
Albena: “The fundamental message from our work is that components of translational machinery can function as transcriptional regulators in the nucleus. We demonstrate for the first time that their extranational role has pathological implications and can cause a neurodegenerative disease in humans. This new concept could help to find a cure for CMT as well as other neurodegenerative disorders. I want to see the patients who donated their biomaterials and provided moral support for our studies being cured. Hopefully, my dream comes true!”

How did the collaboration with others improve the scientific research?
Albena: “With the Scripps Research Institute, we were able to combine two areas of expertise (molecular biology and disease modeling) into one coherent story. Besides this international collaboration we capitalized on the expertise of two staff scientists in our Center - Bob Asselbergh (microscopy) and Ligia Mateiu (bioinformatics). They became an organic part of the team and enhanced our ability to look critically at the research question from different perspectives. Overall, the success of this work relies on the collaboration efforts where you can maximize people’s skills to advance the research.”

What were the major challenges to overcome?
Albena: “The initial tools and results were not good enough. Sven’s first year of studies was very daunting and the experiments failed frequently. But success consists of going from failure to failure without loss of enthusiasm. The same is true for our struggle with the editors of several candidate journals. Although unpleasant, this experience was very rewarding and inspiring. It helped us to emphasize the true value of our findings and strengthen the evidence for our provocative hypothesis.”

What was the most pleasant aspect of the entire process from study design to publication?
Sven: “Assembling the figures with all the data that you have acquired over the years. You finally start to see the bigger picture and think about the flow of your story.”

Bervoets, Wei et al., Nature Communications 2019
A CRISPR KNOCKOUT

Knocking out genes is a great way to learn what they do. After all, if you prevent a gene from doing its job and you notice changes, it’s very likely the gene has something to do with it. There is a caveat, though. Mutations in genes that are required for basic cellular functions and/or reproduction often interfere with the generation of homozygous mutant plants, precluding further functional studies. Additionally, some genes have different functions in different parts of a plant, so the effect of a gene in one part could mask the effect elsewhere.

Now, a team from the VIB-UGent Center for Plant Systems Biology, led by Thomas Jacobs, Moritz Nowack, and Tom Beeckman devised a CRISPR-based tissue-specific knockout system, CRISPR-TSKO, that enables the generation of somatic mutations in particular plant cell types, tissues, and organs. The efficiency of CRISPR-TSKO opens new avenues to discover and analyze gene functions in spatial and temporal contexts of plant life while avoiding pleiotropic effects of system-wide loss of gene function. The work was published in Plant Cell.

We asked Thomas and Ward Decaestecker (one of the first authors of the study and working in the Thomas Jacobs lab) a couple of questions about the breakthrough.

As a child, could you have imagined doing something like this?
Ward: “One of my all-time favorite movies is the first Jurassic Park movie from Steven Spielberg. In this movie they recreated dinosaurs from some DNA found in a fossil mosquito. I always imaged it would be a fantastic job working for InGen, the fictional company in the movie. In the latest movies they even started to genetically engineer dinosaurs. The CRISPR technology would be an excellent technology to do this engineering. In our publication we used this technology to engineer Arabidopsis, a small model plant that is actually a weed. Applying CRISPR to edit the DNA of a weed is exciting, but probably not as exciting as engineering a dinosaur.”

Where did the idea for this research come from?
Thomas: “Rafael (co-first author working in the group of Moritz Nowack) is always stopping me in the hallway to ask hypothetical questions on ways to use CRISPR for developmental biology. One day he asked about making tissue-specific knockouts so that they could study knockouts specifically in their model system, the lateral root cap of Arabidopsis. I didn't think it was going to work as we often observe chimeric mutations using constitutive promoters and I thought the same would happen with tissue-specific promoters. That is, some cells in the tissue would be knocked out, but others would still contain the intact gene and be expressing it just fine. Nevertheless, I offered to help and got him in contact with Ward.

Ward generated the initial constructs for Rafael to check in plants. And after the first proof-of-concept experiment we immediately saw that this was going to work. A number of individual lines were completely knocked out for GFP expression only in the lateral root cap.”

In a hypothetical world where funding and time are not an issue, how would you like to follow up this work?
Thomas: “We would develop a larger collection of tissue-specific promoters and test these with numerous genes that are essential for plant growth and development that cannot be investigated otherwise. It is really challenging to work with essential genes, and I think this system can be used to challenge some long-held theories on the function of certain ones.”
What was the most pleasant aspect of the entire process from study design to publication?

Ward: “The teamwork. We had a lot of meetings to coordinate the research, writing and revisions. Everyone put in a ton of effort and together we got the job done.”

Thomas: “Indeed, collaboration was key in this project. My group and Moritz’s were collaborating from the start and were perfectly complementary. We were able to make the vectors rapidly and evaluate the DNA mutations. Moritz’s group was able to evaluate the phenotypes. As we wanted to expand the biological significance of the project, we wanted to target additional tissue types and genes. For this we asked Tom Beeckman’s group whether they would like to join as they work on root development. Nick in his group suggested targeting YDA in the stomata which led to a spectacular phenotype. We then needed to determine if DNA mutations were actually occurring in these specific tissues. In some cases, this was technically challenging as only a few cells, 5-10% or fewer, of the entire plant were actually targeted. For this we needed the help of Gert Van Isterdael at the VIB Flow Core. After sorting the cells from thousands of seedlings, we were able to clearly show we had specific DNA mutations. A great example of what excellent teamwork can accomplish.”

Decaestecker, Andrade Buono, et al., Plant Cell 2019
HUMAN CELLS IN MOUSE BRAINS

It’s not easy to study human brain disease in animal models. Humans tend to take pride in the fact that we consider our brains unique, so studying them in other animals is a challenge. Nevertheless, animal models are an essential part of our quest for knowledge and a path towards a cure. But what if we can make animal models look more like us?

That’s exactly the breakthrough two groups for the VIB-KU Leuven Center for Brain & Disease Research have accomplished. The group of Bart De Strooper was able to transplant human microglia into mice brains to study Alzheimer’s disease and the groups of Pierre Vanderhaeghen and Vincent Bonin (NERF, empowered by imec, KU Leuven and VIB) showed how human cortical neurons integrated into the mouse visual circuits. Their work appeared in *Nature Communications* and *Neuron*, respectively. We spoke to some of the researchers.

First, Renzo Mancuso, postdoc in the De Strooper lab talks to us about the work behind transplanting human microglia into mice brains.

Where did the idea for this research come from?
Renzo: “This idea came from multiple meetings Bart and I had when I was working with Hugh Perry in the UK and Bart wanted to explore the role of microglia in AD, so we decided to combine our efforts.”

Did you have to learn new approaches to successfully do this study?
Renzo: “It was very exciting because we were setting up multiple things in the lab at the same time we were working on this manuscript. We did not have experience with iPSC/ESC microglia in the lab, there was no certainty that cells were able to graft and integrate in the mouse brain. So long story short, yes, I think we learnt a lot along the whole process.”

At which moment did you realize that this work was going to be so significant?
Renzo: “By January 2018, when we got the first picture of human microglia in the mouse brain. It was when we realized this was actually working out. I think the major challenge was to work in a research context never explored before. The bright side is that you get to see some scientific findings for the first time ever, but that also means you are constantly adapting a troubleshooting along the away.”

How did the collaboration with others improve the scientific research?
Renzo: “Collaboration did not only improve the research outcome, but it made it possible! None of this would have been possible without the contribution of multiple teams and researchers. The VIB Core Facilities were also very important as most of the experiments we performed were complex and required flow cytometry and single cell RNA sequencing. We wouldn't have been able to produce this piece of research without FACS, Single Cell and Nucleomics cores.”

Where do you personally think the next breakthrough lies in this field?
Renzo: “We are right now seeing how the Alzheimer’s disease field is changing, mostly due to the discovery of multiple genetic factors that determine the risk of developing the disease. I am optimistic about the future and believe that the talent and hard work from all researchers in the field will lead to fundamental discoveries on the basis of Alzheimer’s and novel therapeutic approaches in the coming years.”

What was the most pleasant aspect of the entire process from study design to publication? Any lessons you’d like to share?
Renzo: “I think the study design and execution are the most pleasant aspects of any study, but specially the excitement of being the first person in the world seeing a particular new piece of data. This work has also taught me to work hard and smart. If you give yourself room to read, think and analyse the outcome, whatever goal you pursue will be better.”

Next up, we have Pierre Vanderhaeghen and Vincent Bonin, joined by Daniele Linaro and Ben Vermaercke, both postdocs in Pierre’s lab. Here are some of their thoughts on their collaboration investigating the integration of human cortical neurons into mice visual circuits.
Did this study build on previous work by your labs?
Pierre: “In 2013 we reported how to differentiate human pluripotent stem cells into cortical neurons and showed that they could integrate into the mouse brain following xenotransplantation. However, the neurons remained mostly isolated from the mouse brain, which triggered this study, where we developed novel methods to transplant human neurons as single cells within mice brains, followed by their study with unprecedented depth and resolution.”
Vincent: “Pierre’s lab had shown light responses in visual cortex in a different transplantation procedure. We thought, wouldn’t it be cool if we showed you how the human neurons in the living mouse brain develop and start taking on new functions?”

