BIOPARK
CHARLEROI BRUSSELS SOUTH
news

# The Biopark Charleroi Brussels South Newsletter

n°24 — winter 2014

## IBMM - 15 years



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# Mood

**The value of research**

It's self-evident but bears repeating as the year draws to a close: fundamental research is how major scientific advances, and therefore advances in human knowledge, are made, something that is also true of business, medical, and socio-economic progress. The Biopark is an excellent illustration of this fact, because on the Biopark, quality fundamental research was the precursor to new businesses, support to SME, and training for jobseekers, 90% of whom found work within weeks of finishing their course. And indeed, the first stone in the Biopark's foundations was the Institute of Molecular Biology and Medicine.

And because it's the time of year when dreams come true, I have a special wish: that funding for fundamental, free research will continue to command our full attention and be appreciated for its true worth, enabling this research to form part of the best Belgian and international networks. Another truth that bears repeating: researchers need to share and exchange ideas and work together to make progress, whether within an institution – as the IBMM know full well – their university, their country, throughout Europe, or worldwide... We wish you all the best for 2015!

*Serge Schiffmann*
*Vice-Rector for Research*
*Université libre de Bruxelles*

# The IBMM gets a makeover

*The IBMM is now 15 years old and has treated itself to a facelift: the fields in which it carries out research have been refocused, and its networks activated. Here we will meet the new IBMM management team for 2015: Bruno André (President), Laurence Van Melderen (Secretary) and Bernard Robaye (Vice-President and Treasurer).*

## HOW IS THE IBMM LOOKING IN 2015?

*Bruno André:* The IBMM is today home to around 85 researchers (academic, post doc, PhD students), and 13 research groups working in two main fields: molecular microbiology and cellular and developmental biology. Research in *Molecular Microbiology* focuses on viruses – HIV in particular – bacteria, yeasts, and parasites such as trypanosome, etc. that may cause a variety of infectious diseases. *The Cellular and Developmental Biology* research studies complex mammalian cells and embryonic development using a range of models such as mice, xenopus, zebrafish. This research aims to provide a detailed understanding of diseases with genetic causes, and of certain cancers in particular.

## ARE THESE BOTH NEW AREAS OF RESEARCH?

*Bruno André*: Yes, because before we didn't present ourselves in such a focused way, although some of our expertise has a long track record. These two research areas – which were defined with the laboratories themselves – complement a field that was long ago identified as one of the Biopark's strengths: immunology. In 15 years, the IBMM has grown, the laboratories have seen their research mature, and new teams have come to join us. It was time to demonstrate this scientific reality in our communications, too.

## SO IT IS FIRST AND FOREMOST A COMMUNICATION INITIATIVE?

*Bernard Robaye:* We thought that after 15 years of existence, it was time to update the way we communicate about IBMM expertise and strategy. One way in which this is useful is in facilitating links with business. But it was also a chance for us to improve our internal organisation of teams working in the same field and to consolidate synergies, including with researchers on the Erasme campus and in the ULB hospital network, as well as the Institute of Bioinformatics (IB2) and other researchers working on projects closely related to our own.

## CAN YOU GIVE ONE EXAMPLE OF THIS COOPERATION?

*Bernard Robaye:* Several teams at the IBMM are working with the Experimental Medicine Laboratory headed by Professor K. Zouaoui Boudjeltia at the Vésale University Hospital in Charleroi. Their cooperation revolves around research subjects such as atherosclerosis and septic shock. This type of cooperation is very important as it embodies the "M" for "Medicine" in the acronym IBMM, and in particular provides easy access to human research materials (tissue samples, blood cells, etc.).

## HOW CAN THESE SYNERGIES BE INTENSIFIED?

*Laurence Van Melderen:* The best way is simply to bring people together to present their research and form new relationships. This is what happened when the IBMM held a technology workshop this autumn: we took stock of new genetic manipulation tools alongside researchers from the IBMM, Erasme, and other universities who have begun to use this emerging technology, as well as the companies that sell it, etc. In light of its success, with 130 registered attendees, and practical interest, the technology workshop will become an annual event. In January, we held two molecular microbiology mornings: young researchers (PhD students, post-doctoral researchers) working in this field gave a 12 minutes presentation of their research in English, before fielding 5 minutes of Q&A. It was good practice for them, but also a great opportunity to learn and even forge partnerships. Representatives from companies working in this sector were also invited to attend. Once again, this will become an annual event, alternating between our two fields of research, and more projects focusing on these two fields are in the pipeline.

