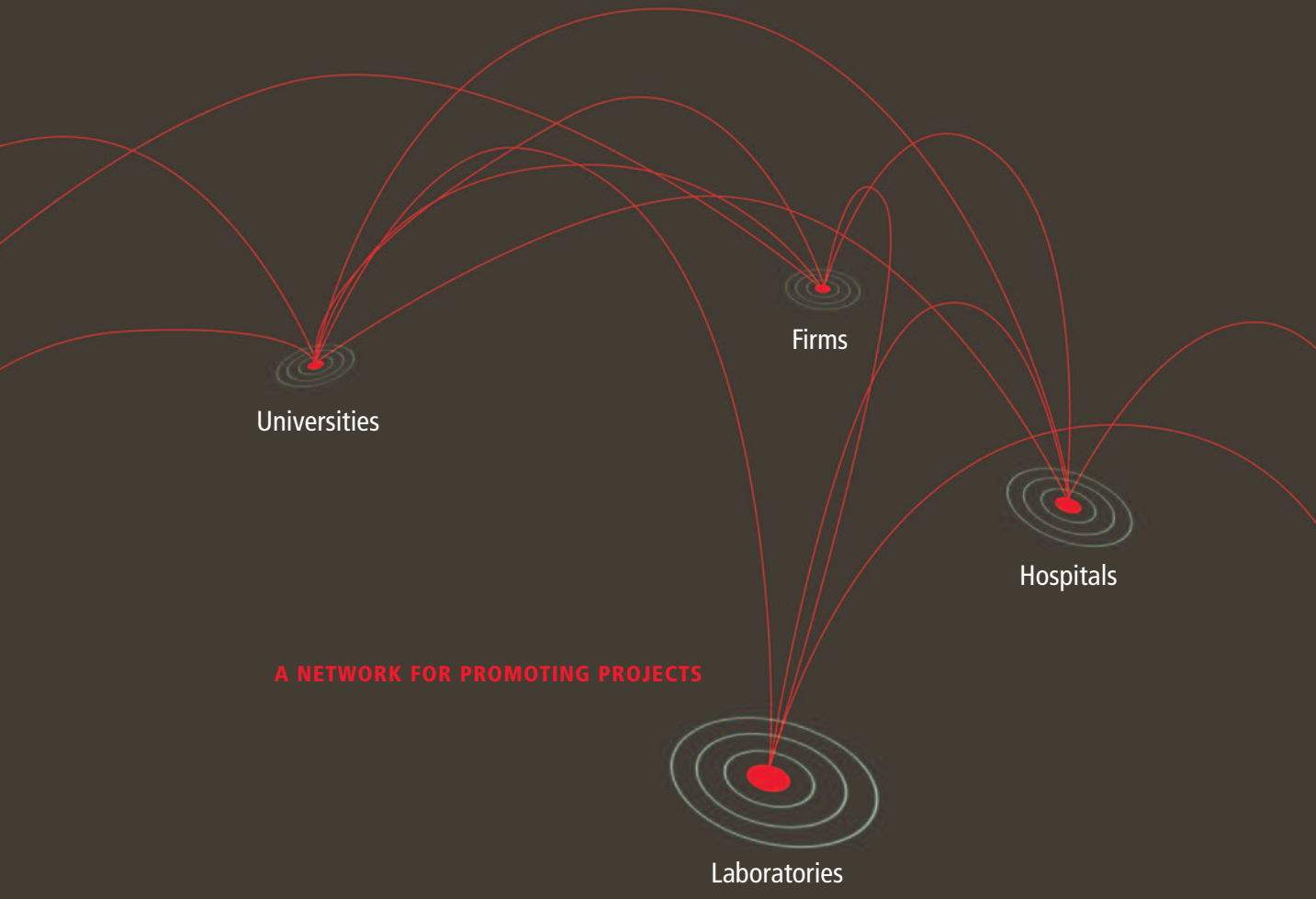
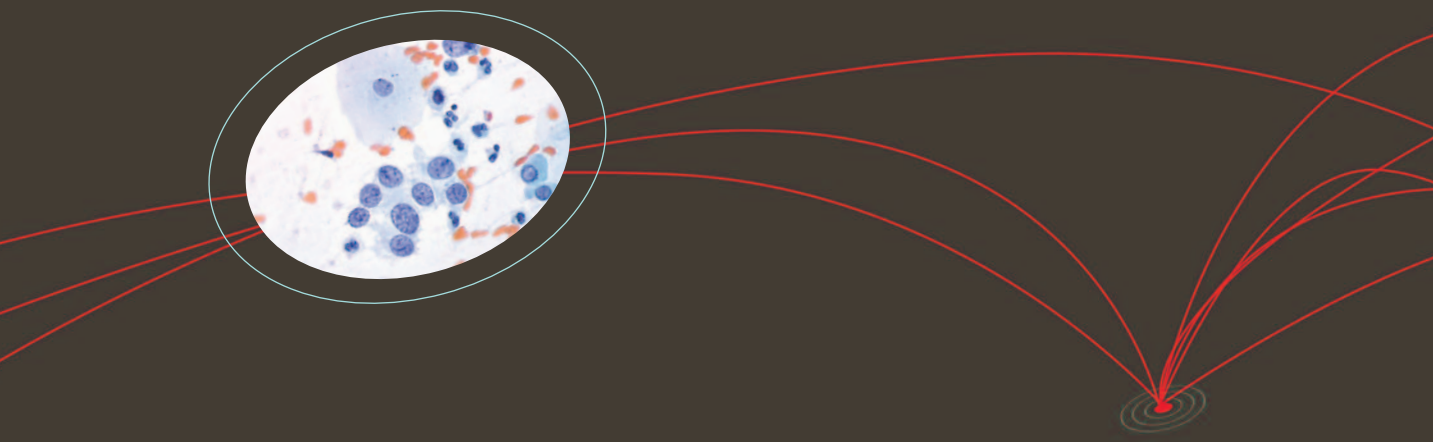


PROGRESS REPORT 2006

CLARA
CANCÉROPÔLE LYON AUVERGNE RHÔNE-ALPES

SPEEDING UP PROGRESS

Under the aegis of the Bullukian Foundation

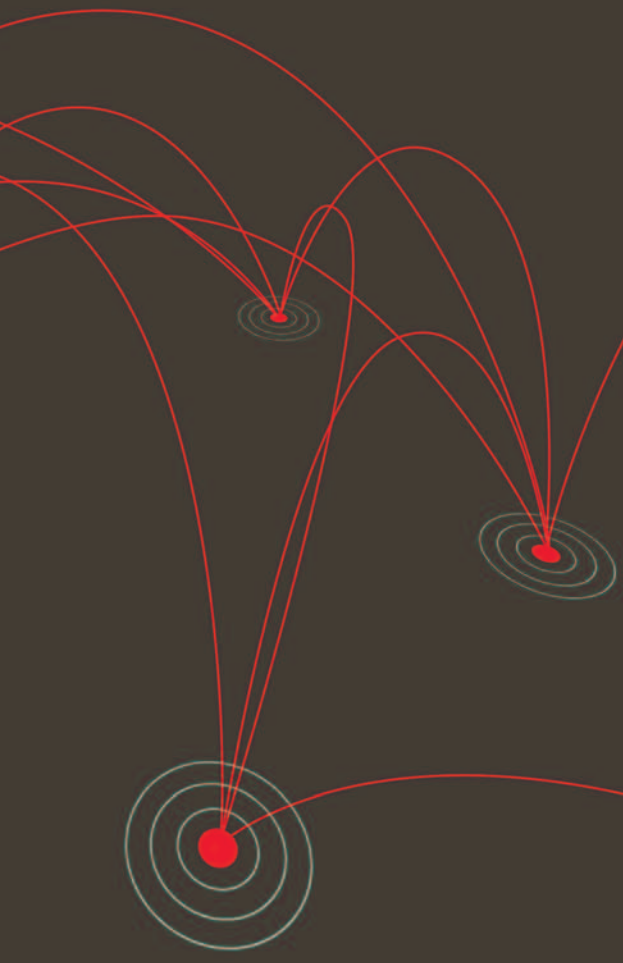


EDITORIAL

In 2006, the region and country saw a number of new initiatives in the field of public research. In this active environment, Cancéropôle Lyon Auvergne Rhône-Alpes successfully stepped up its scientific activities and improved its positioning thanks to better mobilization of its research teams, closer collaboration with institutional partners and continued support from all of its funding providers, local authorities and the French State. We sincerely thank all of these stakeholders: we would not exist without their support and energy. They make the Cancéropôle what it is today. And the Cancéropôle is a reflection of their core values. Here are a few of the most notable observations from this past year:

- The scientific content is gaining in depth and breadth, and CLARA can aspire to become a top-flight reference in Europe.
- The network effect is building momentum and proving more attractive. CLARA is making a name for itself as a catalyst for "speeding up progress".
- The general management of CLARA, a project of major scope, is streamlining and becoming increasingly transparent, which explains why funding providers have shown continued confidence in the initiative.
- While application to industry of network research is one of CLARA's key aims, we cannot yet reap all of the fruits, as research processes cannot be made infinitely shorter: we must let time do its work.
- With CLARA growing and building every day, it is vital to maintain this momentum, as new prospects and challenges emerge on the horizon. CLARA is already preparing for them.

Mireille Guigaz
Executive Director, CLARA



CONTENTS

CLARA defines its position

A CHANGING ENVIRONMENT

The year 2006 was eventful for Cancéropôle Lyon Auvergne Rhône-Alpes, bringing changes at both the national and inter-regional levels and within the network itself.

At the national level, the crisis within the French National Cancer Institute (INCa) was illustrated by major difficulties, the consequences of which have probably not yet been fully measured. This crisis resulted from a number of different factors:

- An improper positioning of the Institute, whose stated ambition of being the arbiter and guide for implementation of the Cancer Plan, quickly turned into a position of a contracting authority that wanted to "do things" rather than "have things done".
- The strong impetus of the Institute's executive body to obtain fast results, thus neglecting the time for explanation and consultation, even among the members of the Board of Directors. As a result, the National Cancer Institute gave the impression of turning a deaf ear to the prerogatives of its oversight bodies and being unaware of the realities in the field, leading to dissatisfaction at all levels.
- Shortcomings in the areas of general and financial management.

This crisis ended only with the resignation of the President (in August 2006) and the announcement that the General Manager was to be replaced.

Without any doubt, this difficult context negatively impacted the legitimacy and credibility of the cancer research networks, which were in the process of completing their emergence and organization phases. Firstly, they were unable to benefit from INCa's support. In addition, they were hampered by criticism and suspicion from research teams and partners, who questioned their ability to implement the Cancer Plan's research strategy and projects. This broke the momentum of the cancer research networks.