Did you have to master new techniques or overcome technical challenges?
Pierre: “This was a risky project, because it was quite possible that these neurons were not connected appropriately within the circuits. Our lab alone was not able to technically tackle this fascinating, but challenging question. This is when we started a fantastic collaboration with the lab of Vincent at NERF, who studies cortical circuits using top notch \textit{in vivo} imaging technologies. Our two labs then worked together closely to image the function of human neurons at the single cell resolution, following visual stimulation of the awake transplanted mice.

Daniele: “My background is in electrophysiology, so most of the topics and techniques of this project were new to me. This was challenging, at least at the beginning, but at the same time it substantially increased my knowledge in several fields, which is certainly one of the greatest advantages in working on such an inter-disciplinary project. On the technical side, the major challenge was certainly having good quality transplantations of human cells into the mouse brain. On the non-technical side, one of the more challenging aspects was having people with very different backgrounds working together towards a common goal. Of course, in the end this proved to be also one of the most rewarding aspects, because everybody on the team learned a lot of new exciting things.”

Ben: “From an imaging perspective, we faced many challenges in consistently recording human neurons with sub-cellular resolution \textit{in vivo}. In the end this increased our technical capabilities and ultimately extended the range of questions that can be addressed in the both labs.”

As a child, could you have imagined doing something like this?
Daniele: “When I was a child, scientists were almost mythical figures and the idea of becoming one as an adult seemed so far-fetched that I never seriously thought about it. Luckily, growing up I found out that if you put in the hard work, becoming a scientist is not only actually possible, but one
of the most rewarding professions out there. True, I learned that doing good science is hard and can feel painstakingly slow. However, I think that a carefully-designed experiment producing the expected results is one of the most rewarding feelings one can hope for.”

Vincent: “No, never in my wildest dreams! But I don’t think you would need to go that far back. While many of the assays employed were developed in the late 1990s, it’s only recently that they have become robust enough and reliable enough to be combined to study human neurons.”

When did this the relevance of this study really strike you? Pierre & Vincent: “One important eureka moment was when we got the first functional imaging data, where we could see human neurons responding to visual stimuli. Because we imaged the visual cortex, we were expecting neurons would respond to visual stimulation of course, but the specificity of response whereby some neurons only respond to specific orientations really took all of us by surprise. This suggests human neurons select their inputs during development.”

This was a great collaborative effort. What were the benefits of having so many minds and different fields of expertise tackling a common question? Pierre: “The joint expertise of our labs made it possible to watch in real time in the living (mouse) brain how human neurons develop, make connections and process information. There was simply no way to achieve this without a close collaboration between our Labs, our Centers, and also between our lab members. We had to put together technologies that are super specific and distinct, from pluripotent stem cell manipulation, to functional imaging of cortical circuits in awake mice, passing by intracellular patch clamp recordings, high resolution neuronal reconstructions, etc. Our colleagues in the Core facilities likewise did a fantastic job that really made the difference for this project, from single cell RNAseq to FACS cell sorting, electrophysiology, high resolution imaging.”

Vincent: “The labs also have complementary expertise in widely different fields, while sharing a strong interest in vision and the neocortex. The choice of visual cortex as target host was critical in that it made be possible to compare human neurons to large body of data acquired in our two labs.”

In a hypothetical world where funding and time are not an issue, how would you like to follow up this work? What does the future – hopefully – hold? Pierre: “Hopefully this world is not hypothetical! We have started several new projects, again through close collaboration between our two labs. We first want to test if transplanted neurons can actually lead to perception and control behaviour in the mouse. We also want to explore whether newly transplanted cells could they lead to ‘rejuvenation’ of the host brain. Finally, we would like to use our model to better understand neurodevelopmental and neurodegenerative diseases.”

Daniele: “A key finding in this study is that we show that the timing of maturation of human neurons is mostly controlled within the neurons themselves, not the environment. This could one day give us tools to ‘reprogram’ aged neurons to a younger state, and lead to a complete change in the way we treat brain disorders, whether related to neuronal loss or aging.”

Vincent: “From a translational perspective, our hope is that similar xenotransplantation approaches will be soon used to do drug screening or to develop treatment for neurological disorders. Fifty years from now, hopefully less, we may use it to repair the human brain after injury.”

What did you enjoy most during this collaboration? Pierre: “The diversity of the people involved, who first had to understand each other to work together. Our joint meetings usually sounded like a mini-Babel tower, with so many diverse mother tongues of course, but also educational background, scientific interests, technological expertise – this project is a clear demonstration that the major strength of VIB lies in the diversity of the minds working here.”

Vincent: “Pierre's passion and that of his lab members alone made it worth our while.”

Linaro, Vermaercke et al., Neuron 2019
Mancuso et al., Nature Neuroscience 2019

Science meets science
TO BECOME, OR NOT TO BECOME... A NEURON

Researchers led by Pierre Vanderhaeghen and Jérôme Bonnefont (VIB-KU Leuven Center for Brain & Disease Research, ULB) have unraveled a new mechanism controlling the switch between growth and differentiation of neural stem cells during brain development. They discovered a specific factor that makes stem cells ‘deaf’ to proliferative signals, which in turn causes them to differentiate into neurons and shape the marvelous complexity of our brain. The findings shed new light on our understanding of brain developmental processes and have important implications for stem cell biology.

The brain is an incredibly complex organ consisting of billions of cells with a diverse range of functions. The mechanisms that orchestrate the formation of this intricate network during development have kept neuroscientists awake for decades.

Pierre Vanderhaeghen and his team study the development of the brain cortex, the outer layer of neuronal tissue that contributes in an essential way to who we are, as a species and as individuals.

“During neural development, a complex cocktail of signals determines the fate of neuronal progenitor cells,” explains Pierre. “These stem cells receive many different ‘proliferative’ signals that instruct them to keep on dividing, generating more and more cells for the growing brain, but at some point, they also need to stop doing this and differentiate. In other words, they need to specialize to become a specific type of brain cell.”

TURNING DEAF AT THE RIGHT TIME TO MATURE INTO A NERVE CELL

Pierre’s team set out to understand how this switch between growth and differentiation is regulated and identified a molecular factor, called Bcl6, that essentially makes progenitor cells ‘deaf’ for the proliferative signals that tell them to keep on dividing, thereby ensuring that differentiation occurs efficiently.

Jérôme Bonnefont, a postdoctoral researcher in Vanderhaeghen’s lab, explains: “We used an extensive set of genomic and cellular tools and found that a protein called Bcl6 acts as a global repressor of a repertoire of signaling components and pathways that are known to promote self-renewal. Since Bcl6 is expressed only in specific subsets of progenitors and neurons during brain development, it allows for the precise fine-tuning of brain developmental processes.”

FATE TRANSITION, STEM CELLS, AND CANCER

Pierre is enthusiastic about the findings: “These results provide important insight into the molecular logic of so-called neurogenic conversion. Thanks to this ingenious switch, differentiation can occur in a robust way despite the presence of many, and sometimes even contradictory, extrinsic cues.”

“We made this discovery focusing on neural stem cells, but I would predict that similar factors act in many stem cells in the embryo and even in adults to ensure proper differentiation,” he continues. “This may be also important in the context of cancer biology, since stem cells and cancer cells usually respond to the same proliferative cues that are precisely inhibited by Bcl6.”

Future work should determine whether and how other repressors in other parts of the nervous system and body can modulate responsiveness to extrinsic cues in a similar way. This will teach us more about differentiation, not only during development, but also beyond in the adult brain and in cancer cells.

Bonnefont et al., 2019 Neuron
**New Insights into How Astrocytes Help the Brain Process Information**

A collaboration between the laboratories of Vincent Bonin (NERF, empowered by VIB, imec and KU Leuven) and Matthew Holt (VIB-KU Leuven Center for Brain & Disease Research) reveals that noradrenaline plays a key role in how astrocytes – star-shaped cells in the brain closely associated with neurons – track distinct information during behavior. The researchers found that astrocytes can integrate information on arousal state and sensory experience.

**Noradrenaline in the Brain**

When we are aroused the hormone noradrenaline is secreted, which helps us to better remember emotional situations compared to neutral ones. In earlier studies, noradrenaline was shown to directly influence synapses – information exchange points between neurons – in brain regions responsible for processing emotions. However, noradrenaline is released across the entire brain and stimulates a class of non-neuronal cells, astrocytes, which listen and respond to locally active neurons. A question remained: do astrocytes integrate this brain-wide signal with the specific activity of local neuronal networks?

**Watching Astrocytes**

To answer this question, Michal Slezak (VIB-KU Leuven Center for Brain & Disease Research) and Steffen Kandler (NERF) used a special microscope to monitor the activity of astrocytes in mice. When mice were presented with visual stimuli, in some cases astrocytes faithfully responded. “It was so exciting! We know that if you check neuronal activity in the brain region receiving inputs from the retina that it exactly mirrors the movement of the visual stimulus. But this is the first time we saw this pattern when watching non-neuronal cells”, says Vincent Bonin, co-lead author of the study.

