



Innovation isn't ordered, it's organized !

When ULB decided to set up the Institute of Molecular Biology and Medicine (IBMM) in Charleroi, many observers asked themselves different questions. What role could the installation of university research teams play in the development of the region ? Wouldn't the jobs created be reserved for over-qualified people from Brussels ? Our researchers also wondered : Will we manage to recruit good students, given the fact that it's so far from Brussels ? How could we attract researchers from abroad to the site ?

10 years later, the different parties are reassured. Today, Charleroi has become a "biotechnology region" : 550 people work in the Biopark, almost half of them in spin-offs from our research institutes. Different players in the sector – the Institute of Pathology and Genetics, the cluster BioWin – have joined the Aéroport.

Nevertheless, the paths leading from the university laboratory to the creation of a company are complex and often unpredictable.

To cite just two recent examples presented in Biopark News : Even if studies on parasites such as the tick and the trypanosome could possibly have industrial and medical applications, the research done by the teams of Professors Etienne Pays and Edmond Godfroid in IBMM is purely «curiosity driven», their wish being to understand how these parasites survive in their different hosts.

The latest development of discoveries from their research has opened new, more applied perspectives and shown once more that so-called basic or non-oriented research can lead to concrete economic development. This non-oriented research is essential to guarantee a strong base for the development of innovations.

The conversion of results from research to innovation, and thus tangible economic effects, is a complex process, often indirect and difficult to quantify. It requires a minimum of high standard research and efficient technology transfer involving interfaces between R&D, incubators, investment funds, etc.

This mechanism is already working in the Biopark, but we're going to be able to reinforce it further, thanks to the support of the Walloon Region. The process of accompanying the creation of a company is going to be enriched by extra financing given to the incubator Wallonia Biotech. This will certainly facilitate new plans for the creation of enterprises in the Biopark.

However, even if we have now reached a critical mass, if we have the ensemble of the innovation chain, we have to stay modest. The Biopark is still young and, to ensure its growth, we have to continue with our open policy and develop collaborations with other bio-regions present in the Walloon Region, in Belgium and throughout the world. For both our

research teams and our enterprises, the competition is international. The stakes are therefore high.

Dominique Demonté,
Director

Biopark Charleroi Brussels South

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From the laboratory to the market

It's not really surprising that studies on parasites like the tick and the trypanosome can lead to industrial and medical applications, as current events in the Biopark have shown. However, in the beginning, the IBMM research teams headed by Prof Etienne Pays and Prof Edmond Godfroid had one principal motivation, to understand how these parasites survived in their different hosts.

The latest developments from their research have opened new, more applied perspectives – in particular, the creation of the spin-off Bioxodes – and has demonstrated once more that so-called fundamental or non-oriented research can lead to concrete, economic development.

To facilitate the transition from the laboratory to the market, an incubation team will soon be set up in the Biopark. This team will accompany the researcher in the different procedures needed to create an enterprise.

Fascinating parasites

Published at the end of 2009, two research studies in the Institute of Molecular Biology and Medicine are on two surprising parasites: the tick, which can help to act against vein thrombosis, and the trypanosome, which decimates cattle in Africa. The research has a potential for development and one of the studies is going to give rise to a spin-off in the Biopark, Bioxodes.



Well known by walkers in our forests, the tick feeds on blood from different hosts, including man. To be able to do this, during its evolution the tick has selected mechanisms which allow it to bypass the defences of its hosts, for example, the inflammatory and immune responses and the clotting of blood. At the site of the bite, the tick discharges a variety of original molecules via its saliva. These molecules are proteins which block the defence mechanisms of the host and are powerful anaesthetics, and efficient anticoagulants and anti-inflammatories.

For more than ten years, in the Institute of Molecular Biology and Medicine (IBMM), Edmond Godfroid's team has been studying the relationships between the tick and its host on a molecular level. From tick saliva the researchers have identified, isolated and characterised molecules with anti-coagulant and anti-inflammatory properties. One of these molecules has remarkable anti-thrombotic properties. This small protein, called Ir-CPI prevents the formation of a thrombus without disturbing the coagulation balance.

