Happy anniversary !

On 1 and 2 October, the IBMM celebrates its 10th anniversary.

Located in the «Rue des Professeurs Jeener et Brachet» (it’s not by chance), our Institute follows on in the tradition of excellence in molecular biology and medicine initiated in the University by the very same Professors Jeener and Brachet.

In 1929, Jean Brachet, then a brilliant young student in medicine at the Université Libre de Bruxelles discovered, without knowing it, molecular biology for the first time ! Jean Brachet showed that thymonucleic acid was a component of chromosomes and that it was synthesized when cells divide after fertilisation. Thymonucleic acid is none other than DNA ! A few years later, Brachet observed that the cells actively involved in protein synthesis are rich in zymonucleic acid : this acid is RNA ! The fundamental basis of molecular biology had been established, that was in 1940.

Jean Brachet was joined by Raymond Jeener : together they founded the Rouge-Cloître laboratory in Brussels. Other brilliant scientists joined them. Rouge-Cloître acquired an international reputation, growing to the point where the laboratories became too cramped. The researchers left the Brussels site to set up a laboratory in Rhode-Saint-Genèse. Here they gathered a second momentum - from a few dozen, they grew to over 150. New research orientations appeared. The laboratories continued to prosper and the Rhode premises, which had originally seemed so huge, became in their turn too small. Several groups went to Brussels and Nivelles. In parallel, a laboratory was taking shape in the Faculty of Medicine in Brussels : first the Laboratory of nuclear medicine which, in 1972, became the Institute of interdisciplinary research in human and nuclear biology. Several years later it was transformed into the Interdisciplinary Research Institute for Human and Molecular Biology, IRIBHM, also of international renown.

In 1999, the laboratories of Rhode, Nivelles and Brussels, which made up the Department of Molecular Biology of the Faculty of Science united and moved to the Aéropole of Charleroi. They were joined by several teams from the IRIBHM of the Faculty of Medicine. The Institute of Molecular Biology and Medicine, IBMM, was created.

Ten years later, the results are indisputably positive. Firstly, from a scientific point of view : IBMM has accumulated publications, citations, prizes, regional research projects, not limited to Belgium but also in other European countries (see article on page 2).

As far as regional development is concerned : the fruit of Objective 1 (Walloon Region, European Union), IBMM gave rise to several spin-offs (see page 4). It is also an attractiveness factor : the competitiveness cluster BioWin and the Institute of Pathology and Genetics (IPG) are now its neighbours. It is also very dynamic : the site has, or will soon have, research institutes, several spin-offs, a multimodal imaging centre (with the Université de Mons), a valorisation unit, an incubator, a unit providing continuous training, a new course (master in molecular physio-pathology)…

10 years after the Biopark Charleroi Brussels South was formed.

Happy anniversary to those who, every day, make IBMM what it is ! And see you on 1 and 2 October during the talks and meetings which sound fascinating.

Martine Labbé,
Doyenne de la Faculté des sciences
Sylvain Meuris,
Doyen de la Faculté de médecine
To understand the biological processes governing the normal functioning of a living organism. An ambitious objective that brings together the about 220 researchers from the IBMM. As it brings together many researchers in biology or molecular medicine.

To take up the challenge, the twelve laboratories of the IBMM have chosen three main research areas.

First, bioinformatics and functional genomics, or the study of the expression and role of genes to enable a better understanding of cell physiology, of molecular mechanisms of the embryo and also of cancer or genetic and infectious diseases (for example, caused by the HIV virus). Secondly, the host/parasite relationships. Namely, the study of the normal and pathological (in case of allergy, inflammation, cancer) functioning of the immune system and the mechanisms by which parasites (trypanosomes, ectoparasites) escape the immune surveillance of their hosts.

Finally, cell biology and imaging, interested in the organisation of the cell and its different “compartments”.

Discoveries
Concretely ? Most recent discoveries have enabled the identification of several molecular mechanisms involved in the development of the nervous system, intracellular trafficking of membrane transporters, latency and reactivation of the HIV-1 virus, in the development and control of inflammation and in the pathogenesis of two human genetic diseases.