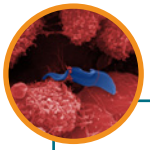
## ARE YOU STILL ENTHUSIASTIC ABOUT YOUR WORK?

*Bruno André:* Yes, and how could we not be? We opened the Institute of Molecular Biology and Medicine 15 years ago, on what was basically farmland. Today, the IBMM stands alongside other research institutes like the IMI and CMMI, etc. as well as the other stakeholders – businesses, training centres, incubators, etc. – that form part of the Biopark. Within the Biopark dynamic, we needed to work together and advertise our specialisms at the IBMM by, for example, making it easier to launch joint research projects or to work with our colleagues at the Erasme campus and the hospitals sector. In 2015, this is exactly what we will do...

*Nathalie Gobbe*

# IBMM: M for medicine…

95% of researchers at the Institute of Molecular Biology and Medicine are from the Faculty of Science, and they carry out research into a variety of infectious and genetic diseases, as well as cancers.



## Sleeping sickness

The trypanosome is a parasite that uses an insect vector, the tsetse fly, to reproduce and spread among its various mammalian hosts. Humans are one such host, and one in which the parasite can cause sleeping sickness, a disease that affects 60,000 people in Africa every year.

IBMM researchers have successfully been able to provide an in-depth description of the molecular mechanism behind sleeping sickness pathogenesis, as well as to outline possible treatment strategies.

Osteoporosis

## Sepsis

Some IBMM researchers branched off from studying trypanosome to look at apoL proteins. Their physiological role is unknown but one such protein seems to be involved in sepsis, formerly known as septicaemia, which takes the form of severe inflammation generally associated with a bacterial or viral blood infection. It leads to death in 30-60% of cases, of which there are 750,000 every year in countries such as the USA. It may become an even greater problem in coming years as the number of infections caused by antibiotic resistant bacteria continues to grow.

Brucellosis

Pena-Shokeir syndrome

Filariasis

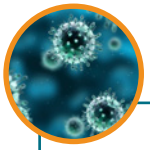
Septic shock

## Obesity

In trying to better understand the role of the apoL1 protein, IBMM researchers observed a potential link with some forms of obesity. Currently classified as an epidemic, obesity affects up to a third of the population in many countries around the world.

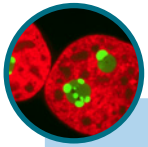
## Cystinosis

Cystinosis is a genetic disease caused by abnormal functioning of cystinosin, a protein used to transport lysosomes, which catalyses the release of cystine present in the cellular compartment. IBMM researchers are studying the link between cystinosin and other lysosome transportation proteins. The aim is to better understand the consequences of an accumulation of cystine in lysosomes for the cell, as well as how cysteamine, the only drug available to treat the disease, works.



## AIDS

Despite the effectiveness of current AIDS combination therapy, so far nobody has recovered from the disease. Currently, the major obstacle in eradicating HIV is the presence of latence reservoirs of the virus that may reawaken following something as innocuous as a cold, for example. A major optimisation of AIDS treatment would be to reduce, or even eliminate these latence reservoirs of the virus, while continuing to treat the patient with effective AIDS therapy to prevent the reawakened virus from infecting new cells. For many years, IBMM researchers have been working to further our understanding of the molecular mechanisms behind this latency, and to discover strategies that will cure patients of their infection.



## Ribosomopathies

With the cells of our body, all proteins are made using nanomachines: ribosomes. Ribosomes are made up of tens of different components that must be assembled precisely to generate functional, reliable machines. When ribosomes are assembled incorrectly our cells fail to produce enough proteins, and those that are produced may contain errors. This exposes us to the risk of developing serious illnesses that have recently become known as ribosomopathies, or “sickness of the ribosome”. Patients suffering from ribosomopathies are often afflicted by cancers, blood cell maturation disorders, and skeletal development problems. IBMM researchers study ribosome biogenesis in human cells and seek to understand how aberrations in the assembly of ribosomes lead to ribosomopathies.