Death

This is a fascinating property when we know that thromboses and thromboembolic diseases, by their venous and arterial manifestations, are today one of the principal causes of mortality in the world. Every year deep vein thrombosis, also called phlebitis, and its complication, pulmonary embolism, are responsible in Europe for more deaths than breast and prostate cancer, infection by the AIDS virus and road accidents combined !

Many anticoagulants are currently on the market and they reduce the effects of thromboembolic disease on the

health. This subject is under intensive research by the large pharmaceutical companies with a view to improving the efficacy of these anticoagulants. They are regularly administered to patients undergoing serious surgery such the replacement of a hip or knee in the elderly, in the case of reparatory surgery in polytraumatised patients following road or workplace accidents, during organ transplantation or, finally, in patients with blood coagulation problems.

Challenge

However, most of the medicines available today have major side effects which make their daily use difficult for the patient. If they are given in too low a dose, thrombosis can occur. If the dose is too high, they can cause



haemorrhages which are difficult to control. The medical world is therefore confronted with a real challenge : to discover molecules with a therapeutic window sufficiently large to prevent thrombotic accidents and avoid haemorrhagic accidents. Protein Ir-CPI, discovered by the IBMM researchers, seems to belong to this class of molecule. In animals, it prevents the formation of the thrombus in deep vein thrombosis, pulmonary embolism and arterial thrombosis models, without altering the coagulation balance or causing haemorrhage.

To become a medicinal product which can be administered to patients, molecule Ir-CPI still has to be evaluated clinically in man. To carry on with this next step, a spin-off, Bioxodes, is being created. Its aim will be to develop the following applications for Ir-CPI : the prevention of deep vein thrombosis, cerebral ischaemia and coronary disease, and also the treatment of the orphan disease, hereditary angio-oedema. It will also investigate the reservoir of proteins in tick saliva, in order to identify new applications in the area of coagulation and inflammation. The intention of Bioxodes is to develop these applications up to the end of phase II clinical trials and then license the results to a large pharmaceutical group.

Trypanosome

Other IBMM research is being done on the trypanosome. This resulted in the publication of an article in the journal «PLoS Pathogens» in December.

For the last twenty years or so, the IBMM Laboratory of Molecular Parasitology has been studying the biology of the African parasite *Trypanosoma brucei*, which is responsible for sleeping sickness in man and nagana which decimates cattle.

Unlike cattle, man has an innate immunity which allows him to kill *T.b.brucei*. Only two clones of *T.brucei* called *T.b. rhodesiense* and *T.b. gambiense* are capable of resisting this immunity and causing sleeping sickness in man.

Under the direction of Professor Etienne Pays, the ULB researchers have managed to understand how man has generated a system of defence against the parasite and how *T.b. rhodesiense* is able to adapt to this defence.

apoL1

The ULB researchers have just reached a new stage which will enable them to design an efficient innovative strategy to fight this dreadful scourge.

They have demonstrated that the human seric protein apoL1, modified by mutagenesis, is capable of killing efficiently



Trypanosoma brucei rhodesiense, the trypanosome pathogenic for man.

The researchers have also shown that, in mice, this protein effectively blocks all development of infection by this parasite and others, especially those responsible for the infection in African cattle.

Published in the journal «PLoS Pathogens» on 4 December, this piece of research constitutes an important advance against nagana which decimates cattle in Africa and also affects cattle in Asia. Given their results, the IBMM researchers propose to breed cattle which produce this protein. Such cattle should be completely resistant to trypanosomes, and they should therefore be productive in endemic regions. In addition, in East Africa, the cattle would no longer be a reservoir for the transmission of sleeping sickness in man. A collaboration is ongoing with INRA, the French National Institute for Agricultural Research.



Objective Incubation

An incubation team is being set up in the Biopark Charleroi Brussels South at the beginning of 2010. On the horizon in 2011, a new building will accommodate the spin-offs in gestation on the site. The development process is being reinforced further.