A correlation has been established between the expression of a given gene and certain pathologic affections, helping to anticipate diagnostic and therapeutic advances in cases of sterility, renal disorders, inflammation and immunodeficiency.

More precisely, the study of membrane transport mechanisms has revealed a new role for the Rhesus factors as ammonium transporters, and their absence has been correlated with pathologies affecting renal function and fertility. The link between Rhesus factors and ammonium homeostasis and the regulation of the pH of physiological fluids is currently under investigation.

An IBMM team has also studied how proteins are targeted towards internal compartments of the cell and has tried to identify the specific signals governing the intracellular trafficking of the membrane transport proteins. The signal which targets membrane proteins inside lysosomes (where they are degraded) corresponds to a short specific chain of ubiquitins.

INPP5E
The objective of functional genetics, a major research area in IBMM, is to attribute a function to each of our 25,000 genes… In this context, a surprising discovery has been made by generating mice deficient in INPP5E, an enzyme which dephosphorylates several intracellular metabolites. Analysis of these knock out mice has enabled us to...
demonstrate that they show alterations in embryonic development characteristic of ciliopathies, rare disorders characterized by anomalies in the construction of eyelashes.

Research on Xenopus, an animal model for the study of embryonic development, has led to the identification of the RNA-binding protein XSeb4R and its post-transcriptional regulator role in the formation of embryonic germ layers, such as the endoderm which develops into the digestive tract and related organs.

Recent work done in IBMM laboratories has identified molecular and cellular mechanisms involved in inflammatory reactions, a pathological response which affects a growing number of people and constitutes a major human health problem.

**Lymphocytes**

The study of the protozoan parasite Trypanosoma brucei and the resistance acquired in man has brought to light the role of the family of apolipoproteins in the lysis of the parasites. Curiously, the same proteins seem to play a role in inflammatory responses, thus opening an unexpected original field of investigation. Other work has shown the importance of the role of an enzyme involved in the regulation of intracellular NAD in the control of inflammatory response discovering a potential therapeutic target. In addition, results have shown that intestinal inflammatory response or colitis (a model for Crohn’s disease) could be controlled by a new population of suppressor T lymphocytes. Among the immune reactions, particular attention has focused on the secretion of antibodies by B lymphocytes and has led to the identification of a population of auxiliary cells which activate B lymphocytes. Finally, the study of the tick (an acarian) has enabled us to show that a protein expressed by the salivary glands not only has an anti-haemostatic activity, facilitating the meal of the ectoparasite, but also inhibits thrombosis in vivo in different mouse models and this without affecting coagulation or bleeding parameters.

All these studies should allow us to envisage new approaches to the treatment of infectious diseases and inflammatory disorders.

> **What was your career in IBMM?**

**Florent Bernard:** I started my doctorate in 1997 under the supervision of Bruno André of the laboratory of yeast cell physiology in the ULB Faculty of Science on the Plaine campus. Two years later, we moved to IBMM. While continuing to work towards my PhD, I supervised the end-of-study research projects of several final year undergraduates and I also took part in the organisation of several events, such as the visit to IBMM of the winners of the biology international Olympiads, having myself been a winner in 1992.

> **You’re no longer at IBMM. What are you doing now?**

**Florent Bernard:** I’m Scientific Officer in the Research Directorate General of the European Commission, in the Marie Curie Network Unit. I’m in charge of implementing the Marie Curie Actions. This consists of financing research into the improvement of the training, careers and work conditions of researchers. The position comprises the conception of actions, evaluation of projects and their follow-up, and the negotiation of contracts. At the moment, I’m managing around sixty projects, each of two to three million euros.

> **What did you get from your experience in IBMM?**

**Florent Bernard:** At IBMM I acquired scientific skills, of course, but my experience also helped me develop a critical eye, assimilate scientific methodology and, above all, approach problems, no matter which, in a rational, precise way - so many contributions which have been useful in my professional life. As a scientist in the political-administrative world, I am also well placed to defend the interests of researchers in the political world. The scientists working at the European Commission play a real bridging role between the scientific and political worlds.
Science and economy

The wager of Objective 1 taken up by IBMM where several spin-offs have seen the light of day, or will do so, in the next few months: this is a real illustration of the close but unpredictable link between basic research and socio-economic development.