However, in some cases visual stimuli did not elicit any response from the astrocytes. The mystery was solved when each event of visual stimulation was analyzed independently – it turned out that astrocytes were active only when the mouse was in motion, and they were silent when the mouse was stationary. Michal and Steffen further tested whether noradrenaline is the molecule responsible for this effect. They used a compound which depletes the brain of noradrenaline and found that astrocytic responses were largely decreased, even when mice were in motion. In other words, noradrenaline is necessary for astrocytes to respond to local stimulation: astrocytes are effectively integrating sensory and behavioral information.

**Big Impact of Little Known Cells**

“This novel finding opens many additional questions. Previous studies on the action of noradrenaline on brain function focused entirely on neurons. Our data highlights that astrocytes can play a much more substantial role than previously thought”, says Michal.

“The idea that astrocytes respond to neuronal activity has been floating around for some time, but evidence for such a system has been lacking in vivo. Our work fills this gap. I just don’t think anyone really expected that the response would be so heavily influenced by the behavioral state of the animal,” adds Matthew Holt, joint lead author. “We now have to work out how this operates at the molecular level and investigate the function consequences for the brain.”

Slezak et al., Current Biology 2019
Understanding Probiotic Yeast

Researchers led by Johan Thevelein (VIB-KU Leuven Center for Microbiology) have discovered that Saccharomyces boulardii, a yeast with probiotic properties, produces uniquely excessive amounts of acetic acid, the main component of vinegar. They were also able to find the genetic basis for this trait, which allowed them to modify the acetic acid production of the yeast. If this unique S. boulardii trait can be further validated to have a probiotic effect in animal models, these results could provide the first genetic basis for S. boulardii’s unique probiotic potency.

A Tale of Mysterious Yeast

In 1923, the French scientist Henri Boulard isolated a mysterious yeast strain from lychees in South East Asia. This yeast turned out to have unexpected and potent probiotic properties. This yeast, called Saccharomyces boulardii, has since been commercialized for treatment of diarrhea and other intestinal diseases. It is now sold in pharmacies all over the world under a wide range of trade names.

Recent whole-genome DNA sequence analysis showed that S. boulardii is closely related to the much better-known Saccharomyces cerevisiae, the yeast species of which different varieties are commonly used in baking, beer brewing, wine making, bioethanol production, etc. The DNA sequence of these two yeasts is actually so similar that S. boulardii is no longer considered as a separate species but as a variety of S. cerevisiae. Why this S. boulardii yeast has been so successful as probiotic, as opposed to the common S. cerevisiae yeasts, has remained a complete mystery.

The Vinegar Mutations

The team led by Johan Thevelein (VIB-KU Leuven Center for Microbiology) found that the production of acetic acid, the main ingredient of vinegar, is a distinguishable feature of Saccharomyces boulardii. Acetic acid is a well-known preservative and strongly inhibits the growth of all microorganisms. But how does S. boulardii produce such large amounts of acetic acid?

Time for a genetic investigation, as Johan explains: “We were able to find two unique mutations in S. boulardii that are responsible for the production of acetic acid. These mutations can act as a genetic ‘fingerprint’ that allows us to distinguish between these two types of yeast and allow the isolation and identification of new S. boulardii strains from nature.”

Based on this knowledge, the researchers were able to implement CRISPR/Cas genome editing to abolish acetic acid production completely as well as switch high into very high acetic acid producers and vice versa. These modified yeast strains can now be used to test the importance of the acetic acid production for the probiotic power of S. boulardii in laboratory animals, which, in turn, may pave the path towards improved treatments for intestinal diseases.

Offei et al., Genome research 2019
A FLY’S PASSENGERS
It’s a sunny summer day and you are having a garden party. A fat black house fly comes on your plate and walks around on your food for a few seconds. Would you still eat it? Rahel Park (VIB-KU Leuven Center for Microbiology) took an in-depth look at the microbes carried by the house flies, and those residing inside their bodies. She identified specific microbial patterns linked to the origin of the flies. Overall, the portion of the potentially pathogenic microbes is low in the total microbial community. However, in a microbe-rich environment, flies readily pick up microbes, making the flies active vectors of pathogens during a disease outbreak.

INSIDE AND OUTSIDE
“The results show that the overall patterns of bacteria found inside the flies are relatively similar between flies from different countries and habitats, suggesting that, as is the case in humans, the species of microbes that live inside the flies are specifically attuned to living there. The flies’ outer surface, however, showed an entirely different picture and harbored an enormous variety of microbes,” says Kevin Verstrepen, who led the research effort in collaboration with Jeroen Raes (both from the VIB-KU Leuven Center for Microbiology) and Bart Lievens (KU Leuven Department of Microbial and Molecular Systems). Kevin continues: “Interestingly, flies isolated from similar niches carried more similar microbial communities, indicating that microbes from the environment are easily picked up on the outer surface of the flies, especially in habitats rich in decaying and fecal matter, such as farms. For fungi, both the internal and external communities varied with country and habitat, suggesting that fungi are mostly hitchhikers rather than long-term residents.”

This study reinforces the idea that during disease outbreaks, when pathogens are prevalent, house flies can be important carriers of potentially harmful microbes.

Park et al., Microbiome 2019
A PoEM ON BREAST CANCER METASTASIS

When breast cancer cells spread through the body, they do so mainly through the lymph system that normally removes excess fluid and waste products from our tissues. Now, scientists from the group of Massimiliano Mazzone (VIB-KU Leuven Center for Cancer Biology) identified a novel subset of immune cells, called Podoplanin-expressing macrophages (PoEMs), that change the tissues near a tumor in a way that promotes the spreading of cancer cells. Getting rid of these PoEMs in a mouse model strongly reduced the ability of breast cancer cells to move to other parts of the body.

LYMPH HIGHWAYS FOR CANCER CELLS

The lymphatic system drains excessive fluid and removes waste products from our tissues. Lymphatic vessels can also play a role in the spread of breast cancer. Growing tumors often put physical pressure on their environment, which makes these lymphatic vessels leaky and easier accessible for tumor cells.

The cancer cells take advantage of these leaks to move through the body and start growing tumors elsewhere, in a process called metastasis. Previous studies have shown that breast cancer cells prefer to move through the lymph system and that more lymphatic vessels near the tumor correlate with a more dire prognosis for patients.

Therefore, therapies that effectively tackle the development and growth of lymph vessels could reduce metastasis and therefore the death toll from mammary tumors, which remain virtually incurable when not detected on time.

PoEMS THAT PROMOTE METASTASIS

The development and growth of lymph vessels near tumors is sometimes supported by a certain type of immune cell. In this new study, Pawel Bieniasz-Krzywiec from the Mazzone team identified a subgroup of these cells, called Podoplanin-expressing macrophages (PoEMs).

But what is the importance of the presence of PoEMs in this specific environment? Massimiliano explains: “PoEMs are characterized by a unique gene signature related to changes in the tumor’s environment. Specifically, they are an excellent source of Collagen 1, which constitutes the supporting scaffold for growing lymphatic vessels. PoEMs also digest some parts of this environment. This liberates various growth factors that stimulate the formation of lymph vessels and gives rise to new routes for cancer cells dissemination.”

The team further observed that PoEMs loosen up the connections between the cells that form the walls of the lymph vessels, which makes it easier for cancer cells to enter these highways. In mice, preventing PoEMs from ‘environmental remodeling’ highly decreased lymph node and distant organ metastasis.

BLOCKING PoEMS TO FIGHT CANCER

These findings provide supportive evidence to targeting PoEMs in humans. With the help of clinicians and pathologists from KU Leuven and UZ Antwerpen, the researchers further tested their findings in human cancer samples. Pawel Bieniasz-Krzywiec provides more details: “On top of the mice results, human breast cancer sample testing revealed a positive correlation between the presence of PoEMs around tumor lymph vessels and lymph node involvement as well as organ metastasis. These observations pave the road towards the use of PoEM blockers in cancer therapy, specifically targeting the cancer-associated lymphatic vessels, without triggering lymphedema associated with current strategies.”

From a broader perspective, the study highlights an emerging concept that properties of immune cells are inherently related to the specific environment they reside in. The study of Mazzone’s team describes for the first time a subset of immune cells specifically associated with tumor lymphatics and promoting their growth.

“Our findings change the way we understand lymph vessel growth near tumors and will surely stimulate new and exciting research in the field,” Massimiliano concludes.

Bieniasz-Krzywiec et al., Cell Metabolism 2019
A study conducted by Georg Halder (VIB-KU Leuven Center for Cancer Biology) discovered that healthy liver tissue surrounding a tumor activates a defense mechanism that restrains tumor growth. Remarkably, the researchers found that hyperactivation of this mechanism above levels normally present in the liver, triggered the elimination of different types of liver tumors in mice. This discovery identifies a novel strategy to fight against liver cancer and could inspire new therapeutic approaches that mobilize normal cells to kill cancer cells.

The study, led by Georg Halder (VIB-KU Leuven Center for Cancer Biology), showed that not only the immune system but also non-cancerous liver cells around liver tumors have the capacity to kill nearby tumor cells. When they experimentally activated this novel mechanism in mice with liver tumors, these mice survived significantly longer and had a drastically reduced tumor burden.

Georg says: “While the study shows that this anti-tumor mechanism exists, how exactly activated liver cells cause the elimination of cancer cells is not known, but it is obviously a highly significant question that we are currently investigating.”