Even if it isn't the only way to turn research into economic development, the creation of a spin-off nevertheless represents the most visible and concrete showcase, especially for the general public. The university now has twenty-four spin-offs, twenty-four enterprises which have sprung up from academic research and often become prosperous companies whose innovation is recognised internationally. Among these twenty-four spin-offs, seven – soon to be joined by two others – are installed in the Biopark Charleroi Brussels South. Together they employ around 220 people on the site. Besides the creation of companies, the process of the protection of intellectual property has also accelerated. In the Biopark the number of patents taken out has multiplied by 10 in ten years.

Seven spin-offs – almost eight, soon nine – in ten years, the result is certainly positive. The university could have stopped there. However, conscious that the process is still complex and very long, ULB wanted to improve things by reinforcing one player, the Wallonia Biotech incubator.

The new team

Thanks to the support of the Walloon Region via the availability of "extraction funds", an incubator team is soon

going to be set up in the Biopark. We'll therefore have on the site all the development players united around a common objective - to encourage the economic development of innovative ideas. The first player in this chain is, of course, the researcher him/herself. The Institute of Molecular Biology and Medicine (IBMM), the Institute for Medical Immunology (IMI) and the Centre for Microscopy and Molecular Imaging (CMMI) will, in the next five years, represent not less than 60 million euros in research contracts. Then comes the technology transfer team. Interface. Thanks to the ESF Convergence programme (Walloon Region, European Union) it has seen itself filled out. The Biopark now has a cell of six people dedicated to the economic development of research in molecular biology and biomedical sciences.

And today, at last, an incubation team - to be put in place the first quarter of 2010 -. Its mission will be to help the future spin-off to evaluate and develop its technology, develop its strategy, create its business plan and raise funds (especially via Theodorus, the ULB investment fund). To put it simply, the mission of Wallonia Biotech will be to facilitate the transformation of an idea into a real business. And to do that, it will rely on the expertise of

another incubation centre, the EEBIC, based on the ULB Erasme campus since 1992. Everything needed to initiate a strategy of incubation integrated into the «Charleroi-Brussels» area and more generally in the entire Walloon Region, since Wallonia Biotech will work closely with other biotech incubators, especially Wallonia Biotech Coaching.

The new building

There's still one important question : Where will we put up these future spin-offs ? The concrete reply : A new building, built by the Intercommunale Igretec, will see the light of day next to IBMM and Wallonia Biotech 1. The first module dedicated to biotechnologies is already completed. In 2011, the Biopark incubator will be able to respond to the special techniques of the biotechnology sector, by accommodating new enterprises in 4000 m² of completely flexible brand-new premises in the "Aéropole" of Charleroi.



WALLONIA BIOTECH 2
BIOMED



Dominique Demonté

« I'm an intrapreneur »

At the beginning of 2010, Dominique Demonté took over the management of the Biopark Charleroi Brussels South - a new step for someone who began his career on the bench.



« Rather than Director, I'd call myself Business Developer of the Biopark Charleroi Brussels South » says Dominique Demonté. The tone is set. He has scarcely taken on the position but already he knows precisely what he wants to make of it. He explains, « I don't have the naïvety or ambition to manage the research institutes or companies of the Biopark, nor indeed the training, development and communication missions carried out there. There are already people there who do this very well. My role is to coordinate, so as to ensure the integrated development of the Biopark and to establish short-, medium- and long-term strategies ».

Researcher

At 38, Dominique Demonté has already had several professional lives. After a first degree in biology at the Facultés universitaires Notre-Dame de la Paix in Namur (FUNDP), he followed on with a PhD in the genetics of yeasts. Nevertheless, research wasn't for him, he was convinced. « I wanted to work in industry. I decided to fill out my CV with a postdoc at the ULB Institute of Molecular Biology and Medicine », he reminisces. He joined the IBMM Laboratory of Molecular Virology managed by Carine Van Lint where he studied the latency of the AIDS virus, in particular posing questions about the way to purge reservoirs of the virus. The subject interested him; however, after five years, his publications written, he decided to move on - he left research.

