



BIOPARK

CHARLEROI BRUSSELS SOUTH

news

The Biopark Charleroi Brussels South Newsletter

n°16 — winter 2012

Companies

A favourable environment	2
Delphi Genetics	4
Bone Therapeutics	6
iTeos	8

CIBLES programme of excellence	9
OncoDNA	10
In brief	11, 12

ULB

UMONS
Université de Mons



Mood

A NEW MAYOR FOR CHARLEROI

We will not even try to hide how happy we are to welcome Paul Magnette. The decision to leave the Federal Government to lead Charleroi's development was a courageous one. He will face some major challenges but Paul Magnette's victory in the elections and his decision to open governance to MR and CDH are two positive initial signals.

The Biopark is one of the uncontested drivers of the Aeropole's economic development. The challenge now is to tie this dynamic to the rest of the city. Issues that require attention include mobility between the city centre and the Aeropole, Charleroi's image, and the quality of life in the city centre.

Charleroi can count on us to face and hopefully overcome these problems, as we hope to continue counting on it.

Dominique Demonté
Biopark Charleroi Brussels South Director



Biopark: a favourable environment for business



Delphi Genetics opens its new green building on the Biopark, Bone Therapeutics is set to begin building work on its own premises, and Biopark Incubator 2 will open its doors to new businesses: without a doubt, business goes well on the Biopark! Marie Bouillez, the director of Biopark Incubator, the campus' "companies nursery", provides us with an overview of the business situation.

WHY IS THE BIOPARK SUCH A SUCCESS WITH BUSINESS?

M. Bouillez: The most influential factor is the dense concentration of stakeholders on a single site, all working in the high technology sector. This proximity fosters the relations and cooperation that flourish easily. For example, iTeos took up residence in Biopark Incubator so that it could take advantage of the nearby research centres and on-site infrastructure (see page 8).

AND COMPANIES FROM OTHER SECTORS ARE ALSO MOVING IN.

M. Bouillez: They are. "VDE Legal" recently joined the incubator, a law firm that specialises in corporate law. They are from Brussels and were attracted to Gosselies by the entrepreneurial dynamic and the number of businesses currently operating from the Biopark. A real demand for this type of service now exists, which explains the appearance of services companies such as them. Even just a few years ago this would have been an unthinkable development.

HOW MANY SPIN-OFFS ARE THERE?

M. Bouillez: The Biopark is currently home to nine ULB spin-offs: Delphi Genetics, DNAVision, Euroscreen, ImmuneHealth, Novasep-Henogen, EndoToolsTherapeutics, Ovizio and a-ULaB are already present, and Bone Therapeutics is scheduled to arrive in 2013 (see pages 6 and 7). The ecosystem that has developed on the site is very important for our spin-offs, and the incubator plays a key role, especially by providing access to



our network of experts. Part of our role is also to facilitate the transfer of knowledge, technology, and resources that may be shared. For example, once per month together with IGRETEC, we organise a meeting between different biomedical companies in order to share information that may affect the sector.

The custom support provided is also vital, especially when creating a spin-off: we work closely with the ULB Technology Transfer Office (TTO) a considerable way upstream from the creation of the company. We provide assistance to backers of the spin-off project as soon as they emerge from the lab, helping them to develop a technology transfer strategy that includes an evaluation, detailed market research, a comprehensive

business plan and, if necessary, assistance with securing funds. The companies are then able to set-up in the incubator and benefit from the Biopark Incubator's network and services as they grow. This definitely represents added value for the Biopark: it is a favourable environment for new projects.

BIOPARK INCUBATOR 2 OPENED IN APRIL, HOW IS IT COMING ALONG?

M. Bouillez: It couldn't go better! We are now home to 11 companies. All of the services you would expect from a Business Centre are available to our clients: flexible workstations that can be hired by the hour or half-day, meeting rooms with cutting edge technology, multilingual reception services, etc. Almost 50% of the building's 2000m²

is currently occupied. The entire building has been fitted out as either office or lab space (partitions, furniture, internet, etc.). Of the 2400m² available, 25% has already been fitted out, mainly by MaSTherCell with their white rooms for use in cell therapy production. In early 2013, we will welcome an additional two companies, and the space currently occupied by existing companies will be expanded. The total fitted space is also set to double.

