

Biotech-

Bio *tech*—

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"Beyond seeding inventions into innovative

Bio tech — FOREWORD

enterprises, time for harvesting has come"

As soon as the first wave of biotechnology rose in Europe, the Wallonia Region saw an opportunity to enter this key sector. The Walloon authorities started to help newborn companies to devise their strategic plans. Moreover, as these start-ups were facing a highly competitive environment, the risk of “sudden death” was great. This did not deter the entrepreneurial mind in Wallonia. On the contrary, biotechnology was chosen as a top priority sector to position the region at the forefront of European Bio-regions. The existing chemical and pharmaceutical companies provided the industrial expertise necessary to appreciate the results of the highly innovative research that was taking place in the universities. The life sciences sector could now enter a new phase of development. The ambition of many of these entrepreneurs has since turned to a rapid expansion and a shift of their activities towards the segments with the highest added values.

The Walloon Region can count on the Directorate General of Technology, Research and Energy (DGTRE), being the “one stop-shop” for research in the region. The DGTRE continually updates its portfolio of grants and subsidies to stimulate innovative research. It actively promotes the appeal of the Region with the help of the Wallonia Export and Foreign Investment Agency (AWEX). These two agencies work in synergy to catalyze the development of this high growth/high value sector.

Together, they act as fertilizer that continues to improve the possibility of harvesting even more fruit!

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WALLONIA AT THE CROSSROADS OF EUROPEAN REGIONS

Wallonia is one of the three regions in the Kingdom of Belgium, situated south of Brussels, Belgium's capital city. The Walloon region is located at the center of a 400-km circle in Europe that encompasses London, Amsterdam, Paris, Strasbourg and Dusseldorf. Wallonia is home to Belgium's French- and German-speaking communities. Its 3.34 million inhabitants live at the crossroads of the Germanic, Anglo-Saxon and Latin cultures. This central location and high level of cross-cultural fertilization explains the quality of the Wallonia entrepreneurial spirit.

The region represents 55% of the Belgian territory and contains most of the country's natural resources like water and forests. Beautiful landscapes with valleys and rivers add to Wallonia's enjoyable lifestyle, blending the Latin way of life with the rigor of northern Europe.

Wallonia has one of the best travel networks in Europe. From high-speed trains to easy air connections for international travelers, and a dense highway network. Moreover, as optical cables have been laid along these highways, they have become true "Infobahn's", leading the region into the "digital age".

According to official economic data, the service sectors predominate in Wallonia, comprising 73% of the regional gross added value and 76% of regional employment.

Wallonia is famous for the highly technical character of its products, though they are mainly considered traditional activities. In recent years, R&D expenditure has increased in the business sector so that it now exceeds the European Union (EU) average. Wallonia's entrepreneurs have accumulated impressive know-how by concentrating on high growth niches in sectors like sciences, aerospace, biotechnology, microelectronics, new material and information technology.

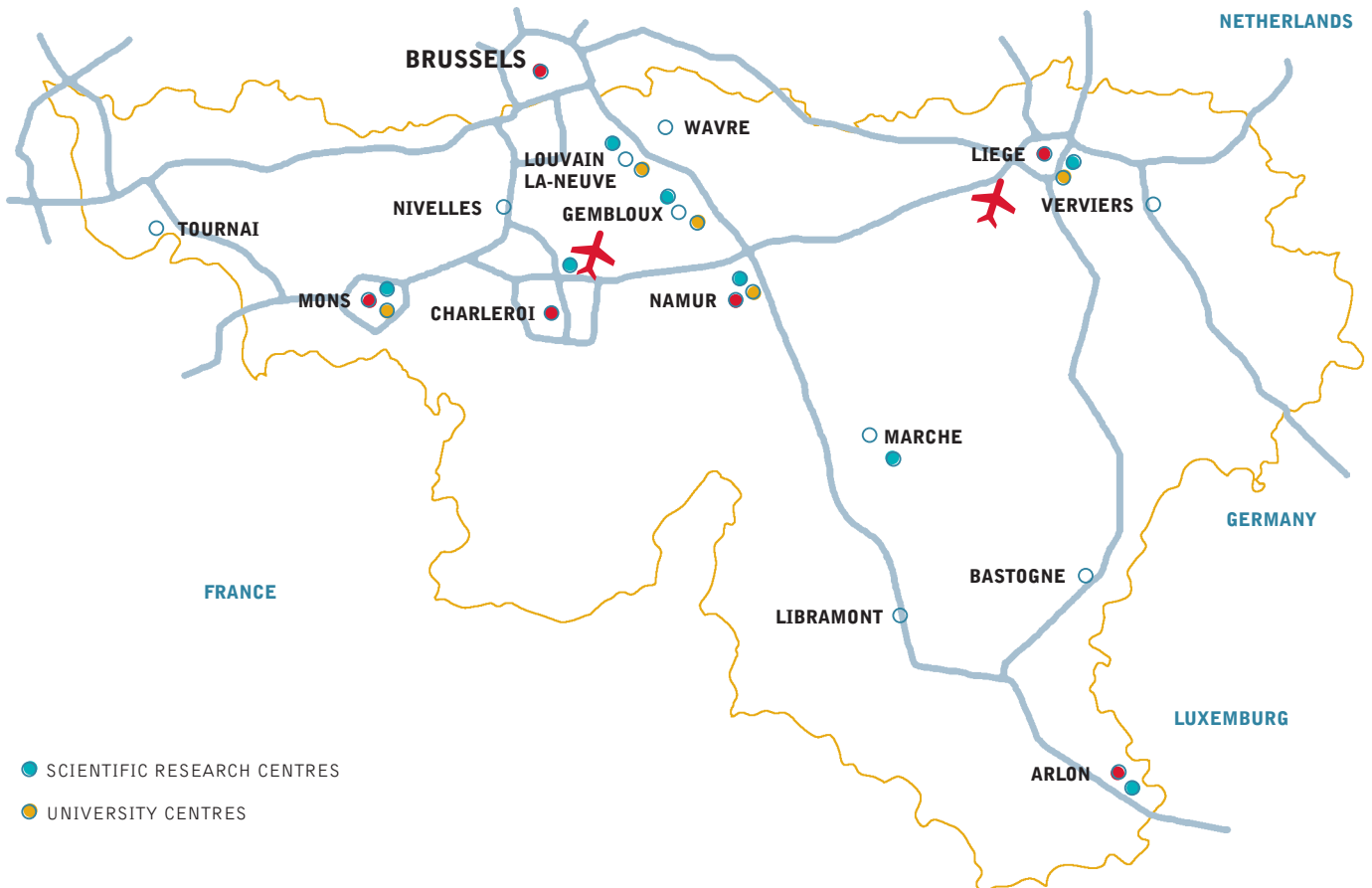
The region is actively building a strategy for research and innovation in order to promote technological development.

Technology sectors accounted for 8.5 % of salaried employment in 2003, but recently, employment has been

increasing rapidly in high-tech manufacturing industries, chiefly in the pharmaceutical and life science industries.

This “innovation system” is based on collaboration between universities, research centers, and financial and public sectors, all of which contribute to the development and extension of the region’s productive base.

Wallonia is also well integrated in the EU as over 75% of its exports are devoted to the EU. Its main exports are mechanical, engineering, chemical and pharmaceutical products.



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THE EXPANSION OF THE BIOTECH INDUSTRY

In the 21st century, Wallonia's biotechnology sector has renewed strength. Dynamic entrepreneurs and innovative research institutes have combined their efforts with local and regional agencies, namely, the **Directorate General of Technology, Research and Energy** (DGTRE), the **Wallonia Export and Foreign Investment Agency** (AWEX) and the important financial arm of the local authorities, the **Société Regionale d'Investissement de Wallonie** (SRIW).

As a result of this cooperation, Wallonia has shown continuous revenue growth in its 69 biotechnology companies. The turnover in 2003 amounts to € 2,376 million growing by more than 19 % since 2001.

Table 1

Biotech activity in Wallonia

	1997	2001	2003	Increase (2001-2003)
Nbr. of companies	25	55	69	+ 25 %
Revenues (mio €)	1,034	1,994	2,376	+ 19 %
Nbr. of employees	3,034	4,461	5,227	+ 17 %

"Source: Data collected and compiled by CRGB, Centre PME and Pi_ (ULg)"

The total number of companies increased from 55 to 69 due on the one hand to the creation of new companies (an increase of 10 since 2001), and on the other to the recent introduction of biotechnology activities in existing companies (an increase of 4). This has helped the region take more than 80% of the country's share of the biotechnology activity, as shown in table 2.

Table 2

Wallonia's share of biotech activity in Belgium in 2003

	Nbr. of Companies	Revenues (mio €)	Revenue % of Total	Nbr. of employees	Employees % of Total
Brussels	24	109	3.77 %	481	6.31 %
Flanders	39	403	13.95 %	1,912	25.09 %
Wallonia	69	2,376	82.27 %	5,227	68.60 %
Total	132	2,888	100 %	7,620	100 %

"Source: Data collected and compiled by CRGB, Centre PME and Pi_ (ULg)"

This success is amplified by the support of large established life-sciences groups based in the region.

Interestingly the 61 small- and medium-size entrepreneurial companies are increasingly contributing to the growth of the sector. The larger contribution in the biotech turnover of Wallonia comes from GlaxoSmithKline Biologicals which contributes to 47 % of the regional figure with € 1,132 million revenues posted in 2003.

There is a common “20/80” rule that states the top 20 companies represent at least 80% of total revenues.

This is even truer in an industry like biotech where very young companies strive to start and create their own niche. Meanwhile, established companies benefit from the technologies generated by small innovative enterprises when their research programs develop into marketable products. Given time, the younger companies will become a key source of innovative products, and inevitably additional revenue.

Table 3

Comparison between SME and large companies in 2003

	Nbr. of Companies	Revenues (mio €)	Revenue % of Total	Nbr. of employees	Employees % of Total
Large	8	1,774	74.66 %	2,914	55.75 %
SMEs *	61	602	25.34 %	2,313	44.25 %
Total	69	2,376	100 %	5,227	100 %

SMEs: Less than 250 employees, annual turnover not exceeding € 40 million, and not member of a large company group.

*Source: Data collected and compiled by CRGB, Centre PME and Pi_ (ULg)”

The total figure includes successful companies that are global leaders in their field, that is, **GlaxoSmithKline Biologicals, Baxter Healthcare, UCB Group and Eurogentec**. They are powerhouses that stimulate the entire sector in the region. They invest heavily in research programs, not only internally, but also externally through cooperation with local universities and smaller biotech ventures.

Moreover, they are local producers and distribute their products worldwide from Belgium.

Table 4

Biotech activity by sector in 2003

	Nbr. of Companies	Revenues (mio €)	Revenue % of Total	Nbr. of employees	Employees % of Total
Healthcare	28	1,878	79.04 %	3,346	64.01 %
Agri-bio	22	306	12.88 %	668	12.78 %
Environment	7	15	0.06 %	70	1.34 %
Technology & Services	12	177	7.45 %	1,143	21.87 %
Total	69	2,376	100 %	5,227	100 %

“Source: Data collected and compiled by CRGB, Centre PME and Pi_ (ULg)”

The leading sectors remain “Healthcare” and the closely linked “Technology and Services”, comprising two-thirds of the companies and more than 80% of the turnover.

“Waste management” is still a relatively young industry borne of the concerns brought about by industrial pollution and the increased environmental protection directives driven by the public authorities at the European level. Companies active in the sector have begun to develop methods to treat waste based on chemical or mechanical techniques.

Biotechnology today is introducing more “eco-friendly” tools and technologies. Bioremediation, for example, uses selected microorganisms to restore soil to its previous state or to cleanse water and air of different types of pollutants.

As “environmental biotechnology” is still mixed with traditional processes, figures provide only the percentage of the biotech techniques used in the larger activities in “waste management”.

The food and agricultural industry represents a very important part of the gross national product in European countries, and this is also true for Wallonia with its large farmlands and forests.

However the “biotech applications” in this sector remain limited. Compared to other Europeans, Belgians are quite receptive to novel foods and products derived from the biotechnology. Legislation enables research to be conducted in this field. Companies involved in genetic engineering of plants are more dependent on consumer choices than those active in cattle selection or in enzyme production.

