The Centre of Microscopy and Molecular Imaging became a reality thanks to financial backing from the European Union and Wallonia (FEDER funds). It’s an innovative resource, an important symbol of the industrial restructuring of Wallonia and, more particularly, of Charleroi. This city isn’t short of signs of renewed vitality, showing a surge in both economic restructuring and cultural activities. What springs to mind, of course, is the airport and its spectacular development, demonstrating our capacity to bring off large scale projects. Just as important, or even more so, is its inseparable Aéropole, the impressive area where we can see the new aspect of the city, resolutely looking to the future. The sustainable development of Wallonia is, in part, happening in this growing cluster.

With the inauguration of the imaging centre in November this year, we’re going a step further in the development of the Biopark. The result of a collaboration between ULB and the UMons in the context of the FEDER Hainaut-BIOMED project portfolio, this resource is further proof of the vitality of our region. The centre is, in fact, one of the few in Europe able to provide its partners with a concentration of resources to their benefit. CMMI, with its interdisciplinary transversal approach, is an excellent example of the positive effects this approach can produce.

Secondly, companies can benefit from a technological environment of high quality, an essential item when we think of the importance of technical performance in the continuing establishment of competitive companies in Wallonia. Fuelled by increasing demands in the competitiveness clusters, we’re working to create job opportunities. In this area too, CMMI serves as an important industrial partner just like, more generally, the different possibilities in life sciences which shouldn’t be ignored.

All this underlines the vital importance of training in a region of excellence like ours, especially in scientific professions which need a high quality labour force, a genuine Walloon trademark. CMMI therefore constitutes a new piece of the transversal structure which the Walloon Government, with the support of the European Union, is setting up to work on the industrial restructuring of Wallonia.

It contributes to strengthening the competitiveness of Biopark in Hainaut and to the benefit of society as a whole - citizens, enterprises and researchers. In fact, when we put into perspective the actions of the Walloon Government and the Government of the Wallonia-Brussels Federation via the "Plan Marshall 2.vert", the declarations of regional and community policies and the allocation of Structural Funds, we can speak about a real concentration of resources and energy for socio-economic priorities, with the aim of creating sustainable development. Projects co-financed in the context of the 2007-2013 European Cohesion Policy benefit from a total budget of 3.129 billion euros, 1.356 billion of which comes from the European Union budget via the Structural Funds FEDER and FSE and 1.672 billion from federal entities. The rest, that is 101 million euros, is provided by various public investors.

More than 3 billion euros therefore, in total, distributed over 109 project portfolios in Hainaut and 111 in the rest of Wallonia and in Brussels... so many development projects the results of which can be found at www.plushaut.be.

Rudy Demotte
Ministre-Président de la Wallonie
It was «a bit of a mad idea», said Robert Muller, its Scientific Director, which becomes a reality on 15 November this year: the inauguration of the centre of preclinical multimodal imaging, CMMI (Center for Microscopy and Molecular Imaging). « Due to its size and complexity such a project was a bit of a fantasy. Its realisation, as often in such cases, resulted initially from small talk and then an opportunity which arose later» Robert Muller tells us.

The idea started to develop in his mind and that of Professor Michel Goldman (then Director of the Institute for Medical Immunology on the Biopark and now Director of IMI, Innovative Medicines Initiative) during a trip to China in 2005. Sharing and completing the imaging equipment in ULB and UMons would increase their research potential and provide an attractive platform for both companies and research centres.

Convergence
From the initial concept to its realisation, progress was rapid. The project was submitted in the context of the European Union «Convergence programme» and the Walloon Region received a budget of 15 million euros. The research teams were in place, working together, exchanging ideas and expertise, the equipment required was identified, ordered and the building work began, below the Institute for Medical Immunology, just next to the Biopark Incubator. The teams moved into their new laboratories in autumn 2011.