Scientific Advisor

Having discovered the coordination of scientific projects during several postdoc years, he imagined entering a company to be responsible for setting up projects. However, another opportunity presented itself, that of integrating the Interface unit of ULB. This was the occasion for him to be in research without being in it completely. He therefore took on this position of development advisor in the biomedical sector. « Being a researcher meant working on a very specialised subject and that wasn't for me. I'm more at home as a generalist, working in different disciplines », he declares. « The work at the Interface is fascinating. For the first time, I could have interests in different projects, all in the area of biomedical sciences. I could also learn about intellectual property, supporting the setting up of projects, relationships with industry... Meeting scientists, helping them develop their projects, that interested me enormously ».

At the same time, the cluster organisations were being established in the Walloon Region. Dominique Demonté participated in the setting up of the health cluster, BioWin. He became the contact between Biowin and the interfaces of the universities in the Belgium's French Community. This collaboration with the BioWin operations cell enabled him to discover another universe, that of industry.

Assistant Director

During these few years, he had the opportunity to work closely with Michel

Goldman, the then Vice-President of Biowin and Director of the ULB Institute for Medical Immunology, who invited him to join his institute. He accepted and became the Assistant Director of IMI. « Working with Michel Goldman was for me extremely enriching. He gave me a strategic vision of the role science can play in economic development. Working in IMI, an academic institute interacting closely with industry, was also very enlightening » he continues.

Dominique Demonté also invested in a major Biopark dossier initiated by Michel Goldman. The project «Hainaut Biomed» was conceived by closely associating research, development and continuous training and it would obtain the support of the Walloon Region and the European Union (Convergence Programme). « This dossier showed us all the added-value obtained by integrating the different sectors of the Biopark into the same project » he observes. « And yet, with the departure of Michel Goldman to Innovative Medicines Initiative where he took over the management in September 2009, we risked losing this coordination role. The university authorities therefore decided to create a post of Director of the Biopark ».

Director

And, in January 2010, Dominique Demonté, who smilingly calls himself an «intrapreneur», that is, someone with a spirit to innovate and use his skills in a structure which already exists, took up his duties. His first motivation ? « To demonstrate in the field that university research plays a key role in regional economic development », he replies without hesitation. He was born and bred in Charleroi, « When I was a student, my father told me that ULB was going to set up a molecular biology centre in the « Aéroport » of Charleroi. I replied to him: « You're kidding ! There will never be molecular biology in Charleroi ! ». Fifteen years on, I have to admit I was wrong and so much the better ».

Philippe Gabant

About Delphi Genetics



A Biopark spin-off, Delphi Genetics has just received the ISO 9001:2008 accreditation. An interview with its CEO, Philippe Gabant.

> Give us a short presentation of Delphi Genetics.

Philippe Gabant : Delphi Genetics is a spin-off which uses unique technologies, patented by the Université libre de Bruxelles, which are linked to the use of bacterial genes, one of which is a poison and the other an antidote. Delphi Genetics was founded in November 2001 by three researchers from the Institute of Molecular Biology and Medicine, IBMM : Michel Milinkovitch, today a professor at the University of Geneva, Cédric Szpirer who is our product development director and myself. As CEO, I manage the R&D with Cédric Szpirer and also manage the daily running of the company. Delphi Genetics employs 12 people - this figure has doubled during the last three years.

> What services do you offer ?

Philippe Gabant : We're a company specialised in genetic engineering, that is, in very simple terms, a company whose technologies enable a more efficient assembly of pieces of DNA. Our technologies are used to study genes or to produce certain biological items such as vaccines. One of our most well-known products is StabyExpress which enables the production of molecules by genetic engineering in the absence of antibiotics. We have licensed it to Sanofi Pasteur who uses it to produce vaccines without the addition of antibiotics during the production process.

> Who are your customers ?

Philippe Gabant : Our customers come to us because they know us to be pure innovators. They mostly come from the world of research. A typical customer is a researcher in the laboratory who buys our kits. Also companies, principally European, ask us for customized R&D services. Finally, our technologies are also licensed for use in production processes.

> How will the ISO 9001 accreditation Delphi Genetics has just obtained help you ?