As indicated in table 5, Wallonia demonstrates from a European perspective a significant strength in stimulating the entrepreneurial mind of scientists and businessmen.

Table 5

Wallonia in Europe (2002)

Year 2002	Europe (*)	Wallonia	%
Inhabitants (million)	385	3.4	0.88%
Biotech companies (number of)	1,878	63	3.35%
Employment (FTE)	82,124	4,969	6.05%

(*) Ernst & Young, ENDURANCE: The European Biotechnology Report 2003 (analysis year 2002)

With less than one percent of the European population, the Walloon Region compares favorably with other European countries. With 4,969 people employed in the sector in 2002, Wallonia boasts biotech revenues of € 2,295 million generated by 63 life science companies. This development is favored by the presence of 7 university centers and 5 science parks active in the field of biotechnology.

The beginning of the 21st century meets the promises.

The presence of highly qualified scientists and skilled technicians enables Wallonia to attract investment in research centers and production facilities. Creation of new companies, mergers and acquisitions, and management buy-outs contribute to the strengthening of the biotech sector in the region.

Sectors

The world of biotechnology is vast and includes many different industries. Their potential applications cover a wide range of sectors like pharmaceuticals, chemistry, agriculture, food production and processing and environment.

For the purpose of this report, four sectors have been distinguished according to the kind of technologies and products generated.

1. Healthcare

- Biopharmaceuticals
- Diagnostics and medical technologies
- Biological research

2. Service and Technology Providers

- Drug discovery services
- Bioinformatics
- Contract manufacturers
- Reagents suppliers

3. Agri-food

- Plants and animals
- Novel foods and ingredients

4. Environment

PHOTO: Molecular structure of cytochrome B562 of E.Coli (CBMN, FUSAGx)

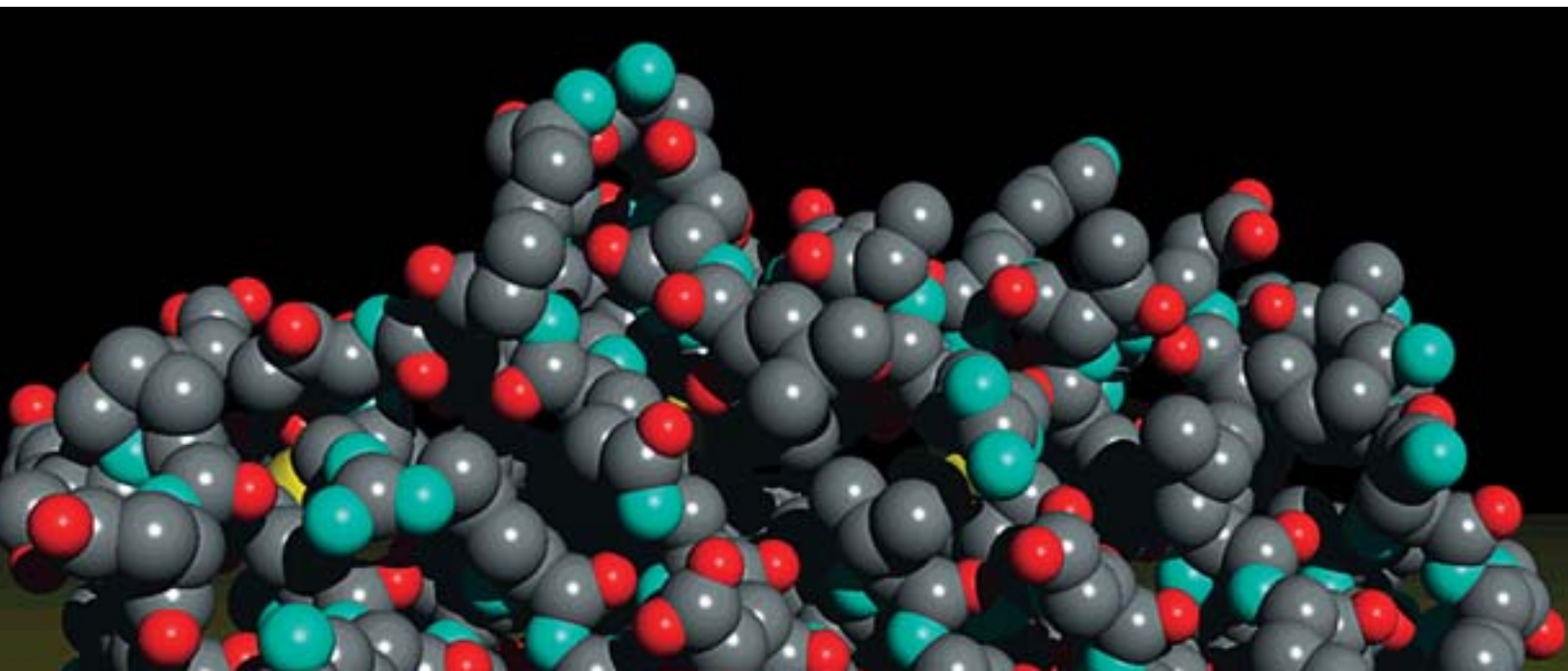


Table 6

Relevant Biotech Events since 2002

2003 January	Creation of Phytisia, a spin-off from the University of Liège
2003 May	Acquisition of an oligonucleotide production facility in San Diego by Eurogentec
2003 May	Henogen acquires 4C Biotech, € 5 million investment for new cGMP facility
2003 July	Implantation of Wetlands Engineering in the Louvain-la-Neuve Science Park
2003 August	Move of the Eurogentec's production to a brand new building in the Liège Science Park
2003 August	Implantation of OncoMethylome Sciences in Liège
2003 August	IBA creates a joint venture with Schering AG to supply FDG for PET imaging in the UK
2003 October	Creation of BioXpr, a spin-off from the University of Namur
2003 October	Start of the GIGA technical facilities
2003 November	Set-up of KitoZyme's pilot plant in Liège
2003 November	Euroscreen received "Belgium's Entrepreneur of the Year 2003" Trophy
2004 January	After Boston, the Florida Proton Therapy Institute in Jacksonville, Florida, USA opts for the IBA system
2004 March	Creation of Aseptic Technologies (spin-out of GSK Biologicals) in Crealys
2004 March	GSK Biologicals investment of € 450 million in Wavre (new plant and QC center)
2004 April	Wetlands becomes SME leader of an integrated project of the European FP6
2004 May	Creation of DNAvision in Aeropole (Charleroi)
2004 June	UCB Bioproducts successfully supplies peptidic active pharmaceutical ingredient for a commercial drug (cardio vascular)
2004 June	Henogen achieves successful phase II clinical trial on new subunit vaccine against infectious mononucleosis
2004 October	Coris BioConcept receives "Wallonia Prize for Exportation"
2004 December	Henogen acquires Dutch spin-off biotech company ImmunoToko
2005 January	Creation of Institute of Medical Immunology (IMI) in Aeropole (partnership between GSK Biologicals, the University of Brussels and the Wallonia Region)
2005 January	Creation of Straticell in Namur
2005 January	Creation of Viridaxis, a University of Louvain spin-off
2005 February	Cardio3, specialized in stem cell cellular therapy, launches its activity in Braine-l'Alleud
2005 September	UCB Bioproducts invests in significant additional cGMP peptide production capacities and capabilities to be fully operational in September 2005

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HEALTHCARE

With more than 400 biopharmaceuticals worldwide and countless new diagnostics and research tools, healthcare is the sector benefiting most from advances in biotechnology.

The "Human Genome Project" produced its first results in 2000 and triggered a wave of company creation throughout the world's healthcare field.

We have chosen to distinguish therapy from diagnostics & biomedicine and research tools.

The first sector is "biopharmaceuticals" and it encompasses different therapies based or derived from biotechnology: recombinant proteins, gene therapy, vaccines and so on.

"Diagnostics and medical technologies" is the second sector and includes diagnostic tools and biomedical instruments.

The third sector is "research tools" and consists of products for research and production, namely, oligonucleotides, peptides, labeled compounds, separation tools, and so forth.

Companies in the healthcare sector usually feature research and development, production and commercial divisions as they are active at the international level.

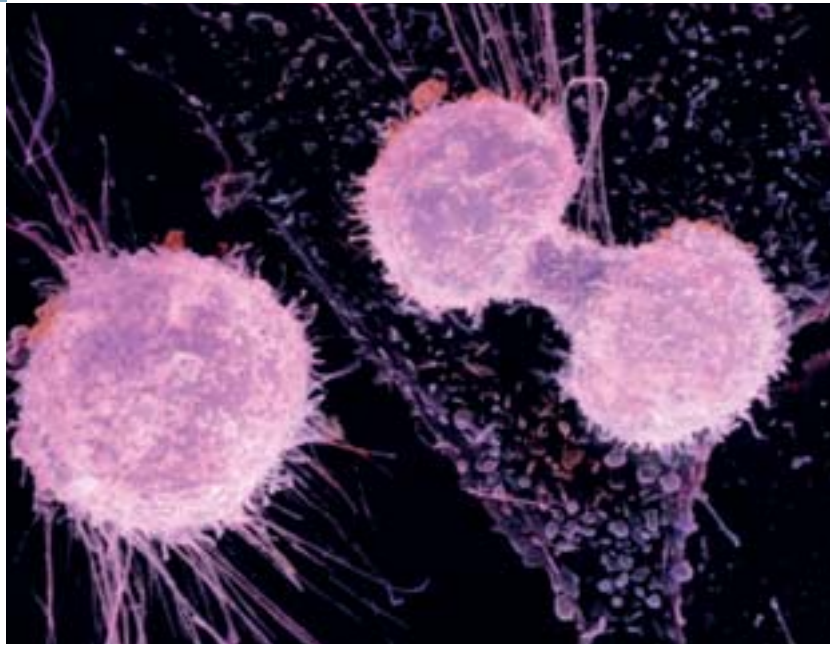


PHOTO: Cellular division ("Gènes et Ethique" Pass © Benelux Press)

BIOPHARMACEUTICALS

GlaxoSmithKline Biologicals

The merger of GlaxoWellcome with SmithKline Beecham has strengthened the leadership position of the global human vaccine subsidiary, renamed **GlaxoSmithKline Biologicals** (GSK Biologicals). They are based in Rixensart, 20 km south-east of Brussels. In 2002, GSK Biologicals enjoyed a healthy 23% share of the world vaccine market, which represents 35 vaccine doses distributed every second.

Success story: from antibiotics to recombinant antigens

This success story began in 1945 with the creation of the RIT company, which started producing antibiotics. The vaccine activity started in 1956 and an ambitious vaccine research program was developed for both human and veterinary purposes. In 1963, the Belgian company looked for a strong global partner. SmithKline & French from the US recognized the company's potential, acquired the business, and built it into a global vaccine powerhouse focusing on human vaccines. In 1986, SmithKline-RIT launched the first vaccine for human use made by genetic engineering (Engerix-B against Hepatitis B, produced in yeast) which boosted the vaccinology research and was at the source of the company's success story.

In 2003, the Belgium company renamed GSK Biologicals, after the successive mergers of SmithKline with Beecham in 1989 and GlaxoWellcome in 2000, achieved a record turnover of £ 1,147 million, steadily increasing at a 13% rate since 2001. Most of the company's activities (90%) are located in Rixensart and Wavre and focus on research and development, clinical trials and production of human vaccines. It now has more than 4,000 employees.

Thanks to the extensive cooperation with Belgian and European universities and to its strong internal expertise, GSK Biologicals features an extremely ambitious research program:

1. Vaccines for "all life stages": paediatric vaccines against S. Pneumoniae, meningitis, rotavirus infections, adolescent vaccines against cervical cancer essentially caused by HPV viruses, adult and travelers vaccines, elderly vaccines against S. Pneumoniae infection and RSV, influenza and varicella zoster virus.
2. Vaccines for the developing world in cooperation with the WHO, PAHO and UNICEF: HBV, poliomyelitis, meningitis, malaria, HIV, tuberculosis, dengue, rotavirus, and so on.
3. "Pharmaccines" or therapeutic vaccines which fight against several cancers: melanoma, lung, breast and prostate cancer.
4. Development of new adjuvants to increase/modulate specific immune responses.

In 2004, GSK Biologicals has achieved promising clinical results in the field of vaccines against malaria and cervical cancer.

