VIB TIMES

QUARTERLY
NEWSLETTER
OF VIB.
SEPTEMBER 2016

VIB

Model organisms at VIB

When a 'like' is not enough

Groundbreaking study on tumor epigenetics

Roadshow for our 20th birthday

No model, no research: why models are at the core of VIB science

Models play a central role in the research conducted at VIB. If you take a look at our publications, the vast majority of them describe work that features one or more models. Naturally, there are a diverse range of models used in different applications. For example, the plant biology research community chose *Arabidopsis thaliana* (thale cress) several decades ago as its main model due to its small size, short generation period and limited genome size. *A. thaliana* has served the plant basic research community very well, and still continues to do so — but like any model, it has its limitations. This has led to the introduction of additional models: poplar for woody plants and corn for food crops, even though these plants need plenty of space in the greenhouse.

Over the years, different model systems from the animal kingdom have also been adopted, such as mice for a wide range of disease studies, *Drosophila* for basic neurological research, *Xenopus* for developmental biology and zebrafish for cardiovascular and related studies. Looking at the numbers, *Drosophila*, mice and zebrafish are the top three models. A major reason for the use of mice in many cases is the availability of an elaborate genetic toolkit that can be utilized to knock in or knock out genes, even though mice are not always the ideal species to use in the study of specific diseases.

The message: each model has its limitations. This is one of the main reasons why some scientists criticize the use of animal models in research. As a result, we must be transparent when it comes to the value and the limitations of animal models — and of models in general.

On the other hand, models have undergone major improvements over the years as our ability to build in more complex pathways grows. In this respect, there is a link with previous issues of VIBnews that cover technologies, as new technologies such as genome editing have sparked a revolution in terms of researchers' capacity to create better models faster, and with more precision. These technologies will also likely catalyze shifts in the types of models that we choose to use in our future research.

René Custers
Regulatory & Responsible Research Manager VIB

MEET OUR MODELS

THE 8 MOST USED EXPERIMENTAL SUBJECTS AT VIB

Each science field or research scope requires the best-fitting model, and each one comes with perks and limitations. Let's take a microscopic look at the most common lifeforms VIB scientists are using to contribute to better lives.

ARABIDOPSIS THALIANA

Arabidopsis thaliana is a type of cress native to Eurasia, and often considered a weed. But in the world of science, it is the model organism used to explore the molecular biology of plant characteristics. The plant can complete its life cycle in just 6 weeks, and many mutants are available to easily and quickly achieve desired characteristics. It also takes up very little space compared with alternative plant models such as corn or rice, and many seeds can be germinated on a small surface. However, a microscope is necessary for many observations, and it can be difficult to handle and isolate tissues. Because *Arabidopsis* is only a model organism, the agricultural applicability of results should always be confirmed in one or more economically relevant crops.

CORN

Corn has become an important food crop around the world, as it easily grows in a variety of climates and conditions. As a result, it is an important model organism for the translation of research-based processes into real applications. It also has particular physical characteristics that make it useful in research, such as large leaf size and growth patterns that allow for high-resolution samples and easy molecular analysis. Because corn is useful in both the field and the lab, these two environments can easily be compared, for even more in-depth insights into conditions, processes and changes. However, corn is time, labor and space-consuming to grow and transform compared with other plant models. Even so, gene editing processes are smoothly conducted in corn, which could lead to a variety of new research opportunities using growing mutant collections.

Front row from left to right: Charlot Versteele, Hilde Nelissen, Kirin Demuynck, Jolien De Block, Xiaohuan Sun

Back row from left to right: Tom Van Hautegem, Lennart Verbraeken, Kim Feys, Bernard Cannoot, Hironori Takasaki, Nathalie Wuyts (VIB-UGent)

DROSOPHILA MELANOGASTER

Also known as the fruit fly, *Drosophila melanogaster* has a brain and nervous system that are just as complex as those of vertebrates, and capable of sophisticated behaviors such as sleep and learning, even as larva. Because its neuronal function and synaptic molecules are easy to study, it is an ideal model for revealing synaptic pathways and neuronal functions that are disturbed in neurodegenerative diseases. In addition, many aspects of neural development and function are similar between invertebrates and vertebrates, including humans. Not only are fruit flies fast-breeding and easy to handle in large numbers, researchers have a huge repertoire of genetic tools available, enabling them to reproducibly work with each neuron in a complete, living animal.

Leen Vanhoutte (VIB-UGent)

Vinoy Vijayan and Ulrike Pech (VIB-KU Leuven)

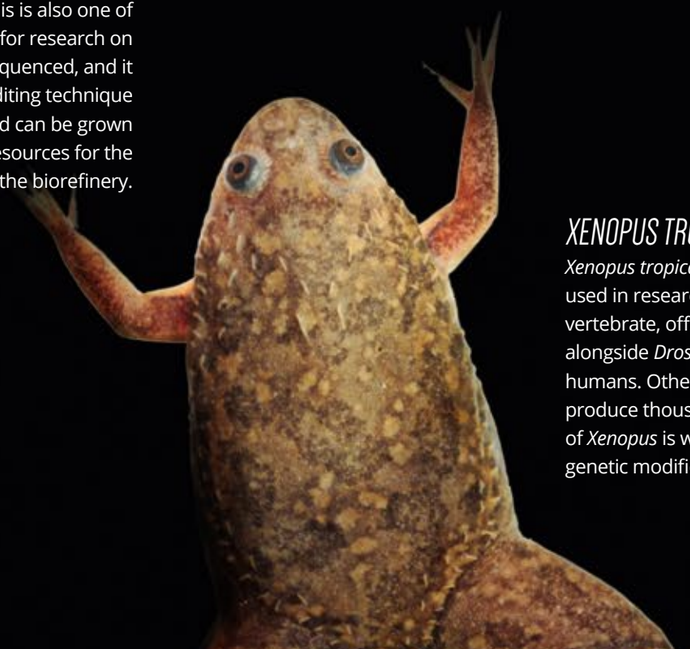
RATS AND MICE

These furry rodents are instrumental in the study of human health and disease, as we share many of the same developmental, anatomical and physiological traits and patterns. Almost every human gene has its "mouse version", and both types of genes are similar in structure, regulation and genome organization. Rats and mice are easily cared for and give birth to large litters, and there are a variety of bred lines to choose from, leading to more reliable research. The genomes of mice and rats are efficiently changed, although creating a genetically-modified mouse or rat is a time-consuming process compared with other simpler models available. Rats and mice must be provided with friendly care and a warm, peaceful and quiet environment to maintain high birth rates and the excellent health needed to be part of a study.

POPLAR

Poplar is a commercial tree species that is cultivated worldwide in plantations for pulp and paper, veneer, packing material, lumber and energy. It is a fast-growing tree that can be vegetatively propagated, and this is also one of the reasons why it has become an excellent model system for research on trees. Furthermore, it has a small genome that has been sequenced, and it can be easily transformed. The new CRISPR/Cas9 genome editing technique works very efficiently in poplar. Because poplars grow fast and can be grown on marginal soils, they are a promising alternative to fossil resources for the production of biofuels and other biobased products in the biorefinery.

Front row from left to right: Paula Oyarce, Sandrien Desmet, Marina Saleme, Lisanne De Vries, Rebecca Van Acker, Barbara De Meester - Back row: Sander Corneillie (VIB-UGent)



XENOPUS TROPICALIS

Xenopus tropicalis is a small aquatic frog native to Africa. Unlike *Drosophila*, which has been used in research for over a century, *Xenopus* is a relatively new model organism which, as a vertebrate, offers significant advantages and opportunities to researchers, and is often used alongside *Drosophila* to translate insights from *Drosophila* research into relevant pathways in humans. Other key features include: neural wiring in embryos is easily observed; female frogs produce thousands of eggs that develop into tadpoles within days, and; the genome sequence of *Xenopus* is well-known and contains no gene duplications, which can confound genetic modification.

Griet Van Zeebroeck
(VIB-KU Leuven)

YEAST

We're all familiar with everyday applications of yeast such as bread and beer, but it is also often used as a model organism to study different aspects of cell biology. Classified as a fungus, yeast cells respond on a unicellular level to changes in nutrient levels, and the responses are clearly observable, leading to insights about cell biology that can be translated to effects in higher organisms. Yeast reproduces rapidly and is very undemanding when it comes to care. As one of the most studied unicellular organisms, its genome is completely known and easily modified via large numbers of gene libraries.

From left to right:
Carlo Milia,
Massimo Santoro,
Xiaowen Chen
(VIB-KU Leuven)

ZEBRAFISH

A small, striped, freshwater minnow, the zebrafish is often chosen as a model in research concerning cancer, drug discovery and the human vascular system. Unlike other animal models such as *Drosophila* and *Xenopus*, the zebrafish has a simple cardiovascular system with an anatomy similar to that in humans. Other advantages of using zebrafish as models include constant size during development, embryo transparency and external fertilization for easy visualization of internal organs, and very fast genetic manipulation. However, as fish, they do lack important mammalian organs such as lungs as well as the divergent immunological elements essential for many common human diseases.