The Network Management Team

At the regional and inter-regional levels, the first organizational effects of the Research Program Law (April 18th, 2006) led CLARA to adjust its roadmap, laid out in December 2005. When the competitive clusters became operational, CLARA explored new channels for collaboration in the field of Cancer. The launching of the call for projects on Research and Care Theme Centers and Networks (RTRS) also helped to mobilize local teams.

Collaboration in the field shifted into high gear with Lyonbiopôle, with the CEA / Léti nanotechnology cluster and, for the Cancer RTRS, with Université Claude Bernard *(see pages 8 to 11 and 38)*.
The potential for shared interests with a number of stakeholders grew considerably. In order to fully capitalize on these opportunities, CLARA must identify and bring in new research teams and find new sources of funding.

The Network Management Team also underwent major changes. Most notably, Jean-Luc Balzer, Deputy Executive Director, Industrial Development and Programs, was recruited by the pharmaceutical industry. He was replaced by Peter Pauwels.

EARLY ASSESSMENT

In this context, the question was raised of CLARA's added value. Rather than avoiding the subject, CLARA decided to confront the issue head-on.

› CLARA as examined by two university students

- **A sociological approach: "The challenges of building inter-regional policy: the example of Cancéropôle Lyon Auvergne Rhône-Alpes (CLARA)."**

As part of a Master's Degree in Sociology at the Paris Political Science Institute (IEP), Audrey Vézian conducted some forty interviews with political leaders, hospital administrators and researchers over a three-month period.

Her study showed that while an inter-regional cancer research policy is desired by all of the stakeholders interviewed, implementation of this policy has proven difficult for the management team in charge of the operations. Not only has the local and national context of the lengthy process to build a cancer research network led to a lack of legitimacy from the point of view of the academic and institutional stakeholders involved, but the network's action is also hindered by a local environment characterized by a strong clash between the academic and industrial mindsets. This lack of stature in relations with local funding providers, academics and institutions, has resulted in a number of obstacles for the policies implemented through the inter-regional organization projects. This is illustrated in CLARA's decision-making bodies by a mostly representation role for academics and institutions rather than a participative role.

The findings of the study were widely distributed within the governance bodies and to the persons interviewed.

- **An economic approach: "Cancéropôle CLARA in Auvergne: an analysis of its economic impact and creation of relevant indicators."**

As part of a Master's Degree in Economics at the University of Auvergne, Alexandre Boulègue attempted to measure the economic impact of a research network such as CLARA.

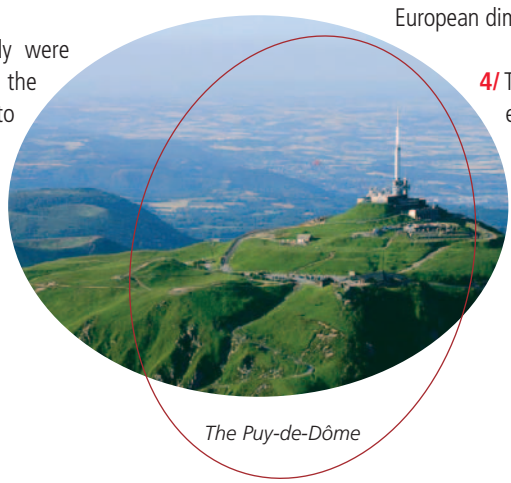
At the Auvergne regional level, this subject proved complex. Nevertheless, four main points can be highlighted:

1/ The cancer research network brings undeniable financial leverage: every year, more than 3 million euros is allocated to Auvergne research teams thanks to the action of the Cancéropôle's Auvergne Cluster (PAC).

2/ Despite a certain weakness within Auvergne's industrial fabric in the field of oncology, the cancer research network is striving to bring new impetus to the region's bio-pharmaceutical sector, which could not be developed spontaneously.

3/ The alliance with the Rhône-Alpes region is a positive factor that brings hope for the future. On its own, Auvergne research could never hope to reach European dimensions.

4/ The PAC's ambitions regarding economic impact are legitimate, but it will take several years before the catalyzing effects can truly be felt.



The Puy-de-Dôme

Assessments conducted by two major funding providers

- **An economic study of the Centre Léon Bérard (CLB) platform**

In a follow-up to the first studies carried out by ALCIMED in 2005, the Rhône General Council (county) wished to examine the economic development potential of the CLB platform, to which it provides 8 million euros in funding *(see CLARA Progress Report 2005, page 17).*

The study showed that construction of the "Cheney D" building will provide new energy for the East Lyon platform in the short term, accelerating the process already initiated by CLB and CLARA. This investment will help constitute a durable critical mass in the research teams and thus lead to the creation of a true "Research Institute", generating visibility for the entire CLARA region. At the same time, it will help to bolster the research *continuum* and to create value by tightening collaboration between the academic and industrial spheres. In addition, this funding is part of the regional research plan and can thus indirectly benefit other organizations, namely Lyonbiopôle.

Centre Léon Bérard

- **An assessment of the Greater Lyon - CLARA partnership**

This study, conducted by LOBYM-Altidiem at the request of the elected officials of Greater Lyon, is based both on a generic assessment of public policy and on the requirement to assess any provision of funding exceeding €100,000.

Two approaches were used: a budgetary/financial approach and a qualitative investigation.

The highlights of this study are as follows:

1/ Greater Lyon has complied with the terms of the Metropolitan Area Contract and its financial commitments are consistent with the project deadlines and the progress in developing facilities *(see page 31).*

2/ The 5 goals that had originally been set for CLARA have been reached, more specifically:

- Building relations between the region's scientific stakeholders on the theme of Cancer;
- Developing technical platforms that combine industrial research and medical care facilities;
- Building Europe's most powerful Nuclear Magnetic Resonance (NMR) facility;
- Implementing a program dedicated to funding start-ups (Proof of Concept);
- Initiating actions that strengthen communication between scientists and help to promote the Lyon metropolitan area around the globe.

The stated expectations primarily concerned four points:

- Defining clearer strategic aims, supported by more effective and efficient means of implementation;
- Shifting from an approach seen as "overly academic" towards a more industry-oriented approach;
- Reducing the cost and complexity of operations, with more easily understandable, better disseminated results;
- Improving relations between CLARA's various stakeholders and with outside organizations.

Lyon

The bibliometric approach

Upon the recommendation of its Scientific Advisory Board, CLARA continued its bibliometrics development in 2006. The Bibliometrics Unit of the Scientific Evaluation Department at the French Institute for Health and Medical Research (Inserm) was commissioned to perform a second study.

The study showed that the Lyon Auvergne Rhône-Alpes region contributed 18% of all publications affiliated with France, placing it second after the Paris region. Lyon Auvergne Rhône-Alpes is associated with a high proportion of top-flight publications: 3.4% of its publications rank within the Top 1% worldwide, demonstrating the high visibility of the region's Cancer research.
Inserm, the International Agency for Research on Cancer (IARC) and the French National Center for Scientific Research (CNRS) hold a unique standing, with 24.9%, 22.3% and 12.9% participation respectively. It should be noted that Inserm's national participation in the field of Cancer is 26.2% and that of the CNRS is 17.2%. IARC contributes to a significant part of the Rhône-Alpes / Auvergne region's international renown, with 5.3% of its publications in the Top 1% worldwide.

The study also highlighted a group of 147 researchers with a high level of international visibility in the field of oncology associated with publications from the CLARA region. Of these, approximately 30% are outside of CLARA, and 40% are at IARC.

Finally, an initial assessment of cooperation within CLARA was conducted. This study distinguished very active collaborative groups, as well as researchers who served as interfaces between these groups. One hypothesis, to be confirmed, is that these "liaison researchers" help to develop cross-disciplinary projects and innovations.

Science in action

In the past, CLARA placed top priority on setting up governance, securing funding and building management models. In 2006, however, the network's main focus turned to its scientific mission.

SCALING UP INTERDISCIPLINARY RESEARCH

Infection and Cancer: a CLARA - Lyonbiopôle collaboration

An initial workshop on Infection and Cancer was held by both organizations on June 22nd, 2006, during which:

1/ A Scientific Board was formed.

2/ 6 core work topics were selected, with the designation of managers for the academic and industrial spheres, in the aim of developing new projects that could be used in applications for future calls for projects.

3/ Several assets were highlighted:

- For most of the cancer causing viruses, there is at least one research team working on the topic within the CLARA region;
- There is a scientific critical mass and the capacity to generate research projects, in particular research transfer projects.

Bernard Mandrand, Lyonbiopôle Scientific Director, and Jean-Yves Blay, CLARA Scientific Director.

INFECTION AND CANCER WORK TOPICS:

1/ Biological resource centers (viral-induced tumor and immunodepressed patient banks, healthy tissue and serum banks, with annotated clinical data)

Coordinator: Raphaël Rousseau, Centre Léon Bérard, with the assistance of Massimo Tommasino, IARC.
Aim: To build a complete collection in the CLARA region.
Status: Key topic, in organization phase.

2/ Epigenetics, telomeres and viral-induced cancers

Coordinator: Eric Wattel, Centre Léon Bérard.
Aim: To bring together the various players and organize the preparation of an application for the 7th Framework Program (FP7).
Status: A project is being set up for the FP7's first call for projects, with potential funding from CLARA.

3/ Immunological response against viral-induced cancers

- Modulation of immune system ligands by viruses (for example Toll Like Receptors - TLR)
- Infection control by the immune system
- Immunological response to vaccination

Coordinators: Geneviève Inschauspé, ENS Lyon, and Massimo Tommasino, IARC.
Aim: To identify players and build a work program on HPV, in order to apply for upcoming Proof of Concept, National Research Association (ANR) or INCa calls for projects in early 2007.
Status:

- An "HCV" project accredited by Lyonbiopôle (partners: Transgène, Epixis, Lyon Civil Hospitals (HCL), Grenoble University Hospital (CHU Grenoble), Inserm and CNRS);
- The ALPHAVAC project, submitted to Lyonbiopôle on the association between cytokine and HCV vaccine (partners: Flamel, Transgène, Inserm, 4 hospital-based teams in Lyon and Grenoble and 2 Swiss teams);
- A project under consideration by Transgène on HPV with a view to CLARA Proof of Concept funding.