By studying tumor tissues from cancer patients and mouse models for liver cancer, the scientists found that the genes YAP and TAZ were activated around tumors in the liver and that this was the driving force of the anti-tumor mechanism.

This observation was surprising because YAP and TAZ are usually highly expressed in different human cancers where they drive tumor cell proliferation and survival. “The identification of anti-tumor functions in genes traditionally considered as tumor promoting genes completely changes how we think about cancer genes and their function in normal tissues,” says Iván Moya, first author of the paper.

However, while this remarkable finding identifies a completely new strategy to fight cancer in mice, this study is the first molecular characterization of this novel anti-tumor mechanism which means that more research is needed to investigate how these findings can be applied to benefit cancer patients. “Indeed, the next step is to test to what degree this mechanism also affects human cancer cells,” says Laura Van den Mooter, also co-first-author.

Moya et al., Science 2019
An international team of scientists, led by Kevin Verstrepen (VIB-KU-Leuven Center for Microbiology) and Steven Maere (VIB-UGent Center for Plant Systems Biology), has discovered that some of the most renowned classic Belgian beers, including Gueuze and Trappist ales, are fermented with a rare and unusual form of hybrid yeasts. These yeasts combine DNA of the traditional ale yeast, Saccharomyces cerevisiae, with that of more stress-resistant feral yeasts such as Saccharomyces kudriavzevii.

**MIXED ORIGINS**

“These yeasts are hybrids between two completely different species” says Jan Steensels (VIB - KU Leuven Center for Microbiology), who coordinated the lab work of this study. “Think of lions and tigers making a super-baby.”

Such interspecific hybridizations are rare and seem to be favored by the domestication process. In this case, the new hybrid yeasts combined important characteristics of both parental species, with the fermentation capacity of normal beer yeasts and the stress tolerance and capacity to form special aromas of more feral ancient yeasts like S. kudriavzevii that haphazardly made their way into the brewery.

The team, supported by industrial partners, has spent five years characterizing the different yeasts used in today’s production of beer, wine, bread and biofuels. The genetic analysis of these yeasts was quite a piece of work, because none of the existing pipelines for DNA sequencing can deal with such mixed origins.

For this the team could, surprisingly, count on the plant expertise of Steven Maere. Steven explains: “Plants have some of the most complex genomes of all living organisms. It is fascinating that complex interspecific hybrids with doubled genomes feature prominently both among domesticated yeasts and domesticated plants.”

**A SURPRISE IN DNA**

“It was a bit of a surprise for us” says Brigida Gallone (VIB-KU Leuven Center for Microbiology), the lead author on the paper. “In 2016, we reported that most industrial yeasts belong to, or arose from the species Saccharomyces cerevisiae, the traditional baker’s and brewer’s yeast. We found that these industrial yeasts are quite different from their wild progenitors, with different subfamilies having adapted to beer, wine and bakery environments. We also noticed that some of the yeasts that were isolated from ancient Belgian beer styles, like Gueuze and Trappist beers, are even more unusual and contained DNA of two different yeast species.”

“It really seems that these unique natural yeasts allowed the development of some of the most renowned beers that Belgium is so famous for,” says Philippe Malcorps, Senior Scientist at the Global Innovation and Technology Center of AB InBev, the world’s largest brewer. The team of Malcorps helped with the isolation of yeasts from some of their spontaneous fermentation beer cellars. Those natural super-yeasts are living witnesses of brewing from pre-industrial ages, adapted to harsh conditions of fermentation of the strong Trappist beers, or survival in the long lagering typical for Gueuze beers.

“One could say that the unique habitat in wooden fermentation barrels created by adventurous Medieval Belgian brewers allowed these new species to thrive until today,” says Kevin.

**A HISTORY OF YEASTS**

Apart from the special Belgian yeasts, the team also collected a large number of hybrids from S. eubayanus and S. cerevisiae, or from S. uvarum strongly adapted to cold fermentation. While it was already known that lager yeasts were hybrids, the complete DNA analysis of a large number of these yeasts showed how these specific hybrids originated in medieval Germany and later spread across different European breweries as the pilsner beers grew more popular.

“It is no coincidence that the origin of today’s beer yeasts lies in Belgium and Germany, arguably the two countries that are most associated with the art of brewing,” says Mathias Hutzler (TU Munich).

In addition to isolating and characterizing additional yeasts from classic breweries, the Verstrepen team is now also using these new insights to create novel hybrids that are even better at making flavorful beer. By crossing different natural yeasts isolated from all over the world, the team hopes to generate new beer yeasts that allow brewers to create new aroma patterns, or brew in a more ecological and sustainable way, for example by limiting cooling or allowing fermentation with a better use of local raw materials.

Gallone, Steensels et al., Nature Ecology & Evolution 2019
Researchers from the VIB-UGent Center for Inflammation Research and Ghent University hospital, together with research teams from the Helmholtz Zentrum in München and the National University of Australia in Canberra, identified a new genetic cause of hemophagocytic syndrome, a rare immune disease characterized by a dangerous and uncontrolled overproduction of cytokines known as cytokine storm. This discovery provides new insights into the human immune system and could inspire new treatments for this deadly immune disease.
WHEN BRAKES ARE NOT WORKING
Uncontrolled activation of the immune system, which occurs in hemophagocytic syndrome, is rare but deadly. It is estimated to afflict 1 in 100,000 children. In a number of children, genetic mutations have been identified that cause this overactivation. These mutations prevent the natural brakes of the human immune system from working. This means that the immune system keeps on fighting, even when the infection has already been resolved.

Early recognition of the genetic mutations causing this fatal disease is crucial for any reasonable attempt to permanently restore a normal function of the immune system. In an international collaboration, research teams at the Ghent University hospital, VIB-UGent Center for Inflammation Research, Helmholtz Zentrum München and the National University of Australia discovered the role of a new mutation in the gene Roquin-1 in a young patient suffering from recurring hyperinflammation, resembling hemophagocytic syndrome.

This research is part of the VIB Grand Challenges Program on primary immune deficiencies. Primary immune deficiencies are a group of diseases in which genetic defects cripple the immune system. Due to their rare and complex nature, primary immune deficiencies are often missed or diagnosed very late. By combining the clinical expertise amongst others present in the partner universities with the scientific knowledge and cutting-edge technology present within VIB teams, the consortium aims to improve diagnosis and treatment of the patients suffering of these rare immune disorders.

FINDING GENETIC DEFECTS
The identification of this new gene variant in a young Flemish boy initiated an international collaboration to understand its role in the human immune system. Using state-of-the-art technology present in the VIB-UGent Center for Inflammation Research together with in-house developed algorithms, the researchers were able to characterize the immune system of the patient at the single cell level.

At the same time, researchers in the Helmholtz Zentrum in München and the National University of Australia were trying to understand the role of mutations in Roquin-1 in mice suffering from immune disease. Comparing the results of the patient with those found in mice revealed both stunning parallels and intriguing differences, which helped to understand the development of this immune disease. These mouse models also allowed the researchers to test and validate alternative treatment options for this rare immune disease.

“The identification of a genetic defect in Roquin-1 by the genetic department of the Ghent university hospital was the start of a very challenging project. Only by teaming up with the research teams in VIB and experts on this particular gene in Germany and Australia, we were able to connect the dots, prove the role of this gene variant and provide insights how this resulted in disease” says Simon Tavernier, first author of this publication.

NEW INSIGHTS IN THE ORIGINS OF IMMUNE DISEASES
By identifying the role of Roquin-1 as a regulator of the human immune system, the researchers discovered a new mechanism how human immune disease can arise. Vigo Heissmeyer (Helmholtz Zentrum, Germany) emphasizes the importance of these findings: “Our research will stimulate the scientific efforts to understand how Roquin-1 functions in the human immune system. It is likely that we will also find additional mutations in Roquin-1 in patients with other immune diseases such as autoimmunity.”

How will these findings impact the life of the patient and other patients suffering from hyperinflammation? According to Patrick Verloo (University Hospital Ghent), the clinician taking care of the patient, this will benefit the patients directly: “The identification of this new mutation might help us to diagnose the disease earlier and start a more suitable treatment.”

Filomeen Haerynck (Primary Immunodeficiency Research Lab, University Hospital Gent) also stresses the significance of the collaborative approach of the VIB Grand Challenge Program, combining the expertise of both clinicians and scientists to reveal the genetic causes underpinning these rare immune diseases. “This kind of translational research is of utmost importance. It is clear that only a profound understanding of the origins of these rare immune diseases will improve the diagnosis and care of these patients.”

Tavernier et al., Nature Communications 2019
The ubiquitin-editing enzyme A20 is a well-known regulator of immune cell function and homeostasis. Here, the labs of Bart Lambrecht, Hamida Hammad and Sophie Janssens (VIB-UGent Center for Inflammation Research) identify a novel component in the A20-mediated decision between life and death. Unexpectedly, rapamycin, a well-established inhibitor of mTOR, strongly protected NK-A20−/− cells from death, and further studies revealed that A20 restricts mTOR activation in NK cells. This study therefore maps A20 as a crucial regulator of mTOR signaling and underscores the need for a tightly balanced mTOR pathway in NK cell homeostasis.