Viral leukaemia and lymphoma

Ciliopathies

Acute myeloid leukaemia

Cancer

## Cerebrovascular diseases

Protected from impacts by the neurocranium, the meninx, and cerebrospinal fluid, the brain is also equipped with a complex biological filter: the blood-brain barrier. This tightly regulated interface between the peripheral vascular system and the central nervous system maintains the homeostasis of the liquid that surrounds the brain, protecting it from pathogens and neurotoxins contained in the blood. The protective, insulating role played by this barrier does however present a major obstacle to the treatment of central nervous system diseases, as it prevents over 98% of potential therapeutic molecules from reaching the brain.

Conversely, a damaged barrier causes too much fluid to accumulate in the brain, fluid that plays a role in the physiopathology of a large number of diseases such as strokes, neurodegenerative diseases, and neuroinflammatory pathologies. IBMM researchers are on the case.

Bone scarring diseases

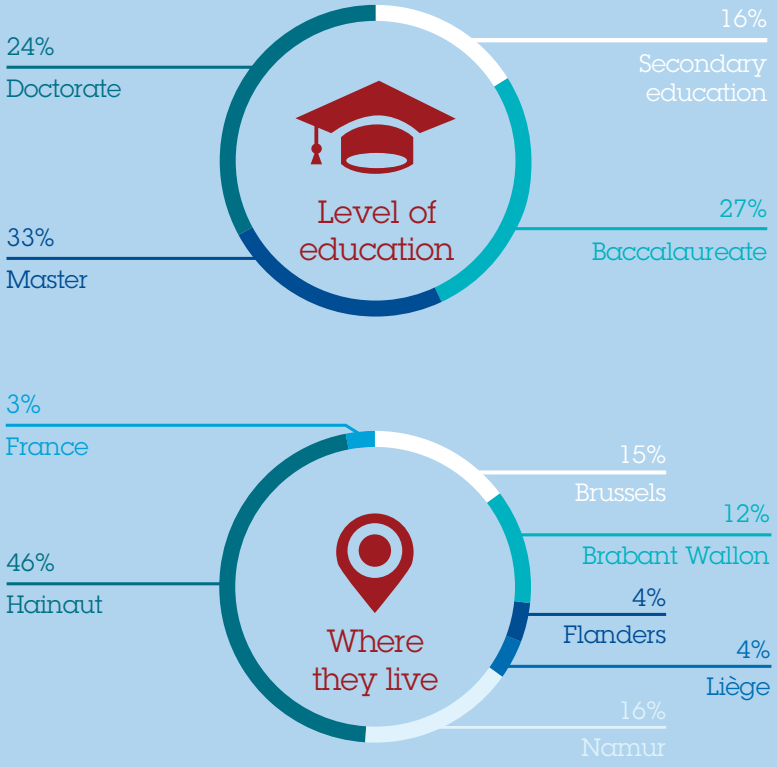
Atherosclerosis

Kidney disorders

Aneurysms

# Biopark: almost 900 jobs

The initial 150 jobs at the IBMM have exploded and today, 15 years down the line, the Biopark employs almost 900 people, representing no fewer than 22 nationalities, with varied levels of education (from secondary to PhD), 80% of whom live in Wallonia, as our latest statistics show.[1]




[1] *Statistics on 15 November 2014, compiled in partnership with Biopark businesses and institutes.*

# Protein structures: crystals of patience

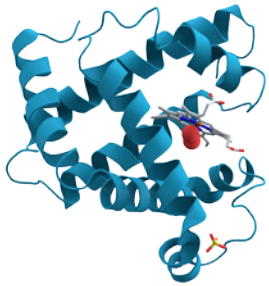
After a long period spent at the VUB, the Cuban researcher Abel Garcia Pino has moved to the Biopark to open a laboratory focusing on the study of protein structures, a new challenge that demands patience and perseverance. We met with the man himself.

A cabinet, a few tables, two chairs, and blank walls: Abel Garcia Pino's office is still quite empty. "I just moved in", the reserved thirty-something points out, "There is a lot to do". Having arrived at the IBMM a few weeks ago, Abel plans to found his research team, the soon-to-open Structural Biology and Biophysics Laboratory. "I always wanted to study structural biology", he explains, "It is one of the rare fields in biology where the result is visible to you. And we can learn a lot about how a protein works just by looking at its structure". The Cuban researcher already had this in mind when he left Havana for Brussels and the VUB where he completed his masters, which he immediately followed with his PhD and post-doctoral research, an education that taught him the virtue of patience: "It can take a lot of time before you finally manage to crystallize a protein", he explains, "It's a lot of work. You need to be able to handle the frustration of failure and start again… and again, and again. Fortunately, it's a fascinating technique and I'm quite determined".