4/ Identification of new cancer-inducing pathogens

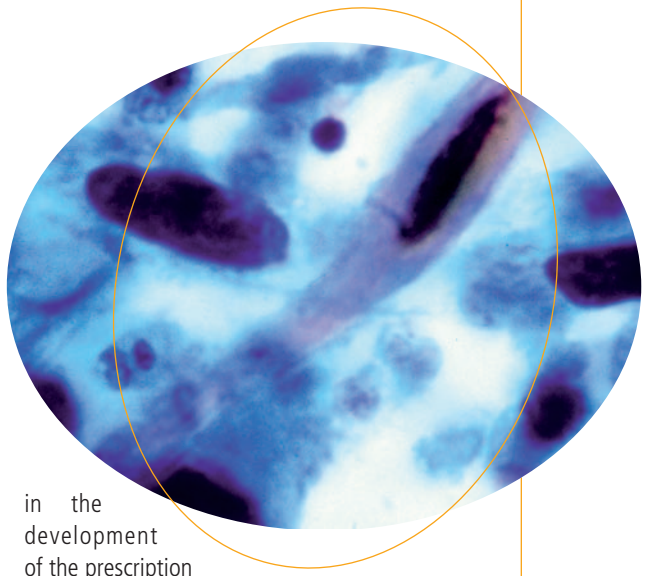
Coordinator: Glaucia Paranhos-Baccala, with assistance from Didier Lamy, bioMérieux
Aim: To assess the opportunity for a project.
Status:

- Startup of the DEMINAP Project, accredited by Lyonbiopôle: use of Toll-like Receptors (TLR) to detect unapparent microorganisms and their ligands for diagnostic and therapeutic purposes (partners: Innate Pharma, bioMérieux, Inserm 590 / Centre Léon Bérard and IARC);
- The emergence of new projects is subject to the Biological Resource Center (CRB) (topic 1), the availability of samples being of capital importance.

5/ Infectious complications of cancer, immune response biology, predictive factors and patient care

Coordinator: Jacques-Olivier Bay, Centre Jean Perrin.
Aim: To identify sub-topics, the players in charge and the research program.
Status:

- A project on the prevention of infections in at-risk hospitalized patients has been filed with Lyonbiopôle. The innovativeness of the project lies in the development of the prescription formula by Hikma Biotech and its association with the immune repertoire analysis protocol developed by ImmunID.
- The topic is to be organized.



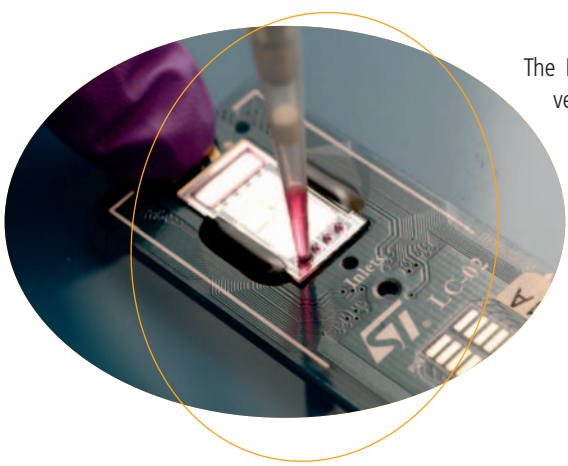
6/ Epidemiology of viral-induced tumors

Coordinators: Franck Chauvin, Loire Cancer Institute (Institut de Cancérologie de la Loire) and Christine Lasset, Centre Léon Bérard.
Aim: To prepare the project in collaboration with the industrial partner (sanofi pasteur MSD).
Status: A project has been submitted to Lyonbiopôle by sanofi pasteur MSD and Clininfo. This project aims to specify the indications for the anti-HPV vaccine.

More information

HCV: Hepatitis C Virus
HPV: Human Papillomavirus
FP7: 7th Framework Programme for Research and Technological Development

Nanotechnology and Cancer: a CLARA - CEA/Léti collaboration



The Nanotechnology and Cancer focus is supported by a very rich local fabric:

- CLARA and its members active in the oncology field;
- CEA/Léti in Grenoble, a world-class player in the field of micro and nanotechnology;
- Rhône-Alpes' leadership in two European excellence networks: Nano2Life and CONTICANET.

In 2006, several events gave rise to collaborative ventures at the regional and European levels:

- **An awareness-raising meeting in Lyon in April 2006**
  A presentation by representatives of CEA / Léti of the available technologies and their first clinical applications helped to raise the awareness among the participating healthcare professionals. This initial forum revealed the potential for interactions between open "technologists" and "technologically-sensitive" clinicians.
- **CLARA's participation at the booth of Nanobio, a Grenoble cluster, at the Nanobio Europe Congress, held June 14th to 16th in Grenoble**
- **A first contact meeting in October 2006 at the CEA in Grenoble**
  This meeting enabled participants to compare the technological solutions developed by Grenoble's nanotechnology specialists with the needs of clinicians in the treatment of Cancer.
  3 topics were highlighted:
  - *In vivo* optical imaging,
  - Minimally invasive sampling,
  - Preparation of blood samples.
  Supporting these topics with specialized workshops would enable operational clinical changes and diversification of the projects set up by CLARA:

Name	Projects	Aims	Partners
Protool	Chemically functionalized silicium tip for molecular or cellular imprints	Nanobiopsy and nanobanking concepts *In vivo* sampling near cerebral tumors	Inserm Unit 318 CEA/Léti
IMOPT3D	Fluorescent 3D optical tomography	Pre-clinical functional imaging, biodistribution and intratumor activity for live mice	Inserm Unit 578, UJF/LEDSS Animage CEA/Léti
	2D system in FRI operational	Activatable fluorescent probes have been developed for the 2D system	
SIMALOC	High-sensitivity, high resolution PETS µ detector (CdZnTe)	Micro Gamma camera for small animal functional imaging	Inserm Unit 340 CEA/Léti
Proof of Concept	Nanobiotix	Activatable nanoparticles (nanobiodrugs™), pre-clinical studies on glioblastoma	Nanobiotix Inserm Unit 433

The Minatec site

- **Closer collaboration between European networks Nano2Life and CONTICANET**

The initiatives to bring these two European excellence networks - Nano2Life (Coordinator: Patrick Boisseau, CEA) and CONTICANET (Coordinator: Jean-Yves Blay, Université Claude Bernard Lyon 1) - closer together were started in Cork, Ireland at coinciding meetings in September 2006. A meeting in December 2006 then enabled the players from the two networks to firm up their involvement in joint initiatives to submit projects for the calls for proposals as part of the European Commission's upcoming Framework Program for Research and Technological Development (FPRTD).

These initiatives for collaboration at the regional and European levels helped to pinpoint some ten potential convergence projects, involving both clinicians and "technology specialists".

On the strength of these assets, the region stands as a center of excellence for convergence projects in the Nanotechnology and Cancer focus area.

Human Sciences and Cancer: a promising new field

The "Public Health and Cancer" focus area is one of CLARA's development priorities. In particular, the Saint-Etienne platform currently under development is being called upon to provide impetus and coordination. With INCa funding as part of the "Core Networks 2005" call for proposals, Franck Chauvin's project entitled *A Regional Cancer Information and Education Resource Center* aims to better involve patients in their treatment and thus improve the quality of care.

The Network Management Team also initiated a program in the field of Social and Human Sciences (SHS) that is an integral part of the National Cancer Plan. Indeed, measure 67 stipulates that the cancer research networks must, through their mobilization and coordination activities, help to *"define a nationally coordinated strategy and development of finalized programs"* in order to strengthen SHS research, which has thus far been the *"poor relation in cancer research"*. More generally, this process aims to develop a multidisciplinary approach to treating the disease in order to better address the multiple dimensions of Cancer. We must not forget that the Human and Social Sciences include Economics, Sociology, Psychology and Anthropology, which are all useful for understanding the disease, its context and the stakeholders involved.

In this climate, an initial seminar on "The Human Sciences and Cancer in Rhône-Alpes/Auvergne" was held in Lyon on November 16th, 2006. Bringing together nearly 70 participants, mainly from the medical and social science spheres, this event aimed to unite SHS researchers and healthcare professionals to discuss potential ways of working together. A participant satisfaction survey conducted after the seminar underlined a keen interest for this type of event, which appears to meet a true need. All of the participants surveyed unanimously acknowledged the usefulness of SHS in the fight against Cancer. CLARA intends to pursue this initiative by helping to build a network based on the topic of SHS and incorporating it into the clinical teams.

In terms of projects, 2006 was relatively productive, as two SHS-related projects received INCa funding. The first was entitled *A sociological analysis of physician participation in clinical research. A comparison of three randomized multicenter trials,* led by Patrick Castel (CNRS, Centre Léon Bérard). The second, entitled *A comparative analysis of anti-cancer policies in France and Great Britain*, was led by François Briatte (Grenoble Political Science Institute/ IEP). Finally, let us once again mention the two studies described on page 5.

Human Sciences and Cancer seminar

CONTINUATION OF THE PROOF OF CONCEPT PROJECT

Two new calls for proposals launched in 2006 helped to build up the project portfolio and reach a funding rate of 83% (€2.5 million out of the €3 million planned). In 2006, the program also received its first encouraging feedback.

Three of the four projects selected in 2005 are in the operational phase

The pilot project, entitled *Treatment of glioblastoma after targeted vectorization of magnetized nanoparticles in tumor cells and magnetolysis*, uniting Nanobiotix and Inserm Unit 433 on Experimental Neurobiology and Physiopathology, started operations in early 2006. It should be noted that the startup Nanobiotix raised €7 million during its second fundraising drive on November 8th, 2006, one year after obtaining its seed funding.

Two projects selected during the first call for proposals in 2005 started in February 2006:

- *Truncated IL-6 as a natural inhibitor of Il-6: an in vivo demonstration,* conducted by OPi, Inserm Unit 590, Centre Léon Bérard, Lyon Civil Hospitals (HCL) and Université Claude Bernard;
- *The treatment of hepatic metastases of colorectal cancer by liver targeting and intra-erythrocyte encapsulation of 5 FU,* conducted by Erytech Pharma, Centre Léon Bérard (Experimental Surgery Unit), Inserm, HCL and Université Claude Bernard (Animage and CIC). It should be noted that Lyon startup Erytech Pharma raised €12 million December 2006, one year after receiving its seed money.

The third project selected during the 2005 call for proposals brought together GENOME express and Inserm Pre-clinical Neurosciences Unit 318 and was entitled *Validating new protein biomarkers for diagnostics and prognostics in oncology*. The firm decided not to continue the project following new strategic orientations after it was bought out by Clinical Data, an American group.

(See the Progress Report 2005, pages 32 and 33)

Five new projects selected in two calls for projects launched in 2006

The second call for projects, published in March 2006, drew 6 applications. Two of these were selected and began work at the end of the year:

- *Therapeutic targeting of cancers using TLR3 agonists,* conducted by Innate Pharma, HCL and Université Claude Bernard;
- *Twist, a new diagnostic, prognostic and predictive marker for aggressive and chemoresistant cancers,* conducted by Covalab and Centre Léon Bérard.