Unique in Wallonia, rare in Europe, CMMI can now provide all analyses (on a scale from molecule to animal) on one site. They have about 700 m² of laboratories and offices in the Biopark. This one stop shopping approach to preclinical imaging – the three unities of place, time and action for all analyses done – obviously optimises the various steps and reduces costs for the customer.

Ten units
The CMMI is organised in ten different units, each supervised by an academic. They are: Electron Microscopy, Automation and Quantitative Morphometry, Holographic Microscopy, Fluorescence Microscopy, Fluorescence Microscopy, Imaging Flow Cytometry, Magnetic Resonance Imaging (MRI), vMlx iv (Positron emission tomography imaging and X-ray tomography), Optical Imaging, vMlx ev (Autoradiography) and Diapath (Immunohistochemistry). By combining different innovative cutting edge technologies and skills, CMMI can provide academic and industrial laboratories with the possibility of analysing a sample by different types of microscopy.

Interactions
Almost twenty people directly financed by the project work in CMMI. They work closely with teams from ULB and UMons (Faculties of Medicine, Science, Applied Science) active on the campuses in Charleroi (Biopark), Brussels (Erasme, Solbosch) and Mons.

They also interact with other players such as Biopark Formation/Training and several companies. In addition to doing recognised collaborative research, CMMI also sets up partnerships with companies and collaborates in the provision of different training courses in medical imaging. This Biopark News will give you an idea…

Welcome to

The Biopark Charleroi Brussels South now has a new research institute. The Centre of preclinical multimodal imaging, CMMI, is inaugurated on 15 November. The story of an exciting adventure which is just beginning…

Do you want to know more?
Go to http://www.cmmi.be


**Research**

**Towards the infinitely small**

*CMMI has state-of-the-art equipment in transmission and scanning electron microscopy. David Pérez-Morga manages this unit which studies various questions not only in molecular biology but also, for example, in botany and nanotechnologies.*

Cells have cilia, sort of microscopic antennae which emerge and bathe in the extracellular liquid, exploring it and playing a sensory role. Sometimes cilia have anomalies in their construction resulting in ciliopathies, rare diseases which can cause renal cysts, the development of anomalies in the eye, skeleton and brain, and also polydactyly, obesity, etc.

Responsible for the electron microscopy unit in CMMI and a junior lecturer in ULB, David Pérez-Morga, is fascinated by the cilia which can cause many diseases. A few months ago, he and the team of his IBMM colleague, Stéphane Schurmans, discovered one of the genes responsible for ciliopathies, INPP5E. In an article published in the journal *Nature Genetics*, the researchers showed that in INPP5E deficient mice there was a decrease in the number of cilia but those which persisted had a completely normal morphology. «We've known about cilia for about fifty years but we don't yet know much about their role, the way they work, their origin, etc. In particular, their role in the development of the embryo is not well known. I was very surprised to see that up to now few scientists have shown much interest but this apparent lack of interest is no doubt linked to the technological limits. Cilia are so small, complex and difficult to see that the use of high technology, like our present electronic microscopy equipment, is necessary», explains David Pérez-Morga.

**Cilia and kidneys**

At the moment the researcher, with his team and some Italian colleagues, is interested in primary nodal cilia present in very early mouse embryos and those in their kidneys which, strange though it may seem, are not yet mature when a mouse is born. Why? When do cilia become mature and therefore functional? And how do they become so? The CMMI team is studying these different questions and is trying to describe the morphology of kidney cilia using electron microscope analyses. «The transmission electron microscope lets us observe very thin cell sections, between 20 and 80 nanometres, while the scanning microscope gives us images of complete small organisms or complete cells whose morphology we can then study. The CMMI is also the only centre in Belgium which provides a service of cryoultramicrotomy, i.e. ultra thin sections under liquid nitrogen at -120°C», adds David Pérez-Morga.