## PROJECTS ALREADY UNDERWAY

Determination that Abel will have to hold onto while his laboratory gets up and running. For the time being, the researcher is trying to source funding to purchase a device to purify proteins, an essential stage in the crystallisation process. The device open the way for a variety of partnerships on the Biopark: "Anyone who works at the cellular level will have the chance to understand things at the molecular, structural level. And for me it will be an opportunity to diversify my future research. It is therefore the perfect place to set up", concludes the researcher, who is not, however, happy to sit and wait. Barely arrived, he has already began joint research with Laurence Van Melderen's laboratory in the same corridor. "She has maintained a longstanding partnership with the VUB laboratory where I was a student", Abel explains, "I have known her for a while already and we have similar interests". And indeed, the Brussels graduate wants to study bacterial persistence and attempt to explain the emergence of antibiotic resistant bacteria, which is also a subject of interest to the Bacterial Genetics and Physiology Laboratory next door. "Now that the proteins involved in this process are known, my research will try to shed light on what happens at a molecular level. The goal is to better understand how the bacterial metabolism is regulated, how resistance factors emerge and, why not, to define interesting pharmaceutical targets", concludes the researcher, somewhat impatient to begin his own projects. Once the protein purifier is in place, it will be a question of slowly attracting PhD and post-doctoral students. While he is keeping his cards close to his chest, Abel Garcia Pino's strategy seems clear, and the researcher confident: "I have always wanted to launch my own research projects, and now is the right time. It's a new challenge", he states plainly.

*Natacha Jordens*



*The structure of a protein (here, myoglobin) provides a lot of information about its function*

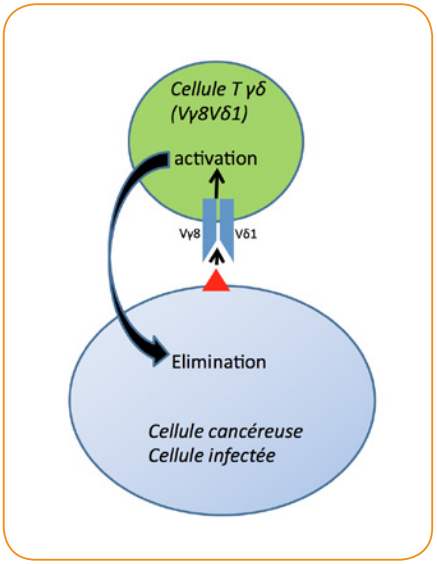
# 2014 Fonds Ithier Award Winner at the IMI

For his research into the role of Gamma Delta T cells in early life, and their possible applications in cancer immunotherapy, David Vermijlen, visiting lecturer at the Faculty of Pharmacy and researcher at the Institute for Medical Immunology, has been awarded the Fonds Ithier Award 2014.

Launched in an effort to promote the fight against cancer at the *Université libre de Bruxelles*, the 2014 Gaston Ithier Award went to David Vermijlen, visiting lecturer at the Faculty of Pharmacy and researcher at the Institute for Medical Immunology (IMI). The award is recent acknowledgement (€75,000 were allocated to the project) for research that goes back several years, and recognition of its significance for the role of Gamma Delta T cells in early life, which encompasses the foetus, new-borns, and early years.

"Cross-disciplinary cooperation between the IMI, the Erasme Hospital, and with other hospitals has enabled us to discover that human *Gamma Delta T* cells (which are unconventional T cells) can fight against infectious agents even before birth", David Vermijlen explains, "We have more recently discovered that these anti-infection Gamma Delta T cells, expressing a Vg8Vd1 receptor, also react to cancer cells".

Present in all humans, these Vg8Vd1 Gamma Delta T cells may be of use in cancer immunotherapy. If the ligand (the molecule bound to a receptor) is identified, then it may become possible to stimulate these Gamma Delta T lymphocytes in order to kill cancer cells *(see figure)*. "The challenge lies in identifying this ligand in order to better understand these cells and the role they play. This could lead to new strategies in cancer immunotherapy being developed", David continues.