The third call for projects, published in September 2006, drew 5 project applications. Three of these were selected, and are scheduled to begin work in early 2007:

- *Treatment of hepatic metastases using focused ultrasound,* conducted by Edap TMS, Inserm Unit 556 and Centre Léon Bérard's Experimental Surgery Unit;
- *Hybrid nanoprobes for multimodal cell tracking imaging in oncology,* conducted by Nano-H and Animage, in collaboration with CREATIS (UMR 5515, U630), GEMPPM (UMR 5510), LPCML (UMR 5620), Inserm Unit 449 and Inserm Unit 548;
- *A robot to assist in minimally invasive cancer surgery,* conducted by EndoControl and the TIMC-IMAG laboratory (UMR 5525UJF & CNRS), in close collaboration with Grenoble University Hospital.

A first set of encouraging results

After two years of existence, the Proof of Concept program has proven successful in terms of both its added value and its working methodology. Eight high-potential projects have been selected.

Throughout this process, CLARA has mobilized partners involved in specifying and running the project selection process, namely the Board of the Business Club, one of whose members chairs the Evaluation Committee. Other partners include ARTEB, Anvar and Amorçage Rhône-Alpes.

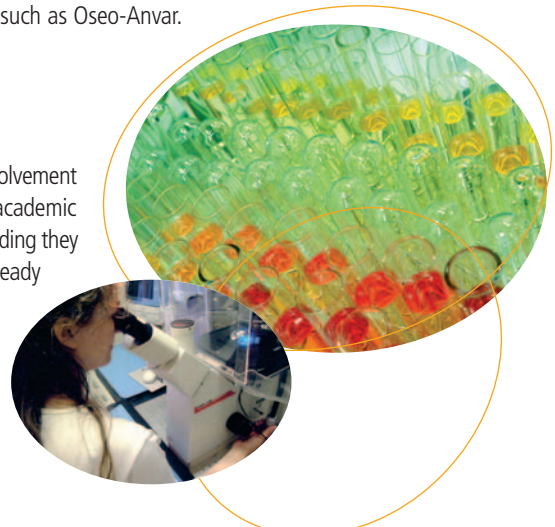
The Proof of Concept program is renowned and respected by partners at both the regional and national levels.

The call for projects launched in October 2006 pointed to a shift in the nature of the projects. There were more applications submitted by start-ups which are newer and more oriented towards medical instruments or technology than towards medicines or even diagnostics. This type of partner requires a higher level of financial support than CLARA can bring to industry partners; it is thus likely to require the mobilization of other sources of funding, such as Oseo-Anvar.

Prospects to be specified

The impact of local authorities' support for the program must be analyzed primarily over the medium and long term.
A full evaluation of the program can only be performed when the first projects are completed, during 2008, or even afterwards if this involves assessing the potential impact for the region (as the average development phase for a medicine lasts approximately 13 years).

Nonetheless, the involvement of firms in CLARA's academic network and the funding they have invested are already clear indicators.



REORGANIZATION OF THE BIOLOGICAL RESOURCE CENTER PROJECT

As the Biological Resource Center (CRB) project was unable to move forward as planned, the Scientific Advisory Board, Guidance Board and Finance Committee all requested a partial assessment. The assessors wrote a progress report and proposals, which were submitted to the project Steering Committee and partners.

These bodies decided to focus the project on the "Information Systems" topic area, and a project manager was named. Based on the progress in the collection of samples for the two pilot projects *Thyroid Cancers and MutaCancer*, the "Retrospective Project and Prospective Project" topic area will be continued.
As a result, the budget forecast for the project was scaled down: it will be at most €100,000.

At the same time, the National Cancer Institute and Inserm took initiatives to build a virtual national tumor library, which justified suspension of CLARA's CRB "Quality and Inventory" focus area. When the time comes, CLARA's CRB teams will join this national program.

FOCUS ON THE PLATFORMS

LYON

› The International Agency for Research on Cancer (IARC)

In 2006, several programs and projects coordinated by IARC benefited from CLARA support, and others were initiated with a view to building a European Cancer Observatory that would enable ongoing monitoring of cancer incidence and mortality.


IARC

• **The ENCR**

The European Network of Cancer Registries (ENCR) brings together some 190 regional and national cancer registries from around Europe. Its activities, interrupted in 2004 due to a shortage of funding, restarted in 2005 thanks to a subsidy from CLARA.

A proposal was finalized to create a central database named GateWay (GW), hosted by IARC, which would contain all of the incidence data from Europe's cancer registries. GW will be the basis for joint descriptive studies on cancer conducted in Europe. Its terms of use and the protocol for submitting data were specified and made public. The "Call for Data" was sent out to ENCR members in March 2006.

As part of the ENCR, IARC set up a course on cancer forecasts in Lyon in September 2006. In July, 98 participants from 11 European countries received training on cancer registration and epidemiological methods.

In terms of communication, the content of ENCR's website was reviewed and updated; the network's activities are regularly promoted on the site. A free publication area is currently being negotiated with the publisher/manager of BioMedCentral. The aim is to periodically publish memos based on ENCR data and the minutes of ENCR general assembly meetings. Finally, a new website on cancer statistics for the general public is currently being designed and should be available online in early 2007.

• Estimating and forecasting cancer incidence and mortality in Europe

As part of the European Cancer Observatory set up at IARC thanks to CLARA funding, estimates of cancer incidence and mortality in Europe in 2006 have been produced. The most recent data on European cancer incidence and mortality have been gathered and forecasts have been made using short-term prediction methods in order to produce estimated incidence and mortality rates for 2006.

Other methods were required to estimate cancer incidence in countries for which no national incidence data were available. These involve forecasting incidence and mortality data provided by cancer registries that are representative of the country. For each European country, the rates estimated for 2006 were multiplied by the estimated corresponding population in order to obtain the best possible estimates of the number of new cases and cancer deaths in Europe in 2006. The results are presented for the 38 European countries specified by the UN and Cyprus, by sex and for 18 cancers *(see insert).*

In 2006 in Europe, 3,191,600 new cases of cancer were diagnosed (not including skin cancers other than melanoma), 53% in men, 47% in women, and 1,703,000 deaths were counted (56% in men, 44% in women). The most frequently occurring types are breast cancer (430,000 new cases, 13.5% of the total), colorectal cancer (412,900 new cases, 12.9% of the total) and lung cancer (386,300 new cases, 12.1% of the total). The latter, with 334,800 deaths in 2006 (19.7% of the total), is the leading cause of death by cancer in Europe, followed by colorectal cancer (207,400 deaths), breast cancer (131,900 deaths) and stomach cancer (118,200 deaths).

• Breast cancer

Breast cancer is the first cancer for which IARC intensified its efforts in order to create a standard for analyzing incidence and mortality data. This work is being carried out by a team featuring P. Autier, J. Ferlay, M. Boniol, C. Héry and M. Beltran. The project aims to set up informatic and biostatistical tools enabling "real-time" analysis of all breast cancer data recorded at IARC. This analysis should then be available to all parties involved in the prevention, screening and treatment of breast cancer. The methods of analysis should also provide indications on the effectiveness of screening and on how decreased use of hormone treatments during menopause impacts the incidence of this cancer.

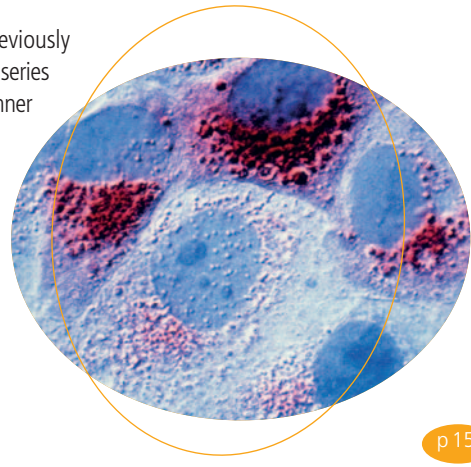
This project will also enable improved comparison of incidence and mortality trends between countries. On the specific topic of mortality, it will help to more accurately estimate to what extent some countries seem to perform better in reducing mortality due to this cancer.

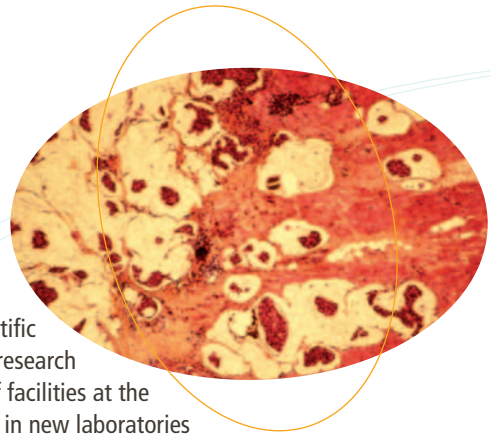
• Survival of children suffering from cancer

Another activity started in 2006 involved writing a series of articles on the survival of children with cancer, using a new period survival analysis method. This group of articles was submitted for publication in *Annals of Oncology,* which had previously expressed its interest in the series (coordinator: Hermann Brenner of DKFZ, Heidelberg).

• The ARCERRA study

This study focuses on the long-term effects of cancer in children. This study is being conducted by the Rhône-Alpes Regional Association of Child Cancer Registries (ARCERRA). A publication is currently being prepared.





South Lyon

2006 was a year of transition, with consolidation of the scientific projects underway and the emergence of new links with clinical research and industrial partners. The year ended with the development of facilities at the South Lyon site, which enabled several research teams to set up in new laboratories in the final weeks of 2006.

The most fundamental projects initiated over the last 2 years generated a number of new scientific exchanges throughout the Gerland/ South Lyon cancer platform, with CLARA teams - in particular the East Lyon and Grenoble platforms - and with other scientific organizations in France and abroad. This process helped ramp up development of the projects, which are now able to bring about truly innovative scientific breakthroughs. Below are a few of the highlights we would like to mention:

- **Cancer epigenetics:** description of telomere signatures, methylation profiles and heterochromatin modifications in certain forms of leukemia and other tumors, in order to identify new markers and therapeutic targets;

- **Biotherapies:** development of molecules interfering with certain targets for therapeutic purposes (apoptosis regulation pathway, telomerase activity and the NF-kB pathway); some of these molecules modulate the response of cancer cells to chemotherapy and radiotherapy;

- **Hormone-dependent cancers:** identification of new targets whose expression is induced by androgens in prostate cancers and description of the role of thyroid hormone receptors in digestive tumors;

- **Immunointervention:** analysis of the role and action of various populations of T lymphocytes and dendritic cells during immune response in various immunization and infection models and during cancers.