**Trypanosome**

For over 17 years, the researcher has been studying one particular parasite, the trypanosome (responsible for sleeping sickness). In an article published in the journal *Science* in 2005, in collaboration with Etienne Pays’ team in IBMM, he showed how a human protein, ApoL1, is capable of killing non-pathogenic trypanosomes. «What we still have to discover is how one of the pathogen sub-species, the trypanosoma gambiense, is capable of countering ApoL1. This is now our next great challenge», says David Pérez-Morga.

**Collaborations**

Although the researcher has his own research subjects, he and his team are also open to other scientific projects. Up to now they have set up around thirty collaborations in ULB and UMons and they also work with other universities and institutes in other countries. Among these, there are several collaborations on cilia and also others with the neighbouring Institute of Pathology and Genetics (IPG). «We give them access to our equipment for the analysis of very rare pathologies» explains David Pérez-Morga. We also work with the ULB Laboratory of Plant Biotechnology (LBV) with which CMMI has just co-published an article in the *Journal of Experimental Botany*. They studied the expression of the Ntann12 protein in the root of the tobacco plant. Other projects are ongoing in the biomedical and plant fields, particularly in the analysis of vaccines and nanomaterials.
Based in Roissy in the region of Paris, Guerbet specialises in the research, production and commercialisation of contrast agents used in MRI technologies, X-ray imaging and nuclear medicine.

The company has been collaborating with Professor Robert Muller’s laboratory in the University of Mons for over twenty years. In fact, Guerbet and the general, organic and bio-medical chemistry group in UMons have been working together on molecular contrast agents, with a view to being able to do increasingly fine-tuned personalised diagnoses and prognoses. «Oncology treatment is costly and often difficult. Using biopsies from tissue tumours we’re now able to evaluate if a treatment will be efficient in a given patient - in other words, to know if the patient is biologically compatible with the treatment. It can also happen that a drug is efficient at the beginning of the treatment but after a certain time it becomes inactive, causes side effects or even becomes toxic. Our tools enable us to predict things like that», explains Marc Port, Research Projects Manager in Guerbet.

Fruitful collaboration

At the head of an R&D team of sixty or so researchers, Marc Port now has over a hundred scientific collaborations set up around the world. «The collaboration with Robert Muller is one of the most fruitful and closest we have with a university laboratory», says Marc Port. «We were looking for specific skills and we found them in UMons. That’s how the collaboration began. Then, over the years, confidence and even friendships were established. We’ve published articles together, applied for patents together, it’s obvious we’ve got the same perception of research and we’ve managed to harmonise both academic and industrial interests».

Nuclear medicine

Based on this success, Guerbet is naturally interested in CMMI where Robert Muller is the Scientific Director. There the company met Professor Serge Goldman, head of the Nuclear Medicine unit in the Erasme Hospital and academic head of NUMIX (Nuclear Molecular Imaging) in CMMI. «For around 4 years, Guerbet has also been oriented towards nuclear medicine. We’re looking for centres of excellence to work with us on nuclear medicine as applied to three large categories of pathologies: oncology, neurodegenerative disorders and cardiovascular disease. We’re looking into, for example, the early diagnosis of Alzheimer’s and early screening for colon cancer», explains Marc Port.

The human contact was good, the scientific exchanges fruitful, and so the idea of setting up a close collaboration with CMMI arose. «Outsourcing means paying to receive a deliverable. The relationship stops there. In Guerbet, we want to go further. We like to discuss with experts, share our knowledge, make our research progress, in short, work with colleagues, regardless of whether we belong to the world of academic or industrial research», says Marc Port.

PPP

The collaboration might be in the form of a PPP (Public Private Partnership), with Guerbet and CMMI researchers all working in the Biopark. The French company has been motivated to create a Walloon branch which will give it the right to enter into a PPP with CMMI. All that remains to be done is to submit the request to the Walloon Region...