There are seven of them - seven spin-offs from IBMM. Each one has its history. We will pinpoint two of them in this Biopark News: Delphi Genetics and DNAVision.

First of all, the older of the two, Delphi Genetics, created in 2001. This Biopark Charleroi Brussels South SME was founded on solid intellectual property developed by Philippe Bernard and Philippe Gabant in the ULB Service of Procaryote Genetics. The researchers of the Faculty of Science developed « poison/antidote » technology, particularly useful in the cloning of genes. In 1992, the researchers registered their first patent which would be, three years later, licensed to the Californian company, Invitrogen.

In 1999, Philippe Gabant joined the IBMM Laboratory of Developmental Biology. Thanks to the First Spin-off financing of the Walloon Region, the researcher developed and exploited new applications of the poison/antidote technology. Two other subsidies from the Walloon Region came to reinforce this research programme. Results in terms of patents: between 1999 and 2002, eight patent applications were made, one patent was acquired from a third party.

In a strong position with this portfolio of patents, Philippe Gabant was joined by Cédric Szpirer, also a researcher at IBMM and Michel Milinkovitch, a Professor at ULB - they created Delphi Genetics. Today the spin-off exploits two patents licensed by ULB. It also pursues its collaborations with IBMM, especially the Service of Bacterial Genetics and Physiology: Delphi Genetics sponsored the Walloon Region Waleo 3 programme project « HYPRO-2COM » concerning bacterial proliferation.

Another spin-off in the Biopark: DNAVision, an SME which employs 18 people in Charleroi and which created, in 2008, a spin-out, DNAVision Agrifood based in Liège.

Expertise developed in the Biopark lay at the origin of DNAVision. In 2002, thanks to the support of Phasing-out of Objective 1, BioVallée was created with, at its core, a department of genomics. This department gathered together researchers who had been trained at IBMM, where they had acquired expertise in the area of DNA technology, particularly in the characterisation of new genetic markers providing responses to biological and medical questions.

A year later, Jean-Pol Detiffe, the present CEO of DNAVision, joined BioVallée. Building on his experience as a pharmacist in industry, he set up a quality environment which could provide services to the pharmaceutical and biopharmaceutical industries.

It was in 2004 that the spin-off DNAVision was created. Its expertise is in both pharmacogenetics, the detection of genetic variations, and pharmacogenomics, tests of gene expression. In April this year, it received a double
quality certification: CAP and GMP, which completed the certifications already obtained: ISO 17025, GLP, CLIA,... DNAVision is one of the only laboratories in Europe with such a vast array of certifications, allowing it to work for both European and American clients. DNAVision has also won several distinctions: Enterprize, Prix wallon de l’innovation technologique, Grand Prix wallon de l’entrepreneuriat,...

Ann Dekoninck, Quality Assurance in GSK-BILOGICALS

> What was your career in IBMM?
Ann Dekoninck: My career in IBMM lasted 8 years and I evolved from undergraduate to post-doctorate. I worked in molecular virology in Carine Van Lint’s laboratory. My thesis was on the bovine leukaemia virus.

> You’re no longer at IBMM. What are you doing now?
Ann Dekoninck: I work in the Quality Assurance Department of GSK BIOLOGICALS. I coordinate different audits by Belgian and foreign regulatory authorities (FDA, WHO, etc), with a view to getting acceptance of new vaccines.

> What did you get from your experience in IBMM?
Ann Dekoninck: The job I do now isn’t really linked to what I did in IBMM. The experience, however, taught me to be independent and autonomous, to adapt to all kinds of situations and to begin my professional life rapidly.

On the programme

On the occasion of its 10th anniversary, the Institute of Molecular Biology and Medicine (IBMM) is organising two days of scientific talks.

**On Thursday 1 October**, after an introduction by Arsène Burny and Jacques Dumont of «Yesterday and Today», it will be the turn of the young IBMM researchers of the Institute to present the research done in their laboratories. The afternoon will end with a talk «Today and Tomorrow» by Muriel Moser (Faculty of Science, ULB) and Marc Parmentier (Faculty of Medicine, ULB).