With the 25 products in the pipeline in 2003 and 20 in clini-

cal trials, GSK Biologicals will lead the pack and continue serving the community with solutions to improve health worldwide. It will remain a global leader in biotechnology and a strong stimulus for research in Wallonia for the years to come.

In Wallonia, GSK Biologicals plays a key role in developing the university research in human immunology. In 1995, it established the Centre de Recherche Interuniversitaire en Vaccinologie (CRIV). The main purposes of the CRIV were the acquisition of basic knowledge in vaccinology and human immunology, the training of experienced immunologists and an important cooperation between different university research teams. After the termination of the CRIV's activities in 2004, these objectives were taken over by the "Institute for Medical Immunology" (IMI), created on the Aeropole of Gosselies, with the partnership of the Wallonia Region and the University of Brussels.

GSK Biologicals also plays a key role in the regional technological development. Its first spin-out (**Aseptic Technologies**) has been created in 2004 in Crealys, to perform an innovative aseptic filling of vials with injectable products.

Baxter Healthcare

Located in Lessines, **Baxter Healthcare** is increasing its investments in its European production unit of blood derivatives. This € 50 million investment made by Baxter (80%) and the Wallonia Region (20%), will be accompanied by a 10% increase in employment from 1,134 up to close to 1,300 persons.

In addition to this significant investment in production capacities, a 165-scientist research and development center based in the nearby city of Nivelles will ensure the company steadily remains at the forefront the latest technological advances.

Eli Lilly

Eli Lilly & Company devotes a major part of its resources world-wide to Research and Development. In the context of this resolute R&D strategy, the **Lilly Development Centre**, located in the Louvain-la-Neuve Science Park with 355 employees, of whom two thirds work on R&D, plays an important role in the development of biologically active substances stemming from research.

PHOTO: Adipocytes precursors (Laboratoire de Biologie Cellulaire, UCL)

DIAGNOSTIC TOOLS AND BIOMEDICAL TECHNOLOGIES

Since the early seventies, Wallonia has embarked on an ambitious program to boost the development of their diagnostics sector. Today, the region remains at the forefront of this field thanks to continuous innovative research.

One of the hot topics in diagnostics is the implementation of the latest DNA chemistry in microchips to create a new technology known as DNA MicroArrays or more simply “biochips”. Two companies are positioning themselves to become leaders in this promising field: **Eppendorf Array Technologies** (EAT) and **Probiox**.

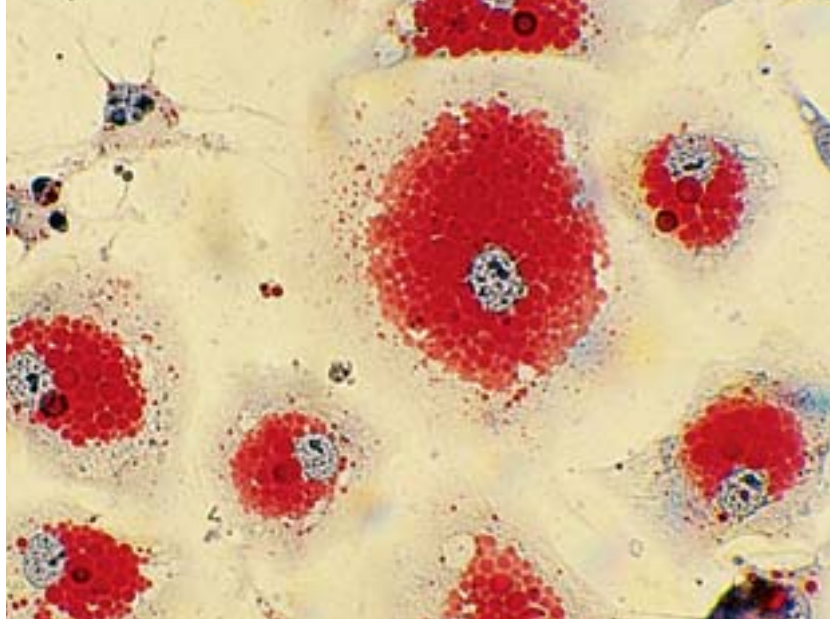
Eppendorf Array Technologies as Competence Center for biochips

To complete the existing supply, Professor J. Remacle, head of the Laboratory of Cell Biology and Biochemistry at the University of Namur, founded Advanced Array Technologies (AAT) in 1999 to commercialize the results of the research performed in his lab with the support of the Wallonia Region.

As a result of combined expertise and an innovative technology patent portfolio, AAT became a leading biochips supplier for pharmaceutical and academic researchers. AAT combines the ability to develop and produce advanced biochips, unique labeling methods for microarrays and next generation microarray formats.

In August 2002, Eppendorf placed its confidence definitively in the Namur company, which became **Eppendorf Array Technologies** (EAT) and is known as the competence center for the arrays and related technologies for the Eppendorf group. Eppendorf AG has now developed its core activities in the business field of biochips in the heart of the capital of Wallonia.

EAT developed a series of high quality biochips products



for quantitative analysis and a growing product pipeline while now having access to Eppendorf’s global distribution network. EAT is setting up full production facilities for biochips in Namur.

The EAT-developed products are part of the Eppendorf basket of research tools for the biotechnology and research laboratories. Eppendorf AG has a worldwide distribution network and has more than 1,600 employees on four continents.

Probiox - Oxidative stress profiling

The birth of **Probiox** in 2001 resulted from the meeting of few actors intent on pooling their acknowledged and complementary expertise in the field of oxidative stress: the “Centre Suprafacultaire de Recherche en Thérapie Cellulaire et Moléculaire” of the University of Liege, displaying an internationally recognised know-how in molecular biology and in the biochemistry of oxidative stress; Professor Luc Montagnier (Paris, France), who chairs the Scientific Board; and Eurogentec, a European leader in the development, production, and distribution of a range of research tools.

When, in an organism, the balance between the level of pro-oxidants and the organism’s antioxidant defense systems tips in favour of the former, there arises a condition called oxidative stress, which favors the development of various diseases, degenerative or not, inexorably linked to that natural phenomenon: ageing. Probiox also specializes in the study and measurement of oxidative stress in the sport, and high-class racehorse markets.

In order to know if people are becoming too “oxidized” and if the antioxidant defenses are too low, Probiox proposes an analytical tool available for determining at any age one’s

oxidative stress status, on a simple blood sample. The profile is based on four types of analysis: (i) antioxidant level measurements; (ii) trace element determinations; (iii) analysis of iron metabolism; (iv) detection of oxidative damage to lipids, DNA, or proteins. All of these analyses are presented graphically as an "Oxidative Stress Rosette".

Biocode Hycel

In 2000, Biocode, an established player in the immunoassay field, acquired Hycel, a French producer of diagnostic reagents and instruments. Through this acquisition,

Biocode Hycel has significantly improved the development potential and automation path of its new system based on a chemiluminescence technology.

On the other hand, Biocode's own research team, with the support of the Chemical Analysis Department of the University of Liege Institute of Pharmacy, discovered new chemiluminescent molecules to be used for the development of a new range of non-isotopic immuno-diagnostics. This has resulted in the birth of the "Pegase project".

Today, Biocode Hycel develops reagents to feed its new versatile bench-top, random and continuous access, walk-away patented automated analyzer (3X3) for immunoassays, clinical chemistry and coagulation.

The 3X3 platform which accommodates disposable universal reaction cuvettes is equipped with a photometer for clinical chemistry and latex immunoassays, a magnetic particles distribution module and a luminometer for immunoassays, and a clot detection module for coagulation tests.

The throughputs, 180, 70 and 120 tests per hour for biochemistry, immunoassays and coagulation respectively, can be doubled by an additional pipetting arm. This system schedules and manages all the tasks commanded by the interface via an Ethernet connection (TCP/IP port), providing laboratories with a multi-functions versatile, innovative and cost-saving tool.

Zentech ... A new road to the future

When Techland started its activities in the early 1980s, it had chosen the specific niche of autoimmunity diagnostics. The continuous dedication to research efforts in this area has proven to be successful over time.

The company's growth was secured by merging with Radim, a larger Italian partner that brought much-needed international exposure and vital expertise in instrumentation at the time of the automation wave.

The Belgian division has always managed to maintain a degree of independence in management. Investment in research in its key domain thereby remained a priority and its novel kits were regular hits on the diagnostics market.

Along with the new millennium, a new era was ushered in for the company. First, a management buy-out separated it from the Italian partner and the now wholly Belgian company is named **Zentech**. Secondly, a strong focus on autoimmunity enables the funding of research programs in both diagnostics and therapy.

New non-isotopic assays are being developed to address the needs of biology laboratories. In collaboration with Henogen, Zentech entered a development program of immuno-absorption columns to cleanse the blood of autoimmune antibodies. This first program to treat vasculitis will open the door to other projects aimed at curing autoimmune diseases.

Funds were needed, and the DGTRE once again supported research programs. In addition, Zentech secured an increase in capital in the amount of 2.25 million through a private investment with a group of institutional investors.

OncoMethylome Sciences

OncoMethylome Sciences (OMS) was founded in 2002 as a spin-out from Tibotec-Virco, a Belgian HIV/AIDS therapeutics and diagnostics company. The Company's offices are located in the Research Triangle Park area of Durham, NC,

USA, in Wallonia, and in the Netherlands. OMS is specialized in molecular oncology diagnostics for early detection and individualized treatment of cancer.

The company's activities are based on validated methylation gene markers and the proven MSP (methylation-specific PCR) technology platform that was developed at Johns Hopkins University and is exclusively in-licensed by OMS.

Aberrant hyper-methylation of genes plays a central role in the early development of all cancers. OMS applies technology for detecting methylated genes. The detection is performed on standard lab equipment for mass-screening and is capable of detecting a few hyper-methylated cells on a background of normal cells. This characteristic makes the technology very effective for detecting cancer early, in readily available samples (such as urine and blood) and achieves excellent specificity and sensitivity in its diagnostic applications. The scientific oncology community has repeatedly expressed the advantages of the MSP technology over other technologies in leading medical journals.

Coris BioConcept

Coris BioConcept develops, produces and sells diagnostic kits based on the immunochromatographic method to detect human enteric and respiratory pathogens. Tests are based on the colloidal gold particle immunochromatographic technique and use coated nitrocellulose sticks. They are quick, simple to use, sensitive, specific, and economical. All kits have received the CE marking for *In Vitro* Diagnostics.

RESEARCH AND PRODUCTION IN BIOLOGICALS

Eurogentec

The story starts in 1985 when Prof. J. Martial and Dr. A. Renard, from the University of Liege Laboratory of Molecular Biology, founded the company. In a couple of years, **Eurogentec** (EGT) emerged as a worldwide leader in the field of oligonucleotide synthesis.

EGT, with its headquarters in the Liege Science Park, has grown into a 279-employee company with subsidiaries in France, Germany, the UK, the Netherlands, and a branch office in Switzerland.