Natacha Jordens

IN BRIEF :

- 18 companies are present on the Biopark, 11 within Biopark Incubator 2.
- 15 of them work in biotech and healthcare, and three others in various support sectors (human relationships, law and infrastructure).
- 9 are ULB spin-offs.
- Almost 50% of the surface available for new companies within the Biopark Incubator 2 is occupied.

For further information on the companies present on the Biopark, please visit www.biopark.be/companies.html

N.J.





At home with Delphi Genetics

On 3 December, Delphi Genetics opened their new 1600m² premises on the Biopark, marking a new stage in the development of the IBMM' spin-off that is negotiating its licences with multinationals.

StabyExpress is the Delphi Genetics signature: developed using know-how from the Institute of Molecular Biology and Medicine (IBMM), Delphi Genetics commercializes this product that enables the production of molecules from genetic engineering without antibiotics.

StabyExpress has already been licensed to Sanofi-Pasteur (June 2009) and GSK (September 2010) and is now also licensed to MSD (known as Merck in the USA and Canada), where it is destined for use not “only” in the production of vaccines, but across all human and animal health fields. “This shows that our technology can be applied to production needs other than vaccines and that we can work with companies from outside the biopharmaceuticals sector, such as those that produce enzymes for the food industry or for diagnostics”, highlights Cédric Szpirer, CEO of Delphi Genetics.

ESCHERICHIA COLI

Since it was founded in 2001, Delphi Genetics has commercialized its technologies used in the study of genes or to produce certain biological components (such as vaccines) through three activities: kits, bespoke R&D, and third party licensing. All of these services are founded upon a single bacterium: *Escherichia coli*, an organism that is well known within the Biopark as it continues to be researched in the IBMM's Bacterial Genetics and Physiology Laboratory, where Delphi Genetics was born. “From time to time we still work with the laboratory, now managed by Laurence Van Melderren. We are sponsoring a Waleo project to design a *Escherichia coli* bacterium with a faster growth rate, a development which would of course increase its yield in the fermenters”, specifies Cédric Szpirer.

For some time now, the SME has been working to diversify its activity: having examined the yeast's potential, Delphi Genetics is now researching the way to adapt its StabyExpress technology to mammal cells and is also analysing its technology's effectiveness in DNA vaccines. Delphi Genetics is leading this research through DNAVAC, a research project from BioWin, the Walloon health cluster competitiveness, with the aim of developing and creating DNA vaccines without the antibiotic resistance gene. They are also taking part in the European Space Agency's AMERE study on cosmic radiation, based on the cultivation of human cells in space.

NEW BUILDING

This summer, Delphi Genetics has left Biopark Incubator I to move across the street into brand new, low energy premises built by the company. The move came at the right time: Delphi Genetics now has its own laboratories that are 100% dedicated to mammalian cell R&D.

“We commissioned a building that will enable us to keep the production and the R&D/ services sides of the business separate. As space was not an issue, we have been able to procure new equipment such as a complete bacterial genome sequencer, a quantitative PCR device, and a protein purifier, all of



which bolsters the range of services we can offer our clients. Our laboratories are ISO 9001 certified, but we are not planning to obtain GMP (Good Manufacturing Practices) certification: it is not really necessary for our type of activity and if we see the need for GMP labs than we can outsource to our neighbours at MaSTherCell or Novasep. Most important for us is maintaining our flexibility: our installations are modular, and we can adapt them to the shape the company takes as it grows”, Cédric Szpirer explains.

Nathalie Gobbe



The Delphi Genetics' low energy building was inaugurated on 3 December in the presence of Paul Magnette, the new mayor of Charleroi

www.delphigenetics.com



GREEN BUILDING

1600m², on 3 floors.

Two activities:

Production, Services/R&D
205m² of office space and meeting rooms, 650m² of lab space, 200m² storage.

Capacity:

45 people.

Low energy building:

“Heated” using energy created by activity in the building.

Budget :

€ 3,5m including scientific equipment.

Opening:

3 December 2012.

IN BRIEF

Founded:

November 2001 by three IBMM scientists – Philippe Gabant, Michel Milinkovitch, Cédric Szpirer – and the ULB.

Number of employees:

15 (including 13 scientists: doctors, graduates, technicians).

CEO :

Cédric Szpirer.



The Bone Therapeutics spin-off continues to blaze its way to the top. Coming soon: new cell therapy products and a new building on the Biopark.