**On Friday 2 October**, IBMM is hosting an academic meeting in the presence of the University Authorities, the Ministers Nollet and Marcourt, and Véronique Halloin, Secretary General of the FNRS. In the afternoon, four renowned scientists will give presentations:
- Bruce Beutler (San Diego), “Forward genetic analysis of innate immune defense”;
- Joel Vandekerckhove (Ghent), “The power of targeted proteomics”;
- Pierre Coulie (UCL), “How to move forward with human therapeutic cancer vaccines?”;
- Enrique Amaya (Manchester), “The inflammatory response during embryonic wound healing”.

The complete programme can be found at http://www.biopark.be (At ‘l’agenda’)

1 and 2 October, in the Point Centre auditorium, Avenue Lemaître 19, Aéropole de Charleroi. 6041 Charleroi.

Participation is free but registration is required.

Information and Registration:
Solange Demeure, 02 650 97 17 or sdemeure@ulb.ac.be
Michel Goldman
« We’ve come full circle »

Director of the Institute for Medical Immunology, initiator of the Biopark Charleroi Brussels South, last September Michel Goldman became Executive Director of Innovative Medicines Initiative (IMI), a new European agency with stimulation of innovation for the benefit of patients as objective.

Medicine, was almost a destiny for Michel Goldman. His father was a family doctor who was also one of the first to teach general medicine at the Université Libre de Bruxelles, his mother assisted, the family lived around consultations. It was obvious to him, though only a child, that he too would look after people who were ill.

After secondary school (at the Athénée Robert Catteau in Brussels), at 16 he signed up to study medicine at ULB. In his 2nd doctorate year, he at last got to the heart of the matter: he discovered the hospital, its teachers, contact with the patient. Enthusiastic, he sought seminars avidly and multiplied his scientific reading. A brilliant student, he then met the person who was to become his mentor, Professor Charles Toussaint, who taught nephrology and whom he met on an internship at the Hospital Brugmann. Having graduated in Medicine with first class honours in 1978, Michel Goldman started a degree specialising in internal medicine – obligatory to work in nephrology. The future specialist entered the hospital Erasme, which had just opened, with one objective: to treat sick people. Charles Toussaint, who also joined the hospital Erasme, nevertheless managed to convince him that a period of research abroad would be an enriching experience, regardless of his future orientation.

Geneva
Michel Goldman obtained a grant from the FNRS and left for Switzerland. He joined the World Health Organization centre of research and training in immunology, which was run by Paul-Henri Lambert who came from Liège. A year later, his first article was accepted in the Journal of Experimental Medicine. These two years led to a PhD from the University of Geneva and an « agrégation » from ULB to teach in higher education. These years were also studded with fascinating encounters, the building of friendships: 20 years later, the researcher, now director of the institute, still collaborates with his colleagues in Geneva.

Back in Brussels, he joined the Erasme hospital Haemodialysis unit, led by Jean-Louis Vanherweghem who worked with him on several research projects. In parallel to his clinical work, Michel Goldman set up a research unit. In the beginning it was composed of a technician and himself, several years later it was to become the Laboratory of Experimental Immunology of the Faculty of Medicine of ULB.

In 1990, Michel Goldman moved to the Immunology-Transfusion Service of the hospital Erasme. He was only just 35 years old. Joined by, amongst others, Arnaud Marchant (today FNRS researcher at IMI and Scientific Director of ImmuneHealth in the Biopark), he reoriented his research towards immunological aspects of infectious diseases.

Charleroi
The laboratory increased in size, one publication followed another, collaborations multiplied... Michel Goldman ended up stopping his clinical work to devote himself full-time to research and his Laboratory of Experimental Immunology. One project led on to another, opportunities were seized, horizons evolved...

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Europe
Given his experience in Public Private Partnership, Michel Goldman was able to use this to the benefit of firstly the University (he became advisor to the Recteur for university-enterprise relations), then the competitiveness cluster Biowan, of which he became vice president in 2006, and lastly, today, Innovative Medicines Initiative, another IMI, which he manages. « I began my career with one priority: to take care of the sick », observes Michel Goldman, « I quickly understood that research would give me the skills and tools to look after people better. I observed later that when research produces useful results, partnership with enterprises is indispensable to succeed in developing a medicinal product. Today, at the head of IMI, I’ll be able to help to facilitate these partnerships, ensuring a dialogue with different associations for people with particular diseases. In a way, I’ve come full circle. »

Acknowledgments
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With particular diseases. In a way, I’ve come full circle.»
Last July, the French company Novasep and Henogen, a ULB spin-off in the Biopark Charleroi Brussels South, announced their rapprochement, that is, the integration of the spin-off into this large international group. Jean-François Pollet, the CEO of Henogen, explained to us the context and objectives of this coming together.