Table 7

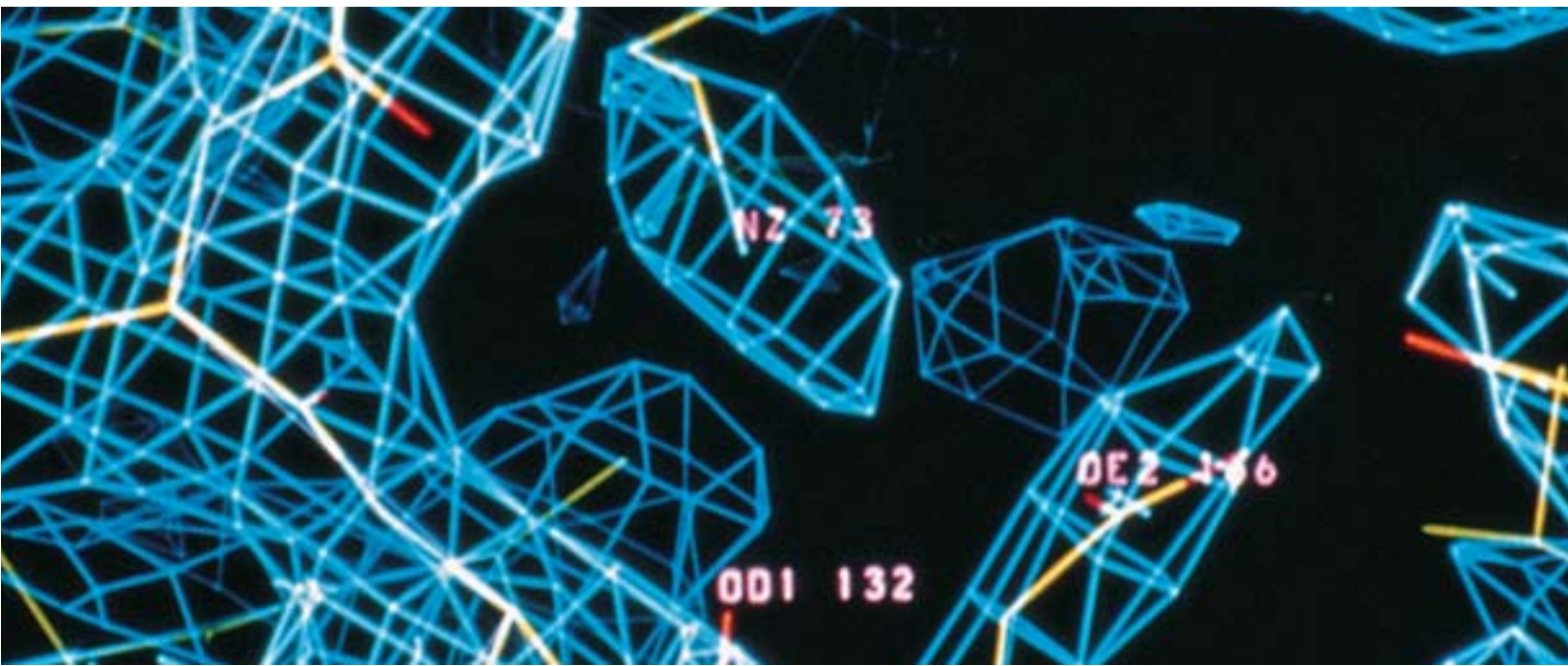
Companies in diagnostics and medical technologies

Created before 2000

Analisis	Reagents and instrumentation
Biocode Hycel	Diagnostics reagents and instrumentation
Biosource	Research and diagnostics reagents
Coris BioConcept	Diagnostics reagents
Diagam	Diagnostics reagents
D-Tek	Diagnostics reagents
Eppendorf Array Technologies	DNA-microchips
Gamma	Diagnostics reagents
Unisensor	Diagnostics for environment and food contamination
Zentech	Diagnostics reagents and special therapy

Created since 2000

Affiland	Affinity supports
Diagenode	Molecular biology diagnostics
OncoMethylome Sciences	Molecular oncology diagnostics
Probiox	DNA-microchips
Straticell	3D skin culture modeling



Under the leadership of J-P. Delwart, the company's CEO, EGT remained consistently profitable in the extremely competitive environment of genomics and proteomics suppliers. Revenues grew from € 12.3 million in 1998 to € 33.3 million in 2003/2004.

Because of this strong balance sheet and an increase of capital of € 5 million, Eurogentec can now push forward its ambitious expansion program:

- External growth will come from expansion of territory. Indeed in August 2001, the company established Nippon EGT joint venture in Japan. In May 2002, Eurogentec took another strategic step opening a North American office. The geographic expansion of Eurogentec continued in 2003 through a partnership with Research Biolabs in Singapore and the acquisition of an oligonucleotide production facility in San Diego (CA, USA) that is now part of EGT North America.

- Invest internally to expand the R&D program, the Contract Manufacturing Organisation (CMO) activity and the distribution of third-party products.

The platform activities of enabling technologies are organized around two business units:

- The "Tools for Genomics and Proteomics" department offers oligonucleotide synthesis with a large range of modifi-

cations, oligonucleotides for In Vitro Diagnostic (IVD), Real-Time PCR products, DNA MicroArray services and a wide range of kits and consumables. It also gathers know-how in the design of peptides, either for antibody production or bioactive peptide purposes. Antibody production in a wide range of animal models as well as peptide, antibody and ProteinArrays are also among its expertise.

- EGT's "Biologics" unit is a full-service Contract Manufacturing Organization (CMO) delivering research, development and production services for cGMP clinical batch manufacturing.

The company offers a complete range of services including gene cloning and synthesis, fermentation, downstream purification and full-scale GMP production of biopharmaceuticals. Projects can be taken from the earliest stage of production process design to the actual manufacturing of GMP lots of recombinant protein or plasmid DNA for human trials or for market supply.

UCB Bioproducts

UCB Bioproducts, a division of UCB Group, a pharmaceutical company, is specialized in custom peptide synthesis and peptido-mimetics for pharmaceutical use.

In the early 80's, some UCB scientists launched an initial development project on small therapeutic peptides. A few

months later the compounds were found to be of little therapeutic interest and the project was stopped. However, the amount of knowledge acquired during the process was not simply dumped; on the contrary, it became the start of a new endeavour. In 1981, with some financial support from the Wallonia Region, and with the industrial expertise and research know-how of the UCB Group, a new company was created: UCB Bioproducts.

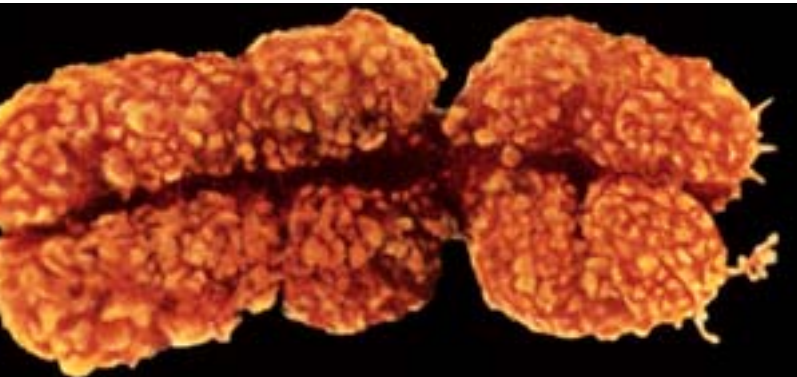


PHOTO: Chromosomes ("Gènes et Ethique" Pass © Benelux Press)

It started by improving and exploiting technology issued from the first project to produce custom peptides for industrial purposes. Building its expertise at a steady pace, UCB Bioproducts became the leader in the field of industrial peptide synthesis year after year.

UCB Bioproducts can provide a complete range of solutions to its customers through a large capacity in its GMP, FDA-approved facilities and its strong regulatory expertise for supporting peptide active pharmaceutical ingredient registration. Thanks to its internal research and its close ties to university departments, it also offers innovative products. From research to production, to preliminary clinical trials and product registration, a comprehensive set of services is available.

Those last years have seen UCB Bioproducts successfully support customers in a large number of projects in various stages of clinical development from preclinical to commercial. This contributed to commercialisation of 3 new Chemical Entities drugs.

With 2004 revenues up more than 20% since 2003 and around 300 employees in Belgium, in US and in Japan, the UCB Bioproducts division is leader in the field of industrial pharmaceutical peptides and currently majority supplier of peptide for commercial new Chemical Entities drugs.

All those achievements are supported by significant capacity and capability investment over the years with culminating point in 2005.

KitoZyme

KitoZyme is manufacturing unique good value biopolymers from truly renewable fungal resources. These biopolymers are characterized by constant high purity, specifications and quality. The product range is based on combinations of sugar units: glucosamine, N-acetyl glucosamine and glucose.

KitoZyme's products apply to global industry players, more particularly in pharmaceutical and medical devices (surgical aids, wound care, tissue engineering), nutraceuticals (cholesterol lowering, arthritis pain relief, weight loss), cosmetics and personal care (antimicrobials), wine industry (clarification, detoxification).

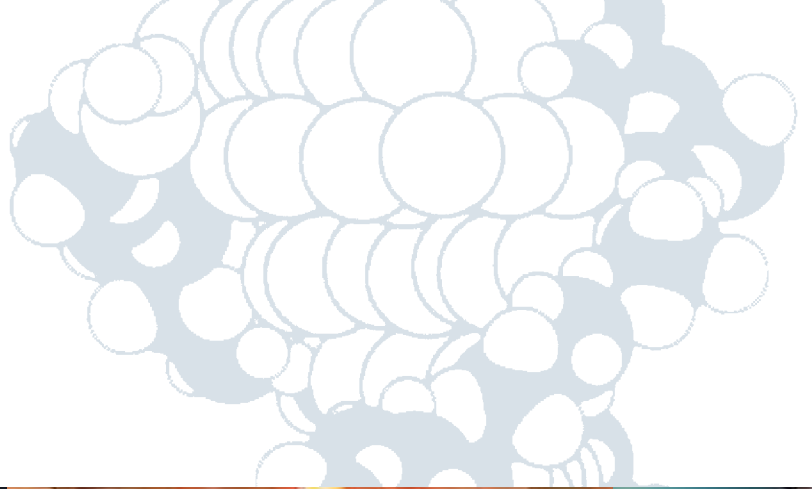


PHOTO: 1/ Somatic embryos colony (Observatoire du Monde des Plantes, Ulg)
2/ GlaxoSmithKline Biologicals
3/ Atomisor (CWBI,Ulg-FSAGx - Photo Houet)

Bio tech-²

SERVICE AND TECHNOLOGY PROVIDERS

The life science industry is growing at a steady pace. In the early days, companies had to follow various research paths and explore new technical fields. Nowadays, they have gathered enough expertise to choose their strategies more selectively and to focus on core competencies. This leaves the door open to newcomers to continue to exploit what is considered non-core to the former. Opportunities arise creating new sub-sectors:

“Drug discovery services” help discover new agents by exploiting specific technologies, namely, genomics, proteomics, pharmacogenomics, functional genomics, and so forth.

“Bioinformatics” bring new software and additional computational power to handle and analyze the considerable data generated by genomics and proteomics.

“Contract manufacturing” extends the production capacity required to manufacture the hundreds of new biopharmaceuticals arriving on the market.

Table 8

Service and technology providers

Created before 2000

Biosiris	Bioinformatics
Eurogentec	Contract research and production
Euroscreen	Ligands and new drugs interacted with membrane receptors
Floridienne	Specialty chemicals
Henogen	Contract research and production
Lambda-Plus	Bioinformatics
Quality Assistance	Contract research and production
Telemis	Bioinformatics
UCB Bioproducts	Pharmaceutical peptides

Created since 2000

Arlenda	Bioinformatics
BioPharma	Contract services
BioXpr	Bioinformatics
Delphi Genetics	Molecular cloning and DNA engineering
Dyax Europe	Phage display based drugs