Vetters et al., Journal of Experimental Medicine 2019

Genetics highlight the central role of microglia in Alzheimer’s disease but at least 36% of AD-risk genes lack good mouse orthologues. Here, the Bart De Strooper lab (VIB-KU Leuven Center for Brain & Disease Research) shows that embryonic stem cell (ESC)-derived human microglia successfully engraft the mouse brain. Upon exposure to oligomeric Aβ, a wide range of AD-risk genes are expressed that are not readily studied in current mouse models for AD. This work provides a unique humanized animal model that will allow elucidating the role of genetic risk in the pathogenesis of AD.

Mancuso et al., Nature Neuroscience 2019

In plants, the full repertoire of redox switches regulating cellular signals remained largely unexplored. Now, the labs of Frank Van Breusegem (VIB-UGent Center for Plant Systems Biology), Joris Messens (VIB-VUB Center for Structural Biology), and Kris Gevaert (VIB-UGent Center for Medical Biotechnology) applied state-of-the-art chemoproteomics to intact Arabidopsis cells and reported an inventory of protein S-sulfenylated cysteine sites in plants for the first time. This is a giant leap forward and entails an important resource that is of high interest for the plant redox community and beyond.

Huang et al., PNAS 2019

In acute inflammation and sepsis, the Glucocorticoid Receptor (GR) loses the competition with inflammatory transcription factor NFκB for the cofactor p300. By this mechanism, found by the Claude Libert lab (VIB-UGent Center for Inflammation Research), GR loses function in the liver. This is a problem because it causes numerous metabolic changes and a lack of anti-inflammatory effects of glucocorticoids.

Dendoncker et al., PNAS 2019

Inflammatory back pain (IBP) is considered so essential in the axial spondyloarthritis (axSpA) diagnostic process that it is recommended as referral parameter in primary care. However, axSpA patients without IBP do exist as well as patients with IBP that do not have an axSpA diagnosis. In this study, scientist from the Dirk Elewaut lab (VIB-UGent Center for Inflammation research) report on the diagnostic utility of IBP according to the ASAS criteria and the individual IBP parameters in several rheumatology settings throughout Europe. Their results suggest that the distinctive impact of IBP is almost fully expressed when physicians refer their patient to the rheumatologist.

de Hooge et al., Annals of the Rheumatic Diseases 2019

Analysis of sequence data from 419 T-cell acute lymphoblastic leukemia (T-ALL) cases demonstrated a significant association between SUZ12 and JAK3 mutations. The Jan Cools lab (VIB-KU Leuven Center for Cancer Biology) shows that CRISPR/Cas9-mediated inactivation of Suz12 cooperates with mutant JAK3 to drive T-cell transformation and T-ALL development. Among the broad genome and gene expression changes observed upon Suz12 inactivation, the integrated analysis identified specific pathways as vulnerabilities in T-ALL cells with combined JAK3 and SUZ12 mutations.

Broux et al., Blood 2019

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Broux et al., Blood 2019
7 #ALS #MotorNeuron #Metabolism #CRISPR

Energy metabolism has been linked to amyotrophic lateral sclerosis (ALS). Yet, motor neuron (MN) metabolism remains poorly studied and it is unknown if ALS MNs differ from healthy MNs. To address this question, the Ludo Van Den Bosch lab (VIB-KU Leuven Center for Brain & Disease Research) compared MNs from ALS patients carrying FUS mutations to their CRISPR/Cas9-corrected counterparts. They show that ALS-causing mutations in FUS did not affect glycolytic or mitochondrial energy metabolism of human MNs in vitro. These data show that metabolic dysfunction is not the underlying cause of the ALS-related phenotypes previously observed in these MNs.

Vandoorne et al., Nature Communications 2019

8 #CharcotMarieTooth #Myelin #ExomeScreening #Neuropathy

Charcot-Marie-Tooth (CMT) disease is the most common inherited neuromuscular disorder characterized by wide clinical, genetic and pathomechanistic heterogeneity. Recently, the gene encoding peripheral myelin protein 2 (PMP2) was identified as a novel cause for CMT neuropathy. The Albena Jordanova lab (VIB-UAntwerp Center for Molecular Neurology) used whole exome sequencing and cohort screening to identify two novel missense substitutions in PMP2 in Bulgarian and German families. This finding significantly expands the genetic and phenotypic spectrum of PMP2-related peripheral neuropathy.

Palaima et al., Orphanet Journal of Rare Diseases 2019

9 #NeuralCircuit #BrainDevelopment #CorticalNeuron #MouseHumanChimera

How neural circuits develop in the human brain has remained almost impossible to study at the neuronal level. Here, a collaboration between the labs of Pierre Vanderhaeghen (VIB-KU Leuven Center for Brain & Disease Research) and Vincent Bonin (NERF, empowered by VIB, imec and KU Leuven) investigated human cortical neuron development, plasticity and function, using a mouse/human chimera model in which xenotransplanted human cortical pyramidal neurons integrate as single cells into the mouse cortex. Their findings provide new insights into human neuronal development, and open novel experimental avenues for the study of human neuronal function and diseases.

Linaro et al., Neuron 2019

10 #Probiotic #Yeast #GenomeSequencing #AceticAcid

The Johan Thevelein lab (VIB-KU Leuven Center for Microbiology) has identified a trait of the yeast Saccharomyces boulardii, sold world-wide as probiotic, that can explain its probiotic potency. The yeast accumulates unusually high amounts of acetic acid, causing strong antibacterial activity. The better-known baker’s, beer and wine yeast, Saccharomyces cerevisiae, produces negligible amounts of acetic acid. Despite their similar genome sequence, two specific mutations were identified in S. boulardii responsible for high acetic acid production, providing the first reliable genetic signature for S. boulardii.

“...will, for the first time, allow us to identify new S. boulardii strains from nature.”

Offei et al., Genome Research 2019

11 #AllergicAsthma #MouseModels #Sphingolipids #ORMDL3

Since 2007, many studies revealed a close association between polymorphisms in the ORMDL3 gene locus and allergic asthma. In yeast, ORMs are well-known regulators of sphingolipid metabolism. This led to the dogma that ORMDL3 controls allergic asthma by modulating sphingolipid metabolism. Nincy Debeuf and colleagues from the groups of Bart Lambrecht, Hamida Hammad and Sophie Janssens (VIB-U Gent Center for Inflammation Research) evaluated the effect of modulating Ormd3 levels in mice by using transgenic models. No effects on cardinal features of allergic asthma were found. This cautions against an overinterpretation of GWAS studies and shows that the role of ORMDL3 in asthma is far from established.

Debeuf et al., The Journal of Allergy and Clinical Immunology 2019
Each year, Clarivate analytics identifies the world’s most influential researchers who have been cited most frequently by their peers over the last decade. No less than 18 VIB researchers are part of this highly acclaimed group of influential scientists.

A SELECT FEW
In 2019, fewer than 6,300, or 0.1%, of all the world’s researchers, across 21 research fields, have earned the distinction of being a globally highly cited researcher. Begin part of this group means a recognition of the exceptional influence in a research field, as demonstrated by multiple highly-cited papers that rank in the top 1% by citations for field and year in Web of Science.

Lieve Ongena (VIB Sr Science policy and International Grants Office Manager): “It is proof that VIB research is influencing others, and that VIB researchers are asking bold research questions of global importance. No method of measurement is perfect, but it is good to try to measure the influence of researchers, and this list tries to do so in an objective and transparent way.”

RICH SCIENCE AT VIB
An impressive 18 VIB scientists join the group of highly cited researchers for 2019, clearly exemplifying the word leading science being done at VIB. Since publications and citations are often called the currency of academic science, it is clear that VIB is rich in outstanding science. We are proud to mention 3 VIB newcomers in this highly cited list: Jan Steyaert, Laurens Pauwels, and Rosa Rademakers. In addition, it is amazing to see no less than 9 members of the VIB-UGent Plant Systems Biology in the list!

Many congratulations to:
- Tom Beeckman (VIB-UGent Center for Plant Systems Biology)
- Wout Boerjan (VIB-UGent Center for Plant Systems Biology)
- Peter Carmeliet (VIB-KU Leuven Center for Cancer Biology)
- Bart De Strooper (VIB-KU Leuven Center for Brain & Disease Research)
- Alain Goossens(VIB-UGent Center for Plant Systems Biology)
- Martin Guilliams (VIB-UGent Center for Inflammation Research)
- Hamida Hammad (VIB-UGent Center for Inflammation Research)
- Dirk Inzé (VIB-UGent Center for Plant Systems Biology)
- Bart Lambrecht (VIB-UGent Center for Inflammation Research)
- Kris Moreel (VIB-UGent Center for Plant Systems Biology)
- Laurens Pauwels (VIB-UGent Center for Plant Systems Biology)
- Rosa Rademakers (VIB-UGent Center for Inflammation Research)
- Hamida Hammad (VIB-UGent Center for Inflammation Research)
- Alain Goossens(VIB-UGent Center for Plant Systems Biology)
- Martin Guilliams (VIB-UGent Center for Inflammation Research)
- Jeroen Raes (VIB-KU Leuven Center for Microbiology)
- Jan Steyaert (VIB-VUB Center for Structural Biology)
- Frank Van Breusegem (VIB-UGent Center for Plant Systems Biology)
- Yves Van de Peer (VIB-UGent Center for Plant Systems Biology)
- Peter Vandenabeele (VIB-UGent Center for Inflammation Research)
- Klaas Vandepoele (VIB-UGent Center for Plant Systems Biology)
The supplier of leading-edge imaging equipment, Nikon, and the scientific leadership of the VIB-KU Leuven BioImaging core join forces in the new Nikon Center of Excellence. This center marks a state-of-the-art imaging facility established as a partnership between a leading research institute, VIB, and Nikon.