Row 1: Debbie Rombaut, Annick De Keyser, Tibby Deckers, Sofie Goormachtig, Astrid Gadeyne
Row 2: Lam Dai Vu, Ive De Smet
Row 3: Bernard Cannoot, Geert De Jaeger, Tom Viaene
Row 4: Yves Van de Peer, Stephane Rombauts

NEW MODEL ORGANISMS ARE THE CREAM OF THE CROP IN PLANT GENETICS RESEARCH

When it comes to economically important agricultural applications of biological research, it's important that scientists use model organisms that allow results to be easily translated from lab to field. VIB's Plant Systems Biology department in Ghent focuses on conducting plant biology research for the development of superior crops that are able to grow in different climates and under many chemical conditions – and the best way to do so is by using wheat and tomatoes as model organisms.

CLOSING THE GAP BETWEEN LAB AND FIELD WITH WHEAT AND TOMATOES

To maximize efficiency and effectiveness, direct research into economically important food crops should be as quick and painless as possible, which makes it ideal for scientists to use actual crops in their experiments. Although no fully sequenced wheat genomes are available because of their complexity, genetic research using wheat is highly relevant to our understanding of gene expression in grains. Like other grains, wheat is an example of an allopolyploid plant, which is a plant with a genome that contains chromosomes derived from multiple species. Wheat is also very sensitive to changes in the environment, which has a huge impact on crop production — and makes wheat research vital to the agricultural industry worldwide.

From left to right: Gwen Swinnen, Linlin Qi, Alain Goossens, Laurens Pauwels, Rebecca De Clercq and Patricia Fernandez-Calvo

The tomato also makes a great model organism, but in different research applications, especially for studies on other popular plants in the *Solanaceae* family including potatoes, eggplants and peppers. Research using tomatoes focuses on fruit development and maturation in order to understand chemical changes that lead to improved taste and nutrition through genome editing. Tomatoes were chosen because they contain a wide range of metabolites that impact taste and nutrition. Although it is possible to obtain gene edited tomatoes, it is a labor-intensive process. As a result, it's more feasible to get these varieties through root culture transformation and transient gene expression in fruit.

TRAINING AT VIB

organizes a science training day on CRISPR-based Genome Engineering (October 27, 2016 in Leuven). During parallel sessions in the afternoon, participants have the opportunity to look at CRISPR-use in plant, fish and mammalian model organisms that can speed up or offer new possibilities for ongoing research.
More info on www.vib.be/training

A HOMAGE TO *E. COLI*, SUPERSTAR MODEL ORGANISM

What immediately springs to mind when you read the words 'model organism'? Most of us would shout fruit flies, Arabidopsis*, rats and mice, or yeast. Yet, we often forget the one modest organism that paved the way for all the previous ones:* Escherichia coli*, a bacterium that lives in intestines.*

Actually, *E. coli* was one of the very first model systems for molecular biology. Discovered in 1885 by Theodor Escherich, it has been commonly used in experiments ever since. Thanks to its fast growth and reproduction rates – it doubles in quantity every twenty minutes! – *E. coli* just as quickly proved itself a lab champion.

THE FOUNDATION OF BIOTECHNOLOGY

The very essence of a model organism is that it provides insights into the workings of other organisms – something *E. coli* did con brio! We owe it nearly everything we know about prokaryotic genetics and molecular biology, like gene regulation, bacterial conjugation, transduction, and much more.

So let's give *E. coli* the credit it deserves, as one of the heroes of modern biotechnology.

NEUROSCIENCE AND PLANT BIOLOGY TEAM UP TO EXPLORE ENDOCYTOSIS

Some research projects apply more than just one model organism. As many basic cell processes are quite similar across lifeforms, the exact effects of molecules can be compared in different organisms. One example is the multidisciplinary research carried out by the labs of Patrik Verstreken (VIB-KU Leuven) and Jenny Russinova (VIB-UGent). In plants, fruit flies and human cells, they discovered the mechanisms by which inhibitors of endocytosis disrupt energy metabolism.

When molecules (such as proteins) come near a cell, they can be engulfed by it. This process is called endocytosis. The paper, published in Nature Communications, unveiled the actual biological consequences of ES9, a molecule that inhibits endocytosis. By comparing the effects on plants (*Arabidopsis*), fruit flies (*Drosophila*), and human cells, the team showed that differences in cell physiology systems may require the development of plant-specific or animal-specific inhibitors for medical uses.

Patrik, your neuroscience lab joined hands with Jenny's plant biology lab. What was the driver behind this collaboration?
Patrik: "We are both interested in how cells communicate with each other. Some of these mechanisms, such as endocytosis, are quite similar. When Jenny's lab began isolating inhibitors of the process, we were obviously interested in assessing whether the compounds that are active in plants also affect flies. The findings also tell us that apparent plant-specific compounds or insect-specific compounds may have to be treated with care, as these tools may have more far-reaching effects than originally assumed."

Jenny, what important lesson do you take from this research?
Jenny: "Plant researchers sometimes use small molecules discovered in the mammalian field, assuming they have the same mode of action. But although biological processes can be very similar, the differences in cell physiology can cause varying results. For example, we observed that ES9 and the known drug TyrA23 cause acidification of the plants' cytoplasm, thereby inhibiting endocytosis. Because extracellular spaces in plants and mammals have an opposite pH, such drugs will affect cytoplasmic pH differently. This means we have to use compounds with the greatest caution and carefully attune them to the right organisms."

Let's also ask some other contributors about the project. Wim, what about next steps and plans moving forward?
Wim Dejonghe: "Our findings open pathways to develop ES9 through chemical processes into a specific plant endocytosis inhibitor. We're also looking forward to further studying the effects of extracellular pH on plant receptor activation and internalization."

And finally: Sabine, what struck you the most about the outcomes of this research?
Sabine Kuenen: "Not only did ES9 treatment in *drosophila larvae* result in endocytic phenotypes, resembling mutants that we had studied before in the lab, also mitochondrial function was severely affected, pointing out that additional effects can be induced when using inhibitors, especially when using them in different model organisms."

Dejonghe et al., Nature Communications 2016

VIB ALUMNI: CAMILA ESGUERRA

Camila Esguerra has found a haven in Oslo. "This will – probably – be my home for a long time," she assures. As a group leader at the Biotechnology Centre of Oslo, part of the University of Oslo, and with the intention of progressing from an associate to a full professorship at the School of Pharmacy in the future, she thinks long term.

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

Of course, there's another reason why she and the Norwegians get along like peas in a pod: they are all fond of fish. Specifically zebrafish, in Camila's case.

Why has the zebrafish been a recurring theme throughout your scientific career?
Zebrafish have a high genetic, pharmacological and physiological similarity to humans, and they have multiple advantages over rodent models. The fish larvae are small (less than 5 mm long) and optically transparent, which allows easy visualization of tissues. Adult zebrafish produce hundreds of offspring per week, and the embryos develop fast. These features are combined together to form an ideal *in vivo* model suitable for medium-throughput phenotypic screening in microtiter plates. Behavioral analysis and electrophysiology are also possible on zebrafish larvae. One of the major advantages of this model however, is how easy it is for researchers to perform bioactivity tests of small molecules - compounds can simply be added to the water surrounding them.

When you relocated from Leuven to Oslo, you brought along your interest in epilepsy as well?
Absolutely. When I was in Leuven at the Department of Pharmaceutical and Pharmacological Sciences, we established several zebrafish seizure models, including one for Dravet syndrome (DS), a severe early-onset form of epilepsy. Last year, we published a study that found that the serotonin agonist fenfluramine reduced epileptic seizures in one of the models we developed. In Oslo, I want to further combine genetic and chemical approaches in zebrafish, not only to shed light on the mechanisms of seizure generation, epileptogenesis and treatment resistance, but also to apply our expertise to other neurological diseases such as schizophrenia and Alzheimer's.

From 2003 to 2006, you worked in the VIB lab of Désiré Collen and Peter Carmeliet after four years with Mermaid Pharmaceuticals in Hamburg. Isn't that an unusual career path?
I already knew Peter Carmeliet from when we were both at the Whitehead Institute in Boston in the early 1990s. I even worked with him for a short time. There was a rumor at the Whitehead that I was a 'good cloner', so Peter sort of confiscated me. Ten years later, I was with Mermaid and we ended up in the middle of the 9/11 period. We really had a hard time obtaining sufficient financing, so Désiré and Peter gave me the opportunity to build a zebrafish facility in Leuven. Actually, they were very generous because they also allowed me to finish my PhD - after normal working hours, of course. As a result, I actually graduated from KU Leuven.

You've been in Oslo now for a year and a half. Is there a difference between doing science in Belgium vs. Norway?
For many people, it seems that I've moved to the 'periphery' of science in Europe. But honestly, it does not feel that way. The intense networking that occurs between labs in Norway and other Scandinavian countries should not be underestimated. It is considered a natural duty to find research partners in Norway, Sweden, Finland or Denmark. If you receive infrastructure funding, you are even obligated to engage in collaborations. The Scandinavian connection offers a large pool of opportunities and talent.

REPORTER ON THE ROAD: WHEN A ‘LIKE’ IS NOT ENOUGH

When you do research on neurodegenerative diseases as common and devastating as Alzheimer’s or Parkinson’s, it’s easy to pitch your work to a wider audience. Generally speaking, the people I meet are interested in what I do, or at least happy that I am interested in it on their behalf. Most of them are glad to know their tax money is invested in research that can help us understand and (hopefully) eventually cure the illnesses that they or their loved ones may suffer from. Consequently, most of the ‘science communication’ I have been involved in, both inside and outside of VIB, has been smooth sailing.