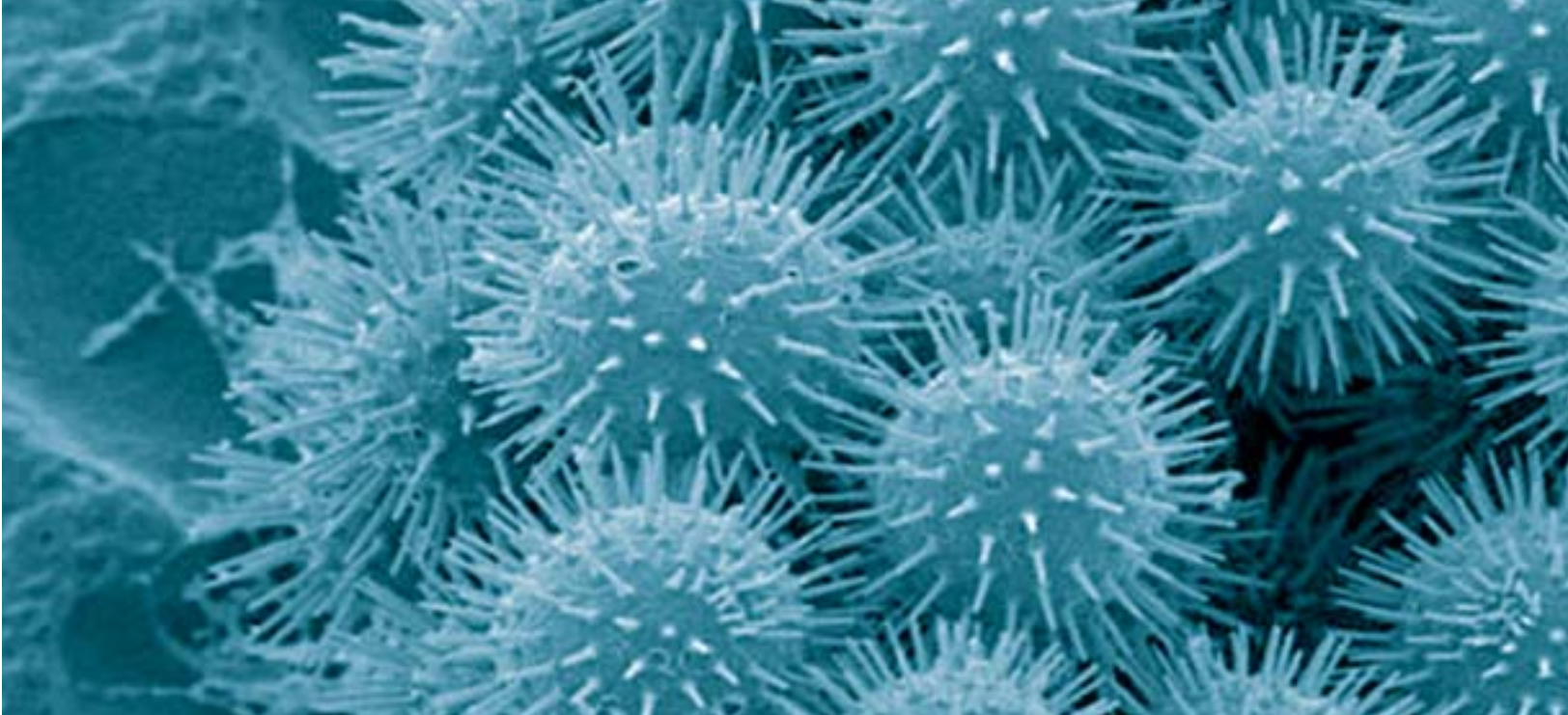


PHOTO: Cunnighamella elegans (Unité de Microbiologie, UCL)

DRUG DISCOVERY SERVICES

Delphi Genetics

Delphi Genetics, a University of Brussels spin-off founded in November 2001, develops services and products in the field of DNA engineering. Its first product line, the “Staby Express” kits, increases the yield of protein production using *E. coli*. These products are distributed by Takara-Bio in Asia and Eurogentec in Europe.

The products developed by Delphi Genetics are based on the use of unique technologies using bacterial poison-antidote genes.

Delphi Genetics has also built up a network of research collaboration with other companies for the development of new approaches in DNA engineering.

The company is also involved in a research consortium aimed at accelerating the design of laboratory animal models; this research program has received the “Eureka” label. Delphi Genetics intends to develop new vector tools allowing a better approach for the construction transgenic animals.

Dyax Europe

Dyax is a biopharmaceutical company focused on the discovery, development and commercialization of antibodies,

small proteins and peptides as therapeutic products for medical needs that have not yet been met, particularly in the areas of inflammation and oncology. The company is located in Cambridge, USA, and operates its European subsidiary in Liege, known as **Dyax Europe**.

Dyax uses a patented phage display technology to identify a broad range of small protein, peptide, and antibody compounds that can be used as therapeutics. The company currently has two recombinant proteins in phase II clinical trials. DX-88 is being studied in two indications (hereditary angioedema and cardiopulmonary bypass), while DX-890 is being studied for cystic fibrosis.

Euroscreen

Euroscreen is specialized in an area of biology known as G-protein coupled receptors (GPCRs). Different GPCRs are on the surface of each human cell and wait for specific signals (ligands) which will then activate an exact function within the cell. In fact, about 90% of all signals received by our cells are transmitted through the binding of specific ligands of GPCRs on our cell surfaces. It is perhaps not surprising then that about a third of the drugs in use or in development at pharmaceutical companies today are either GPCR ligands or block the binding of GPCR ligands.

Founded in 1994, Euroscreen applied its GPCR science to create a business selling GPCR products, services and research tools which biopharmaceutical customers purchase for their own GPCR research programs, while the

company also established a new drug development group of its own. The profits from the sales of the products and services are used to pursue its drug target programs which now allow Euroscreen to partner its drug development programs with biopharmaceutical companies. Indeed, the company's capabilities have already resulted in partnerships with Solvay for the discovery of new GPCR targets plus technology transfer and a recent drug development collaboration with Cephalon Inc. for the rapid identification of drug candidates in the fields of neuroscience and oncology.

Euroscreen and its academic partner, University of Brussels, have cloned and characterized more than 20 of the 230 currently characterized human GPCRs over the last 15 years, resulting in a substantial patent portfolio. Among such patents, Euroscreen has rights to the CCR5 receptor and antibodies, for the important use in blocking the entry of HIV virus into human cells as a new therapeutic modality in the treatment of AIDS. Several companies are using the CCR5 receptor as a target such HIV drug development and will be entering into license agreements with Euroscreen for access to this intellectual property. Other patented targets for Euroscreen's licensing efforts include ORL1/nociceptin, several purinergic receptors and SHIP2 for use in type II diabetes.

BIOINFORMATICS

With the publication of the first complete genome sequence in early 2001, genomics and proteomics are at the forefront of biotech news. The massive amount of data now available can only be exploited with the fastest computers and most sophisticated software. Computers and processors continue to grow according to Moore's law, doubling speed and performance every 18 months. Software is another matter...

Bioinformatics aim at analyzing this mass of new data and providing adequate solutions.

University labs, especially those in Liege and Gembloux, as well as in Namur and Louvain-la-Neuve, play a leading role in this field.

Biosiris develops activities in the field of simulation and molecular modeling of biological molecules. The company aims to collaborate with pharmaceutical, cosmetic, biotechnological and food companies in developing research

activities. Through its in-house technology platform and its members' expertise, Biosiris helps industrial groups discover new therapeutic molecules, understand the working mechanisms of biological systems and select innovative research trends.

Its specificities are the study of proteins, drugs and membranes with respect to their sequence-structure-activity relationships. This expertise allowed Biosiris to work with several different proteins and to suggest mutations to improve stability, generate complementary peptides, improve or prevent protein interactions, modify the insertion of a peptide/protein in a biological membrane, and so forth. In addition to these customized services, Biosiris also developed an efficient method for the prediction of antigenic properties (B epitopes).

Lambda-Plus is one of the very few European companies to provide worldwide services of expertise in cutting-edge computing skills plus a background in CRO, a vast set of Electronic Data Capture (EDC) solutions and innovative technological solutions associated with customized services to meet each and every client's specific needs. Lambda-Plus offers a wide range of solutions to computerize the data collection process usually carried out through a conventional paper approach: EDC using PC, PDA/tablet PC or a scanning technology.

Telemis is a spin-off of the University of Louvain and is active in multimedia technological solutions based on three core competencies: transmission, image and security. These "high-tech" products find specific applications in various fields including medicine and pharmacy.

BioXpr, a University of Namur spin-off, offers services and products in the field of bioinformatics, applied to R&D in the life sciences sector. The company can design advanced and progressive software to speed up R&D, create intelligent databases to enhance data, process proteomics or genomics data, and so on.

BioXpr offers fifteen years of experience in bioinformatics applied to life sciences, and in 2002, its algorithms were ranked in the world's top three for protein structure prediction algorithms.

Arlenda was created in 2003 as a spin-off of the University of Liege by an inter-disciplinary team of experts in laboratory analyses and statistics. The mission company develops, validates and commercializes an integrated suite of indus-



trial solutions dedicated to all phases of analytical procedures, from the early optimization to its routine use.

CONTRACT MANUFACTURING

Henogen: A 5 years-old mature spin-off of the University of Brussels

The creation in Gosselies of a “biotechnopole” which gathers most of the biotechnology research activities of the University of Brussels offers a fertile soil for start-up enterprises. Professor A. Bollen’s laboratory has a longstanding relationship with GSK Biologicals that lead to the creation of **Henogen**.

With the help of a venture capital fund, GSK Biologicals and the University of Brussels raised the initial capital of € 1.5 million to create the company early 2000.

Benefiting from years of expertise in preventive medicine and bioengineering, Henogen can speed up projects in human vaccine and gene therapy fields, and recombinant proteins in general.

In mid 2004, the company successfully completed a phase II clinical trial for a new vaccine against the Epstein-Barr virus, which is responsible for mononucleosis and is often present in different forms of lymphomas. In October 2002, the EEC labeled this vaccine “orphan drugs” for the prevention of post-transplantation lymphomas; the clinical development is ongoing.

Henogen has also developed a new molecule, the recombinant soluble human tissue factor for tissue and bone repair

as well as for surgical glue. The development, the production under GMP constraints and the demonstration of its safety in pre-clinical models have been successfully accomplished. Clinicals trials of this new pharmaceutical product are ongoing since mi-2004.

Henogen’s services range from the early stages in research to production of batches for clinical trials in GMP facilities, which have been validated by the General Inspection of Pharmacy in Belgium. Current partnerships with GSK Biologicals, Pasteur Institute of Paris, Stallergenes and Immuteq show the company’s broad scope of activities.

With a team of more than 80 scientists, Henogen is ready to tackle new challenges in the future, focusing on establishing its own line of biopharmaceuticals products in the transplantation area, demonstrated by the late 2004 acquisition of ImmunoToko.

Eurogentec

Out of the two Eurogentec’s business units, called Eurogentec’s “Biologics” unit, is a full-service Contract Manufacturing Organisation (CMO) delivering research, development and production services for cGMP clinical batch manufacturing (see also page 16).

Bio tech-²³

AGRI-FOOD

For centuries, biological processes have been used to transform natural raw material into food and other finished products. Famous examples include beer, cheese, yogurt, bread and wine, which all benefit from fermentation by microorganisms. These “traditional biotech” products represent an important part of the food industry. Modern biotechnology introduces genetic engineering for the development of new plant species and the improvement of existing crops. This enables the production of non-allergenic foods and cholesterol-free nutriment. New transgenic plants produce therapeutic proteins. Transformed seeds feature an increased resistance to insects or a capacity to sustain extreme climatic conditions. Modified animals show improved resistance to deadly diseases. Cattle can be genetically selected and bred to provide improved meat quality, as well as to produce pharmaceuticals in their milk.

Occupying 55 % of the Belgian territory, Wallonia is rich in farmland and forests. The people live close to nature and learn from it. This helps to boost strong research in agricultural and forest sciences.

Gembloux, Liege and Louvain-la-Neuve are renowned university centers where top research programs are conducted. Close communication with the industry enables technology to move from research labs to the market. The provincial authorities also promote biotechnology research with the “Centre d’Economie Rurale” (CER) in Marloie. This center helps the agricultural communities with veterinary services and top-class disease detection and diagnostics. Moreover, this close-to-the-field expertise enables the CER to become a provider of antibodies and biologicals for the industry.

Sugarbeet and chicory are widely cultivated in the region. Local university laboratories are renowned for their advanced research in development of plant quality and yield improvement. The industry has taken advantage of their expertise and developed genuine industrial processes for its exploitation.

Cosucra group Warcoing: From Chicory to Inuline

Cosucra Groupe Warcoing is a pioneer in exploiting industrial chicory for the production of sugar and fibres. Thanks to its own research and its tight contacts with the universities, it was able to develop an efficient extraction and transformation process for chicory inuline.

Cosucra Groupe Warcoing is also involved in the research and breeding of industrial chicory. The group develops different biotechnology methods such as culture in vivo, molecular markers, and marker assisted selection to accelerate and rationalize conventional breeding.

Galactic

Galactic develops original techniques to exploit and produce higher quality lactic acids from pure sugar with nature-friendly processes. For example, the company has developed a biodegradable polymer, the PolyLactic Acid (PLA), which is a promising, substitute to traditional thermoplastics. With thousands of possible applications in the industries of food, cosmetics and pharmaceuticals, the lactic acids potential of growth is enormous and will ensure the future success of the company. Galactic is a living proof that biotechnology can be helpful to the environment. Other natural substances are also exploited by biotechnology. Several companies play an active role in developing new substances and additives for the food industry.

As a majority shareholder, Finasucre provides strong financial support to Galactic. This helped the company to become, in a short time, world leaders in the production of lactic acid and lactates.



Beldem: Leader in food ingredients technology

Beldem (Andenne) is a leading growing company in food ingredients. It produces enzymes that are mainly used in baking and milling sectors but additional growth comes from products for animal feed. Beldem produces also on the same site baker's yeast and yeast extracts in a recently built production facility. In Saint-Vith, Beldem produces dry and liquid sourdoughs for bread quality improvement.