«This PPP is very important for Guerbet because there aren’t many multimodal platforms like CMMI where you have the complete chain, from the synthesis of a product to its evaluation for imaging. I can’t think of one real competitor in Europe. It’s also interesting because in nuclear medicine we’re short of space. CMMI has the room to accommodate researchers. Finally, working with competent people is of great value to us. For example, when I have a discussion with Professor Serge Goldman, he gives me the clinician’s point of view. He compares my research approach to the needs of his patients. Thanks to these exchanges, we can better orient our scientific programmes and equipment requirements», says Marc Port.

For CMMI, the interest in working with a company like Guerbet is just as high. It’s the very demonstration the technological choices and scientific expertise of CMMI are coherent, attractive and, in the end, will create economic value in the Biopark. The partnership and the resulting exchange of skills is also the occasion to select new projects in the future and increase research capacities in CMMI… a perfect chain, once the Walloon Region has added its vital link.
**Training in imaging**

Based on the skills and equipment found in CMMI, Biopark Formation/Training has set up a training cycle on Imaging. This begins with a day of introduction to (preclinical) molecular imaging on 8 December.

**Overall picture**

This is the type of public the Biopark Formation/Training cutting edge training course on 8 December is targeting. In one day they will get an overview of molecular imaging today and of its applications via theoretical presentations, case studies and a visit of CMMI, the new Centre of molecular imaging.

It’s also aimed at all the players in the industrial and academic biotechnology sector, for example, technicians, researchers and final year and PhD students who need an introduction before sitting down in front of the instruments, and teachers in «Hautes Ecoles» who could then train their students in these cutting edge technologies. This cycle is also accessible to job seekers, directly or as part of a long-term training programme such as BIOPOLY or BIOCEL. Thanks to financing from the «Académie universitaire Wallonie-Bruxelles», there’s a special tariff for training in imaging for ULB and UMons PhD students.

**Specific modules**

The first module of the cycle will give an overview of preclinical molecular imaging. Biopark Formation/Training, in collaboration with teams from CMMI, intends to develop modules specific to the technologies found in the Centre. Some half-day modules will be organised in 2011 and 2012. In addition, cutting edge modules in multi-spectral imaging by flow cytometry and optical and electronic microscopy are already in their catalogue. «In these state-of-the-art courses, we alternate theory and practical demonstrations. We rely on the CMMI experts who advise us, or even give the courses, and on the cutting edge equipment of the Centre used for the demonstrations », explains Erika Baus.

Organised for the first time on 8 December, the introductory training in preclinical molecular imaging has already been approved and is subsidised by the BioPharE programme of the competitiveness cluster BIOWIN. (It’s therefore not so expensive for the trainees.) The objective of BIOWIN is to strengthen the development of skills critical for the strategic, scientific and operational excellence of the members of the health-oriented competitiveness cluster.

«Our objective is to provide an overview of the potential of molecular imaging. These new technologies, with a wide variety of areas of application, are sometimes not yet very well known», says Erika Baus, a trainer in Biopark Formation/Training and coordinator of the Imaging courses.

The Biopark Formation/Training team started from the concept that industrial and academic research laboratories often hesitate to invest time and money in imaging technologies. Some of the instruments are indeed expensive and, in addition, many technologists, researchers and project managers often find it difficult to identify the potential applications of the techniques. But when they decide to use them, they have to be able to discuss with their future service providers. They have to know the possibilities and limits of imaging, define the characteristics of the samples to be supplied, be conversant with the background and technical vocabulary without necessarily being able to do the experiments themselves. In the same vein, a company or academic laboratory which wants to strengthen an area of research or start working in a new area might wonder if one or several imaging techniques could be useful. They therefore need to understand their potential and limits.

You can consult the training agenda and sign up on the BIOWIN web site (http://www.biowin.org).
Marjorie Vermeersch
«I turn on the radio and I settle down by the microscope»

With a diploma in clinical chemistry, Marjorie Vermeersch works in electronic microscopy in CMMI. A look at the career of this skillful enthusiastic young woman.