Liesbeth Aerts

All of that changed when I wrote a piece on a far more controversial topic – animal experimentation – for a magazine in Flanders. Suddenly, insulting tweets appeared, people posted comments containing inaccurate facts, and in a response piece, my words were taken out of context and misrepresented for the whole world to see.

I must admit that it shook me up a little – not that I was surprised. I knew this debate was emotionally loaded and that negative responses were inevitable. However, I had underestimated how much time and energy it would drain from me, and how much these public reactions and my inability to respond to them would get to me.

Why me?
In the turmoil that followed, I second-guessed my decision to write an opinion letter. Why had I thought it was a good idea in the first place? After all, it did not really involve me anymore. I no longer work at VIB-KU Leuven, or at any other Belgian or European research institute for that matter. The pending revision of EU legislation on animal experimentation would not have any direct impact on me or my work. Besides, I am not the most suitable person by far to speak up about this topic. The last time I performed experiments involving animals was seven years ago. Surely, other more experienced and senior people were in a much better position to address these issues, especially to the press.

Why not me?
In the heat of the moment, these excuses didn’t occur to me. I had responded to the press the way I did because what I read had hurt me as a scientist. I may not be an expert, but my reputation had been dragged through the mud just as much as that of any other researcher. I may not be directly involved in animal experiments on a regular basis, but I work with cell lines derived from animals, requiring animal serum. I use antibodies generated by my colleagues through the use of animals. As a result, the purpose and methods of my work were also criticized. My ethical standards were questioned.

I care enough about my research to spend evenings or weekends in the lab, to lose sleep over it, to get frustrated, to discuss it over and over again, even with friends outside of work. Looking at it that way, it was not at all strange to take a defensive position when the work I so firmly believe in was publicly put into question.

Discussing progress and hope is easy. I figured that if I truly cared about scientific outreach, I should not shy away when the conversation gets tough. Staying silent about the difficult subjects does not help either — it just feeds fear and ignorance. Having decided that responding publicly was the right thing to do, I wondered why so few scientists did.

An uncomfortable silence
Why did the same articles stir so little reaction in my colleagues? Bart De Strooper reacted, as he has in the past. Why was no one else taking our side in this public argument? Did they also ask themselves the same question I did: “Why me?”

To be fair, what I wrote was shared and liked on social media, within my own and hopefully other people’s scientific and academic networks. But out there in the public sphere, nobody refuted inaccurate claims in the comments section. Were there really no other scientists following the debate? Why was no one else from any of the 22 Belgian institutes that had claimed days earlier to communicate better about animal experimentation speaking up?

It is not enough that we pat each other on the back and return to our lab work. We need to have this conversation where it matters: with the public, the animal right activists and the legislators. The least we can do is make our voices heard. I know my piece will not make “extremists” change their minds, but it provides another view, hopefully balancing the perspective of the silent majority. The same is true for other controversial topics such as genetic modification, a discussion currently flaring up in full force with the surge of CRISPR/Cas.

The online conversations I had confirmed again that the scientific enterprise is a big black box to outsiders. How can they know why animals are still needed, or what is allowed and what isn’t? We cannot expect legislators to make evidence-based policies if we do not communicate how science works or, at the very least, call out people who misrepresent it.

Now, I know what you’ll say: “We don’t have time for that!” And you are perfectly right, you don’t have time. But you can make time. We are so busy chasing high-impact publications that we neglect the issues that have very real impacts occurring right before our eyes. We know our science matters, and it is up to us to tell people how and why. No one else can do it for us.

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

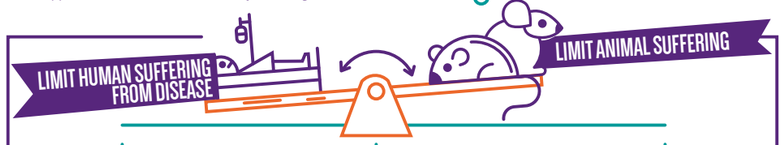
THE USE OF ANIMALS IN MEDICAL RESEARCH

A responsible balance

FACTORS THAT SWING THE BALANCE

- The goal of the research and the prospected human or animal benefit resulting from that research.
- The existence of non-animal alternatives for the research.
- The number of animals used.
- The application of measures to limit any suffering to the animals.

Ethical committees oversee the strict application of the three R's principle and determine which way the balance swings.



REPLACEMENT

If there is a non-animal alternative, it must be used.

REDUCTION

If the experiment can scientifically correct be done with fewer animals, then the number must be reduced.

REFINEMENT

If there are ways to limit any suffering, these measures must be applied.

NO ANIMAL EXPERIMENT WITHOUT APPROVAL FROM AN ETHICAL COMMITTEE

ANIMAL CARE IN PRACTICE

Appropriate housing with good lighting, correct temperature and humidity.

Access to plenty food and water.

Health and welfare monitoring by a designated veterinarian.

Certified training of all personnel involved in animal experiments

ANIMAL MODELS

Animal models generate important knowledge about diseases and help to identify and validate relevant targets for developing new therapies. Modern genetic tools allow the creation of animal models that mimic the human disease condition in an ever more precise manner. Worldwide there are many thousands of different animal disease models in fruit fly, zebra fish and especially mice.

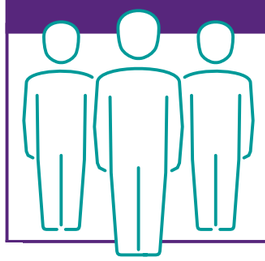
NON-ANIMAL METHODS

Non-animal methods are used whenever possible, but cannot currently fully replace animals.

Non-animal methods such as the use of cell cultures or computer modeling approaches are used in most if not all lines of research.

It is less complex to develop non-animal methods in more applied toxicological research than for basic biomedical research. In particular cell culture based systems are already widely used in applied toxicological research.

It is not realistic to expect robust alternatives to be developed in the near future for the use of animals in the study of complex interactions in basic biomedical research.



ETHICAL DUTY TO PROTECT HUMAN SUBJECTS

There is an ethical imperative to protect human clinical trial subjects to undue harm or suffering. This is why medical ethical review boards demand solid experimental data from pre-clinical research before allowing a trial drug to be administered to a human being. Such data can in most cases only be produced using live animals. There are no robust non-animal models that can uncover unexpected side-effects.

ANIMAL EXPERIMENT STATISTICS

In Belgium in 2014 664.471 animals were used in experiments (this is a grand total that includes medical research).

68.6% were rodents (mostly mice)

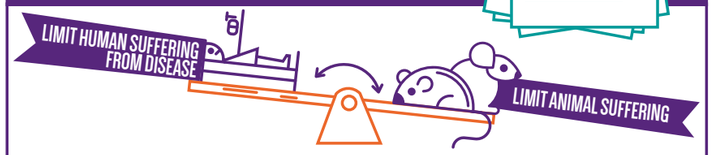
20.2% were fish (mostly zebrafish)

0.3% were dogs and cats

0.007% were primates

STRICT ADMINISTRATIVE REQUIREMENTS

On top of the moral and animal care obligations there are very strict administrative requirements. Some of them do not contribute to the welfare of the animals and only lead to biomedical researchers and animal care takers spending more and more time on paperwork. It's not only the moral obligation that makes researchers think twice before considering an animal experiment.



We must be careful not to shift the balance too strongly in either direction. Making the legislation even more strict will endanger important medical research in favor of overly exhaustive paperwork which does not contribute to animal welfare.

WHY ANIMAL MODELS ARE STILL VITAL TO BIOMEDICAL RESEARCH

Animal models are designed to represent human conditions because of our many shared characteristics. This is relevant because the more similar to humans the model's studied molecular pathways are, the more predictive the outcome of the study will be.

MODELS TODAY: SMARTER, BETTER, AND MAKING REAL IMPACTS

Activists criticize the validity of animal models, citing examples of experimental outcomes involving animals that were not very predictive of the human condition. However, they neglect the many cases when animal experiments and models have been critical in the development of major therapies. Today's models are much better than those from just twenty years ago, and their relevance, quality and smart design are keys to generating significant societal impact.

DEVELOPERS OF NON-ANIMAL MODELS HAVE THEIR WORK CUT OUT FOR THEM

Over a million EU activists signed a motion to phase out the use of animals in research, but the European Commission has proposed instead to boost progress in ethical lab practices and fuel the development of non-animal alternatives. In this context, the Commission will hold a conference in December 2016 in Brussels to debate the validity of animal models and how best to apply scientific advancements to develop non-animal approaches. It is crucial that this debate is well-informed regarding the value and limitations of animal models, and also that expectations about the development of non-animal alternatives are well-managed, since they will not be viable for use in basic biomedical research in the short to mid term.

This is why VIB has developed an infographic on the use of animals in medical research. This infographic will be communicated to policymakers and other relevant stakeholders through appropriate channels.

THE RISE OF A SCIENCE ICON: THE GUINEA PIG

Guinea pigs have long been synonymous with 'test subjects' – and that's no coincidence! The chubby rodents have been used in medical experiments since the late 1800s, and have contributed to various scientific breakthroughs ever since.

The discovery of adrenaline? Guinea pigs. The discovery of vitamin C? Guinea pigs (which can't produce it themselves, just like humans). The development of antibiotics, asthma medicines, artificial heart valves? You get the picture...