Vital links with clinical research also enabled the emergence of many projects. Highlights include:

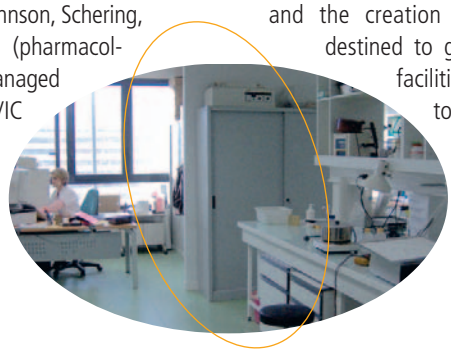
- The growth of the platform dedicated to pharmacological screening and modeling of the effect of anti-cancer treatments, pooling clinical, pharmacological and biomathematical expertise, in which the projects aim to:
  1/ Model new medicines and their interactions with various biological processes in order to optimize their pre-clinical and clinical development;
  2/ Track pharmacokinetic/pharmacodynamic relationships to adjust therapeutic effects, including in the complex biomolecular model, such as monoclonal antibodies;
  3/ Develop new molecules (anti-angiogenics, kinase inhibitors, etc.) in phase I;
  4/ Conduct clinical trials with new methods of adjusting the dose and release of anti-cancer medicines, using a mathematical model that enables real-time control of hematotoxicity and antitumoral effect: an original proof of concept clinical trial is underway in the field of breast cancer.

- As part of the ETOILE project to create a carbon ion hadrontherapy research and care center, building an international multidisciplinary (biology, physics, radiotherapy, imaging, etc.) research network on the effects of carbon ions in cancers sensitive or resistant to conventional radiation therapy, using *in vitro* models and animal models.

- As part of the Lyonbiopôle competitive cluster, development of new monoclonal antibodies for therapeutic purposes in the treatment of viral-induced lymphoma.

- The startup of new programs, some of which are funded by the INCa calls for projects in clinical research (PHRC) and rely on Lyon Civil Hospitals' Biological Resource Center (in particular the tumor library), which involve the identification of new diagnostic and therapeutic markers in patients, such as:
  - Genomic and proteomic analysis of breast, prostate and urinary bladder cancers (PHRC in 2005 and 2006);
  - Alterations in gene and protein expression in lymphomas and chronic lymphocytic leukemia, as part of national (PHRC 2003) and international consortiums;
  - Analysis of bcr-abl gene mutations in patients with chronic myeloid leukemia treated using imatinib;
  - The study of telomere shortening in elderly patients treated for ovarian cancer using chemotherapy (PHRC 2006).

The potential for economic development is also growing, with a number of industrial partnerships. Notable examples include EFS Electronics (development of a 2nd device for chemotherapy-hyperthermia in carcinosis), Génopoïetic (clinical trial on a vaccine in carcinosis), OPi (pharmacology for the marketing approval application for a monoclonal antibody), bioMérieux (validation of an early diagnostic marker in breast cancer), Innate Pharma (immunotherapy), Cyclacel (*in vitro* studies on new anti leukemia molecules), Roche/Genentech (worldwide trial for the recording of new indications for a monoclonal antibody, coordinated in Lyon), Jansen/Johnson & Johnson, Schering, Astra-Zeneca, sanofi-aventis (pharmacology, modeling and locally-managed clinical trials), and the PRAVIC (OPi) and BIOVAX (sanofi, Becton-Dickinson) projects as part of collaborative ventures with Lyonbiopôle. A project on the development of agonists of an immunomodulating agent in collaboration with Innate Pharma and Lyon Civil Hospitals (HCL) was also funded as part of CLARA's Proof of Concept call for projects.



Finally, the scientists at CLARA's Gerland/South Lyon platform also played a vital role in organizing oncology research. Our teams were actively involved in projects to create and accredit research units with Inserm, CNRS, Université Claude Bernard, Lyon's Ecole Normale Supérieure graduate school and HCL. Several of them are part of the "Innovations in Infectiology" advanced research network (RTRA) accredited in 2006 and of the "Synergie Lyon Cancer" Research and Care Theme Network. They are also a stakeholder in liaison organizations recently accredited by INCa, such as the HCL-CLB platform for the molecular genetics of cancer and the national reference center located in South Lyon for the treatment of rare peritoneal tumors.

Thanks to funding from local authorities, particularly Greater Lyon, the work to develop and equip the 1,400 sq. m. facilities refurbished by Université Claude Bernard and HCL at the South Lyon Medical Federative Research Unit (UFR) has enabled several teams to set up and share a high-level technical platform. This will help boost interaction between the Gerland site (where a new BioSafety Level 3 laboratory has also been equipped) and the South Lyon Teaching Hospital.

This year of transition thus saw many new programs and the creation of a true scientific momentum destined to grow even stronger thanks to the facilities and equipment made available to researchers.

East Lyon

At the East Lyon platform, two hospitals manage major programs.

The first, led by the Léon Bérard Cancer Center (CLB), focuses on Structural and Functional Genomics. Coordinated by Alain Puisieux, its main aims include:

- Identifying prognostic markers and predictive markers for response to treatment;
- Pinpointing new therapeutic targets and developing innovative therapies;
- Identifying circulating markers (early diagnostic factors and therapeutic follow-up markers).

This project is part of CLB's interdisciplinary clinical and biological research program on describing the molecular composition of cancers. It is run in tight collaboration between research teams at Inserm Unit 590 (managed by Alain Puisieux) and CNRS Unit 5238 (managed by Patrick Mehlen), as well as teams at Lyon's Rockefeller University (CNRS Unit 5201), the Lyon Ecole Normale Supérieure graduate school (CNRS ENS Unit 5161), IARC and the Clermont-Ferrand Genetics Laboratory (managed by Yves-Jean Bignon). This joint effort led to the creation of three original programs in structural genomics (the *MutaCancer* and *CirBioCancer* projects) and functional genomics (the *InaCancer* project) between 2004 and 2006. These three programs, developed in direct interaction with fundamental research projects, received positive assessments from the Scientific Advisory Boards of INCa and Centre Léon Bérard. The initiatives rely on partnerships with firms (including GENOME express, bioMérieux and TRANSAT).

- **MutaCancer and InaCancer**

The *InaCancer* project was initiated by CLB's Molecular Oncology Unit and developed as part of a collaborative network bringing together Inserm Unit 590 (Alain Puisieux), CNRS ENS Unit 5161 (Eric Gilson), CNRS Unit 5201 (Marc Billaud), the teams in Infection and Cancer Biology and Molecular Carcinogenesis at IARC (Pierre Hainaut and Massimo Tommassino), Inserm Unit 578 (Elisabeth Brambilla) and Lyon firm TRANSAT. InaCancer aims to build original cell models that trace the natural history of tumor progression, from the normal epithelial cell to the invasive cancer cell.
Related to the work carried out at Inserm Unit 590, breast cancer is the first type of tumor to be studied. To date, 26 different lines showing specific alterations have been obtained using normal human mammary epithelial cells (HMEC). Description of these lines is continuing at CLB's Molecular Oncology Unit.

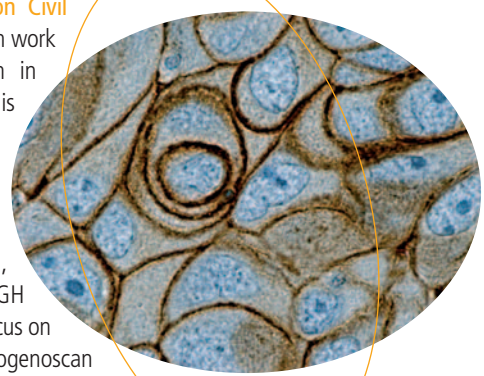
The *MutaCancer* project is run by CLB's Molecular Oncology Unit as part of a collaborative venture with the Clermont-Ferrand Genetics Department (Yves-Jean Bignon) and with Grenoble firm GENOME Express (F. Pons). The project, started in late 2005, is a high throughput mutation research program applied to cancers (breast cancers, colon cancers, lung cancers and neuroblastoma). This project received INCa funding in 2005.

As regards direct sequencing, 273 genes involved in p53-dependent, BRCA1 and PTEN pathways were selected and the first genes presenting potentially harmful mutations are currently being studied in primary tumors (breast cancers, colon cancers and neuroblastoma) and in normal tissue in order to assess the frequency of the mutations. The second approach being used, GINI, involves an experiment on inhibiting Nonsense-mediated mRNA Decay (NMD) in the cell lines being studied.

- **CirBioCancer**

  The *CirBioCancer* project, which received the backing of CLB's Scientific Advisory Board in December 2005, followed by that of INCa in September 2006, aims to highlight tumor-related gene alterations in the peripheral blood by analyzing circulating DNA. CirBioCancer will be conducted with close collaboration among hospital laboratories - CLB's Molecular Oncology Unit and Pathology Department, the Pathology Department at Edouard Herriot Hospital (HCL), academic research teams (Carcinogenesis Mechanisms and Biomarkers, IARC; Inserm Unit 590, and the Molecular Pathology Laboratory at the Lausanne Pathology Institute) - and an industrial partner (bioMérieux) as part of Cancéropôle Lyon Auvergne Rhône-Alpes.

The second program, led by Charles Dumontet, is based at Lyon Civil Hospitals (HCL). Construction work on the new facility began in January 2006 and delivery is scheduled for June 2007. This platform will feature technologies enabling the use of high-throughput DNA chips to study genotyping, transcriptome and the CGH array. The first projects will focus on lung cancer (the Pharmacogenoscan Protocol by Christian Brambilla), myeloma (inter-group IFM) and breast cancer (CLB projects).



GRENOBLE

CLARA's Grenoble platform places top priority on proteomics, nanotechnology and functional imaging to treat cancer patients.

In 2006, the platform was nearly completed thanks to the purchase of more than 75% of the equipment required. The platform's functional organization was also established between:

- The hospital, with its research cluster bringing together technological resources at the biology innovation center, the biological resource center and the oncology research unit;
- The 2 newly accredited Inserm/UJF research centers, one dedicated to cancer research and the other dedicated to the neurosciences (including brain tumors).

This development was possible thanks to the significant efforts of the 3 parent organizations, Inserm, Université Joseph Fourier (UJF) and Grenoble University Hospital (CHU), in terms of redeploying staff and creating jobs at the technical platforms.

Finally, 2006 saw the opening of the platform to regional, academic and industrial cooperative ventures. In addition, the Biopolis business incubator, located at the healthcare facility, is now open and the first group of biotech firms have set up shop there.

At the "proteomics" platform, analysis of proteins using SELDI TOF devices (François Berger at the CHU facility and Karin Sadoul at Institut Albert Bonniot) has been operational for 3 years, with conclusive findings on distinguishing various histological types of tumor tissues, and on biological liquids in the diagnosis of cancer.
Analysis using a MALDI TOF-TOF Applied 4800 mass spectrometer (Michel Sève) is now up and running and the first proteins described using this device are chromatin-associated proteins. A new 2D nano chromatography device has been added to the platform, thanks to funding from the Nanobio program. Inserm has just created an engineer position for this platform, as the Institut Albert Bonniot research center was set up. In early 2007, an Affymetrix system (François Berger in collaboration with bioMérieux) will enable the platform to perform transcriptome analysis.