Biopole: Specialist in enzyme purification

Another active player in enzyme technology is **Biopole**, which develops and commercialises innovative products based on its expertise in human and animal secretory molecules. Biopole was the first company to implement the use of lactoperoxidase and lactoferrin in nutraceuticals, animal feed, oral healthcare and cosmetics products. Future development will enable Biopole to enter the industrial food enzymes production, specially the industrial enzymes purification by HPLC at industrial scale.

Belovo: Egg Science & Technology

Belovo was the first company in Belgium to benefit from regional financial support in the biotech sector. In 1980, the SRIW's support helped Belovo grow into a multinational company led by originality and high technology. Belovo has acquired a solid international reputation for its range of highly functional egg products, including egg powders, refined egg ingredients (Lysozyme, Avidin, Lecithin) and low cholesterol shell eggs (Columbus).

The company continues to invest in R&D programs in egg science and technology. Working in a GMP environment, the company is able to meet the strict requirements of the food and pharmaceutical industries throughout the world. Among major successes recorded by the company are the launches of pharmaceutical grade lysozyme, infant food grade egg yolk lecithin and Columbus egg and foods.

Progenus

Based on a technology platform of DNA and genetic information analysis, **Progenus** is a company which today proposes solutions to breeders, retail chains, meat processors and consumers in need of a reliable system to ensure animal selection, animal and species identification and meat products authenticity. By using DNA tests in animal breeders, a Gene Marker Profile program is carried out in order to select the best animals to improve milk or meat quality and quantity. Likewise, species identification of meat products or animal identification from the farm to the consumer is important for economic, religious and public health reasons. Progenus has developed specific genomic DNA probes that distinguish between DNA samples of most species such as pigs, horses, sheep, cattle or fish.

Phytesia

Phytesia, a University of Liege spin-off, specializes in the production of high added value plants. The company develops and markets new micropropagation products for horticulture, floriculture, agriculture, forestry, conservation and industrial applications.

Phytesia has perfected techniques for germination and in vitro cultivation, acclimatization and large-scale production of hardy orchids from Europe, North America and other temperate countries.

DNAVision

The research and development company **DNAVision** provides expertise in molecular biology, especially in the field of genetic analysis. With state-of-the-art instrumentation and methods validated in a quality environment, the company provides analytical services designed for the health and agro-alimentary industries.

DNAVision, founded in May 2004, already provides various application notes emerging from scientific expertise acquired mainly in the laboratories of the University of Brussels in the field of characterisation of genetic polymorphic markers.

PHOTO: 1/ CRA-Gembloux (photo Marc Deckers) -

2/ In vitro callus proliferation (Observatoire du Monde des Plantes, Ulg)



Table 9

Companies in Agriculture and Food**Created before 2000**

Artechno	Microbacteria and culture media
Avecon	Environmental additives
Beldem	Food additives and enzymes
Belovo	Egg and egg derivates
Biochem Europe	Enzyme purification and refining services
Biopole	Enzymes
Bioplant in Vitro	Plant breeding
Cosucra Groupe Warcoing	Plant engineering
Enzybel	Enzymes
Enzyme & Derivates	Enzymes
Galactic	Lactic acid and derivates
Horpi Systems	Biological control products
THT	Lactic bacteria and derivates
UCB Bioproducts	Diagnostics products for food contamination

Created since 2000

DNAVision	Food analysis
KitoZyme	Biopharmaceuticals chitosanes derived ingredients
Phytisia	Plant breeding
Progenus	Animal selection
Quality Partner	Food analysis and cosmetics
Viridaxis	Biological control products



Bio tech-²⁴

ENVIRONMENT

Our planet deserves to be protected from pollution or perhaps even restored to its “natural” condition wherever possible. Biotechnology can help reach this ambitious and noble goal.

Indeed, “Environmental Biotechnology” can be defined as the use of microorganisms, in particular bacteria and fungi, to restore and eventually improve the quality of the environment.

Bioremediation, for example, uses microorganisms to restore soil to its previous state or to cleanse water of different types of pollutants. This is more than wishful thinking as the worldwide market for bioremediation of organics and metal contamination of groundwater has been estimated to reach 1 billion per year.

Each university in Wallonia would like to play its role in helping to improve well-being and keep the region “clean”. Therefore specific research departments conduct “Earth-friendly” research programs. Dedicated support from the DGTRE, through its focused funding programs, has helped universities and companies to pool their interests and to bring out innovative services. Moreover universities and companies can use the services of the Library of Mycology of the University of Louvain, the fourth world collection of fungi with 26,000 species. This led to the development and use of bioremediation to recycle specific pollutants.

Realco

Founded in 1968, **Realco** is now based in Louvain-la-Neuve. By using enzymes and bacteria, Realco uses biotechnology for cleaning and water purification. Their R&D efforts represent more than 10% of their turnover and the company conducts several ambitious research pro-

grams with universities of Louvain, Brussels and Liege. This has led to a patent that demonstrates the importance of using enzymes as early as possible in the purification of waste water.

Biorem

Biorem is a company engaged in the in-situ treatment of soils and aquifers contaminated by various range of hydrocarbons. The concept of Biorem is consisting on the gathering of all the different functions involved in the sanitation treatment in one unique unit, added to a proper bioremediation technology.

The different steps of a biological treatment are rationalized, preventing all kind of incompatibility problems of the equipment, and bringing an efficient solution to the inhibiting factors in a bioremediation process. The treatment units are able to inoculate homogeneously in the soil and the subsoil microorganisms that have been purposely designed for the type of pollutant. A remote monitoring process can avoid many human interventions on the treatment location, and allows continuous supervision of the work.

Agrostar

For the past twenty years, **Agrostar** has been producing microorganisms for environmental use, known as biological starters. In this way, Agrostar offers its customers and industrial partners a truly integrated service from applied research to the set up of practical methods of use from the development of specific breakdowns to the industrial production in fermentor vessels,... Therefore Agrostar can

provide the scientific and technical support which all those who distribute or prescribe biological starters are entitled to expect.

Wetlands Engineering

Wetlands Engineering, a fast growing innovative start-up, develops the production of fungal biomass and enzymes (laccases) for bioremediation of aromatic compounds (dyes, colored wastewater,...). Complementarily, the company produces hardware and software systems for bio-processes: innovative sensors for biotech, equipped fermentor, wastewater treatment unit, research compost pilot device, and industrial aerated composting technology. Wetlands Engineering is the SME leader of an integrated project of the European sixth framework project dealing with the introduction of industrial biotechnologies in the dye and dying industry (www.sophied.net). This huge project coordinates the R&D efforts of 26 partners in 10 countries with a total budget up to € 10 million.

The companies offering their expertise in this field are presented in the table 10.



Table 10

Companies active in the environment biotech field

Created before 2000

Agrostar	Biological starter enzymes
Biorem	Bioremediation
EcoTerres	Waste management
Realco	Waste management solutions

Created since 2000

Wetlands Engineering	Waste treatment
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Photo: 1/ Laboratoire de Biochimie et Biologie Cellulaire, FUNDP
2/ Lyophilisator (CWBI, Ulg-FSAGx - Photo Houet)
3/ Rhodotron TT200 (Ion Beam Applications)
4/ Auxine induced tomato root (Observatoire du Monde des Plantes, Ulg)



Bio tech-

**WALLONIA:
A REGION FOR GROWTH
AND SUCCESS**

3



Bio tech-³¹

EXCELLENCE IN RESEARCH: THE BIOTECHNOPOLES

If financial analysts were to rate Wallonia on the basis of Fundamentals and Technical Analysis (TA), they would certainly refer to the region as a “Strong Buy”!

Fundamentals imply “Excellence” found in people and infrastructure, whereas TA looks for strong support and “Excellence in Incentives”.

Aware of the importance of knowledge-based innovation, the Wallonia Region has always promoted high quality education. Indeed, it actually finances and hosts nine university centers and scores of research institutes that produce hundreds of science graduates.

The breakdown of students registered in major Universities in 2003, in life and medical sciences, is given in Table 11.

This high concentration of “brains” constitutes a reservoir of talented and well-educated scientists. Biotechnology is among the fastest growing fields and expertise ranges from plant engineering to the latest genomics and proteomics technologies.

A strong will of academics to increase the value of research led to nurturing “excellence” in relations with the industry.

This further stimulates the companies that are the region’s driving force: GSK Biologicals, UCB Bioproducts, Eurogentec, Baxter Healthcare, Eli Lilly, Cosucra, Beldem, Belovo and many others are paving the way to success.

Tableau 11

Students registered in Universities in 2003 (*)

	UCL	ULg ¹	ULB	FUNDP	FUSAGx	UMH	Others ²	Total
Science³	3,605	3,132	3,457	1,158	999	547	1,057	13,955
Medical sciences⁴	4,801	4,450	3,565	967	-	223	-	14,006
Total	8,406	7,582	7,022	2,125	999	770	1,057	27,961

(*) abbreviations are explained in the table at the end of the brochure

¹ Including FUL (Fondation Universitaire Luxembourgeoise)

² Others include FPMs, FUSL and FUCaM

³ Applied sciences, agricultural sciences and plant engineering

⁴ Medicine, dental & veterinary sciences, pharmacy and physical training sciences

Source: Cref2004

Tableau 12

Science and Technology Parks containing most of the biotech companies in Wallonia

Location	Name
Science Parks	
Gembloux/Namur	Crealy Science Park
Gosselies/Charleroi	Aéropole
Liège	Liège Science Park
Louvain-La-Neuve/ Ottignies-LLN	Louvain-La-Neuve Science Park
Mons	Initialis Science Park
Technology Parks	
Seneffe	Seneffe Technology Park
Ghislenghien	Business Park Qualitis

Located in the centre of Western Europe, Wallonia is ideally positioned to address neighbouring markets as well as the rest of the world. The creation and extension of science and business parks from Mons to Liege form a long “Valley” stretching from the west to the east of Wallonia.

The high concentration of universities and large healthcare companies has contributed to the creation of centers of excellence in biotechnology: the “biotechnopoles”.

The Pole of Liege

The **University of Liege** (ULg) has a long and strong tradition regarding both collaborations with industries. Understanding that innovation can come from all directions, the ULg has implemented a policy of “crossborder” cooperation between different faculties and departments.

The first example is **GIGA** (“Groupe Interdisciplinaire de Génoprotéomique Appliquée”).

Located within a building of the University Hospital, GIGA is a unique structure composed of 4 axes:

- The Centre of Biomedical Integrative Genoproteomics (CBIG): a multidisciplinary research center counting 280 scientists of the ULg focusing on genoproteomic approaches of cancer and inflammation;
- Core facilities in bioinformatics, genomics, proteomics, transcriptomics, transgenics (mouse and zebrafish), and protein production;
- Laboratories and offices for biomedical businesses;
- A training center in biotechnology dedicated to continuing education for career development.

Through its wide range of skilled expertise and know-how in the expanding field of functional genoproteomics, GIGA acts as a hinge between university research and biomedical companies.

GIGA is financially supported by local, Wallonia and European authorities, with a total budget for the 2003-2006 period that amounts to € 56 million. Furthermore, in the continuity of the GIGA project, 2005 has been the year of the launch of the INTERREG III ALMA-GRID project. Its main objective is to build a virtual laboratory environment allowing multiple academic core facilities to co-operate. They will provide a world leading service to companies and academic research by using the synergies of competencies. This project is combining the scientific leading edge

competencies of the four participating Genome Centers: GIGA (University of Liege), Molecular Biotechnology Institute (RWTH Aachen), Genome Centre Maastricht (University of Maastricht), CenStat Centre (LUC Diepenbeek).

The **University of Liege** (ULg) has merged theory, learning, knowledge and business in various research centers, among which the **CART** (Centre for Analysis of Residues in Traces), the **CEIB** (Interfaculty Centre of Biomaterials), the **CRPP** (Centre de Recherche sur les Protéines Prion), the **CIP** (Centre for Protein Engineering University) and the **CRGB** (Research Center for the Management of Bio-Industries).

The **BioLiege** association, playing a central networking role in Walloon biotechnology and numerous spin-offs offer an extremely supportive environment around the ULg. Besides, the University of Liege has also put a strong emphasis on the water management through the **Aquapole** created in November 2003.