ALL BEGINNINGS ARE DIFFICULT

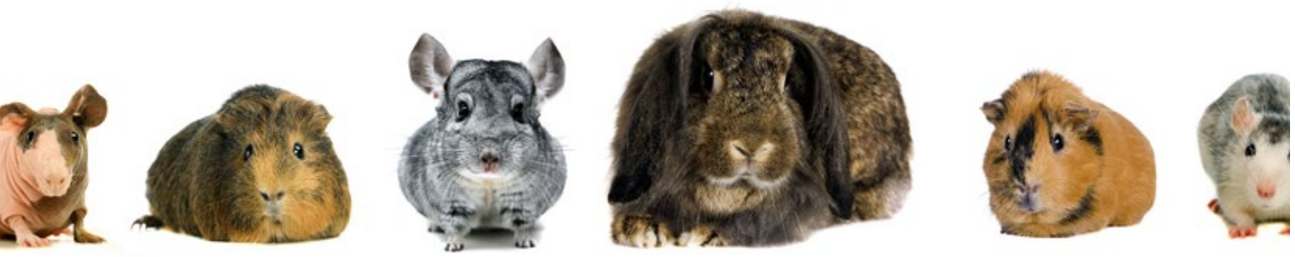
The furry creature's rise to fame had a bumpy start, though. In 1890, Robert Koch, a German country doctor, announced he'd found a cure for the most pressing medical issue of the time: tuberculosis. His test subjects? You guessed it again: guinea pigs. However, when Koch's first attempts failed to translate into a vaccine, his favorite test animal became an unflattering metaphor for the difficulties of medical research.

FROM ZERO TO HERO

Guinea pigs wouldn't gain a more winning reputation until after WW2, when English ecologist Kenneth Mellanby wrote 'Human Guinea Pigs'. The booklet's title refers to the willing test subjects who helped reveal the cause of scabies transmission among soldiers – keeping many brave men out of the hospital. Talk about a hero story!

LOST IN TRANSLATION?

Conejillo de indias. Cobaye. モルモット *(morumotto)*. From Spanish and French to Japanese, the guinea pig metaphor is present in many languages. Yet, their linguistic reign is far from undisputed. They have to compete with 'test rabbits' in Dutch *(proefkonijn)*, German *(Versuchskaninchen)* and Finnish *(koekaniini)*. Meanwhile, the Hungarian language *(подопытный кролик)* seems to go for 'test mice', probably due to the rise of rat and mouse research between the 1930s and 1960s.



HIGHLIGHTING CHROMOSOMAL DELETION TO MOVE CANCER RESEARCH FORWARD

In a typical cancer cell, up to one-quarter of the genome is lost due to chromosomal deletions on a massive scale. The subsequent vulnerabilities can't be revealed by studying these genes individually. By generating cells with chromosomal alterations that mimic human cancers, the team of Anna Sablina (VIB-KU Leuven) allows researchers to assess the role of particular chromosomal deletion in cancer development and progression.

While most cancer research studies individual genes or non-coding RNAs, Anna and her team went for the bigger picture by focusing on large-scale chromosomal deletion. Through chromosomal engineering, they managed to model aberrations that are commonly observed in cancer patients. Surprisingly, these deletions led to phenotypes that are completely different from what was found in studies of single genes or micro-RNAs. Anna and PhD students Yanyan Cai and Jonathan Crowther talk about the ins and outs of the project.

What does this mean for cancer research in general?
Anna: "It indicates that chromosomal deletions should be considered as distinct mutational events. Furthermore, I'm convinced that applying chromosomal engineering will make it possible to generate a library of human cells that represent the diversity of genomic abnormalities observed in cancer cells. Not only will this help us better understand the human cancer genome, it will also provide a useful platform for identifying drugs that are able to selectively kill tumor cells with a particular chromosomal abnormality."

What were the major challenges of this project?
Anna: "To learn about cancer biology, you need to mimic alterations observed in cancer patients as closely as possible. Also, because I've never pursued such a high-risk project, it was quite challenging for me to convince both the ERC committee and my team members to take the leap."

Jonathan: "For me, it was deciphering the association between chromosomal deletion and its effect on drug responses in breast cancer patients. Without the existence of pre-established cancer patients' cohorts, such as The Cancer Genome Atlas (TCGA), we would have been hindered in identifying these associations."

Yanyan, how long did it take to generate cell lines with chromosomal deletion?
Yanyan: "It took us over a year

and a half. We tried many different approaches to increase the genome editing efficiency and to detect, isolate and screen modified clones. To be honest, it was quite a frustrating process."

What factors contributed to the team's success?
Yanyan: "First of all: persistence, because we liked the project so much, and our uncommon approach resulted in completely new information. The other crucial thing was the collaboration of several people with completely different backgrounds. For example, I learned a lot about time management and project coordination."

Jonathan: "Working in a multidisciplinary group was certainly a big plus. As a bioinformatician, I had the pleasure of working with people with hands-on approaches to genome editing, cell culture techniques, and molecular biology applications. This project certainly gave me a greater appreciation for molecular biology."

Anna: "When I was describing the project to the evaluation committee, Sir Paul Nurse (Francis Crick Institute, London and member of VIB's institutional advisory board) asked me whether I consider myself a biochemist or a geneticist. Along the way, I realized that you have to be both if you're doing functional genomics."

Cai, Crowther, et al., Cancer Cell 2016

MULTIDISCIPLINARY APPROACH FOR GROUNDBREAKING STUDY ON TUMOR EPIGENETICS

A group of researchers lead by Diether Lambrechts (VIB-KU Leuven) explored the mechanisms that cause increased levels of methylation in tumor genes — information that is vital to the adaptation of therapies to fight different types of tumors. Methylation is one of the ways that gene expression is different in tumor cells, which leads to different conditions inside a tumor. One of the changes that occur in solid tumors is a lack of oxygen, or hypoxia, which leads to the spread of the disease to other parts of the body.

Cancers usually start with a single cell that has mutated, and the mechanisms that are behind these mutations are well-known. Tumors are not only different from their tissues of origin genetically, but also epigenetically, which has to do with the way genes are expressed rather than the genes themselves. Bernard Thienpont, a postdoctoral researcher who collaborated on the study, gives us inside info about the boundary-breaking research, which was published in Nature.

Bernard, what are the significant lessons learned?
Bernard: "There are two that really stand out to me. The first is that the environment inside a tumor can have a huge impact on the way genes are expressed, and the second is that epigenetic mutations do exist. The second one is notoriously difficult to demonstrate, and we managed to go a long way towards proving that genetic changes aren't required to cause epigenetic changes in a tumor. These understandings give us more insight into the tumor development process, potentially leading to new, inexpensive and reliable detection methods and more targeted therapies."

What did you find was the most important experience in this project?
Bernard: "Our investigations crossed the borders of many disciplines, and I found this especially enriching. The combined proof that was delivered in each of these different biomedical domains really pushed our research forward tremendously, and inspired trust in ourselves and in our reviewers to accept our findings. "Multidisciplinarity" isn't just a science buzzword – for this project, intersections between domains were crucial to our success."

What was one of the major challenges?
Bernard: "Understanding a key reaction on a kinetic level was the most challenging, since the enzymes we were studying were not stable, and the reaction conditions had to be very specific. It was tough to fine tune each of the reaction components to develop a reproducible experiment."

Do you have any good anecdotes about the project?
Bernard: "I was always surprised that nobody else had really explored this idea, since it was such an obvious line of investigation for me. Interestingly, a group from Chicago already studied this mechanism, but in the one cell type that turned out to be the exception to the rule. We were lucky not to be scooped!"

Thienpont, Steinbacher, Zhao, D'Anna et al., Nature 2016

As one of our Expert Scientists, Sven Eyckerman knows all about the 'tech' in 'biotechnology'. Together with his VIB-Ghent University research team, he has been working on several innovative biotechnologies. A recent example is the generic Virotrap platform, as seen in VIBnews June. Shortly after, Sven and his team came up with yet another pioneering technique. They developed a set of universal protein tags that go by the acronym of 'PQS' and enable protein quantification via targeted proteomic techniques. Sven talks you through the how and why of this new tool and tech innovation in general.

TALKING PROTEIN TAGS, NOVEL IDEAS AND TECH INNOVATION

Gaining an accurate view of a protein's cellular concentration remains challenging: antibody-based approaches and alternative quantification strategies both have their own limits. In close-knit collaboration with two other VIB-UGent teams, Sven and his team members zoomed in on one specific, proteomic method: Selected Reaction Monitoring (SRM). Resulting in a brand-new research technique, their multi-disciplinary work was published in the online, open-access journal *Scientific Reports*.

What was the main trigger for developing this new research technique?
Sven: "SRM is a method that quantifies the 'best mass spectrometry' in a protein to monitor the expression level of that protein, its abundance so to speak. But there's a catch: multiple of these 'best' peptides need to be selected for each studied protein, making assay development difficult. That's why we envisioned a universal SRM assay based on protein tags."

How did you turn this idea into a workable tool?
Sven: "We teamed up with the bioinformatics research group of Lennart Martens and the proteomics lab of Kris Gevaert. Together, we looked for peptides with excellent properties for SRM-based detection and quantification, properties that were absent from all the available proteomes of model organisms. These peptides can now be used as protein tags. That way, it's no longer necessary to set up an SRM assay for each protein of interest, saving researchers a lot of time and effort."

Does this open up new perspectives in your field of study?
Sven: "Using the CRISPR/Cas9 system, we also managed to effectively tag endogenous proteins. This adds a powerful new aspect to genome editing, crucial to new research. In addition, it is possible to address specific important biological issues that impact people's lives."