The "*in situ* molecular detection" platform (Elisabeth Brambilla and Philippe Lorimier, CHU engineer) brings together techniques, equipment and personnel dedicated to *in situ* study of proteins using immunohisto-chemistry and *in situ* nucleic acid hybridization (Dominique Leroux). This platform, which has been operating for several years, now features more sophisticated devices thanks to CLARA funding. Furthermore, INCa and the Hospitalization and Healthcare Organization Division (DHOS) selected this platform for experiments on a new preservation system.

In 2006, **the cancer molecular genetics platform** (Marie-Christine Favrot, Dominique Leroux and Elisabeth Brambilla) was accredited by INCa. As a result, the platform will be equipped with a multiwell quantitative PCR system and a pyrosequencer.

The EPIMED platform (Sophie Rousseaux) is operational, with an engineer position created by UJF. The sharing of knowledge and technical expertise in epigenetics has enabled the platform to develop its first analysis tools, such as the repchip.

Likewise, **the immunological follow-up platform** (Patrice Marche) is operational and should serve as a Grenoble-based liaison between CLARA and the Infectiology RTRA Research Network.

In the area of imaging, **the non-invasive small animal imaging platform** (Jean-Luc Coll and Véronique Josserand, an engineer with funding from Génopole) brings together a set of devices enabling *in vivo* tracking of fluorescent molecule expression by normal and malignant cells in mice, and the study of the biodistribution of fluorochrome-marked molecules. The equipment, purchased thanks to CLARA and designed in collaboration with CEA/Léti, involved an industrial transfer. This activity is being carried out in liaison between the Nanobio program and CLARA. Nanobio funding enabled the purchase of additional equipment. The platform was opened to firms this year on a contractual basis. Likewise, thanks to CLARA, Daniel Fagret's laboratory validated a prototype of a SPECT camera developed by CEA/Léti. Other important advances were made in small animal and human NMR (Chantal Remy and Jean-François Lebas). Continuation of this program on the imaging platforms will be made possible by high-level funding as part of the State-Region Project Contract (CPER) 2007- 2010.

Joseph Fourier University (UJF)

SAINT-ÉTIENNE

The Loire Cancer Institute (ICL) initiated CLARA's regional public health platform, led by the team of Franck Chauvin, Yacine Merrouche and Dr. Ruch (The Hygée Center for Cancer Information, Prevention and Education). This platform, to help organize public health research and activities in the field of cancer, will be built on the Saint-Etienne university campus. It will be home to research programs in a variety of prevention-related fields.

In addition to driving public health research for the region, this team is working on its own topics. Several programs are already in progress:

Primary Prevention

- A regional campaign to promote early diagnosis of cancer in persons over 75 years of age.
- Factors for accepting or refusing HPV vaccination in primary prevention of cancer of the cervix.

Secondary Prevention

- How informational documents given to women called in for breast cancer screening impact participation. A national multicenter study.

Tertiary Prevention

- Development and assessment of therapeutic education programs in the field of cancer. Current topics include fatigue and pain. Future subjects include nutrition and compliance with oral chemotherapy. National multicenter studies (this topic is specific to ICL).
- The impact of quitting smoking on post-surgical lung complications. A regional multicenter study.

This research activity is being developed and is formalized in contracts obtained during competitive calls for projects in 2005:

- The Massif Central and European project (FEDER),
- The French National Cancer League from the "Teens and Cancer" call for projects,
- An INCa contract from the "Human and Social Sciences" call for projects,
- An INCa contract from the "Clinical Research" call for projects,
- The 2006 national Hospital Clinical Research Program (PHRC),
- Contracts with firms.

The Loire Cancer Institute

When the platform is operational (it will be open to the public in 2008), programs for assessing activities on primary prevention of cancer will be set up by the region's various teams participating in the platform.

Another topic being explored by ICL is hematology research, under the supervision of Denis Guyotat and Lydia Campos. The members of this team were members of an accredited research team at the Saint-Etienne facility. As part of the CLARA organization process, this team relocated to the East Lyon - Inserm platform and works on its own specific research topics.

CLERMONT-FERRAND

In 2 years, the Cancéropôle's Auvergne Cluster (PAC) has proposed more than 50 scientific projects, 21 of which have been awarded funding. All of these projects are interregional and involve collaboration between various institutes.

Nutrition and cancer is the PAC's signature topic within CLARA. It involves both fundamental and clinical research and relies on an INCa-accredited core interregional network and on the Clermont-Ferrand Human Nutrition Research Center, one of only three in France. This topic aims to clarify the impact of nutrients on the various stages of cancer, from carcinogenesis to the nutrition of cancer patients, to the adjuvant activity of food in anti-cancer therapies.

There are three fields of action in this topic area:

- Biomechanical studies on the protective effect of certain nutrients (such as retinoid metabolites and phytoestrogens from tomatoes and soy beans) on the development and occurrence of hormone-dependent cancers (breast cancer and prostate cancer), on experimental models and in clinical research.
- Evaluation of the consequences of cancer on patient nutrition, with the prospect of developing a nutritional intervention strategy for cancer patients. Three cancers are targeted: ENT carcinomas, colic carcinomas and skin melanoma. The epidemiological aspect of this work is being carried out jointly with the Saint-Etienne platform.

- Increasing sensitivity to chemotherapy through a low-methionine diet. This topic is based on original work conducted in Clermont-Ferrand, showing that methionine deficiency increases the sensitivity of melanomas to nitrosyl-urea treatment *in vitro* and *in vivo* in animals. Colic carcinomas and melanomas are currently being studied.

Imaging: This topic is being explored based on the expertise of Inserm and clinical teams in the development of radiotracers, from pharmacology up to clinical trials in humans. There is a highly favorable industrial environment composed of pharmaceutical firms specialized in the production and marking of tracers (benzamides and fluor-18-deoxyglucose). One of the aims is to develop specific melanoma and cartilage tracers for diagnostic purposes (scintigraphy). The long-term objective is to develop molecules enabling specific internal radiotherapy or radiochemotherapy leading, among other things, to potential industrial applications.

Centre Jean Perrin

Functional genomics and "post-genomics" aim to understand the molecular disorders that govern cell transformation. Five topics have been selected: the study of transcriptome in hormone-dependent cancers; high-throughput sequencing of genes involved in mammary tumors (the "Mutacancer" program); the study of the first phases of development of prostate and adrenal tumors using transgenic animal models; the study of genetic instability,

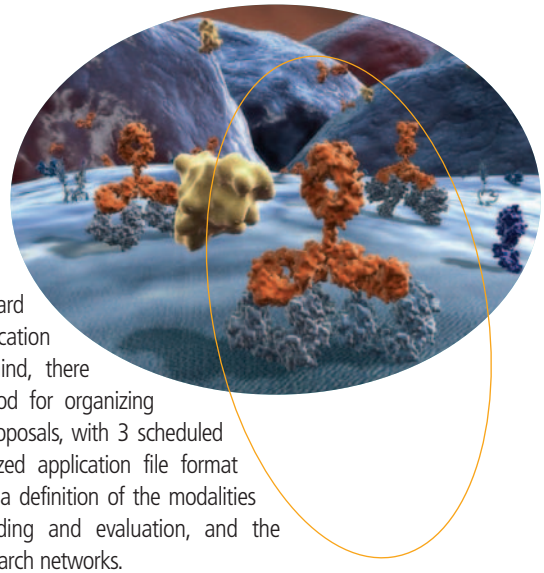
relationships between expression of some cytokines and the chemosensitivity of cerebral gliomas and malignant lymphoproliferations; and the study of non-BRCA genes causing hereditary predisposition to mammary cancer in humans.

Other projects in the fields of oncogeriatrics, oncogenetics, bioinformatics, economics, and social and human sciences have also received funding.

The close working relationships between researchers in the Auvergne and Rhône-Alpes regions and the periodic work meetings have strengthened the teams in a "win-win" virtuous circle, which got off to a promising start in 2006, with the first concrete results expected in 2007.

Finally, cancer research has been included in the next State-Region Project Contract (CPER) for 2007-2013 in Auvergne. In addition to the funding received from the Auvergne Regional Council and Clermont Community on a regular basis, this guarantees that the region's cancer research teams will continue to be strengthened.

THE PROJECT PORTFOLIO



In 2006, the number of calls for projects in the field of cancer increased, particularly from INCa, either on its own behalf or in conjunction with partner associations.

CLARA issued 28 calls for projects, 20 of which drew 77 application files. At the end of January 2007, 25 projects were selected, resulting in a 32% success rate and funding allocations of €2,669,000 (in comparison with the 15 projects selected in 2005).

In terms of prospects for 2007, INCa and the cancer research networks aim to make their procedures more homogeneous, to apply consistent rules to the calls for projects and a standard format to the application files. With this in mind, there will be a new method for organizing upcoming calls for proposals, with 3 scheduled sessions, a standardized application file format and procedures, with a definition of the modalities for payment of funding and evaluation, and the role of the cancer research networks.

> Projects selected by INCa in 2006: see appendix 1
> Hospital Clinical Research Program (PHRC) projects: see appendix 2
> Oncology projects selected in the STIC 2006 procedure: see appendix 3
> European projects: see appendix 4

> Projects funded by the Cancer Research Association (ARC): see appendix 5

The Cancer Research Association (ARC) is a major funding provider for cancer research projects that are fundamental, clinical or preventive in nature. It provides three types of funding: grants which aim to support young French or foreign researchers during their training; subsidies which aim to support French laboratories during specific research projects; and funding for equipment, intended to provide regions with the latest technology as part of its facility development policy.

> Projects funded by the National Cancer League

The National Cancer League is France's leading funding provider for cancer research. As the data on funding granted by the League to projects undertaken in the CLARA region were not available at the time this report was published, please check the League's web site (www.ligue-cancer.net), where this information will be published in the near future.

> Projects funded by the BCRF

The Breast Cancer Research Foundation (BCRF) has supported a breast cancer research program within the CLARA network since 2005.

The BCRF is an American foundation, funded by Estée Lauder and dedicated to providing financial resources for breast cancer research. The Foundation has been active since 1995, but until 2005 provided funding only for North American teams. Since then, it has financed one hundred projects per year, including 15 outside of the USA. These projects are selected by the Foundation's Scientific Advisory Board, which then contacts the investigators.

Within CLARA, the BCRF has funded an integrated research project, composed of several teams, since 2005. This project, which brings together Inserm Unit 590, Centre Léon Bérard, CNRS, Edouard Herriot Hospital, Université Claude Bernard, IARC, and the Pathology Department at Clermont-Ferrand's Centre Jean Perrin, aims to understand the role of stromal cells, namely immunocompetent cells, fibroblasts and fibrocytes, in tumor progression.