How does the Vg8Vd1 TCR receptor identified in earlier research interact with cancer cells? What does the receptor recognise/detect? What role does the ligand play? These are all questions that David Vermijlen will endeavour to answer over the coming months.

*Damiano Di Stazio*

## DAVID VERMIJLEN: PROFILE

- **1990-1995 :** Bioengineering degree at Ghent University.
- **2003 :** Thesis on the defence mechanism of the liver's Natural Killers (immune system cells), VUB Faculty of Medicine and Pharmacy.
- **Up to 2003 :** Assistant in the Laboratory of Cellular Biology and Histology at the VUB.
- **2003-2006 :** Post-doctorate in the Immunobiology Laboratory at King's College London.
- **Since 2006 :** Researcher at the Institute for Medical Immunology, IMI.
- **Since 2012 :** Visiting lecturer at the ULB Faculty of Pharmacy.

# First Enterprise. A win-win project

Born of a partnership between GSK and the CMMI, the First Enterprise project "Nanoparticle Vaccine Industrial Preparation Platform" will provide a researcher with two years of full time employment with the company, as well as a work placement within the research unit.

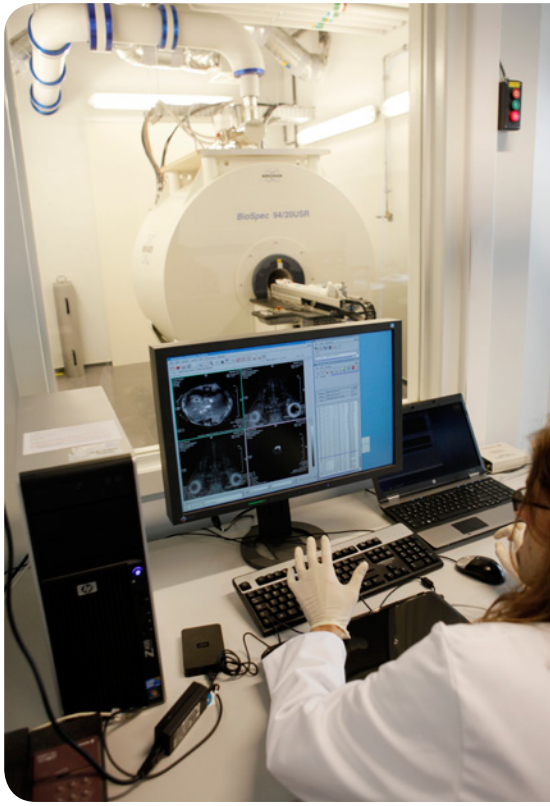
A First grant (FIRST University Colleges, FIRST Spin-Off, FIRST Enterprise, etc.) sees a young researcher receive two years of funding from the Wallonia (and GSK, for this project in particular). And what is the aim of these programmes? To create the proper conditions for real collaboration between various stakeholders in research who are willing to benefit from each other's experience by sharing scientific expertise and technical facilities. "The programmes provide an opportunity to share sophisticated facilities and expertise, as well as to learn about the restrictions and occasionally differing objectives that these stakeholders pursue", explains Dominique Demonté, Director of the Biopark. "Furthermore, it falls neatly under the objectives of the ERDF that financed the CMMI, such as enabling the transfer of skills between universities and businesses".

The First Enterprise Project in particular enables businesses to employ a researcher to carry out research, providing training through a work placement within a research unit (universities, certified research centres, etc.). Indeed, this describes the adventure that GlaxoSmithKline (GSK) and the Centre for Microscopy and Molecular Imaging (CMMI) have embarked upon with the "Nanoparticle Vaccine Industrial Preparation Platform" project.

"The project sets out to develop a procedure to create links between the structure (size, ultrastructure, surface properties) and biological activity of the nanoparticle formulae developed by GSK", explains Pol Harvengt, Expert Scientist at GSK. These tools will be used to study the impact of some of the nanoparticle's physicochemical properties, such as their size or the composition of their surface layer.