Where does your fascination with new technologies come from?
Sven: "When I was twelve, I remember getting a science book. The cover featured a picture of what looked like the Apollo lunar module that was used to land on the moon. It took me a few years to figure out what was really in the picture: an electron microscope image of a bacteriophage, a minuscule device that 'lands' onto bacteria to inject them with a lethal substance. I think this finding prompted my interest to study biotechnology, while the people I met during my career further encouraged and inspired me."

What usually kick-starts novel ideas?
Sven: "New ideas often come from a certain frustration about what is – or rather isn't – possible using today's research methods. To give just one example, it used to be impossible to investigate protein complexes without destroying the cell. That triggered us to come up with a new research technique: the Virotrap concept was born.

New ideas also pop up when I lie awake at night. Or when I perform repetitive tasks in the lab and let my mind wander. Coming to think of it, that might not always be beneficial for the experiment I'm carrying out… Seminars and conferences can get your creativity flowing as well, especially if they address topics outside your own research domain. Many technological developments are the result of a crosspollination occurring between two fields of study."

Vandemoortele G., Staes A., et al., Scientific Reports 2016

TECHWATCH: CALLING ALL INNOVATION AFICIONADOS

Sven: "Technology is evolving almost ludicrously fast. Staying up-to-date has become quite a challenge, while early access to new technology can profoundly impact your research. That's why VIB's TechWatch is such a unique and powerful asset. Mark Veugelers and Halina Novak, responsible for TechWatch at VIB HQ, know exactly what's possible technologically. Why not contact them directly about your research question or need, instead of browsing through the TechWatch technologies list on the website? And if certain technology turns out to be unavailable, I'm confident that VIB's tech freaks will be happy to take the challenge!"

QUICKSCAN

1

#Biological noise #tumor growth #systems biology

Individuals in a population of cells often show different growth rates, even if all cells are genetically identical and in the same environment. Using a combination of mathematical modeling and experimental work, Bram Cerulus and colleagues from the Kevin Verstrepen lab (VIB-KU Leuven) show that this so-called “noise” in growth rates has a complex and counterintuitive effect on the overall growth rate of the population, with increased differences in growth rates associated with healthier cell populations. The results do not only allow more accurate modeling of growth rates of microbes and tumors; they also shed new light on the costs and benefits of biological noise on the healthiness of cell populations.

Cerulus et al., Curr Biol. 2016

2

Gene duplication # Flowering plants

Gene duplication is an important mechanism for increasing genetic novelty. The lab of Yves Van de Peer (VIB-UGent) investigated duplicate gene retention in more than 9,000 gene families shared between 37 flowering plant species. For these gene families, duplicate retention appears to be highly non-random across genomes and duplication events. The investigation found that genes with functions related to genome integrity and organelles always appear as single copies, and genes that interact with the environment are consistently kept in duplicate.

Li et al., Plant Cell 2016

3

#CRISPR #domestication

The domestication of wild plants has provided us with crops that meet the needs of humans. Selected traits are often caused by mutations in cis-regulatory elements, which regulate the expression of related genes. These generally result in subtle changes in, for example, the tissue specificity of gene expression, and were unconsciously favored by farmers to avoid pleiotropic effects, which are caused when one gene influences two or more unrelated genes. Learning from domestication, Gwen Swinnen and Laurens Pauwels from the Alain Goossens lab (VIB-UGent) propose genome editing of cis-elements as a strategy to improve crops.

Swinnen et al., TIPS 2016

4

#Diagnostic Biomarker #SYNE1

Recently the lab of Peter De Jonghe (VIB-University of Antwerp) was involved in the expansion of the SYNE1-associated clinical spectrum with identification of mainly truncating recessive SYNE1 mutations causing multisystemic diseases rather than pure cerebellar ataxia. Given the gene size, conserved missense variants can be found in 5.6% of unaffected carriers. Muscle immunohistochemistry provides a valuable diagnostic biomarker for clarifying the pathogenicity of SYNE1 missense variants.

Mademan et al., Brain 2016

5

#SORL1 #Alzheimer’s disease

The SORL1 gene has been associated with Alzheimer’s disease (AD), and rare genetic variants of this gene have been singled out as potential causes of early-onset AD (EOAD). In a large European group of 1255 EOAD patients and 1938 control individuals, the Christine Van Broeckhoven lab (VIB-University of Antwerp) found an enrichment of rare SORL1 variants in EOAD patients. Interestingly, a certain type of variant that is predicted to cause abnormally short proteins was only identified in patients. These patients also had more often a family history of AD, further implicating a role for these mutations in development of the disease.

Verheijen, Van den Bossche et al., Acta Neuropathologica 2016

6

Redox-sensitive adherence #Gastric cancers & ulcers

Helicobacter pylori is a leading cause of peptic ulcers and gastric cancer. The bacterium adheres blood group antigens, or carbohydrates that cause an immune response, to the lining of the stomach. Kristof Moonens from the Han Remaut lab (VIB-VUB) provides structural and mechanistic insight into the BabA adhesin, which is the adhesive produced by the bacterium. This adhesin comes in many forms in terms of its structure and function, but it relies on a chemical reaction that is vulnerable to N-Acetylcysteine, a redox-active drug.

Moonens et al., Cell Host & Microbe 2016

7

Zeb2 #Dendritic cells #Development

Research conducted by VIB and its affiliates has implicated Zeb2, a gene regulating a protein with a critical role in organ and tissue formation, in the development of NK and T cells. NK and T cells are used by the body’s immune system to fight infection. Recently, Charlotte Scott & Bieke Soen from the labs of Bart Lambrecht & Geert Berx (VIB-UGent) have shown that Zeb2 is also critical for the development of dendritic cells (DCs), which help NK and T cells destroy pathogens. The loss of Zeb2 in cells resulted in fewer DCs and a change in the cell division process.

Scott et al., J Exp Med 2016

NEAT1 AND SAMMSON: SIMILAR, YET DIFFERENT ANTI-CANCER TARGETS

A team of researchers led by Chris Marine (VIB-KU Leuven) has shown that NEAT1, a long non-coding RNA, plays an important role in the survival of highly dividing cells – cancer cells in particular. The research has a striking similarity to earlier findings by the Marine lab about SAMMSON, a long non-coding RNA gene on which the growth of aggressive skin cancer is highly dependent. Chris is happy to shed some light on the similarities and differences between both papers.

A large share of the human genome has long been considered 'junk DNA', because it doesn't contribute to proteins. However, recent insights indicate that many non-coding RNAs play an important role in biological processes and diseases after all. NEAT1 and SAMMSON are prime examples.

Chris, in what way are the NEAT1 and SAMMSON papers similar?
Chris: "The two projects each identified a long non-coding RNA as a potential anticancer therapeutic target. NEAT1 and SAMMSON are also both 'trans-acting', which means that they function away from the locus they originate from. In both cases, we identified the proteins that control their expression: p53 in the case of NEAT1, SOX10 in the case of SAMMSON.

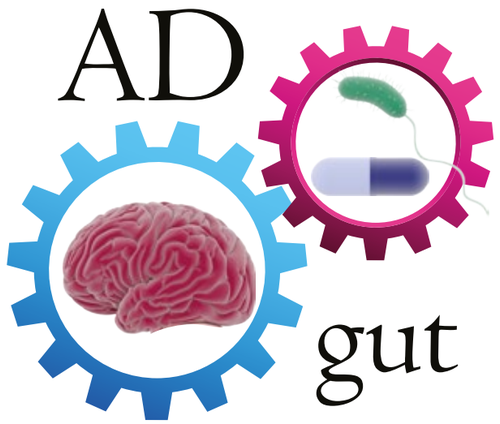
Importantly, both are cancer-cell specific therapeutic targets: they are required for the growth or even the survival of cancer cells, but they are dispensable for normal cell function. This means NEAT1 and SAMMSON can both be safely targeted *in vivo*, using an antisense-based therapeutic approach, which is clinically-compatible. And lastly, both RNA molecules have a clear potential as biomarkers, either of melanoma malignancy (SAMMSON) or as a predictive marker of response to chemotherapy (NEAT1)."

There are some remarkable differences as well.
Chris: "Yes. First of all, SAMMSON is a melanoma-specific RNA molecule, whereas NEAT1 is not restricted to one specific cancer type. Secondly, SAMMSON functions by modulating the biology of mitochondria, which provide energy to the cancer cells. NEAT1, on the other hand, contributes to the assembly of 'paraspeckles', subnuclear particles in the cell nuclei of cancer cells that prevent accumulation of DNA damage.

All told, our data highlight that lncRNAs are capable of transacting a wide repertoire of regulatory functions."

SAMMSON paper: Leucci et al., Nature 2016

NEAT1 paper: Adriaens et al., Nature Medicine 2016



WILL GUT FLORA STOP ALZHEIMER'S DISEASE?

In the previous issue of VIBnews, you could read all about the first major results of the Flemish Gut Flora Project, the long-term research project into gut bacteria. The findings of Jeroen Raes (VIB-KU Leuven) and his team indicated several links between health and the billions of bacteria in our intestines. A recent study on mice has now uncovered a new association: Alzheimer's disease. To pursue the new lead, a European research partnership was set up. And Jeroen and his team have joined the quest.