Philippe Gabant : It shows the market that we are capable of integrating our innovative character into an industrial quality system and this therefore opens new commercial opportunities.

> Your SME is growing. What is your principal challenge today ?

Philippe Gabant : Doing good science isn't complicated for us - we were trained in ULB ! However, since we come from the academic world, we didn't have any knowledge of the market. We've had to develop a commercial strategy, set up a distribution network for our kits, etc. Delphi Genetics is, by definition, a company unique in the world because it commercialises technologies and products invented by us and our colleagues. It's all the more difficult because the market won't wait for us. We're currently working towards stabilising our range of services, conti-

ning the increase in sales of our kits and increasing substantially our revenue from licensed technologies. Beyond these economic objectives, our driving force is still the same : to manage to do elegant science using innovative technologies.

> What's the interest of being in the Biopark Charleroi Brussels South ?

Philippe Gabant : We have collaborations with research centres all over Europe, including ULB. The geographical proximity in the Biopark allows us to follow projects more closely : we like working with our neighbours. The researchers we rubbed shoulders with when we were in IBMM have since completed their PhDs and most of them have left the university. We bump into those who have replaced them every day in the laboratories, the library or the cafeteria. We're getting to know each other - all this facilitates collaborations. Being in the Biopark brings added value.

iGEM : IBMM team award

Led by Laurence Van Melderen and Gilles Vanwallendael of the Institute of Molecular Biology and Medicine (IBMM), a multidisciplinary team of ULB undergraduates, PhD students and professors in biology, bioengineering and bioinformatics won a prize at the 2009 iGEM Jamboree, the prestigious international synthetic biology competition.

The ULB-IBMM team won the prize for the best natural «BioBrick», for their project on the production of «natural» glue, i.e. a bio-glue produced by a bacterium. The glue has great qualities as it is non-toxic, biodegradable, can be used on wet surfaces and is three times more adhesive than super glue !

No fewer than 112 teams participated in the 2009 competition, held at MIT in Boston. Six teams received major awards, there were 9 special prizes – one of which was awarded to the ULB-IBMM team – and 8 prizes for the best project in each category.

Biopark : New entities

Two entities have just been set up with the aim to manage the activities of the Biopark Charleroi Brussels South : Firstly, the Biopark Bureau, which brings together the different players present on the campus (research institutes, technology platforms, enterprises, development, training, communication, service support) and, secondly, the Biopark Strategic Committee, run by the academic authorities of ULB and comprising the members of the Bureau and representatives of the Boards of Governors of ULB and the Université de Mons. In addition, a Director of the Biopark has been appointed - Dominique Demonté. Find out about him on page 5.

Biopark Formation accredited and approved

Good news for Biopark Formation which has just obtained the approval «Chèques-formation» from the Walloon public service DGO, Economie, Emploi et Recherche, for its training in «Flow cytometry», «Molecular biology» and «English courses specific to life sciences». Another piece of good news - Biopark Formation has also had its flow cytometry modules recognised by BioWin.

IBMM : A new laboratory

In the autumn a new research team was set up in the Institute of Molecular Biology and Medicine (IBMM) : the laboratory of Cell Nucleus Biology, led by Birthe Fahrenkrog, previously of the University of Basel in Switzerland.

DNAVision and BGI-HK partners

DNAVision, a ULB spin-off in the Biopark Charleroi Brussels South, and the Beijing Genomics Institute-Hong Kong (BGI-HK), a spin-off of the Beijing Genome Institute in Shenzhen, have finalised a strategic alliance to improve their positions in the area of new generation sequencing.

<http://www.dnavision.be>

Advanced training

Biopark Formation is starting new advanced training modules in the first quarter of 2010.