«When I explained what I do to my mother, she didn’t believe me. She always thought of me an excitable quick-tempered person... a difficult temperament to reconcile with the meticulous precise work I do. But when I go to the lab, I turn on the radio, settle down by the microscope and nothing can disturb or annoy me, even if I do sometimes swear a little!», says Marjorie Vermeersch.

The young woman is overflowing with enthusiasm and it shows. With a diploma in clinical chemistry from the «Haute Ecole Louvain en Hainaut» (Fleurus), Marjorie began her professional life on the ULB Erasme campus. «When I was a student, I really liked histology, the precision of the techniques involved, the delicate work to be done... I therefore chose a subject in histology for my final year project and it eventually led me to the Laboratory of Pathological Anatomy headed by Isabelle Salmon. On 15 July, just after I got my diploma, I already had a job» she remembers.

At IBMM

She then worked for two years in the Laboratory of Pathological Anatomy. «It was really fascinating, I learnt a lot and participated in very interesting research linked directly to clinical applications. For certain diagnoses I sometimes even went to the operating theatre with the doctors. The link with the patient was immediate, very motivating. But it was hard work – 12 hour days were not unusual – and the travelling between La Louvière, her native town, and Brussels (or rather being stuck in traffic jams) was exhausting. Marjorie therefore decided to look for work closer to home. It was 2001, the Institute of Molecular Biology and Medicine (IBMM) had been inaugurated two years earlier. They were looking for a lab technician, Marjorie applied and was taken on. She joined the Immunobiology Laboratory, headed by Muriel Moser and stayed there eight years, moving from cell culture to histology, which became her speciality.

At CMMI

A new professional opportunity then presented itself. David Perez-Morga told her he was looking for a technician for the new electron microscopy section in one of the 10 CMMI units he managed. She thought about it, hesitated a little and then decided to take the plunge. She joined CMMI in 2009.

«Electron microscopy is derived from histology. In both cases, you make sections of cells or organs, for example, which you stain and observe. In histology you work on tissues but in electron microscopy you work on a scale 1000 times smaller and you can see inside the cells themselves with a great deal of precision. It was a new challenge for me», explains Marjorie Vermeersch. She accepted that challenge. She enjoyed the finesse and dexterity indispensable in electron microscopy, and the variety of subjects and range of techniques also delighted her. «At CMMI, I can work not only on the trypanosome and dendritic cells but also meet the demands of a plant or nanoparticle laboratory! Each time there’s a problem, you have to think of the best technique to solve it, test it, verify it... We’ve also set up collaborations with companies who ask us to validate their samples, we then move from pure research to quality control», says Marjorie and she goes on «Electron microscopy techniques continue to evolve, we have to read a lot, update our knowledge constantly. For example, I went to Montpellier to learn ultracryotomy. In Belgium only CMMI provides this service. The technique involves making sections under a flow of nitrogen at -120°C, allowing us to work on samples of between 50 and 100 nanometres». At first she thought she might be bored in the laboratory but she now admits there’s no fear of that...

Her pastimes ? «My pastimes are those of my two children!» she smiles. «My daughter is mad about horses and, even though I’m scared of them, I spend my weekends at the riding school!». Marjorie is happy to swap her lab coat for a kitchen apron. There too she opts for delicate painstaking work. «Don’t expect me to prepare a stew for you. I prefer verrines of appetisers, dishes with little fiddly bits or with instructions such as «mix cream at 80° with a paste at 120°» confesses the young woman.
An interview with two researchers who participate in the CMMI adventure

Christine Decaestecker,
DIAPATH (Digital Image Analysis in Pathology)

> Tell us about your career in a few words.
Christine Decaestecker: As a mathematician, I did my PhD in data analysis and then specialised in machine learning in the IRIDIA research group (ULB). During a long-term collaboration with Professor Salmon (Laboratory of Pathological Anatomy at the Erasme Hospital), I became interested in the specifics of anatomoclinical data and in techniques for analysing images suitable for providing objective quantitative descriptors for pathological cells and tissues. Today I’m the president of the biomedical section of the Ecole polytechnique de Bruxelles (ULB) and FNRS senior research associate at LISA (Laboratory of Image Synthesis and Analysis). I also co-manage the DIAPATH unit at CMMI with Isabelle Salmon.