Scientists from the Ecole Polytechnique Fédérale de Lausanne in Switzerland found the link between the composition of gut flora and the development of Alzheimer's disease. Teaming up with the Jeroen Raes lab, they are now forming a European research consortium called AD-gut.

Unexpected ally in battle against AD
The mission is clear: AD-gut will explore new methods to map the microbial composition of our gut flora in a quick and precise way, in order to find out which intestinal cultures speed up the development of Alzheimer's disease.

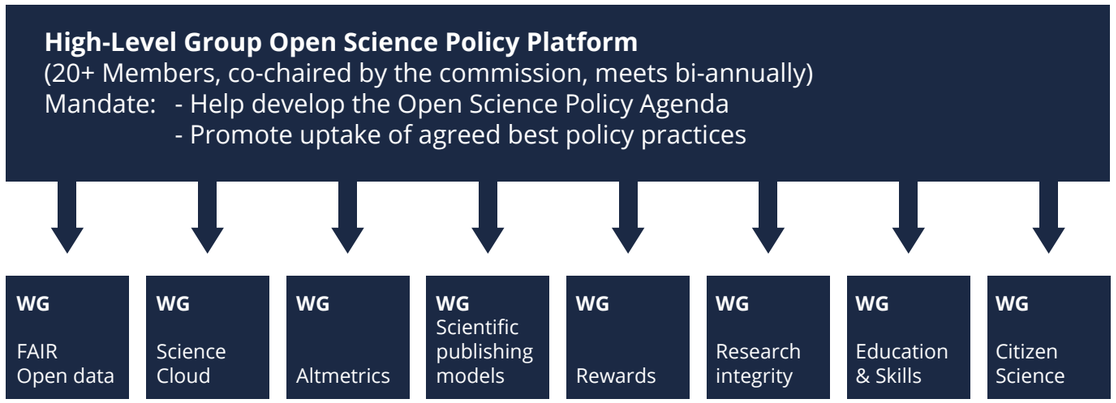
Jeroen: "The discovery of this link is of crucial importance. It opens up a whole new avenue in the battle against this incurable disease. We hope that our research can help detect the disease at an earlier stage. In addition, we will examine whether it's possible to develop specific probiotic cocktails that can change the gut flora in such a way as to stop the development of Alzheimer's.

OSPP

WELCOMING OPEN SCIENCE WITH OPEN ARMS

VIB is a founding member of EU-Life, an alliance of top European life sciences research centers with the goal of supporting research excellence in Europe. EU-Life was recently appointed by the European Commission to represent research institutions on its new Open Science Policy Platform (OSPP), which aims to revolutionize European science by promoting Open Science policies and guidelines across domains, borders and research communities.

OPEN SCIENCE POLICY PLATFORM



The purpose of Open Science? To make scientific information available to a wider inquiring audience, from professional scientists to amateur inquiring minds, for bigger impacts and broader reach.

DEMOCRATIZING RESEARCH ACCESSIBILITY

Michela Bertero will speak for EU-Life as an institutional stakeholder in the Open Science Policy Platform, EU Commissioner Moedas' new high-level advisory group. This group was formed by the Commissioner to provide expert advice on policy actions needed to radically boost the quality and impact of European science via the promotion of Open Science – which is the movement to make scientific information available to the greater scientific community, from amateur to expert. OSPP will engage with the wider European science and research community and their member organizations to support the implementation of best practices and guidelines for Open Science.

5 TOPICS, 8 WORK GROUPS

The European Open Science Agenda will address five main topics. First, it will foster the inclusion of Open Science practices in educational programs and focus on guaranteeing the quality of Open Science. Second, it will seek to remove barriers to Open Science by creating incentives and awarding researchers for contributing to it. Next on the agenda is the mainstreaming of open access policies to research data and publications, which is related to the development of Open Science research infrastructures to improve data hosting, access and governance. Finally, the platform intends to embed Open Science into society as a socio-economic driver, making science responsive to societal and economic expectations.
At the same time that the OSPP panel was announced, EU member states also agreed on the ambitious new target of making all publicly-funded scientific papers freely available by 2020. During the next two years, 8 OSPP-steered working groups will be established to develop action plans around issues that must be addressed to meet Open Science objectives. Key topics include open science clouds, citizen science, research integrity, altmetrics and more.

READ MORE IN THE EU-LIFE NEWSLETTER

Through EU-Life, VIB researchers gain shared access to the expertise, technologies and facilities of 13 partner research institutions. The newsletter is intended to generate intra-alliance awareness and interest, with the ambition of presenting a competitive advantage to EU-Life participants.

Subscribe to the newsletter at http://eu-life.eu/content/eu-life-newsletter

"With the rise of the digital data era, an EU policy that concerns access to knowledge and data sharing is urgently required in order for European science to stay cutting-edge, while safeguarding opportunities to translate scientific results into economic growth. VIB is extremely pleased that EU-Life is represented on the Open Science Policy Platform."

Lieve Ongena, VIB Senior Science Policy Manager

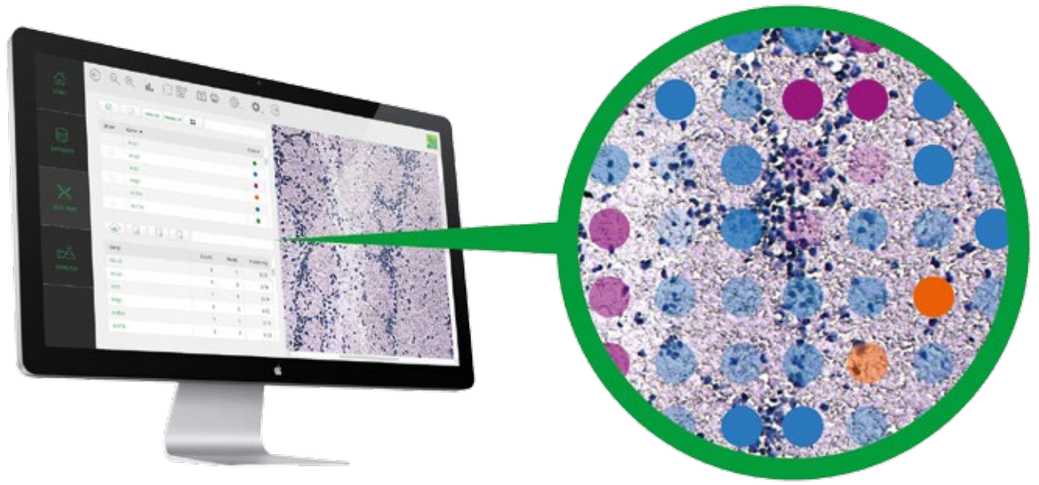
NOW IN E-BOOK FORMAT: THE GMO REVOLUTION

Did you know that the very cradle of genetically modified organisms (GMOs) is found in Belgium at the University of Ghent? No wonder our country, and VIB specifically, has always been one of the world's pioneers in gene technology. Two years ago, Wim Grunewald (VIB IP manager) and Jo Bury (VIB Managing Director) wrote a book on how GMOs could be useful in solving current and future agricultural issues. And as of now, you can read the e-book on your tablet or e-reader for free.

In The GMO Revolution, Wim and Jo offer balanced and fact-based insights into how GM crops could be useful in making agriculture more sustainable, safe and productive. They give plenty of examples of pressing problems – and how to tackle them with GMOs ranging from potatoes that can protect themselves against late blight and trees that can be used in biofuel production, to vitamin-packed 'golden rice' and wheat containing a safe form of gluten.

Haven't been able to lay your hands on a copy of the book yet? Or do you prefer reading on a screen?
Easily download the English e-book version (ePub format) at www.vib.be/plant-news.

More of a paper fan? Then order it here:
www.lannoo.be/gmo-revolution.



TECHNOLOGY WATCH: NOVEL WAYS TO LOOK AT THE TRANSCRIPTOME

Spatial Transcriptomics offers scientists novel insights into biology by enabling RNA sequencing in 2D

Technologies for gene expression analysis have changed dramatically in the last few years. From Northern blotting and microarray-based gene expression profiling all the way to RNA-sequencing. Deciphering the transcriptome is showcasing amazing insights into how individual cells work. Two recent platforms have created quite a stir in life sciences research, as they transcend the classical bulk-transcriptome approaches.

A WHOLE NEW WORLD: 2D VISUALIZATION OF GENE EXPRESSION REVEALED

An exciting "next-gen transcriptomics" approach enables the visualization and quantification of gene expression in a spatial tissue-based context (Stahl et al., Science 2016). The technology, initially developed at Karolinska Institute, is being commercialized by the company Spatial Transcriptomics. Their method, RNA sequencing in 2D, starts by attaching a tissue section onto a gridded microarray, packed with approximately 1000 different spots containing oligo-dT probes with location-specific barcodes. After histological analysis and imaging, the cells are lysed. The cellular RNA diffuses directly from the tissue section onto the array, hybridizing to the oligo-dT.

Following cDNA synthesis on-chip, the cDNAs are eluted, converted into a library and sequenced, whereby the barcodes in each sequence define the original 2-dimensional location of the RNA at high resolution. Data visualization of the tissue section image with gene expression data allows the determination of which genes are expressed in specific tissue areas and in what quantity. The technology enables novel types of bioinformatics analyses of gene expression, which are extremely valuable in research and diagnostics.