Nikon and VIB strongly believe that an open exchange between academia and industry is decisive for the rapid advancement of science and technology. Therefore, the Center of Excellence will be the go-to place for showcasing the latest technology and advanced training for researchers and company representatives alike.

Better equipment for better insight
The announcement of the Center of excellence went hand in hand with a scientific symposium and a celebration. The event was a great success with more than 100 international participants.

Patrik Verstreken, the director of the VIB-KU Leuven Center for Brain and Disease Research, the hosting center of the VIB Core facility Leuven, is enthusiastic: “This is a great opportunity. We need the best equipment, and we need it now.”

The new center will, for example, enable the analysis of tissue sections of mouse models for neurodegenerative diseases in an increasingly automated fashion. This will allow the researchers to look at earlier time-points of diseases and quantify multiple aspects like the plaque burden in Alzheimer’s disease faster and in more detail.

Research meets industry
Geert Van Minnebruggen (VIB Head of Core Facilities): “Generally, such company and research institute partnerships are important in modern life science research. Through this interaction we are able to have demo instruments and to do beta testing. Via this interaction, the core facility provides access to state-of-the-art machinery and measurement time.”

Sebastian Munck (Expert technologist of the VIB Imaging Core): “The key to success is to start with the best images possible, as this will determine the potential of the discovery. Therefore, the partnership between the VIB and Nikon is a big chance and will be an attraction pole for researchers near and far.”
On November 6 VIB and KU Leuven officially opened the NextGenQBio platform. This state-of-the-art project was granted to VIB and the Stem Cell Institute Leuven (SCIL) within the purview of the Hercules Foundation financing for large scale research infrastructure. The platform is unique in Belgium and combines several cutting-edge technologies. This will provide major insights into the basic biological mechanisms of complex systems and facilitate the translation of these insights into drug discovery programs.

A triple punch
The technologies involved are a centralized platform that connects high-throughput screening (HTS) technologies with high-content imaging (HCI) to enable high-throughput high-content screening (HT-HCS). Added to this, a centralized cell culture platform was established for automated culturing of a broad range of cell types, including induced pluripotent stem cells (iPSC). And to top it off, there is a package of comprehensive bioimage analysis software and IT infrastructure for automated image analysis, data visualization and data storage.

Catherine Verfaillie (SCIL, KU Leuven): “This triplet of technologies enables multi-parametric HCI on conventional cell lines, but also on human stem cells to capture human pathology as accurately as possible. By combining HTS with HCI and automated image analysis, the effect of a large amount of perturbants can be assessed at the cellular level, including rare events.”

“The opening event was overbooked with attendees both from academia and the industry showing the broad interest for this unique screening and cell culture platform.”
Frederic Rousseau, VIB-KU Leuven Center for Brain & Disease Research
FWO GRANTS TO MASTER NEW TECHNOLOGIES

Two postdocs in the Christine Van Broeckhoven lab (VIB-UAntwerp Center for Molecular Neurology) received FWO funding for stays in the USA as visiting scientists.

Eline Wauters completed a research stay at the University of Pittsburgh in the lab of Gang Li (Aging Institute, UPMC, University of Pittsburgh) to learn the experimental procedure of REEL-Seq. This is an unbiased high-throughput technology to identify genomic variants that modulate the binding of regulatory proteins. Eline will use this technology to identify functional genetic variants that are located within a quantitative trait locus identified in the Belgian GRN founder family. These variants are expected to influence the onset age of GRN-related frontotemporal lobar degeneration.

Rita Cacace will visit the lab of Lennart Mucke at the Gladstone Institute of Neurological Disease (University of California, San Francisco). She is keen to learn state-of-the-art techniques in the field of neuronal hyperexcitability related to neurodegenerative brain diseases. Rita is particularly interested in data analysis of functional neuroimaging techniques like MEG to map brain activity. She will use the acquired knowledge to further investigate the consequences of DPP6-Kv4.2 loss and neuronal hyperexcitability in dementia.

DID YOU KNOW...

• that the multiplex protein imaging platform of Akoya Biosciences has been evaluated in a joint effort between Tech Watch Innovation Lab, the Core Facilities and VIB research labs, and is now accessible through the VIB Biol Imaging Core?
• that the Tech Watch Innovation Lab projects can be followed through Basecamp?
• that the Tech Watch Innovation Lab recently collaborated with the Nucleomics Core/Neuromics Support Facility to set-up service for all VIB scientists on Oxford Nanopore Technologies?
VIB AND BGI ANNOUNCE STRATEGIC PARTNERSHIP

BGI Group headquartered in Shenzhen, China, is the world’s largest genome research organization innovating at the forefront of genomic technologies. Together with VIB, they have agreed to pursue a partnership striving for excellence in science and leadership in technology.
By signing a Memorandum of Understanding, VIB and BGI have agreed to share knowledge, technology, and expertise in order to accelerate progress in genomic research and enabling technologies in a broad scientific field including health care and agriculture.

Through this strategic collaboration, VIB and BGI will establish joint research programs and conduct co-developments on innovative applications of single cell sequencing, health monitoring omics and more.

Johan Cardoen, Co-Managing Director of VIB: “Over the past years, VIB has heavily invested in the development and applications of state-of-the-art technologies. Exchanging and bundling our expertise with BGI is a recognition of VIB’s excellence in science as well as in technological development and innovation. This partnership is expected to generate newly applicable scientific results and the next generation of enabling and disruptive technologies in the life sciences.”

Jian Wang, President and co-founder of BGI: “VIB is a well-renowned international life sciences research institute with a strong focus on translating basic scientific results into pharmaceutical, agricultural and industrial applications. I foresee a great synergy between the two organizations with the integration of our respective expertise and capabilities in our fields working towards our shared goal to apply science and innovation for the benefit people and the environment.”

DID YOU KNOW...

• VIB’s Bio-incubator was listed in Labiotech’s 20 Best Biotech Incubators in Europe?
• FierceBiotech named VIB spin-off Confo Therapeutics, a drug discovery company building a unique pipeline of GPCR target-ed therapeutics, as one of its ‘Fierce 15’ Biotech Companies of 2019? This solidifies its reputation as champion of innovation and creativity.
• AgroSavfe, a VIB spin-off that develops new biocontrols for use in agriculture, raised €35 million in Series C financing?

37
As an entrepreneurial research institute VIB seeks to translate the results of its scientific investigations to societal value. To encourage this entrepreneurial mindset across the institute and beyond, VIB’s Innovation & Business team organizes an annual Technology Transfer training course. During this course, the VIB Innovation & Business Team, together with guest speakers from industry, outlines the tech transfer activities and process while detailing the practicalities of making technology transfer happen. Topics at the basis of tech transfer include Intellectual Property Rights with a focus on patents; business development activities including licensing, negotiation and deal-making; as well as incubation of projects towards spin-off creation.

During this one week course the participants bring on their own business idea to work out a pitch for a (hypothetical) new company, which is contested and evaluated by a professional jury.

This year, the Award for Best Pitch went to the team of Marlies Vanden Bempt (VIB-KU Leuven Center for Cancer Biology) and Dorine Sichien, Djoere Gaublomme, Florencia Linero, Elisabeth Gilis (VIB-UGent Center for Inflammation Research). Well deserved - but as the jury was impressed by all of the pitches, we want to congratulate all participants!

Selected testimonials from course participants

“The course takes time and effort for a week, but it gives a complete overview of what to know about IP rights and Tech Transfer in general. I think that every scientist who plans to work in applied research should take this course.”

“It was a very good opportunity to learn about the process behind filing a patent and starting a biotech business. It was also very interesting to learn how VIB’s team does that. The presentations were well done and during the break and dinner we could interact with the VIB Innovation & Business team, which was very interesting. I really liked the course, I learned a lot and it was one of the best VIB courses that I have followed.”

“During the course, I learned more about the tech transfer work of VIB and as a VIB postdoc, I am proud to hear the Innovation & Business team’s effort and success.”

“It was nice to meet some members of the VIB Innovation & Business team in person and get an insight into their day-to-day responsibilities and learn about potential career paths outside of academia.”
VIB RESEARCH LEADS TO NEW BLOOD TEST FOR CHRONIC LIVER DISEASE

Developing biochemical methods to study protein-linked glycans started out as the PhD research project of Nico Callewaert, in 2001-2002 in the VIB group of Roland Contreras. Few methods were then available to allow research into these protein modifications. Nico (VIB-UGent Center for Medical Biotechnology) rapidly saw the discovery’s potential for diagnostic purposes, as glycans change with disease. For years Nico and his team persevered...