> Henogen was the first ULB spin-off in the Aéropole of Charleroi.

Jean-François Pollet: Henogen stemmed from the ULB Applied Genetics Service and it will celebrate its 10th anniversary this year. Henogen is a pharmaceutical and bioengineering company specialized in contract development and production of new biopharmaceutical substances. Its company has a wide range of skills to stand in for or accompany our partners in their research and development activities, process development and GMP (Good Manufacturing Practice) production of products up to Phase III clinical trial materials.

It has grown rapidly over these 10 years. Having begun with a small group of SGA researchers, Henogen now employs 105 people and has two bioproduction sites, one on the Aéropole of Charleroi and the other in Seneffe. Our shareholding has also evolved: composed of ULB (80%) and GlaxoSmithKline Biologicals (20%) at the moment of its creation, it then opened up to the SRIW and the group IMBC. At the end of 2008, we realised that if we wanted to continue to grow, to accompany our clients a little further in the process of developing and getting on the market their new therapeutic and prophylactic substances, our company would have to open its capital to other shareholders. At the beginning of 2010, we will have increased capacity in Seneffe and this site will be oriented towards multi-product activities. In parallel, we are going to invest in new equipment which will allow us to do aseptic filling of finished products. We will progressively move our bioreactors and fermentors towards disposable single-use systems, which will have great benefits in terms of management and economy, at the same time allowing us to scale up on our sites, thanks to less bulky systems.

> And what will Henogen bring to Novasep?

Jean-François Pollet: As I was saying, our enterprises are complementary. We too come with our portfolio of around a hundred clients - academic institutions, SMEs or start-ups, and also major players in the pharmaceutical sector. Novasep is also active in the contract manufacturing of active pharmaceutical ingredients but it is, at present, more oriented towards products manufactured by chemical synthesis. For Novasep, the interest of our acquisition is our expertise in purification processes and the equipment developed by Novasep.

> What’s in this acquisition for Henogen?

Jean-François Pollet: Novasep had a turnover of 325 million euros in 2008, it has about ten sites in the world and employs around 1200 people. For Henogen, this acquisition therefore means that we enter a large group: joining Novasep will provide new impetus to the development of our share of the market worldwide. It’s the opportunity to increase our range of services to our present clients and to get in contact with new clients. We will also benefit from synergies within the group, in particular the very wide expertise in purification processes and the equipment developed by Novasep.

> Will there be any changes in the near future?

Jean-François Pollet: The Charleroi site has been working at cruising speed for a while. It’s possible to manufacture several products in parallel and to work with all types of expression vectors and various living microorganisms: E. coli, yeasts, L. lactis, mammalian or insect cells, viral vectors or attenuated living pathogens. On the other hand, our site in Seneffe, which was acquired in 2004, needed investment to expand. Fifteen days after our acquisition, the decision to invest 1.8 million euros was taken and our Seneffe site is now being transformed. At the beginning of 2010, we will have increased capacity in Seneffe and this site will be oriented towards multi-product activities. In parallel, we are going to invest in new equipment which will allow us to do aseptic filling of finished products. We will progressively move our bioreactors and fermentors towards disposable single-use systems, which will have great benefits in terms of management and economy, at the same time allowing us to scale up on our sites, thanks to less bulky systems.

> You are one of the important players and the oldest « enterprise » on the Biopark Charleroi Brussels South. What kind of relationship do you have with your neighbours?