THE BEAD OF A DIFFERENT SEQUENCING TECHNOLOGY

A second approach that goes beyond bulk population analysis for decoding cellular heterogeneity consists of single cell RNA sequencing. To isolate and sequence thousands of single cells, droplet based methods are frequently used. Single-cell transcriptomic technologies such as Drop-Seq (Macosko et al., Cell, 2015) and In-Drop (Klein et al., Cell, 2015), have now also found their way to commercial platforms, which is where the Chromium platform from the company 10x Genomics is making waves (Zheng et al., in press, 2016).

The Chromium instrument allows droplet-based loading of more than 48,000 single cells per experiment. Individual cells are collected in droplets containing barcoded oligos on beads, whereby up to a million different barcoded beads can be used per experiment, ensuring that each cell will have a unique matching bead and oligo. Cells are lysed in the droplets and the mRNAs are captured on the beads, with cDNA synthesis performed in each droplet. After breaking the emulsion, a bulk library prep is made and the sample is ready for RNA-seq. After sequencing, the barcodes allow the sequencing reads to be grouped back to the mRNAs from individual cells.

TRANSCRIPTOMIC TECHNOLOGY IN THE FORECAST

Even more exciting times are ahead for the transcriptome, since there are about a dozen companies that have plans to launch new instruments or platforms to look at gene expression. From direct RNA sequencing to detect novel base modifications to ultra-long reads for the comprehensive profiling of RNA-splicing, these technologies will ensure exciting new discoveries.

Several VIB scientists are using these technologies in their projects and, given their potential, we expect broad appeal to all of VIB.

In case you have a cool idea on how to use/develop transcriptomics tools, please contact techwatch@vib.be or call Mark Veugelers at VIB-HQ.

CORE FACILITIES: MOVING TOWARDS SMART RESEARCH PARTNERSHIPS

Science and technology are becoming increasingly intertwined. Without high-tech infrastructure, many breakthroughs in life sciences wouldn't be possible. But due to the rapid pace of technological advance, individual researchers can no longer master the whole panoply of techniques. Moreover, research institutes cannot afford to acquire every single technology. We answer to this call for more efficiency by centralizing expertise and equipment in core facilities – a process that VIB set in motion internally already a while ago, and that we are gradually expanding beyond our institute's walls.

Our own 9 core facilities provide support in a wide array of omics fields and house specialized scientific equipment and services for each discipline. Since 2012, we have stretched our access to expertise and resources internationally through Core for Life, an alliance of VIB and 5 other renowned European life science institutes: EMBL (Germany), VBCF (Austria), CRG (Spain), FGCZ (Switzerland) and MPI-CBG (Germany).

Sharing resources: a prerequisite for scientific leaps

The July issue of *EMBO* reports featured a paper on institutional core facilities, written by Geert Van Minnebruggen (Head of Core Facilities at VIB) and his five peers of the other Core for Life institutes. The authors advocate the core facility concept by highlighting their strategic needs, operational benefits and future collaboration models.

Geert, how do the 6 Core for Life partners collaborate in terms of technology?

Geert: "On a regular basis, technology experts working at the local core facilities come together and discuss promising new technological developments. They then investigate the potential advantages of making a group purchase and pooling the technology. Sometimes, only one core facility buys the new tool, after which the other institutes know where to go when they lack the technology for their research project. For example, VIB is Core of Life's leading partner in Nanobody generation, which means we possess the most know-how and equipment in this domain."

Are expertise or research protocols being exchanged as well?

Geert: "Yes, we also talk about new cooperation strategies and organize technology workshops. If one of our partner institutes has acquired a new tool or adopted a new protocol, our people travel over there to master the technique – and the other way around. Another important interaction lies in benchmarking. In the field of proteomics, for example, all Core for Life members verify test samples on a regular basis in order to ensure consistent data quality levels. This also acts as a sort of quality label for research carried out by VIB or a partner institute, enabling us to underline our professionalism to industry partners, thus strengthening private-public partnerships."

Can you give us a glimpse of the future of core facilities?

Geert: "At VIB, we are currently setting up a 10th core facility in the domain of metabolomics, an emerging field that holds great promise for precision medicine. We have also recently joined forces with Genomics Core at UZ Leuven and we are joining a cancer research consortium at Ghent University. Companies will also become crucial partners to establish common platforms in the forms of joint ventures, spin-offs or ad hoc collaborations. And because we at VIB are convinced that technology will be the engine that propels science forward, we want to be in the vanguard of what I like to call 'smart partnerships'."

Meder et al., Embo Reports 2016

HOW TECH TRANSFER TRANSFORMS NEW TECHNOLOGIES INTO LIFE-IMPACTING SOLUTIONS

People in and around VIB are well aware of our adage: basic research as a starting point for tangible solutions that benefit society. But translating a paper or a technology into a groundbreaking new drug or agricultural application doesn't happen overnight. The importance of the tech transfer process was recently illustrated by a study led by Nico Callewaert (VIB-UGent) and Jan Steyaert (VIB-VUB). The paper presents a technology platform for synthetic biology, and is a great example of how innovation and entrepreneurship go hand in hand.

The study Modular Integrated Secretory System Engineering In Pichia pastoris To Enhance G-Protein Coupled Receptor Expression, conducted in the VIB labs of Nico Callewaert and Jan Steyaert was published in the May issue of ACS Synthetic Biology (see box). It is the second VIB paper that concerns the complex field of membrane protein expression technology.

Nico, can you describe the research in a nutshell?
Nico: "We provide a technology package that integrates four engineering modules in the yeast Pichia pastoris. Our goal was to increase the expression of membrane proteins to quantities that allow studies and screenings, and, ultimately, drug development. We used the human G-protein-coupled receptors – also known as GPCRs – as examples of these proteins. Located on the surfaces of cells, these molecules receive chemical signals and pass them on. Because these GPCRs play an essential part in a wide variety of processes and diseases, they are attractive drug targets."

Impact through expertise
The research is a prime example of one of our cornerstones: cross-departmental collaboration. The joint effort of Nico's Medical Biotechnology Center and Jan's Structural Biology Research Center has established VIB even more firmly in the global biotechnology firmament. The second typical VIB feature is, as mentioned, the clear tech transfer component, which funnels the findings into the next phase: the development of new medical solutions.

Jan: "This publication describes yet another application of our expanding Nanobody®-enabled platform for the stabilization of difficult to handle proteins including membrane proteins, amyloidogenic proteins and protein complexes. Together with Brian Kobilka (Stanford University), we applied similar methods to stabilize and elucidate the first active signaling structures of GPCRs. These results were conductive in awarding the 2012 Nobel Prize in Chemistry to Robert Lefkowitz and Brian Kobilka.

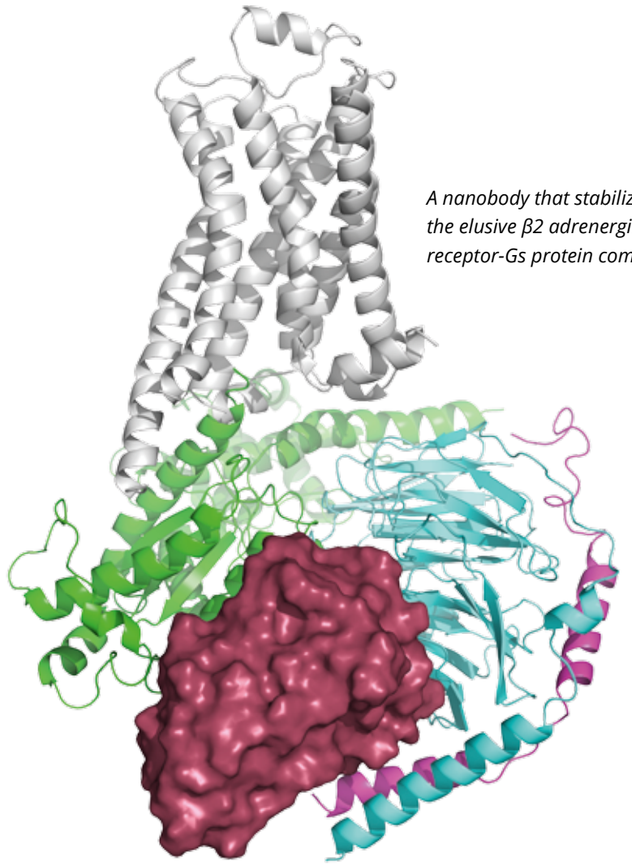
Last year, VIB and VUB created Confo Therapeutics, a spin-off that builds on the same technology to allow easier investigation of GPCRs, which can be a tremendous advantage for drug discovery."

One study, two sequels
Bridging the gap between research and the market is an important aspect of the job of Carla Snoeck, Manager New Ventures at VIB. She points out that basic research is more than a crucial threshold for follow-up studies, as generally assumed – it can also immediately serve as the basis for innovative products and technologies with huge impact.

Carla: "As Jan and Nico are both basic researchers, they conduct the kind of science that doesn't always immediately lead to concrete applications. But they develop so-called 'enabling' technologies that are instrumental to elucidate novel targets and underlying biological mechanisms – which is, after all, our core business. In addition, these platform technologies can be applied in numerous domains. That gives them huge societal and economic relevance."