If one thing can be said of Bone Therapeutics, it is that this spin-off is constantly evolving. The company entered the cell therapy sector in 2006 and since that time it has grown from 3 to 50 employees and multiplied its funding by five to reach €30m, becoming a mini-pharma in and of itself.

Bone Therapeutics researches, tests, and manufactures cell therapy products and its success is founded upon two pillars: “Our human outlook is our main asset. The founders of the company were all previously clinicians and were therefore enthusiastic to develop treatments for patients. Many things can be tested in a laboratory, but the findings

cannot always be applied to people”, confides Enrico Bastianelli, the CEO. “The second key to success is quality, both of the products developed and the work carried out. We offer highly targeted solutions for bone diseases that cater to real medical needs. This means that we need a competent team, capable of carrying out demanding, conscientious work”, he adds.

CLINICAL TRIALS

Bone Therapeutics is a specialist in debilitating bone and joint diseases, most of which are without a cure. Its main targets are osteonecrosis of the hip (a rare disease that destroys the joint) that affects those aged 30-50 and pseudoarthrosis (when fractures fail to heal spontaneously). PREOB® was developed to treat these diseases. An autologous product, it is developed from the patient's own calf, turned into a drug and then readministered.

Phases I and II were combined in order to test the product's toxicity and effectiveness, and phase III is currently underway. This phase is intended to reproduce and validate the results obtained during the pilot phase and to test product safety on a larger patient sample (130 in total) and across more sites (20-25 centres throughout Europe). “When PREOB® was implanted into some patients it either halted or reversed the disease's progression. It improved hip function while

causing a significant reduction in pain. This key study marks the final stage before authorisation to bring the product to market”, Enrico Bastianelli reports excitedly.

Bone Therapeutics is also working on another treatment: ALLOB®. This allogenic product will also help to heal stubborn fractures. The paperwork for the clinical trial will be submitted during the first half of 2013 and the trial will begin later the same year. Another product, MXB®, is a cellular matrix combination that targets more serious diseases such as bone defects or losses.

GROUNDWORKING CEREMONY

In parallel, Bone Therapeutics is set to build its own premises at the Charleroi's Aéroport. Located at the roundabout in front of Biopark Incubator 2, the 3 hectare site is waiting for work to begin. Planning permission has already been obtained and only the financial closing remains to be completed before the foundations can be laid in early 2013. Biopark was the natural choice of location. The company wanted to remain within the *Académie Universitaire Wallonie Bruxelles* and chose to be located in Gosselies. “We wanted to set up in an established science park where we would be alongside other biotech companies. Choosing to remain in the region is also a



nod to Wallonia who has loaned us its financial support, without which this amazing project would not have been possible”, he explains.

The company will be fully installed within the Biopark Charleroi Brussels South: the administration, the researchs labs, the GMP production space and the quality control section. “Part of our building will also be home to Promethera, a company that specialises in the development of cell therapy for liver disease. Each company will continue with their own work while sharing a workspace and services”, the CEO goes on. Work is expected to last two years, with the official opening taking place in 2015.

Sandrine Rubay

www.bonetherapeutics.com



Bone Therapeutics' teams should move into their new premises in 2015, accompanied by the company Promethera



PRESIDENTIAL VISIT TO THE BIOPARK

Bronislaw Komorowski, the Polish President (centre), listens closely to the explanation provided by Gaetan Van Simaey (CMMI, left) during his visit to the **Centre for Microscopy and Molecular Imaging (CMMI)** on 13 November. As part of his official visit to Belgium, the Polish President also attended the signing ceremony for an “agreement on cooperation and relationship” between the Biopark and **Lodz Regional Park of Science and Technology**, which focuses on nano and biotechnology and stands to benefit from Biopark’s experience in these fields, while our campus will be able to boost its international visibility.

N.J.





iTeos: 3 targets, 4 years to prove themselves

iTeos Therapeutics opened its first laboratory in Biopark Incubator 2 in October. The company aims to validate and develop several immunomodulator molecules, some of which have already made good progress towards clinical trials.



Cancer cells have more than one trick in their DNA that lets them evade the immune system. One such evasion mechanism is immunosuppression: the ability of cancerous cells to reduce the immune response they provoke. “Immunosuppression makes other treatments, such as anti-cancer vaccines, less effective”, explains Michel Detheux, the CEO and cofounder of iTeos, a new spin-off from the “Ludwig Institute for Cancer Research” (LICR) and the *Université Catholique de Louvain*. “iTeos’ goal is to develop candidate medications to reestablish an immune response to tumours and then work in synergy with the other available treatments”.