- Flow cytometry :
 - Introduction to flow cytometry
1 March 2010 (9h00-12h30);
 - Applications of flow cytometry
1 March 2010 (13h30-17h00);
 - Applying a cell phenotyping protocol
5 March 2010 (9h00-17h00);
 - Drawing up a cell phenotyping protocol
8 March 2010 (9h00-17h00);
 - Multispectral imaging by flow cytometry or « ImageStream »
12 March 2010 (9h00-12h30)
- Molecular biology :
 - PCR troubleshooting (optimisation and resolution of problems)
26 February 2010 (9h00-12h30)

For more information, go to www.biopark.be/formations/

CIBLES evaluated

The programme of excellence CIBLES has had its first evaluation : a very positive result for this important research programme – around 25 million euros invested over five years – launched in January 2008 with the support of the Walloon Region.

Managed by ULB - IBMM (Biopark Charleroi Brussels South) and IRIBHM (Erasmus Campus) – the objective of CIBLES is to identify and validate new therapeutic targets in areas important for human health and for pharmaceutical and biotechnological activity in Wallonia. Associating closely university teams (ULB, UCL and ULg) and companies (UCB, GSK and Euroscreen sponsor the programme), CIBLES focuses its therapeutic interest on the central nervous system, inflammation and cancer. Its three areas of research are G protein-coupled receptors, promising intracellular targets and stem cells. A group of experts composed of both industrialists and academics – CNRS/INSERM Montpellier and the Universities of Milan and Zürich – evaluated the three areas of the project, taking into account both scientific and economic criteria. Their opinion was very positive - the experts emphasised the quality of international publications and the number of patents granted. This committee also fixed the research priorities for the next few months.

A Chinese at IMI

Since November 1st 2009, IMI has welcomed a doctoral fellow granted by the Chinese government. Dr. Qing Yuan is a surgeon. He will pursue, in the team of Veronique Flamand at the Institute of Medical Immunology, a thesis initiated in the Organ Transplanter Center of the Changzheng Hospital at the Second Military Medical University of Shanghai, on the understanding of immune mechanisms involved in the graft rejection in transplantation. This doctoral thesis will be co-directed within the Université Libre de Bruxelles and the Shanghai University.

Notreregion.be

On the initiative of the Charleroi-Sud Hainaut Strategic Development Committee, a surprising campaign has been launched in the region : to rediscover it and find out the good news go to <http://www.notreregion.be>. The Biopark Charleroi Brussels South is a partner in this unusual initiative.

IBMM : Genomes duplication and evolution

From the sequencing of genomes, we know that the duplication of the chromosomes of a species (followed by multiple rearrangements) has happened in many places in the tree of life. Traces of such genetic events are still visible in genomes today, as in that of the yeast used by Prof. Bruno André's Molecular Physiology laboratory (IBMM) to study the regulation of membrane transport proteins. The two copies of a duplicated gene often evolve in different directions and hence make the functions of the cell more elaborate. This is what Prof. André's group has just shown in the case of a gene encoding a transcriptional activator of the genes involved in amino acid transport. Bioinformatic analyses first showed that this gene was duplicated during genome duplication in an ancestor of the yeast. The two genes then diverged : the first intervenes when the external environment contains a low concentration of amino acids, the second plays its role when the environment is rich in amino acids. The cell is therefore in a better position to adapt to different environmental conditions. This study, published in *The Journal of Biological Chemistry*, provides a further example of the importance of genome duplication during evolution.

Biomedical group

Through the impetus given by the Intercommunale Igretec, a «biomedical» working group has been set up in Charleroi. The group brings together the players of the sector, from industry, hospitals and research centres. All the partners of the Biopark Charleroi Brussels South have, of course, joined this group, from which different common actions should soon emerge.

DNAVision : A new certification

DNAVision has obtained the certification Illumina CPro™ for its application of Infinium genotyping. This is a further recognition for the spin-off which is the only genomics company in the world to be ISO17025 accredited, CLIA certified, CAP accredited and GLP and GMP certified.

<http://www.dnavision.be>

Delphi Genetics : BL21 (DE3) on sale

BL21(DE3) chemically competent bacteria in a convenient format. BL21(DE3) is the most widely host used for protein expression using /E. coli /and T7 expression system. Each tube contains 100µl of competent /E. coli /BL21(DE3), which is sufficient for one high efficiency transformation.

<http://www.delphigenetics.be>