Then, in collaboration with Hans Van Vlierberghe of UZ Gent this finding evolved into a tool that could diagnose liver cirrhosis of the subtype that predisposes patients to the development of liver cancer. This was also made possible by the generous support of the Foundation Fournier-Majoie, IOF of Ghent University, the FWO and the contributions of many clinicians.

Based on this work, the UK company Helena Biosciences launched the Glyco Liver Profile at the Liver Glycomics Congress in Ghent this fall. This new diagnostic product strives to become an essential part of how medical professionals diagnose, monitor and predict chronic liver disease. A critical advantage is that this new test is non-invasive, in contrast to current methods.

“We started to see this as a major technology that could be used in clinical practice. However, using protein glycan profiling (‘glycomics’) for disease diagnosis was totally new for even the largest diagnostics companies. It necessitated that we completely described the chemistry and clinical sample preparation, which took us many years. Finally, to ensure that it would find its way to patients and hospitals, the help of a commercial partner with a suitable clinical instrument was needed. Along came Helena Biosciences, and we have worked closely with them to bring this innovation to the patients.”

Nico Callewaert, VIB-UGent Center for Medical Biotechnology
In the course of 2019, or in early 2020, we are seeing a growth in the number of VIB group leaders.

For the first time in VIB’s history we welcome(d) an abundance of new female group leaders and expert scientists (8 out of 9), including a new female director in Antwerp. Out of the 9 new PIs, 6 were (internationally) recruited from outside VIB and 3 deserved an internal promotion. Nationality-wise, we see 4 Belgians and 5 foreigners (UK, Italy, Portugal, Singapore, Switzerland). We thank all centers for their initiatives in attracting and securing a much more diverse PI landscape.

Below you can read their goals and aspirations for their research group for the coming years. We wish them all the very best in their new role and we count on you for their smooth integration within the VIB community.

**VIB-UGENT CENTER FOR INFLAMMATION RESEARCH**

**Charlotte Scott**
Group leader starting January 1, 2020

“My research career to date has focused on understanding the biology of two types of immune cells, namely dendritic cells and macrophages, in healthy individuals. Now that we begin to understand these cells better, moving forward at VIB my lab will focus on understanding which types of these cells are present during different liver diseases and what they’re doing in these settings. We hope to better understand which of these cells might represent viable targets for future therapeutic strategies and how we should aim to target them.”

**VIB-UGENT CENTER FOR PLANT SYSTEMS BIOLOGY**

**Hilde Nelissen**
Group leader since January 1, 2019

“Our research group is interested in improving crop productivity and adapting our current crops to the future challenges caused by climate change. More specifically, we study the molecular and cellular basis by which plant organs grow under various conditions. We aim to decipher the instructor networks that govern organ size under normal, as well as drought conditions. We will also assess the impact of the networks on plant yield stability. Understanding growth regulatory networks will allow us to direct plant breeding and enhance our success rate in selecting higher yielding crops.”
Karolien De Bosscher  
Expert Scientist since January 1, 2019

“Nuclear hormone receptors are ligand-regulated transcription factors and intracellular drug targets in a wide range of diseases including inflammation, cancer and metabolic disorders. Unfortunately, many of these drugs suffer from drawbacks partly due to uncharacterized cross-actions. My lab pursues the working hypothesis that a re-wiring of nuclear receptor cross-talk mechanisms towards unconventional, more favorable, nuclear receptor hetero-dimerization is possible. The underlying idea is to influence gene expression patterns such that enhanced therapeutic benefit may come within reach.”

Janine Brunner  
Group leader starting February 1, 2020

“In my lab we work on the structure and function of membrane proteins. We are interested in lysosomal ion channels that are essential for efficient degradation of contents in these cellular recycling organelles. Malfunction of the involved channels may lead to fatal neurodegenerative disorders like Parkinson’s disease. A second focus is the biology of lipid transporters and synthases, where we are specifically looking at the origin and function of lipid asymmetry, and the involvement of key lipids in cell signaling. We follow a multidisciplinary approach that is based on structural biology complemented with biochemistry and biophysics, infused with light microscopic techniques and electrophysiology. I look forward to contributing to the success of our institute and am excited to start my new lab at the VIB-VUB Center for Structural Biology.”

Charles Van der Henst  
Group leader starting January 1, 2020

“Our lab focuses on a deadly human pathogen called Acinetobacter baumannii, which was recently ranked as ‘top 1/critical priority’ by WHO. Yet, this multidrug-resistant bacterium remains poorly characterized, despite an established clinical impact worldwide. Our approach is situated at the interface between microbiology, genetics, infectiology, molecular biology and host-pathogen interactions associated with drug screening strategies and microscopy-based monitoring. This multidisciplinary aspect is a prerequisite to understand the complexity of this bacterium and the associated infection strategies as a whole. We aim to improve our understanding while fighting A. baumannii at the same time. To do so, we combine both fundamental and applied researches, with an emphasis on the pathogenic potential and antivirulence strategies.”
Sandrine Da Cruz
Group leader since October 1, 2019

“I am very excited to join VIB-KU Leuven to pursue my long-standing interest in the mechanisms of neuronal growth/death and muscle denervation in amyotrophic lateral sclerosis (ALS), a fatal paralytic disease with no cure. My team and I are committed to work towards a better understanding of the pathogenic pathways and ultimately developing potential therapeutic strategies to treat ALS, as well as other neurodegenerative diseases including frontotemporal dementia (FTD), the second most common dementia after Alzheimer’s disease.”

Lynette Lim
Group leader starting January 1, 2020

“Information processing in the brain depends on specialized circuits that are formed by distinct types of neurons. How these different nerve cells emerge and mature during development remains a fundamental question in neurobiology. I am interested in understanding how developmental programs are coordinated and integrated dynamically to generate functional circuit. We employ an interdisciplinary approach that combines mouse genetics, metabolomics, and novel methods in single-cell RNA sequencing, with cutting-edge imaging techniques and bioinformatics to define how developmental programs influence brain circuit formation.”
Goodbye to...
In the course of 2019, we said goodbye to 2 group leaders who have decided to pursue their scientific career elsewhere while they will still be partially connected to VIB to finish some projects and to guide PhD students towards the finalization of their doctoral work.

Adrian Liston (VIB-KU Leuven Center for Brain & Disease Research) has taken up a group leader position at the Babraham Institute in Cambridge (UK) and Dietmar Schmucker (also VIB-KU Leuven Center for Brain & Disease Research) went to the University of Bonn (Germany).

We wish them both tremendous success.

Patrizia Agostinis
Group leader since March 1, 2019

“My lab focuses on studying the interface between (dying) cancer cells and stromal cells in the context of cancer biology and therapeutics. We aim to unravel how dying cancer cells communicate with their environment and to identify vital cancer cell-derived factors that allow the establishment of a proficient dialogue with the immune system. We believe that this is crucial to improve existing or design novel anticancer therapies based on their ability to kill cancer cells while successfully engaging long term anti-tumor immune responses. We are also keen to understand whether and how heightened autophagy in cancer cells, or in the tumor vasculature, enables tumor outgrowth and subverts anti-tumor immunity.”
Christine Van Broeckhoven (VIB-UAntwerp Center for Molecular Neurology) received the career award for science communication from the Royal Academy of Belgium on November 18th. The jury specially appreciated her unwavering dedication to breaking the taboo concerning dementia and her work emphasizing the crucial importance of scientific research as well as its ethical and societal dimensions.

Philip Van Damme (VIB-KU Leuven Center for Brain & Disease Research) is chair of the Valéry Perrier Against ALS Fund, which was founded in memory of Valéry Perrier, who died from the terrible disease. With the fund, his family and the doctors who treated him hope to raise awareness about the disease, as well as support the research of Professor Van Damme. The aim is to promote research on the causes and mechanisms of the disease, and to identify new and improved therapeutic goals.
Lucia Chavez-Gutierrez (VIB-KU Leuven Center for Brain & Disease Research) received the International Proteolysis Society (IPS) Young Investigator Award 2019. This award was newly established to specifically honor upcoming scientist in the field of proteolysis. The IPS Council appreciated Lucia’s recent ground-breaking research on gamma secretase function.

Each year, EMBO elects promising young scientists to join its Young Investigators Programme. For 2020, 27 young scientists were selected. Two of those work in Belgium: Bert De Rybel (VIB-UGent Center for Plant Systems Biology) and Martin Guilliams (VIB-UGent Center for Inflammation Research).

Jean-Christophe Marine (VIB-KU Leuven Center for Cancer Biology) has received the Society for Melanoma Research 2019 Outstanding Research Award. This award recognizes his important contributions to melanoma research and furthers the goal of the Society for Melanoma Research, which is to eradicate melanoma.
The most important aspect leading to a successful career is self-knowledge. That is the shared conclusion of the speakers at the 5th annual VIB postdoc day that took place on October 10th at the Thagaste Monastery in Ghent.

This year’s anniversary edition, entitled ‘Stairways to Success’, gathered speakers from diverse sectors in life sciences. All the speakers were asked to disclose the meaning of success according to their personal experience, which resulted in lively discussions and enlightening tips and tricks towards a successful career.