Can you describe some possible applications of Jan and Nico's study?
Carla: "They are developing generic technologies that enable the structural and functional characterization of proteins that are notoriously difficult to purify and to study with any available method today, hereby focusing on the highest hanging fruits. The combination of solid scientific data and external validation by academia and industry emphasizes the uniqueness of these technologies and its broad application potential in different fields. The current study can for example be used to tackle bottlenecks in drug discovery and product development trajectories. The best proof are the ongoing collaborative partnerships and spin-offs in the pipeline."

Claes et al., ACS Synthetic Biology 2016



A nanobody that stabilizes the elusive β2 adrenergic receptor-Gs protein complex

EFMC AWARD FOR CUTTING-EDGE GPCR TECHNOLOGY

Jan's pioneering work in the field of Nanobody®-enabled structural biology, which revealed the structural complexity of GPCR transmembrane signalling, was honored in late August with an Overton and Meyer Award, handed out by the Prous Institute for Biomedical Research. This prestigious prize rewards the developers of new technologies in drug discovery and is part of the European Federation for Medicinal Chemistry (EFMC). Congratulations, Jan!

More info on www.efmc.info.

ABOUT ACS SYNTHETIC BIOLOGY

Founded in 2012, ACS Synthetic Biology is a peer-reviewed scientific journal in the relatively new field of synthetic biology. With MIT's Christopher Voigt as editor-in-chief, it has become one of the most respected and widely-read specialized journals in just a couple of years.

Sven Bervoets

LEXOGEN RESEARCH AWARD FOR SVEN BERVOETS

The Lexogen Research Award is dedicated to the development of innovative technologies that go with next-generation sequencing (NGS). One of this year's winners is Sven Bervoets (Albena Jordanova lab, VIB-University of Antwerp). He receives a QuantSeq Library Prep Kit with 96 preps and one lane of Illumina HiSeq 2500 with 100bp single reads.

"This award allows us to apply QuantSeq technology to analyze the transcriptome of Drosophila models of peripheral neuropathies due to mutations in aminoacyl-t-RNA synthetases," says Sven. "These ubiquitous proteins govern the correct translation of the genetic code, and on top of that have additional non-canonical functions. Our approach will reveal the underlying disease mechanisms and shed light on the commonalities between affected enzymes of the same functional class causing similar clinical presentation. It might even create opportunities for improved diagnosis and potential treatment for patients around the globe."

Patrik Verstreken

PATRIK VERSTREKEN JOINS FENS KAVLI NETWORK OF EXCELLENCE

During the FENS Forum in Copenhagen, Patrik Verstreken (VIB-KU Leuven) has been selected to join the FENS Kavli Network of Excellence for young neuroscientists. The group promotes neuroscience through scientific exchange and communication. Since its creation, three meetings have been held, resulting in several scientific collaborations, numerous opinion articles in the European Journal of Neuroscience, and the creation of the Best Thesis and Best Mentor in Neuroscience Awards. The latter were attributed for the first time during the FENS Forum in Copenhagen.

Patrik was chosen among 15 outstanding FENS-Kavli Scholars, which were elected from a strong pool of talented neuroscientists from across Europe. "I am confident that the now fully established Network of Excellence will continue to foster scientific interaction, collaboration, advocacy, and outreach," commented Professor Barry Everitt F.R.S., President-Elect of FENS.

CLAUDIA BAGNI WINS ERNEST SOLVAY PRIZE

On May 3, Claudia Bagni (VIB-KU Leuven) received the Ernest Solvay award, one of the three prizes handed out by the Queen Elisabeth Medical Foundation (QEMF). This Belgian non-profit organization supporting research in neurosciences awarded Claudia and her team for the project "CYFIP1-pathies: shared pathways in intellectual disabilities and psychiatric disorders".

In her lab, Claudia studies the molecular, cellular and behavioral aspects of a group of neurodevelopmental and neuropsychiatric disorders, namely Fragile X Syndrome (FXS), Autism Spectrum Disorders (ASDs) and Schizophrenia (SCZ). With the support of the Queen Elisabeth Medical Foundation, she was able to make significant progress on the role of the Fragile Mental Retardation Protein and its interactor CYFIP1, two key synaptic proteins. All this culminated in the winning research project, which identified important mechanisms involved in these disabilities during embryonic development and early postnatal life.

The Claudia Bagni Group

FRANCIS IMPENS RECEIVES ODYSSEUS GRANT

Francis Impens (VIB-Ghent University), is one of 25 researchers to receive an Odysseus grant. Issued by Flanders Research Foundation (FWO), this grant aims to give outstanding researchers the financial means to build their own research group and perfect their project internationally.

"I plan to create a small research group to investigate bacterial infection models through innovative, proteomics-based approaches," says Francis. "The growing antibiotic resistance requires a better understanding of the fundamental mechanisms used by pathogenic bacteria to infect their host. In this way, we can potentially identify new targets for therapeutic intervention."

Francis Impens

BIOTECH TOUR:
A ROADSHOW FOR OUR 20TH BIRTHDAY

1996 marked the start of an amazing journey that decisively put Flanders on the global biotech map. From our founding fathers Jo Bury and Rudy Dekeyser's initial 'plan from scratch' to a world-class scientific community, we've come a long way in a relatively short timeframe. It's all the more reason to celebrate our 20th birthday in style … with a 5-month VIB biotech tour.

During our traditional annual biotech day, the general public is welcome to snoop around in our labs and explore the practical applications of our research. Widely appreciated by young and old alike, this 'open house' will have a slightly different approach. Our tour will stop in all the cities where we have a partner university, with one main goal: immerse as many people as possible into the wondrous world of life sciences. The kick off of the biotech tour on October 5, 2016 will take place at the same time as the celebration of 20 years VIB at BOZAR in Brussels.

TOUR WITH 5 KEY STOPS

EXPO - OCTOBER 2016

BIOTECH TALK - THURSDAY OCTOBER 13, 2016

How can people contribute to Alzheimer's and gut flora research, amongst others?

Christine Van Broeckhoven (VIB-University of Antwerp), Jeroen Raes (VIB-KU Leuven) and Herman Goossens (Antwerp University Hospital- University of Antwerp)

EXPO - NOVEMBER 2016

BIOTECH TALK - WEDNESDAY NOVEMBER 30, 2016

TedX Life is Science – Discover the passion for research, art and relevance for society

Speakers to be revealed soon.

SPREAD THE WORD AND STIR THE PASSION!

During the biotech tour, we'll talk about DNA, genomes and proteins. We'll present nifty tools and showcase our latest breakthroughs in the fields of brain and cancer research, gut flora and auto immune diseases. And we'll also give you a sneak peek at what we have in store for sustainable agriculture and biofuels.

Long story short: it'll be your achievements that steal the scene! Feel free to share or retweet messages (#biotechtour) or to spread the word within your faculty or organization and talk about it during a family dinner or barbecue with friends. If we all pitch in, the biotech tour is bound to stir thousands of people's passion for science.

UPCOMING VIB CONFERENCES

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

The goal of Hallmarks of Cancer is to convene global leaders in the cancer research arena to enhance our understanding of the key aspects of cancer and how to promote translation of this knowledge into the development of more effective therapeutics. The meeting should provide a high-profile forum for exchanging ideas and establishing a dialogue amongst clinicians, scientists and drug development companies. Keynote speakers are Lewis Cantley, Weill Cornell, US and Laurence Zitvogel, Gustave Roussy, FR.

ER stress, autophagy & immune system
January 26-27, 2017 - Bruges

How do ER stress and autophagy impact on inflammation and immunity? Discover the latest findings and meet the world's leaders at the first edition of the VIB conference ER stress, Autophagy & Immune system. 18 top scientists confirmed their presence. Keynotes are David Ron, Cambridge Institute for Medical Research, UK and Beth Levine, HHMI & Texas Southwestern Medical Center, US.

More info on www.vibconferences.be

EXPO - DECEMBER 2016

BIOTECH TALK - WEDNESDAY DECEMBER 14, 2016

How does VIB look for answers to the big challenges concerning health, sustainable food and energy production?

Bart Lambrecht (VIB-UGent) and Wout Boerjan (VIB-UGent)

EXPO - JANUARY 2017

BIOTECH TALK - WEDNESDAY JANUARY 25, 2017

VIB is known for its research in cancer, neurology, and even beer and chocolate.

Diether Lambrechts (VIB-KU Leuven), Patrik Verstreken (VIB-KU Leuven) and Kevin Verstrepen (VIB-KU Leuven)

EXPO -FEBRUARY 2017

BIOTECH TALK - MONDAY FEBRUARY 20, 2017

Apotheosis in the Flemish Parliament
Why do we need basic research?

Program and speakers to be revealed soon

More info on **www.biotechtour.be** (Dutch only).

A GLANCE AT 'SCIENCE ON THE ROAD' OF LAST SCHOOL YEAR

The VIB schoolproject 'Science on the Road' (Wetenschap op Stap) aims to sparkle the enthusiasm of kids in life sciences by bringing a real (Dutch speaking) researcher into their class room. Last year's edition, around 100 scientists engaged themselves in visiting 136 classes, reaching more than 3000 little scientists.

More info on www.vib.be/wetenschapopstap

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MARK YOUR CALENDAR

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

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

Biotech Tour
October 13, 2016 - Antwerp

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

Biotech Tour
November 30, 2016 - Hasselt

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

Biotech Tour
December 14, 2016 - Ghent

Biotech Tour
January 25, 2017 - Leuven

ER stress, autophagy & immune system
January 26-27, 2017 - Bruges

Apotheosis Biotech Tour
February 20, 2017 - Brussels