In particular, the following research programs are being funded:

- Dendritic lymphocytic infiltrates: description and prognostic impact (I. Treilleux, F. Penault-Llorca),
- Purification and functional description of plasmacytoid dendritic cells (pDC) present in primary breast tumors (N. Bendriss-Vermare),
- Purification and functional description of regulatory T-cells (Treg) present in primary breast tumors (C. Ménétrier-Caux),
- The contribution of infiltrating cells in tumor progression in 3D culture models (C. Dezutter-Dambuyant, J. Valladeau),
- The role of pDCs and Treg lymphocytes in murine models of spontaneous tumors,
- Molecular alteration of tumor cells involved in the regulation of lymphocyte infiltration (A. Puisieux, J.Hall, C. Caux),
- The role of estrogen receptor methylation (L. Corbo),
- Apoptosis of tumor cells and anti-tumor immune response (P. Mehlen, C. Caux).

The funding enabled the acquisition of a Tissue Micro-Array device and analysis software application that made it possible to analyze the stroma and lymphocyte infiltrates on a series of more than 500 patients in extension studies, linked with a database of clinical data. The project is continuing in 2007 thanks to support from BCRF, with the development of a research program on rare breast cancers.

> Corporate-funded projects: the Merck example

Merck Santé, a pharmaceuticals firm located in the Rhône-Alpes region, decided to set up a special partnership with CLARA.

After entering the French cancer treatment market in 2004 with the launch of a new targeted immunological therapy (Erbitux®, a monoclonal antibody), Merck Santé wishes to continue its development in the treatment of cancer using innovative therapies. It has organized a number of partnerships with various institutions and close collaboration with public and private research teams, thus demonstrating the company's commitment to developing and sharing its knowledge.
In addition to Merck Santé's participation in the network's Business Club, its collaboration with CLARA has led to the setup of two research projects since 2005. The first focuses on the medical practices of patients suffering from a rare malignant tumor. With €700,000 in funding, this project involves a four-year collaborative study, another sign of Merck Santé's desire to be a partner in CLARA's long-term development.
A second project, on the treatment of ENT tumors in the Rhône-Alpes region, was finalized in late 2006. This project will receive €402,500 in funding between 2006 and 2009.

The Merck Santé Headquarters in Lyon

Merck Santé is investing in the future by providing the public with innovative cancer therapies. CLARA remains a special partner, bringing together various stakeholders in the field of cancer, such as academics, researchers and representatives of the corporate world.

CLINICAL RESEARCH

INCa's Clinical Study Groups (GEC)

The Clinical Study Groups (GEC) set up by the National Cancer Institute are composed of 10 to 15 members, one-third of whom are non-French.

The missions of the GECs are as follows:

- To compile a list of all of the clinical trials open for enrolment in France;
- From these trials, to select the ones that should receive INCa support;
- To propose a trial for each indication where there is currently no study underway. This will guarantee, in the long term, that all patients suffering from cancer can take part in a clinical study.

Four of these GECs are coordinated by CLARA members:

- **Radiotherapy GEC (Françoise Mornex)**

  Started in 2005, this was the first of the 28 groups created by INCa. It is composed of 15 oncologists and radiotherapists, bringing together expertise in all of the sub-specialties of the disciplines, including representatives of SFRO, SFJRO, SNRO (French Radiologists Associations), quality control of the treatments, representatives of ESTRO and EORTC for Radiotherapy, and 3 foreign members (from Switzerland, Belgium and the UK).

  In the beginning, its activities consisted of listing French clinical trials, or those with French participation, in which radiotherapy was used. One hundred and twenty four were listed, and 74 corresponded perfectly with the definition laid out by INCa (not including support for costly innovative technology (STIC) and industry sponsors). Next, a list was compiled of the trials that the group wished to give INCa accreditation (20 trials). Trials focusing solely on radiotherapy that did not receive funding and/or promotion in the absence of assistance from the pharmaceutical industry were also listed. The group is awaiting guidelines from INCa in order to continue its activities, since not all groups have completed this final step. Updates are performed on a continual basis.

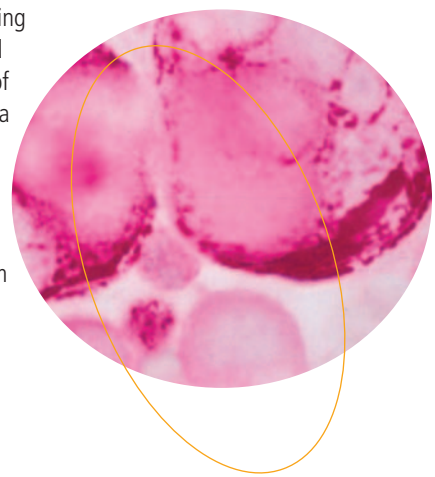
  This program is run in partnership with the SFRO, and these activities were presented in detail at the last SFRO conference (on November 15th, 2006 at the Palais des Congrès in Paris), which was attended by several INCa personalities.

- **Ovarian GEC (Isabelle Ray-Coquard)**

  Frontline ovarian cancer and relapse ovarian cancer are the two focuses of this study group.

  As regards frontline ovarian cancer, the activities focus on the following areas:
  - New adjuvant treatments;
  - Ovarian cancer and translational research;
  - Ovarian cancer, sexuality and patient quality of life;
  - Assessment of medical and surgical practices in early-stage ovarian cancer;
  - Treatment of localized ovarian cancers;
  - The role of lymphadenectomy;
  - The role of intraperitoneal chemotherapy.

  As regards relapse ovarian cancer, the activities focus on the following areas:
  - New tools for assessing the efficacy of medicines, including new therapies, and the development of new efficacy criteria (such as clinical benefit);
  - The role of surgery in relapse;
  - Redefining platinum sensitivity.



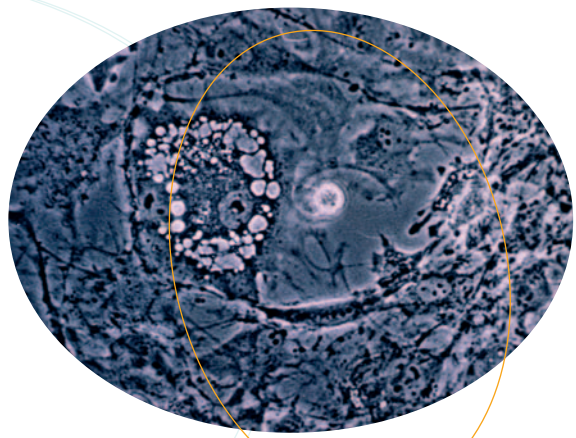
- **Oncogeriatrics GEC (Jean-Pierre Droz)**

The Oncogeriatrics GEC is composed of 8 member oncologists, hematologists and geriatricians. There are 3 foreign members (from Italy, Switzerland and the UK) in the group.

The group undertook the following activities:

- Specifying the minimum criteria that define a trial as being an "oncogeriatrics" trial. This is based, in part, on the methodology of the trial as well as on the equal participation of oncologists and geriatricians. Some form of geriatric assessment is required in these trials.
- The group took an inventory of the known studies in France that could be considered as having an oncogeriatric perspective. The catalog includes some forty studies that were analyzed either using the full protocol or the synopsis. Crosschecking was conducted in order to pinpoint these various studies, using either information from INCa or from the French National Federation of Cancer Centers, or from the groups themselves. Key leaders in the various types of tumors were contacted for this purpose. Ten trials are consistent with the definition of a clinical trial in oncogeriatrics. They have been ranked based on the specified criteria.
- A review of potential research fields is currently underway, investigating the fields of geriatric methodology that may be missing in the framework of cancer treatment. It is also focusing on the fields that are insufficiently studied in the various types of tumors.

As of today, the GEC meets 3 or 4 times per year and produces a report, a list of the trials underway and research prospects to consider.



- **Sarcoma GEC (Jean-Yves Blay)**

The Sarcoma GEC includes physicians from the French Sarcoma Group (GSF) and foreign representatives of the European Organization for Research and Treatment of Cancer (EORTC) (from Switzerland, the Netherlands, Belgium and Italy).

In 2006, the Sarcoma GEC identified and accredited 25 active protocols in France. 8 protocols are currently being set up and will be active in 2007. A Public Health research program, designed to assess strategies to improve treatment of these tumors at various stages of the disease, is currently under discussion with INCa, as part of the application to the call for proposals on Rare Tumors.

The Sarcoma GEC meets several times per year, in particular at the GSF's annual conference.

The Auvergne Rhône-Alpes Assistance Platform for Clinical Research on Cancer (PARCC-ARA)

The Rhône-Alpes / Auvergne region has created a platform to assist in the development of Clinical Research, which is one of the Research priorities of France's national Cancer Plan. CLARA and the platform have signed an agreement that makes the platform the hub of the cancer network's clinical research activities. Also joining the initiative are other partner organizations that help to conduct clinical trials in compliance with established standards, in both data management and assistance in patient recruitment and follow-up (Clinical Investigation Centers of the four University Hospitals). To date, this appears to be the only regional partnership in France that brings together all of the organizations involved in cancer clinical research.

The main mission of the platform is to increase the region's cancer clinical research potential, in both quantity and quality, by helping investigators to design, plan, coordinate, manage and analyze their clinical trials. This support falls into two categories: methodological support and operational and/or financial management of research-related activities. Another mission involves fostering the emergence of a clinical research strategy in the field of cancer and carrying out studies, so that the greatest possible number of patients has access to innovations in therapy.

In terms of accomplishments, the PARCC-ARA has provided methodological support to clinicians in the region who wish to set up a regional or national project, and, from time to time, has given financial support to help complete projects already underway.

The launching of its own projects, approved by the Steering Committee, illustrates the willingness of the PARCC-ARA to take part in identifying top-priority research topics for the region and, insofar as possible, to carry out some of this research if it does not have other sources of support.

In addition to academic research, PARCC-ARA also wishes to extend its activities to include partnerships with the corporate sector. For the time being, this primarily involves development consulting for small biotechnology firms located in the region. If the conditions are right, this partnership could lead to clinical research activities that call upon the platform's expertise.

Governance and management

GOVERNANCE

During 2006, the performance of CLARA's governance illustrated 3 key points:

1/ The system is robust and productive: it enables all partners and stakeholders - whether politicians, institutional leaders or researchers - to express their ideas on subjects within their scope of competency.

The Steering Committee ensures the coherence of the overall policy between the local authorities that provide funding for CLARA and the French State: it is truly the strategic crossroads between the regional in-the-field view and the national priorities of the Cancer Plan.

The Guidance Board took the initiative to create an Executive Board in order to help it work more effectively and develop enhanced communication with the Network Management Team.

The Finance Committee proved itself as a major body within the network. Not only does it reflect CLARA's interregional character, through the examination of all of the financial issues, but it has also developed its own multi-year vision enabling it to rise above political and institutional cleavages. In addition, by regularly requesting reports from the Network Management Team on all of CLARA's activities, it provides a stimulus to promote better monitoring, greater transparency and stronger collective energy.