Stefan Wellens (KU Leuven) started by explaining that a career is not linear, but the outcome of acting on opportunities. Once you have found an opportunity it comes down to self-branding. Hans Van de Water (The Floor is Yours) showed how to stand out from the crowd by creating a concrete story-line with a wow-factor. According to Carine Steurs and Pegah Rouhi, recruiting consultants for industry at MODIS, postdocs already possess the right amount of hard skills and should focus on the development of soft skills that match their personality.

Ype Boersma (Academicpositions.com) informed us about the 5 most common trends for academic recruitment. When you can’t seem to find the right job description, but you have an innovative idea, a start-up might be the thing for you. Entrepreneur Colm Ryan passionately shared his move from postdoctoral researcher to cofounder of Reagent Genie and advised us to never stop dreaming.

Translational biotech is definitely encouraged by VIB and they provide the necessary support as indicated by Elisabeth Stes from VIB’s Innovation & Business team. Next was an interlude by Umeshree Govender (Accenture Strategy) who demonstrated her extravert storytelling competency, a must-have talent for consultants.

Kodi Ravichandran, group leader at the VIB-UGent Center for Inflammation Research and the University of Virginia explained how hiring the right people and establishing a healthy lab culture contribute to his success and that of his team members. Annemarie Van Nieuwenhuijze holds a group leader position as senior scientist at Ablynx, a Sanofi Company, and agrees that leadership and project management courses are a valuable contribution for success.

To finish the day, the invited speakers contributed to a vivid panel debate and gave us their ultimate piece of advice: a postdoc is a productive time during which you learn on a daily basis. Turn failure into learning and stay positive.

The VIB Postdoc committee would like to thank VIB for its support, the speakers for the informative talks and all participants for their contribution to make it an interactive and fruitful event.
The conference is planned to be as broad as possible, encompassing almost all fields of life sciences. The students will be able to listen to top scientists in their research field, but also have the chance to peek at fields that they do not directly work in. In fact, many discoveries were done by looking over the hedge! VIBes is the perfect occasion to get out of the lab and be inspired by speakers from various disciplines. A few big names that will be present: Paul Nurse (Francis Crick Institute, UK), Madeline Lancaster (MRC Laboratory of Molecular Biology, UK), Antonio Lanzavecchia (IRB, CH), Helene Steiner (Cell-Free Technology, Open Cell, UK) and many more!

Moreover, the symposium is preceded by half a day of workshops on communication with a non-scientific audience, building confidence on stage, and better visualization and presentation of data. There are also workshops on possible career opportunities in- and outside of academia, insights into the future of science, etc. Internationally renowned trainers are invited to share their experience and knowledge.

There will be plenty of networking opportunities and social activities, including a visit to the wonderful city of Leuven and a great final party!

Participants can submit an abstract for a poster and/or oral presentation before January 16, 2020. The Early bird deadline is January 29, 2020.

Register via www.vibconferences.be
SUCCESSFUL MICROBES: 
BIOTECH DAY 2019

Despite the gloomy weather, Biotech Day 2019 was a great success. A large number of visitors enjoyed a range of presentations and activities that provided a glimpse into the marvelous world of microbes.

No sun? No problem!
Sunday, October 20, 12u30. Dark skies. Stubborn veil of rain. And an estimated 4000 visitors for Biotech Day! Researchers and companies from all over Flanders gathered at campus Arenberg, Leuven to give the general public a (sometimes literal) taste of the power and relevance of microbes.
Five years of organizing VIB Conferences has made us realize that we could finetune our website. During the summer break we did a complete overhaul of the website, based on feedback from users. The new website features an updated look and feel. We hope this will make the registration process easier and improve your overall conference experience.

**Added registration options**
A new feature allows for group bookings. If you’re an administrative assistant or want to sign up a group of lab members in one go, now you can!

**Enhanced profiles and abstracts**
Networking is essential during conferences. For this we created expanded profiles. You can now add a photo and LinkedIn link. Once you register for an event you will see this info for other attendees a week prior to the start of the event and up to two weeks after it finished. This will make it easier to contact new collaborators you met during a VIB conference.

Accepted abstracts will also be visible online during this period for registered attendees of the event. This way you can come to the meeting even more prepared.

**Update your account**
For those of you who had already made an account on the previous website, you will have to make a new one. We’ve simplified this process and it should not take more than a few minutes.

We hope you will enjoy the new website and we look forward to seeing you at future VIB Conferences!

Visit [www.vibconferences.be](http://www.vibconferences.be) for more information.
DID YOU KNOW...

On October 10-11, 2019, the second edition of The Brain Mosaic: Cellular heterogeneity in the CNS took place. More than 270 people from all over the world gathered at the University hall of KU Leuven for 2 days filled with groundbreaking neuroscience.

THE BRAIN MOSAIC: PIONEERING AND EXTENDING BRAIN DATA

DID YOU KNOW...

LIFE AT VIB NEVER STANDS STILL. A SEMINAR YESTERDAY, A GROUND-BREAKING PROJECT TODAY, AN INNOVATIVE TECHNOLOGY LAUNCHING TOMORROW... STAY IN THE LOOP WITH THIS OVERVIEW.

Did you know that...

- already two VIB scientists appeared in the EOS podcast series? Let us hope that the example of Stein Aerts (VIB-KU Leuven Center for Brain & Disease Research) and Stijn Mertens (VIB-KU Leuven Center for Microbiology) will be followed by many VIB colleagues!

- Katharina Held (VIB-KU Leuven Center for Brain & Disease Research) won the early investigator award for her paper in the Journal of Physiology? Her paper is about mutations in voltage-sensing domains. Electrifying!
For this conference we had the pleasure to have two conference reporters: Nicola Fattorelli and Vinoy Vijayan from the VIB-KU Leuven Center for Brain & Disease Research.

Let’s give them the floor:
Nicola describes day 1: “The symposium opened with a keynote lecture by Sten Linnarsson (Karolinska Institutet, SE) who inspired the audience with an overview of the single-cell transcriptomics work that his lab has been pioneering, including the comprehensive description of the mouse brain atlas and the RNA velocity concept. The first plenary session already gave us the big picture of the Brain Mosaic conference, i.e. leading speakers in the field giving an extensive description of cellular heterogeneity in the major animal models’ brain cells.

Stein Aerts (VIB-KU Leuven Center for Brain & Disease Research, BE) and Scott Waddell (University of Oxford, UK) introduced the fly brain, Bosiljka Tasic (Allen Institute for Brain Science, US) went back to mice, while Barbara Treutlein (ETH Zurich, CH) moved on to primates and explored cerebral organoid development, comparing human and other great apes.

The afternoon session of day 1 was mainly dedicated to Spatial Transcriptomics, a groundbreaking technique which allows mapping gene activity in tissue samples. The speakers showed how this spatial information can be added to single-cell transcriptomics, and that we’ll be soon able to reach sub-cellular resolution!

The last session covered new developments in methods of omics data integration and gave some insights on how powerful computational analyses can be in understanding the complexity of the data we collect.” Vinoy looks back at the second day: “Day 2 kicked off with a keynote address from Ido Amit (Weizmann Institute of Science, IL). His talk focused on new applications of single-cell technologies to study the immune system’s role in disease in intricate detail. Following the keynote, there was an excellent line-up of speakers focused on new technologies and brain diseases, especially Alzheimer’s and Parkinson’s. The overall message was that there is a lot more variability at the level of the genome and the transcriptome in disease conditions. New technologies like single cell are helping us appreciate this.

The final session of the conference switched focus to the level of brain function at the neural circuit and whole brain level. Jayaram Chandrashekar (HHMI Janelia Research Campus, US) talked about the Janelia Mouselight Project – a huge undertaking that combines massive human and technological resources to generate a platform for molecular characterization of individual neurons in the brain. Taken together with genomic, transcriptomic and proteomic technologies described earlier in the conference, it seems that we are approaching a ‘golden era’ for neuroscience research. An era where we can study the amazing diversity of the brain at many different biological levels.”

- Lia Martina (VIB-UGent Center for Medical Biotechnology) won a prize for her presentation during the EMBO-FEBS Lecture Course on Species island in Greece? Science in the sun.
- the exterior of the new building for the VIB-UGent Center for Medical Biotechnology is finished? The labs are currently being installed. Ooh, shiny new things.
- Yves Dondelinger and Mathieu Bertrand (VIB-UGent Center for Inflammation Research) won the Octaaf Dupont Prize? The prize recognizes an academic work on physiology with application of biotech methods. Phine job, guys.
- newly minted Shubhada Kulkarni (VIB-UGent Center for Plant Systems Biology) was profiled as first author by the journal Plant Physiology? Immortal fame awaits.
- Valerie Uytterhoeven and Disha Shah (both VIB-KU Leuven Center for Brain & Disease Research) each received a grant from Alzheimer’s Association (AARF grants).
- the BioRxiv paper from the Jan Steyaert lab (VIB-VUB Center for Structural Biology) on Megabodies was picked up by the community immediately? After only one day online it was already labeled and communicated “as a promising preprint reaching the top 10% altmetric score within the first month after publication”.

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MARK YOUR CALENDAR

Applied Bioinformatics in Life Sciences (3rd edition)
February 13-14, 2020 - Leuven

VIBes in Biosciences 2020
March 11-13, 2020 – Leuven

Translational Immunology
March 26-27, 2020 - Ghent