For GSK, the main benefit of the project will be the researcher learning the skills needed to assess and select imaging technology. This technology should enable nanoparticle vaccines to be characterised, evaluated *ex vivo,* and their activity monitored *in vivo*. "This experience at the CMMI will give GSK the opportunity to acquire the skills needed to evaluate the very best imaging techniques", Dominique Demonté continues. It could make a real contribution to the selection and approval of new nanoparticle formulae. These techniques are not currently available within the company.

*Damiano Di Stazio*



# A new cell therapy MasterClass scheduled

A MasterClass will be held on 31 March at Biopark Training, aimed at current and future business owners, a new addition to the prospectus focusing on how to build partnerships to market goods and services in the cell therapy sector.

A major biomedical and pharmaceutical challenge, cell therapy will once again be the hot topic at Biopark Training in March 2015. “Cell therapy is a major strategic objective for the Biopark campus and Wallonia in general”, explains Arnaud Termonia, Director of Biopark Training. “This can be seen in the five cell therapy companies, members of bio.be, who work together as part of the Co-ACT platform: Beta-Cell, Bone Therapeutics, Cardio3 BioSciences, Promethera Biosciences, and TiGenix who aim to create 2000 jobs by 2017. For several years now, cell therapy has received the active support of the Marshall Plan, and is one of the main priorities of the Biowin competition cluster”.

The 1 and 2 April 2015 will also see a special cell therapy event on the Biopark: *B4B-Connection Cell Therapy* (Buzz4Bio Conferences). The event is designed to “enable sector players take part in formal (specialist conferences, presentations, etc.) and informal (networking breaks, cocktails, and networking lunch) networking”.

It is against this backdrop that Biopark Training is launching its cell therapy MasterClass as part of a day-long event (31 March) dedicated to building partnerships to market cell therapy goods and services. “We think it’s important to support and enrich the event with training activities”, Arnaud Termonia goes on. “Two themes will be dealt with over the course of the day”, adds Béatrice Goxe, Scientific Coordinator and Trainer at Biopark Training. “The first part will focus on better relations with Belgian and French regulatory bodies, while the second will deal with how to find new partners to finance cell therapy activities”.

On the agenda, top flight speakers including Eric Halioua on sourcing capital outside Europe, Alan Fauconnier on financial assessment, and Jean Van Nuwenborg on regulatory affairs.

The target audience? Current and future CEOs from specialist cell therapy companies, as well as all sector players looking to found subsidiaries or diversify their partnerships in France and Belgium.

*Damiano Di Stazio*

## COURSE PROGRAMME

- Introduction to legislation on cell therapy products
- Group activities with role play coached by regulatory experts
- Introduction to the main sources of funding for cell therapy businesses
- Two case studies
  - o Sourcing capital outside Europe
  - o How to float on the stock market
- Group activities with role play coached by regulatory experts
- Closing cocktail dinner

# An alternative to histology?

Currently, preclinical research into bone repair is carried out through a mainly histological approach. By using a combination of imaging methods, the OSTEOMOD project - born of a partnership between the CMMI and Bone Therapeutics - sets out to offer an alternative to histology.

In regulatory terms, one of the critical phases in the preclinical development of drugs in general, and cellular products in particular, is the *in vivo* validation of their effectiveness in models similar to their clinical application. This stage requires that methods for *in vivo* analysis, often difficult to set up, need to be created and approved.

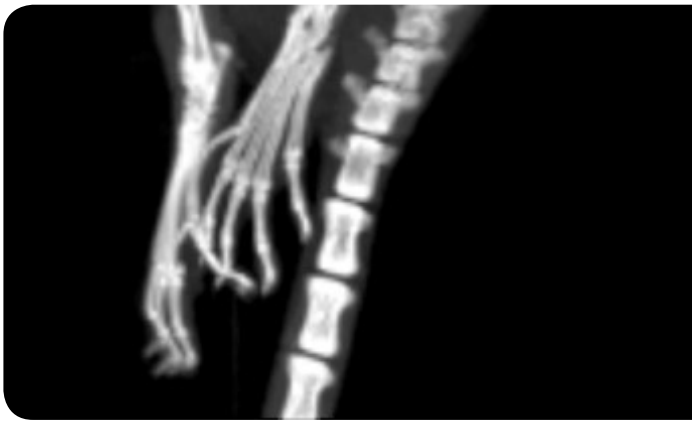
At the time of writing, preclinical research into bone repair is carried out via a mainly histological approach. It is a relevant, essential, and ethically acceptable approach for simple models. It becomes unwieldy when using animals for *in situ* kinetic studies of bone repair commissioned for complex fractures: the study is a lot longer in duration, and intermediate samples mean animals must be sacrificed.