IN THE PIPELINE

The company is looking into three enzymes involved in immunosuppression, two of which were identified inside the Belgian branch of the LICR by the second cofounder of iTeos, Professor Benoit Van Den Eynde, and his

team. “Our most advanced programme targets an immunosuppressive enzyme expressed by a sub-population of cells that form the tumour”, explains Michel Detheux. “We then discovered an inhibitor for this enzyme that had already been tested on humans for another application. This gained us a head start of a few years on development, and we hope to be running clinical trials for this candidate medication within two years!”. The two other enzymes studied by iTeos are indoleamine and tryptophan-2, 3-dioxygenase (IDO and TDO), for which the company has been performing high-throughput screening in an effort to identify the inhibiting molecules. The company hopes to develop an “immunomodulator clinical candidate” of one of these enzymes by 2016.

MISSION: EXCELLENCE

The path has been laid out for the young spin-off that has already made a number of contacts with major global pharma. Currently, the 5-person company is funded through a €6m grant from *Wallonia* and €3m of private investment, a major part of which comes from the LICR. iTeos has chosen to set up in Gosselies. “As I had already worked as a manager of Euroscreen, I was already familiar with the Biopark”, reveals Michel Detheux, “and it provides me with the most

services that could be useful to my company”. The CEO lists the CMMI, the effective animal house facilities, and the practical services offered by Biopark Incubator. “Irrespective of where a company comes from, excellence is what matters”, concludes the iTeos manager who hopes to convince the sector within four years.

Natacha Jordens

www.iteostherapeutics.com



Benoit Van den Eynde (left) and Michel Detheux (right), cofounders of iTeos.

CIBLES: an investment for the future



The programme of excellence CIBLES, launched in 2008 by *Wallonia*, is now nearing completion. Participating teams are now displaying their results.

Coordinated by the ULB, the CIBLES project focuses on three research strands, each sponsored by partners in industry. For five years now, the participating teams from the ULB, UCL, and ULg have attempted to identify and certify new pharmacological targets that may be of use in treating diseases linked to chronic inflammation reaction, the nervous system and cancer. “The programme has enabled us to develop great experimental tools that will be of great use in our future research. It is an investment in the future”, explains Etienne Pays, the head of the Molecular Parasitology research unit. His laboratory is carrying out research under strand 2 which is sponsored by GSK and focuses on promising anti-inflammatory products. Their research has lead to the study of apolipoprotein L-1 (apoL-1), which is involved in resistance to trypanosome infection and that also has a

modulating effect on the immune system. “We discovered that these proteins change the behaviour of dendritic cells that monitor immunity and increase the effectiveness of the immune response, especially during viral infections. We also believe it to have cancer-fighting properties and intend to look into this over the next years”.

AND THAT IS NOT ALL...

These dendritic cells are also influenced by some regulatory lymphocytes that have been studied by the neighbouring Immunobiology laboratory that is also participating in research strand 2. The team has learned that lymphocytes that express the receptor CD27 dampen the immune response by transferring this receptor to dendritic cells. This is a never-before seen process. “The goal is to fully understand the process”, explains Muriel Moser, the head of

the Immunobiology research unit, “but also to learn how we can influence the regulatory lymphocytes to dampen or accentuate the immune response. They could then turn into precious allies used in combination with existing therapies”. The laboratory is also about to conclude a public-private partnership between *Wallonia* and GSK that will enable them to continue their research, with a special focus on diabetes: a disease triggered by an autoimmune response.

CIBLES has enable these teams to take a step forward towards the discovery of new therapeutic targets. And while there remains a long way to go before candidate medication is developed, the leads discovered during the programme already hint at promising results.