Jean-François Pollet: Excellent, we work with the research centre ImmuneHealth and we would like to establish increasingly regular contacts with other Biopark players, especially with Delphi Genetics and DNAVisión. It is obvious that, dealing with the needs of our respective clients, appearing together on certain occasions, we increase our attractiveness by demonstrating the added value chain present in our region. Together, we can effectively offer our clients a complementary range of services. Players in the Biopark Charleroi Brussels South reinforce each other, showing a common showcase to different institutions and enterprises looking for partnerships in the area of pharmaceutical development.
Two rare diseases outsmarted
For over 10 years Stéphane Schurmans’ team in IRIBHM has been studying the function of several genes involved in intracellular signalling, amongst these, INPP5E.
The IBMM laboratory generated mice deficient in the INPP5E gene and discovered that they displayed many alterations in embryonic development. There was enough evidence to enable the scientists to recognize ciliopathies. This new class of rare pathologies is characterized by a defect in the construction of the cilia, sort of antennae which elongate the cell in order to probe the extracellular medium. The IBMM researchers demonstrated that the INPP5E protein is, in fact, located in the cilia of cells and that inactivation of the INPP5E gene causes instability of the cilia. On the basis of the results they obtained, the Belgian group contacted two teams of researchers: in the UK, Dr. Geoffrey Woods of Addenbrooke’s Hospital in Cambridge and, in the US, Dr. Joseph Gleson of the University of California in San Diego. They had published articles suggesting that MORM and Joubert syndromes were probably ciliopathies caused by a genetic anomaly situated on the long arm of chromosome 9, which corresponds to the location of the INPP5E gene in man. The British and American laboratories searched for, and found, mutations in the INPP5E gene in the DNA of patients suffering from these two rare diseases. Experiments on these human INPP5E enzymes mutated in the ULB laboratory confirmed, like in the mouse, an instability of the cell cilia.
This research was published in Nature Genetics on 9 August of this year.

Biopark Training
From autumn 2009, in addition to the existing training, Biopark will provide specialised English courses for people working in life sciences, and also training in flow cytometry. The latter gives training in image streaming and the software Flowjo. For more info, see: www.biopark.be/ formations

Collaboration between Euroscreen and Novartis
Euroscreen SA, a leader in G Protein Coupled Receptor science, announced a Research Collaboration Agreement with Novartis to discover new targets for possible application in certain disease areas. Financial terms of the deal were not disclosed.
Information: www.euroscreen.be

AIDS : new advances
For many years Carine Van Lint, of the IBMM Laboratory of Molecular Virology, has been studying the molecular mechanisms which regulate the expression of HIV-1 genes. In collaboration with Prof. Nathan Clumeck’s team at CHU Saint-Pierre, the researchers in this laboratory have just demonstrated that treatment combining a deacetylase inhibitor (already used clinically for other illnesses) with an inducer of NF-kappaB reactivates viral expression in ex vivo cultures of reservoir cells isolated from the blood of seropositive patients under multitherapy. Reactivation by this combination is synergistic, that is, more efficient than the addition of the effects of each activator alone. These results, published in the journal PloSONE of 30 June, constitute proof of the principle of therapeutic potential co-administration of the two different types of HIV-1 activators, in the presence of an efficient anti-HIV-1 therapy, with the aim to reduce effectively the pool of cell reservoirs latently infected by HIV-1. However, the researchers did not observe transcriptional reactivation in around 40% of the blood samples tested. They emphasize the importance of identifying other reactivators of viral latency and of testing them in combination with those used in their study. New therapeutic perspectives for AIDS are opening up.

New director of IMI: Oberdan Leo
On 15 September, Oberdan Leo succeeded Michel Goldman as the Director of IMI. President of the Belgian Society of Immunology, Oberdan Leo teaches immunology and cell biology at ULB and at the Université de Mons. He has published around a hundred scientific papers. His research interests are focused on the activation and differentiation of T lymphocytes and the control of inflammatory responses. Michel Goldman takes over the management of another IMI: the Innovative Medicines Initiative (see « Career » on page 6).

Collaboration between BioXpr et DNAVision
BioXpr SA and DNAVision are joining forces to offer pharmaceuticals and red biotech industries a global and seamless service in genetic analyses. This collaboration will revolved around microarrays, miRNA and Next Generation sequencing. The first joint service being launched seamlessly covers the design, the experimentation, the analysis and interpretation of microarray projects.
Information: www.dnavision.be