Funded by *Wallonia*, the CWALity OSTEOMOD project is the fruit of a partnership between Bone Therapeutics and the Center for Microscopy and Molecular Imaging (CMMI), and uses a combination of imaging techniques to provide a non-invasive alternative to histology. It can obtain reliable results with no need to sacrifice animals and provides truly dynamic *in situ* monitoring of repairs to bone defects. "OSTEOMOD falls under the 3 'R' Rule", reports Enrico Bastianelli, Director of Bone Therapeutics, "Reduce, Refine, and Replace. Reduce the number of animals used in the experiment, Refine the methodology used, and Replace animal models".

"The CMMI and Bone Therapeutics have been working together now for several years", explains Gaetan Van Simaeys, a researcher at the CMMI and the Erasme Hospital Nuclear Medicine Department. Thanks to our cutting edge biomedical imaging equipment, we are able to develop quantitative indications in imaging".

"The CMMI brings high added value, in particular thanks to its solid background in bone and cartilage imaging", Enrico Bastianelli continues. "It's not the first time that we have called upon this expertise: CARTIM, a cartilage imaging project to evaluate therapeutic products designed to reduce joint damage caused by arthritis, is another example".

*Damiano Di Stazio*



*Mouse femur fracture microCT, as will be realized by the CMMI as part of its collaboration with Bone Therapeutics in the project OSTEOMOD.*

## A NEW PARTNERSHIP FOR BONE THERAPEUTICS

In November, Bone Therapeutics announced the launch of a 2-year partnership with Kasios in France, during which they will work to develop a new product for use in spinal fusion procedures. Sponsored by the Wallonia, the project combines technology from each company: cell therapy using donated osteoblasts in ALLOB® by Bone Therapeutics, and the synthetic micro-granulated bone substitute *TCP* by Kasios.

Both partners hope to develop a new approach to healing spinal lesions by combining these two products, in particular during the osteoconduction process in which the grafted material acts as a medium for the growth of new bone.

# In brief

## THE ACIDIFICATION ENABLES APOL1 TO WORK

Another front page image for the CMMI! After *Science, Eukaryotic Cell,* and the *Journal of Microscopy,* it is now *Molecular Microbiology's* turn to choose a photo from the centre for microscopy to illustrate its November issue. The image accompanies an article by Laurence Lecordier and the team at the **Laboratory of Molecular Parasitology (IBMM),** headed by Etienne Pays, about man's natural immune mechanism against the African parasite Trypanosoma brucei, an immunity that was probably acquired when man's ancestors appeared on the African continent.

The laboratory had previously discovered that this immunity is associated with the serous protein APOL1: the protein forms pores in the trypanosoma's digestive compartment, which kills the parasite. In this most recent publication, the team has identified the parts of the parasite that enable APOL1 to work. The different components are all involved in the gradual acidification of the digestive compartment, thereby proving that this acidification is necessary for APOL1 to work in trypanosoma.


## INFLAMMATORY PROTEINS CONSTANTLY DEGRADED

TTP/Tis11 family proteins are factors involved in the downregulation of several different families of genes, including those involved in the inflammatory response: in too large numbers, these proteins may constitute a major impediment to the immune response, while too few of them may make it easier for inflammatory or auto-immune diseases to take hold. This means that regulating levels of proteins belonging to this family is crucial to the organism, but the mechanisms governing this regulation remain little understood.

In an article published in *Molecular & Cellular Biology,* Cyril Gueydan and the team at the **Molecular Biology of the Gene Laboratory (IBMM)** revealed the mechanism through which cells degrade TTP/Tis11 family proteins. But unlike the traditional degradation mechanism in which a degradation *marker* is attached to the target protein (ubiquitination), TTP/Tis11 proteins are constantly identified and degraded by cellular machinery. It is the balance between this constant elimination and the synthesis of new proteins that regulates intracellular levels.

Since then the team has been trying to understand the details of the degradation mechanism in immune system cells, in an effort to shed light on its potential involvement in triggering and controlling the immune response and any associated diseases.

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