Natacha Jordens



3 RESEARCH STRANDS, 5 TEAMS

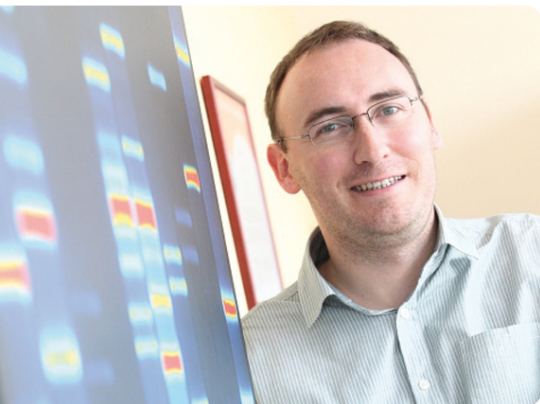
5 Biopark teams were taking part in this programme. In addition to the Immunobiology and Molecular Parasitology units, the **Molecular Virology** laboratory is also carrying out research under strand 2. The **Molecular Cell Physiology** and **Developmental Genetics** units respectively are working on Strand 1, sponsored by Euroscreen and focused on receptors coupled to G proteins, and Strand 3, which researches the roll of stem cells in cancer and central nervous system diseases, in partnership with UCB.

N.J.



OncoDNA is open for business

Jean-Pol Detiffe, the founder and former CEO of the spin-off DNAVision, has just created a new company on the Biopark: OncoDNA.



IN WHICH SECTOR DOES YOUR NEW SME, ONCODNA, OPERATE?

JP Detiffe: As its name indicates, OncoDNA focuses on the DNA analysis in oncology used to both monitor and treat patients in an effort to provide “personalised” medicine that is adapted to the genomic profile of the patient’s tumour.

WHO ARE YOUR SHAREHOLDERS?

JP Detiffe: We have obtained over €2m in funds from Bio.be (an IPG subsidiary), Sambrinvest, various private investors including Jean Stéphane (former CEO of GSK Biologicals) and François Blondel (former CEO of IBT, the brachytherapy company) who chairs the board of directors,

as well as regional funding from the technological development department.

ALTHOUGH ONCODNA IS A NEW COMPANY, IT ALREADY BOASTS CONSIDERABLE EXPERIENCE.

JP Detiffe: That’s right. We can rely on the expertise of the Institute of Pathology and Genetics (IPG), which is also home to our offices: IPG is the 3rd leading laboratory in Europe in terms of tumour analysis volumes, with around 50% of all hospitals in French-speaking Belgium sending their samples to IPG for analysis. We combine this expertise in anatomopathology with the cutting edge DNA sequencing techniques that I developed during my many years at DNAVision. We also benefit from a scientific committee that includes Martine Piccard and Christos Sotiriou from the *Jules Bordet Institute* in an advisory capacity.

HAVING ONLY JUST OPENED, YOU ARE ALREADY IN BUSINESS?

JP Detiffe: Yes. As of now we are providing customised tumour analysis through different product lines that range from the sequencing of a targeted panel of genes to whole genome sequencing of a tumour; we will soon be opening a dedicated web

portal for oncologists that will enable them to quickly get data online, as well as to view the selected treatment and monitor the state of the patient’s tumour.

DO YOU ALREADY HAVE A TEAM IN PLACE?

JP Detiffe: Yes, we have already hired several employees with skills in bio-informatics or marketing and who work together with the IPG biologists, doctors, and technicians to whom our analyses are outsourced.

Nathalie Gobbe

www.oncodna.com





FORMING OLFACTORY EPITHELIUM AND THE CEREBRAL CORTEX

In two new articles published in *Cerebral Cortex and Developmental Biology*, scientists from Eric Bellefroid's **Developmental Genetics Laboratory** at the IBMM have identified the Dmrt5 transcription factor as a key regulator in the development of the olfactory system and cerebral cortex.

The first study looks into the role played by Dmrt5 in forming the olfactory epithelium in amphibian embryos and the team has shown that it plays an important role upstream from the cascade of genes that control neuronal differentiation. Furthermore, it suggests that this factor acquired a role in neurogenesis at a very early stage of evolution as a related gene with a very similar function exists in the sea anemone *Nematostella vectensis*.

The second study shows that Dmrt5 is required for the development of the caudomedial cerebral cortex. The main authors of this publication, Amandine Saulnier and Marc Keruzore, tell us more: "Our results show that Dmrt5 is active in the initial stages of cerebral cortex development, controlling the formation of a major signalling centre involved in regionalisation of the cortex, the cortical heme, and modulating the expression of other transcription factors involved in cortical identity".

N.G.

PARIS-GOSSELIES: A FRUITFUL PARTNERSHIP

PQLC2. No, it is not some obscure code but rather the name of a protein discovered by a group of the *Université de Paris Descartes*, the *Centre National pour la Recherche Scientifique* (CNRS), and **Bruno André's** team at the **IBMM's Molecular Cell Physiology Laboratory**. PQLC2 transports basic amino acids (arginine, lysine, and histidine), to the cytoplasm from the lysosome, an organelle that "digests" cellular waste. The existence of a protein performing this metabolic function in humans has been known for over 20 years, but until now all attempts at biochemical identification and cloning of its gene had been in vain.