> What does the DIAPATH unit at CMMI consist of?
Christine Decaestecker: DIAPATH provides an integrated solution for histological analysis and the identification, characterisation and validation of protein biomarkers by the analysis of images and data. Our approach is integrated into the modern anatomopathologic approach which is really evolving towards digitisation. Digitisation of cytological and histological sections has advantages, especially for archiving and access to standardised reproducible analytical techniques by the analysis of images, generating quantitative data available for statistical analysis. From a medical point of view, this also facilitates the exchange of «cases», enabling us to benefit from the experience of colleagues. In medicine we can also use digitised slides for teaching purposes, for example, making the material easily accessible to students. Our biomarker platform is focussed on proteins, key players in metabolism. We identify the presence and location of a protein inside tissues by using different immunohistochemistry techniques applied to the sections of the tissue to be studied. The labelled histology slides are scanned and the digitalised images generated then analysed. These images are useful in hospitals to establish a diagnosis and also to evaluate the response to a treatment. In clinical and preclinical research they can be used to identify, for example, new diagnostic, prognostic or therapeutic biomarkers.

> What do you think the principal asset of CMMI is?
Christine Decaestecker: It’s the one stop shopping. At CMMI, a large number of skills and techniques are brought together for imaging analysis, ranging from a molecule to a small animal. More specifically for DIAPATH, it’s the implementation of a long collaboration between my group in the Faculty of Applied Science and that of Isabelle Salmon in the Faculty of Medicine. Technicians, biologists, physicists, IT specialists and engineers work together in DIAPATH, taking part in what has become a major trend today, digital pathology.
Gilles Doumont, NUMIX (Nuclear Molecular Imaging)

> Tell us about your career in a few words.

Gilles Doumont: I’m a biochemist by training. After a final year project in the Department of Molecular Biology in ULB, I did a PhD in oncology at IBMM and then a post-doc in the Netherlands Cancer Institute (NKI) where I worked on breast cancer. After five and a half years there I decided to come back to Belgium and started working at CMMI in April 2011.

> Which part of CMMI do you work in?

Gilles Doumont: I work in NUMIX (Nuclear Molecular Imaging). We do three types of imaging: firstly, in vivo nuclear molecular imaging (positron emission tomography, PET, and tomoscintigraphy or single photon emission commuted tomography, SPECT, on small animals injected with a radiotracer), secondly, in vivo anatomic imaging (commuted tomography or CT scanning) and, finally, ex vivo resolution molecular imaging of sections of radiolabelled tissues (autoradiography). With our equipment, we’re able to do non-invasive metabolic functional cell imaging in real time, with high sensitivity and good resolution. I’m in charge of projects in our team, from identification of the needs of the customer, definition of experiment protocols, acquisition and analysis of images, to the generation of results and writing of reports.

> What do you think the principal asset of CMMI is?

Gilles Doumont: The key players in CMMI are also researchers at ULB and UMons, reputed in the scientific community. CMMI benefits from the expertise they have acquired over many years. The interactions are continuous and mutually enhancing for everyone. It can only be a benefit for the basic research done in the Biopark and the technological services provided to third parties. It is important for CMMI to provide customised services. We listen really carefully to our customers, whether they are academic laboratories or private companies.

Lab’Insight

There will be a Lab’Insight dedicated to biomedical imaging on the Biopark on Friday 25 November from 9h to 13h. What’s the idea of this? During the morning companies will meet university laboratories and French Community «Hautes Ecoles». It will be a morning to discover the expertise and, who knows, maybe set up collaborations. Centred on biomedical imaging, the Lab’Insight will be in the Biopark Charleroi Brussels South and participants will be able to visit the new CMMI.

Information and registration at http://www.labinsight.be

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