The Pole of Gosselies (Charleroi)

From basic research to economic value, the Aeropole Charleroi brings it together at its biotechnology pole or “Biopole ULB Charleroi”. A unique structure in Wallonia, it has been supported by academic, Wallonia and European financial commitments and is driven by a common vision.

The **University of Brussels** (ULB) has concentrated in the biopole the best of its life science research activity: **Institute of Molecular Biology and Medicine** (IBMM) and **Institute of Medical Immunology** (IMI).

Established at Charleroi since 1999, the IBMM is mainly dedicated to teaching and academic research. This institute enjoys a high degree of international fame, and operates in many fields of biotechnology. Born of an innovative partnership between the University of Brussels and GSK Biologicals, with the support of Wallonia Region, the IMI is active in several fields: development of new immunotherapy strategies for transplant rejection, autoimmune diseases and allergies, definition of new vaccine strategies applicable to the neonate, the development of new tests evaluating vaccine efficiency and security. Indeed, a number of spin-off companies have already been

established in the Biopole, among which **Henogen, Euroscreen, Delphi Genetics, Aliwen, DNAVision** or **H-Phar**.

The non-profit organization **BioVallee** facilitates the transformation of research results into innovating products and services that can be then marketed to or by the nearby start-ups. BioVallee was founded in 2001 at the initiative of the University of Brussels (ULB), the University of Mons (UMH) and Igretec. It specializes in genetic construction and analysis, two rapidly expanding fields that involve many sectors of activity: health, agri-food, agriculture, environment, etc. The center also provides scientific, logistic, financial and administrative services to start-up companies in the sector.

Closely linked cutting-edge technologies and diverse fields of application caused BioVallee to develop partnerships and alliances. Strong links have been established with the University of Liege but also in France (Lille and Grenoble) and will further continue with the United Kingdom, Germany and the Netherlands. The center works closely with its neighboring incubator company, Wallonia Biotech, to identify the needs of companies in the region and to offer its services, either to develop new products or to improve their production processes.

The Pole Gembloux – Namur

The **University of Namur** (FUNDP) comprises more than 4,000 students and enables close connections between various departments, especially the faculties of medicine and science and the computer sciences institute. This led one of the laboratories to embark in PCR and DNA research early. Professor Remacle created AAT in 1999 (now **EAT**) to tackle the need for advanced and affordable microarrays.

BioXpr, founded in 2003, provides expert services in the field of bioinformatics. More recently, in 2005, another biotech company, **Straticell** was created, performing three-dimension skin culture modeling for in vitro toxicology and toxicogenomics

The **University of Gembloux** (FUSAGx) is mostly dedicated to agricultural food and forestry sciences. Its world reputation attracts more than 250 students from abroad. With 1,000 students, it is one of the largest centers of excellence

in this field in Europe. The FUSAGx is collaborating with the ULg in the “**Centre Wallon des Bio-Industries**” (CWBI), which exploits microbiological diversity to develop genuine industrial processes. As a result, several companies were created, namely, **Agrostar, THT, Artechno, Avecon** (with the University of Ghent-RUG), **Biotreatment** and **Microbelcaps**.

More recently, several spin-off companies were developed. These companies are **Biosiris** which offers bioinformatics tools to predict the tridimensional structure of different proteins, amino acids or potential therapeutic agents, **Progenus** which developed a gene-based diagnostic tool to evaluate the milk production ability of cattle, and **Bionext** which developed biopesticides (strain of yeast) that are efficient against post-harvest diseases on apples and pears.

Midway between Namur and Gembloux, the FUNDP and the FUSAGX contributed to the creation of the **Crealy Science Park**.

Crealy covers an area of one square kilometer with 67 % of the park already occupied by high-tech companies; among them, biotechnology is represented by **Aseptic Technologies, Coris BioConcept, Biopole, THT, Artechno** and **Lambda-Plus**.

The Pole of Louvain-la Neuve

Many research projects in biotechnology are carried out at the **University of Louvain** (UCL), both in Louvain-la-Neuve and on its biomedical campus in Brussels.

In Louvain-la-Neuve, the **Institut des Sciences de la Vie** (ISV) brings together 24 research groups from different faculties and departments. All these groups, involved in basic and applied projects, are using molecular and cell biology approaches to investigate the functioning of the living world, from the molecule to the whole organism.

The **Christian de Duve Institute of Cellular Pathology** (ICP) pursues investigations in a great variety of fields. This diversity generates particularly fruitful exchanges that are made possible, beyond the differences among subjects, by the common concepts and methods characteristic of modern biology.

ICP also houses the Belgian branch of the Ludwig Institute for Cancer Research, active in the field of cancer immunology and cancer genetics.

The **University of Louvain** (UCL) has always maintained and continues to develop a strong relationship with the industry as demonstrated by the success of their 2.25 km² Louvain-la-Neuve Science Park.

More than 120 high-tech companies employ 4,300 people in R&D and production. The field of life sciences is represented by such well-known names as **Ion Beam Application** (IBA), **Abbott**, **Ajinomoto**, **Eli Lilly**, **Pfizer Animal Health**, **Sankyo Pharma** and **Wyeth**. Additional smaller start-ups have joined the park including **Wetlands Engineering**, **Enzymes & Derivates**, **Creative Research Solutions** and **Realco**. Recently, **Bayer CropScience** selected Louvain-La-Neuve Science Park for its R&D and testing team.

IBA: a growing leader

In 1986, **Ion Beam Application** (IBA) began as a spin-off of the UCL Cyclotron Research Centre and has grown to become world leader in cyclotrons and proton therapy. In 2003, its annual turnover was € 257.7 million. More than 1500 employees work in 49 locations in 12 countries around the world.

IBA has been listed on the EuroNext stock exchange since 1998 and is a component of the Bel-20 index. It still works in close cooperation with the UCL and also acts as a key supplier of cyclotrons to **International Brachytherapy** (IBt), a world leader in radioactive implants for the treatment of cancers (prostate). IBt was founded by four US scientists who chose Wallonia as the base for their company because of the excellence in technology of the UCL, the presence of IBA and the strong support of the Wallonia Region government in terms of research funding. IBt is based in the Technology Park of Seneffe, a few kilometres from the UCL.

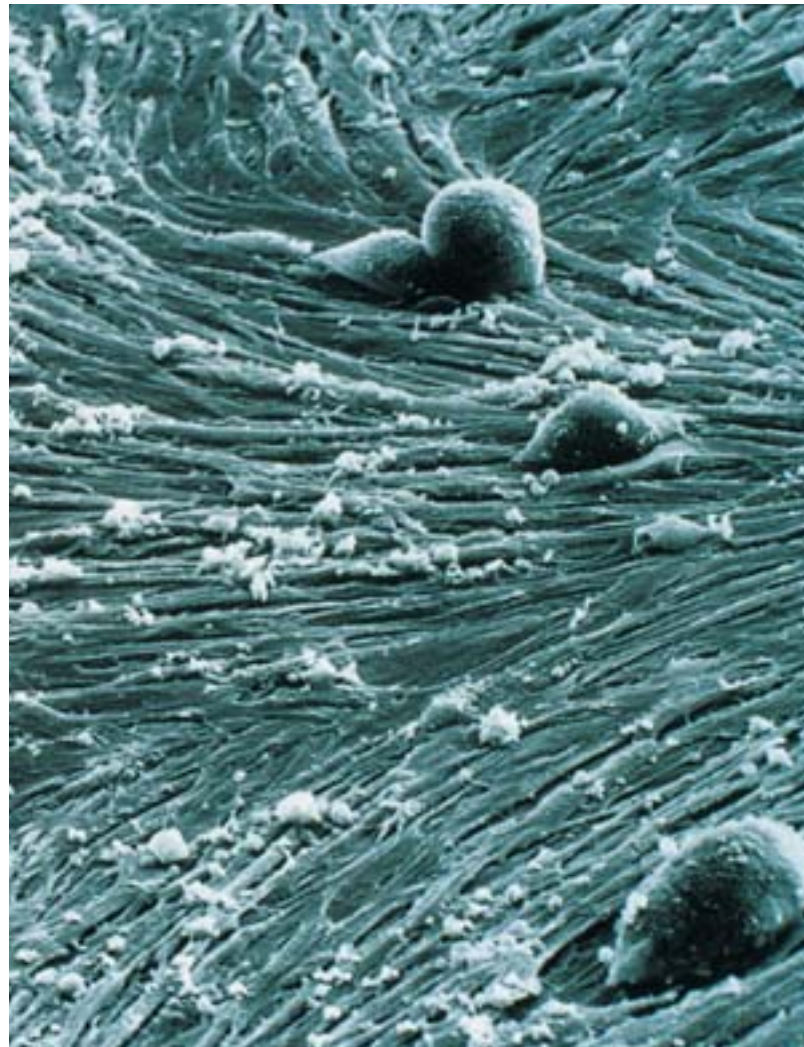


PHOTO: Langerhans islets in vitro (Laboratoire de Biologie cellulaire, UCL)

Bio tech-

3²

EXCELLENCE IN
INCENTIVES

“Science and knowledge are like a beautiful engine, but money is like the fuel to get it running!”

Wallonia features a biotechnology sector in which the quality of the scientists and the financial incentives are very attractive.

Innovation comes through renewed commitment and actions in research.

The universities often generate cutting-edge ideas, which find fertile ground in the new start-up companies.

So when the Wallonia Region government put biotechnology on the top of its priority list, it was not just on paper, it also meant that real funds were made available to start companies, to finance innovative research and to develop promotional tactics and strong international partnerships.

Thus *the money is there, and even more - the people to help you in your project evaluation, in your international expansion and in your search for global partners.* Wallonia entrepreneurs have always looked beyond the country's frontiers to export their innovative products and advanced technology.

This export-oriented culture and a central location in Europe are clear advantages for any company based in the region.

The two Wallonia government agencies in conjunction with a strong financial arm (the **SRIW**) work in synergy to actively increase the odds of success of any new venture: the **Directorate General of Technology, Research and**

Energy (DGTRE) and the Wallonia Export and Foreign Investment Agency (AWEX).

Evaluating and funding scientific projects is the task of the **DGTRE**. Companies can ask the DGTRE to share the risk of investing in innovative research and development. The experienced staff at the DGTRE has designed a comprehensive series of financial incentives and subsidies to meet the needs of companies from start-ups to established enterprises. This is a real engine of growth for the sector in Wallonia and a strong stimulant for companies to exploit research results.

The first set of incentives is managed by a team dedicated to exploiting results from research programs within universities and enterprises. The most popular is the “recoverable advance”, an interest-free loan that covers up to 70% of

Tableau 13

Wallonia Region support in biotech applied research (in € million)

Year	Enterprises	Universities	Total
2000	11.8	11.5	23.3
2001	7.7	17.6	25.3
2002	7.2	30.1	37.3
2003	9.4	14.3	23.7
2004	14.2	19.4	33.6

applied or development research expenditure of the enterprises. It is reimbursable as an annual fee representing a percentage of product sales. Other possibilities include grants for feasibility studies and technology transfer.

Another department in the DGTRE is more focused on academic applied research. Their series of subsidies usually covers research expenses including 100% of the salary of researchers in universities or young start-ups. It aims at increasing the scientific potential within the laboratories and capitalises on it by transferring it into industry.

The **DGTRE** team closely monitors the rapid advances and common changes in biotechnology. Consequently, it regularly tailors funding “programmes” that meet the needs of the pioneers in special domains. This enables early entry into the latest technology fields.

“Waleo” is the latest campaign that covers the recent advances in technologies that directly benefit human medicine. The total 2002 Waleo budget was € 17.4 million and a budget of € 20 million is planned for the 2005 campaign.

The total amount spent by the Wallonia Region to sponsor research and development in biotechnology has been consistently rising over the past years as shown in the table 13.

Through the **AWEX**, regional authorities offer strong support for international expansion of Walloon-based companies. The AWEX provides a wide range of financial incentives designed to promote exports and international joint ventures. As a foreign investment agency, AWEX has the general responsibility of attracting foreign investment to Wallonia. This includes seeking out and providing information to potential foreign investors. The Agency also offers a pro-active follow-up service to investors already established in Wallonia. In addition, it is in charge of identifying new foreign investors for the acquisition of industrial sites under a restructuring process.