The study, published in *PNAS*, details the discovery: Prof. Bruno André's team first discovered three "PQ" proteins in yeast. Their colleagues in France then confirmed the presence of a human equivalent within lysosomes and revealed the molecular properties of PQLC2.

This discovery sheds light on the treatment mechanism for patients suffering of cystinosis, where cystine accumulates in the lysosomes: patients are treated with "cysteamine" that converts the cystine trapped in the lysosomes into a lysine-like compound, which is then able to leave the lysosome thanks to PQLC2. This study will therefore further help the understanding of this diseases and lead to the development of more effective treatments.

This work was made possible through the support of the Cystinosis Research Foundation

N. J.

ELIMINATION OF PROTEINS

For a cell, the ability to eliminate a particular protein from its surface membrane is crucial in order to adapt as conditions change within its environment. The IBMM's **Molecular Cell Physiology Laboratory**, under Bruno André, had previously shown that the elimination of these proteins is triggered when they are linked to a signal molecule, ubiquitin, provoking their endocytosis and degradation within the lysosome. The team's latest publication in *Molecular and Cellular Biology* describes the cascade of biochemical events that trigger the modification by ubiquitin of an amino-acid transporter of the yeast plasma membrane. They show that arrestin-like proteins play a pivotal role in the control of this protein's ubiquitination and endocytosis. This research sheds new light on how cells selectively eliminate certain proteins from their plasma membrane, mechanisms which must be understood in order to control the target proteins in a number of drugs.

N.G.



TIS11 ACCELERATES RNA DEGRADATION

In their latest article published in the *Journal of Biological Chemistry*, the Cyril Gueydan's **Molecular Biology of the Gene** (IBMM) research unit sheds light on the RNA degradation process. The elimination of RNA, the copy of genetic information to be turned in to proteins, is an essential process for the cell to respond quickly to changes in its environment, such as to stop an immune response. To degrade the RNA, the cell must destroy the "polyA tail" found on the end of the molecule, enabling it to remain stable. In this article, the research team proves how important the protein TIS11 is in this process: it recognises and targets specific RNA sequences and accelerates the degradation of the polyA tail. The results were obtained using cells taken from the drosophila, animal model whose simplified immune system means that the appearance and disappearance of RNA molecules can be observed readily and in great detail. The researchers will now endeavour to understand how TS11 causes the degradation of RNA, before possible proceeding to transpose the results to human cells in order to shed light on the role played by this protein in the immune response.

N. J.

CONTROLLING IMMUNE RESPONSE

A healthy immune system reacts to danger signals – bacteria, viruses, or cancer cells – and a first wave of inflammation sounds the alert and stimulates the body to go on the offensive. Once the danger has passed, the inflammation must cease in order to avoid an excessive reaction. This means that the period for which the inflammation lasts must be controlled. However, this control is disturbed in a number of diseases and can lead to septic endotoxic shock which may prove fatal, or assist the development of diseases such as cancer, arthritis, asthma, or multiple sclerosis.

Véronique Flamand's team at the IMI and Abderrahman Hachani at Imperial College London, a former PhD student at the ULB, have both contributed to Ezra Aksoy's research while she was a doctoral student at the IMI, before she occupied her current post as a researcher at Barts Institute of Cancer – University of London. They have just made a major advance by discovering the enzyme that controls the body's inflammatory response. This key lipid kinase is called PI3K P110delta and provides precision regulation of the inflammatory response in order to avoid any excessive reaction that may cause damage to the organism. The PI3K P110delta enzyme balances the immune response by regulating a particular type of immune cells: dendritic cells. Published in *Nature Immunology*, this discovery provides interesting new opportunities for vaccines, immunotherapy for cancer or even chronic inflammatory diseases.

N.G.



A full house for the latest immunology course by Biopark Training. On Friday 16 November, over 100 trainees were on the Biopark campus for the first module of "Immunology for Beginners" taught by Professor Oberdan Leo (IMI). This first module is a prerequisite for those with no background in immunology to sit the six other available modules. In light of its success (in all around 280 students registered for the cycle), Biopark Training is already planning a new cycle for 2013.

N. J.