Created in 1979, **SRIW** and its subsidiaries together form the **SRIW Group**, the mission of which is to provide long-term financing to companies in Belgium and abroad, with the objective of promoting either directly or indirectly the economic development of the Walloon Region.

They participate in projects for redeployment, modernization or growth of the companies concerned.

The financial resources which the SRIW group brings to its partners are attributable to activities which are principally directed towards the long term.

The flexibility of the SRIW enables it to adapt to individual cases. Each project is specifically studied and the most appropriate solution is applied; the solutions include direct equity participations, convertible or non-convertible loans, subordinated or senior loan, warrants, and so forth. This contrasts with the conventional, short-term financing covered by traditional bankers.

Tableau 14

The local public investment companies

Province	Investment company
Hainaut Western part	HocclInvest
Hainaut Southern part	SambreInvest
Hainaut Central & Eastern part	Invest Borinage Centre
Luxembourg	InvestSud
Liège	MeusInvest
Namur	NamurInvest
Brabant Wallon	NivellInvest
Liège German Community	OstBelgienInvest

To fulfill its missions more efficiently, the SRIW created a series of “Specific Development Centers” in charge of specific sectors, such as Technowal and CD Technicom for New Technologies and Ecotech Finance for environment.

Since 2000, SRIW, Technowal and its subsidiaries have invested in 23 companies from the Life Sciences Sector, among which: **Aseptic Technologies, Biocode Hycel, Biopole, BioXpr, BioXtract, Cardio3, Eurogentec, Henogen, Horpi Systems, H-Phar, KitoZyme, Oncomethylome Sciences, Probiox, Quality Assistance** and **Zentech**, for a total investment of nearly € 50 million.

Besides its traditional core activities, the SRIW:

- has participated in the creation of several VC funds, i.e. **Start-It**, dedicated to investment in start-up companies in the biotech and high tech sectors, **E-Capital** targeted at fast-growing companies and some university funds.
- has expanded outside the country’s boundaries through the creation of **Cossom**, a subsidiary handling foreign inter-

national investments.

- works actively in cooperation with the eight local provincial investment companies providing early stage financing and with university funds for seed capital.

- networks regularly with venture capital and private equity funds to grant substantial financing rounds and to secure sequential investments for rapidly growing companies.

With the DGTRE in charge of research and scientific aspects and the SRIW managing investments, the Wallonia Region offers an efficient combination of support and stimulus to the biotechnology community.

To obtain its required funding, the biotechnology sector in Wallonia can also count on an active and rapidly growing pool of private venture capitalists and private equity funds and on strong university support.

Venture capital funding is available from private funds that help start-up companies to raise seed, early stage or follow-up capital. Specialized venture capital funds such as **Mara Ventures** or private equity funds from large institutional investors (**ING Private Equity, Fortis Private Equity, KBC Investco, Dexia Ventures...**) support Wallonia biotechnology companies through equity or mezzanine financing. In addition, these investors participate in mixed funds together with universities and local and regional investment companies.

The universities themselves, in addition to providing high quality education that fulfills their "social" role in society and nourishes the employment market with trained scientists, actively participate in the economy as they now create additional wealth through spin-off companies. To get the best return on such investments, most of them have set up their own venture capital fund.

The University of Louvain set up **Sopartec**, a seed capital and technology transfer company and virtual incubator. It played a key role in the development of the listed companies **Ion Beam Applications** (IBA) and **International BrachyTherapy** (IBt). It also manages the **Vives** fund, created with public and institutional investors to provide early stage financing for high technology companies.

The University of Liege, in cooperation with the local investment company, **MeusInvest**, created **Spinventure** to finance stages preceding the establishment of new start-ups, such as feasibility and market studies, as well as stud-

ies on industrialization and commercialization. In its second stage, it also offers seed capital.

In recent years, the University of Brussels has created the **Theodorus** fund to provide seed financing to the spin-offs issued from academic research of the institution. Similarly, the University of Mons and the Polytechnic Faculty of Mons have jointly created the **IMBC-Spinnova** fund, and the University of Gembloux has created **Gembloux Valorisation** for the same purposes.

As universities keep on considering the importance of capitalizing on research conducted within their labs, the currently remarkable rate of creation of spin-offs is expected to be sustained the coming years.

Bio tech — TIME TO HARVEST

With excellence in human resources and research, and financial incentives and grants, Wallonia has entered the third millennium with a decisive commitment to support a knowledge-based economy.

Biotechnology strongly remains at the top of the region's priority list. The sector continues to boom and opportunities arise to exploit the fantastic results from the research laboratories based in the universities. Entrepreneurs have found regional authorities and local industry to be extremely helpful in setting up a base to start their activity. Consequently many companies have found a fertile environment for rapid expansion and ambitious new development programs.

Wallonia has proven its ability to exploit the best opportunities and fruits arising from its innovative research. Indeed, the staggering progression of the number of enterprises active in the biotechnology sector, from 55 in 2001 to 69 in 2003, helps the region place itself in the top ranks in Europe.

Wallonia can create wealth. This strategy of stimulating the sector increases the region's wealth as shown by a "gross regional product" issued from the biotechnology activity that grew from 1,994 million to 2,376 million in a two year period.

Wallonia can create employment. Hard hit in the early 1970s, the region can reconstruct itself and thanks to its intelligent investment in education, it brings highly educated and specialized youngsters to the workplace, giving them hope for the future and *real employment* opportunities. Today, the biotech sector employs close to 5,000 scientists and technicians, up from 3,000 five years ago (large and entrepreneurial companies together).

Recent years have shown the great potential and richness in the region.

Wallonia has become a master of creation, innovation and knowledge.

The region is proving its ability to turn promises into successes.

We invite you to participate in this process of value creation.

We welcome you to join us and generate welfare together.

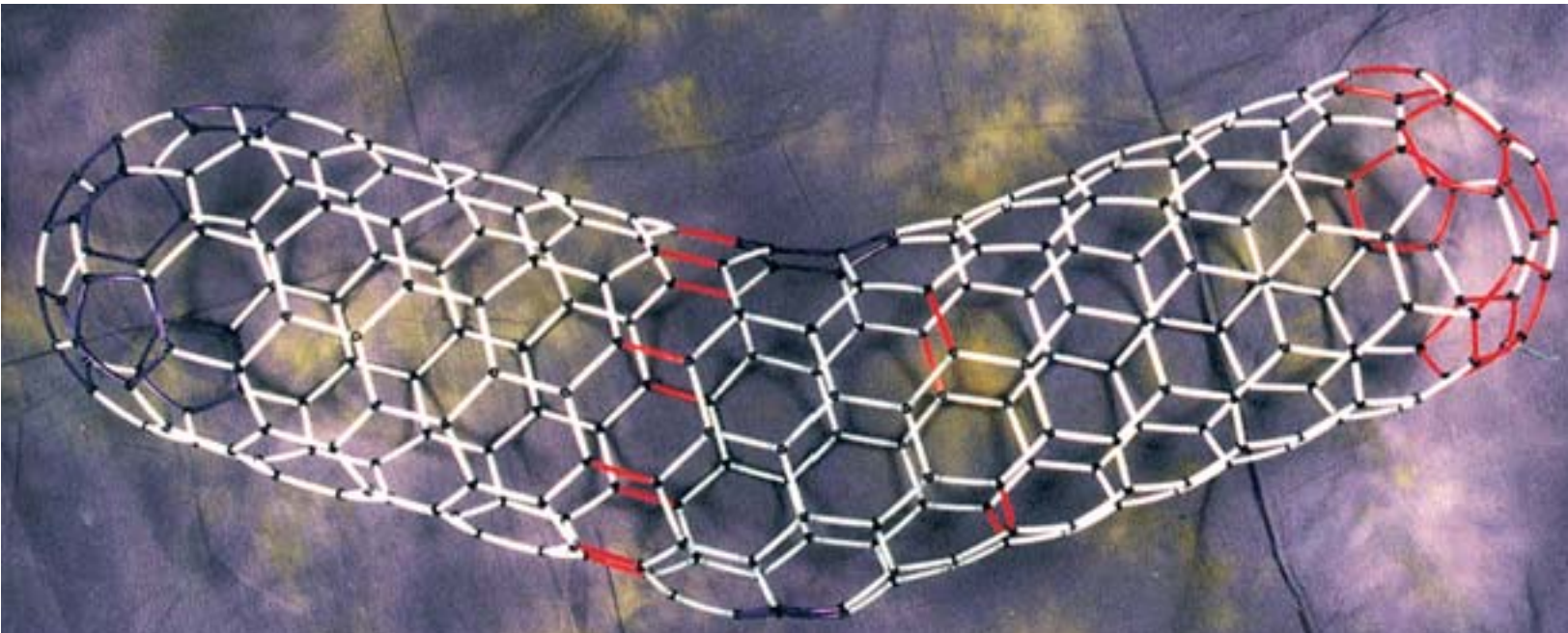


PHOTO: Carbon nanotube modeling (FUNDP - RMN - LISE)

Bio tech-

USEFUL INFORMATION

Abbreviations

Terms

AIDS Acquired Immune-Deficiency Syndrome

cGMP Current Good Manufacturing Practice

CMO Contract Manufacturing Organization

CRO Contract Research Organization

DNA DeoxyriboNucleic Acid

EDC Electronic Data Capture

ENT Ear, Nose and Throat

FDG Fluorodeoxyglucose

FP6 Sixth Framework Program

GMP Good Manufacturing Practice

GPCR G-Protein Coupled Receptors

HBV Hepatitis B Virus

HIV Human Immune-Deficiency Virus

HPV Human Papilloma Virus

IVD In Vitro Diagnostic

HPLC High Performance Liquid Chromatography

MSP Methylation Specific PCR

PCB's Polychlorinated Biphenyls

PCR Polymerase Chain Reaction

PDA Personal Digital Assistant

PET Positron Emission Tomography

PLA Polylactic Acid

QC Quality Control

R&D Research and Development

RSV	Respiratory Syncytial Virus
TA	Technical Analysis
TCP/IP	Transmission Control Protocol/Internet Protocol
VC	Venture Capitalist

Companies and institutions

AAT	Advanced Array Technologies
AWEX	Wallonia Export and Foreign Investment Agency
CER	Centre d'Economie rurale
CART	Centre d'analyse des résidus en traces
CBIG	Centre of Biomedical Integrative Genoproteomics
CEIB	Centre Interfacultaire des Biomatériaux
CIP	Centre for Protein Engineering
CRGB	Research Center for the Management of Bio-industries
CRIV	Centre de Recherche Interuniversitaire en Vaccinologie
CRPP	Centre de Recherche sur les Protéines Prion
CWBI	Centre Wallon des Bio-Industries
DGTRE	General Directorate for Technology, Research and Energy
EAT	Eppendorf Array Technology
EGT	Eurogentec
FDA	US Food and Drug Administration
GIGA	Groupement Interdisciplinaire de Génoprotéomique Appliquée
GSK Biologicals	GlaxoSmithKline Biologicals
IBA	Ion Beam Application
IBt	International BrachyTherapy
IBMM	Institute of Biology and Molecular Medicine
ICP	Institute of Cellular Pathology
IMI	Institute of Medical Immunology
ISV	Institut des Sciences de la Vie
LUC	Limburgs Universitair Centrum
OMS	OncoMethylome Sciences
PAHO	Pan American Health Organization
RIT	Recherche Industrie Thérapeutique
RUG	Universiteit Gent
RWTH-Aachen	Rheinisch-Westfälischen Technische Hochschule Aachen
SRIW	Société Régionale d'Investissement de Wallonie
THT	Techno-High-Technology
UNICEF	United Nations Children's Fund
WHO	World Health Organization

Universities in Wallonia

FPMs	Faculté Polytechnique de Mons
FUSL	Facultés Universitaires Saint-Louis
FUCaM	Facultés Universitaires Catholiques de Mons
FUSAGx	Facultés Universitaires des Sciences Agronomiques de Gembloux - University of Gembloux
FUNDP	Facultés Universitaires Notre-Dame de la Paix – University of Namur
UCL	Université Catholique de Louvain – University of Louvain
ULg	Université de Liège – University of Liège
ULB	Université Libre de Bruxelles – University of Brussels
UMH	Université de Mons-Hainaut – University of Mons

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