The Scientific Advisory Board (SAB) has truly come into its own. Under the active and vigilant presidency of Christian Bréchot, Managing Director of Inserm, the research teams are strongly encouraged to meet the demands of international quality standards, to build new collaborative ventures with one another, to promote partnership and to use assessment methods. In practice, from session to session, the members of the SAB made recommendations for actions that have already enabled CLARA to move forward in the strictly scientific domain.

2/ The system may, nevertheless, appear bureaucratic and complex for those on the outside, and CLARA's organization is often criticized as being unclear.

Without totally denying this opinion, it seems that there are many other public organizations that are more bureaucratic than CLARA, namely the Public Interest Group (GIP) type of organization, which certain authorities seem to encourage.

3/ This governance provides structure and helps to support and bring value to the projects undertaken in the network.

Among the recommendations made by these various bodies, the key points are as follows:

- The request to begin an assessment/ benchmarking procedure, with the involvement of the funding providers, in 2007;
- The request that everyone begin thinking about the evolution and reworking of CLARA's scientific strategy in order to prepare it for new challenges, namely at the European level, and to implement a new multi-year financial contract policy;
- To provide greater support for public/private-sector initiatives and research transfer activities.

CLARA's Scientific Advisory Board

MONITORING OF PROJECTS AND PLATFORMS

Since September 2005, the Network Management Team (NMT) has been working to set up an operational system to monitor the platforms and projects. This aims to make the program more transparent, and particularly to ensure the most effective use of CLARA funding *(see the CLARA Progress Report 2005, pages 18-19).*

This monitoring process has been used to do an inventory and hierarchy of all of the projects currently underway. It has produced its first results, as it has directly contributed to the following achievements:

- Monitoring of the Network Management Team's projects by drafting an action plan and project review on a bi-monthly basis. The reports are then sent on to the Finance Committee.
- Building a database of all CLARA research projects that received INCa funding during the 2003-2006 period.
- Publishing a guide on procedures and funding for the Auvergne region and a chart of the funding procedures for the Clermont-Ferrand and Grenoble platforms.
- Developing performance indicators for CLARA platforms and pilot activities for the South Lyon, East Lyon and Grenoble platforms.

One example of a performance indicator chart (Network Management Team, bi-monthly review, November 28th, 2006)

Cancéropôle Lyon Auvergne Rhône-Alpes Management chart for the CLARA program			November 28th, 2006 – Version 3	
NMT projects			LEVEL OF RISK: Low / Medium / High	
NMT Projects		**Risk**	**Situation**	**Decision / Action**	**Aim**
Calls for Projects	INCa Calls for Projects		• Calls for Projects 2006: 33 calls for projects compared to 5 in 2005. To date, 27 projects published, including 7 since June 2006. Next calls for projects not handled by CLARA. • Handling: 73 projects filed via CLARA in 2006, including 46 since 06/23/06. • Convention in preparation for Partnership with University of Lausanne and Milan Tumor Institute as part of Europe Twinning Call. • INCa considering allocating 7% of funding for calls for projects to project management.	• Finalize database (XLS and ACCESS) of CLARA projects funded by INCa • Prepare for transfer of management of INCa funding by CLARA team. • As part of the INCa call for Projects entitled Mobile Clinical Research Teams (EMRC): specify joint position for DIRC, networks (Oncora, Concorde, Oncauvergne, Arc Alpin, Oncoloire) ARH and CLARA on the CRAs at general public hospitals and, if possible, at private centers.	• To incorporate the projects selected in the 2006 calls for projects in CLARA's monitoring program.
	European Calls for Projects		• 7th FPRTD: 20 project lines related to CLARA activities identified (14 Cancer topic lines + 6 Healthcare topic lines). 6 project initiators found, including 3 multidisciplinary projects mainly in Lyon. The process for answering CFPs specified. Note on CLARA's 7th FPRTD policy written. Meetings held with Europe units (Inserm Transfert, Esus and CNRS). Training run by SB on the 7th FPRTD.	• 7th FPRTD: Implement action plan and share it with CLARA management (12/01/2006). Prepare for meetings planned for 12/06/2006 at CLB and 12/07/2006 at UJF. Collect project sheets to send to national contact.	• Position CLARA projects on priority topics prior to 7th FPRTD calls for projects. • If necessary, implement specific CLARA actions at European level by complementing work of Europe units already set up (and by informing them of CLARA actions)
	Other Calls for Projects		• RTRS-CTRS Cancer file: Setup of application launched by HCL (G. Salles), CLB (A. Puisieux) and Lyon 1 with CLARA funding (support from Algoé). Filing with Ministry of Research December 22nd, 2006. • Carnot Label File: Call for projects launched – deadline: 12/20/2006	• RTRS-CTRS Cancer file: Quickly mobilize directors of RTRS-CTRS founding and partner institutes to specify respective contributions and budget. Identify industrial partners that can be involved in project. • Carnot Label file: specify relevancy of CLARA support to set up candidacy file.	• RTRS-CTRS Cancer file: Emphasize CLARA momentum in Lyon to leverage funding for Cancer.

The performance indicator chart is created using information from one-to-one interviews with the members of the Network Management Team held before the review meeting. This analysis and summary of the projects helps to pinpoint the main achievements and highlight the points to be dealt with together during the project review meeting.

This process does not aim to analyze all of the key events listed in the Master Plan, but rather to focus on a given period: two months before and two months after the review meeting.

The agenda of the review meetings is determined based on the main risks to be dealt with as shown by the performance indicators. This analysis of the risks for a given period helps to anticipate difficulties that lie ahead, to make a hierarchy of them and to generate potential solutions.

A short-term action plan for the project team is determined during the review meeting and summarized in the list of decisions. This meeting, based on a "decision-action" approach, enables each member of the team to leave with their own roadmap of the subjects discussed.

FUNDING

Cancéropôle Lyon Auvergne Rhône-Alpes has distinguished itself from the 6 other cancer research networks, thanks to the amount of multi-year funding granted by its local authorities, in particular those of Rhône-Alpes (the Region, Greater Lyon, the Rhône County, the Loire County and Saint-Etienne Métropole) and, to a lesser degree, those of Auvergne (the Region, Clermont Community and the Puy-de-Dôme, Allier, Cantal and Haute-Loire counties).

Concerning Rhône-Alpes, most of the funding is earmarked for investments (equipment and construction) for the platforms. Greater Lyon significantly contributes to the Proof of Concept program *(see pages 12 and 13)*. In Auvergne, we can observe a better balance between funding for investments and funding for operating expenses. The research projects are funded by the French State, via INCa, following competitive calls for projects *(see page 23)*. The various funding providers are thus complementary.

Summary of the multi-year scheduling of the CLARA program, 2003-2006

- **Status of the main sources of funding in the Rhône-Alpes area**

Liberté • Égalité • Fraternité
RÉPUBLIQUE FRANÇAISE

AMOUNT IN THOUSANDS OF €	2006					TOTAL	
Recipient (funding)	**Investment approved**	**paid**	**Operation approved**	**paid**	**Total paid**	**Overall total approved 2003-2006**	**Overall total paid 2003-2006**
High-field NMR (MENRT)		1 170,00			1 170,00	5 400,00	3 240,00
Emerging cancéropôles (MENRT)						3 923,00	2 900,70
INCa calls for projects (INCa)*			2 669,00			6 145,00	1 530,00
Proof of Concept (DRRT RA)						37,00	37,00
Biological Resource Center (FNADT RA)						108,00	108,00
HCL: University hospital for Biological Resource Center (Ministry of Health)						1 027,00	1 027,00
Network Management Team (FNADT RA)						216,00	216,00
Network Management Team (INCa)			350,00	350,00	350,00	700,00	700,00
Total		**1 170,00**	**3 019,00**	**350,00**	**1 520,00**	**17 556,00**	**9 758,70**

* The amount shown for INCa includes the amounts granted to scientific projects selected in the 2006 calls for projects. These sums will be paid over several years.

RhôneAlpes Région

AMOUNT IN THOUSANDS OF €	2006					TOTAL	
Recipient	**Investment**		**Operation**		**Total paid**	**Overall total approved 2003-2006**	**Overall total paid 2003-2006**
	approved	**paid**	**approved**	**paid**			
Grenoble University Hospital	528,00	169,00			169,00	1 347,76	717,76
Joseph Fourier University	878,00					1 963,00	352,00
Inserm Grenoble	70,00					453,00	345,00
Subtotal Grenoble	**1 476,00**	**169,00**			**169,00**	**3 763,76**	**1 414,76**
Saint-Étienne University Hospital	410,00					410,00	
High-field NMR	1 500,00	450,00			450,00	7 000,00	4 105,00
Proof of Concept			260,00	260,00	260,00	260,00	260,00
Network Management Team			520,00	520,00	520,00	2 144,00	1 464,00
Total	**3 386,00**	**619,00**	**780,00**	**780,00**	**1 399,00**	**13 577,76**	**7 243,76**

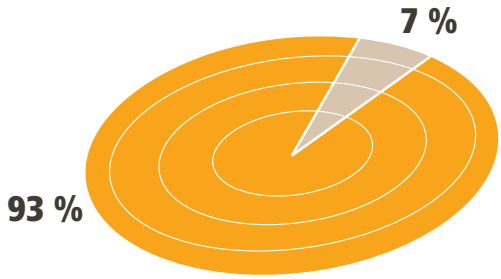
RHÔNE
LE DÉPARTEMENT

AMOUNT IN THOUSANDS OF €	2006					TOTAL	
Recipient	**Investment**		**Operation**		**Total paid**	**Overall total approved 2003-2006**	**Overall total paid 2003-2006**
	approved	**paid**	**approved**	**paid**			
Centre Léon Bérard - East Lyon		900,00			900,00	7 500,00	900,00
Network Management Team				600,00	600,00	1 651,00	1 151,00
Total		**900,00**		**600,00**	**1 500,00**	**9 151,00**	**2 051,00**

GRANDLYON
communauté urbaine

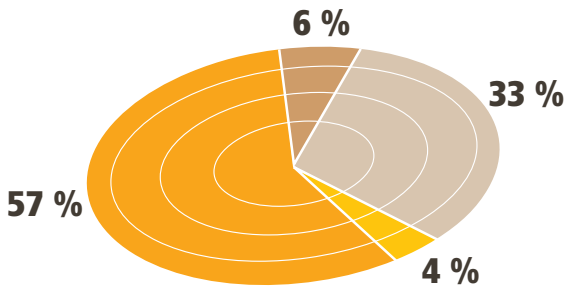
AMOUNT IN THOUSANDS OF €	2006					TOTAL	
Recipient	**Investment**		**Operation**		**Total paid**	**Overall total approved 2003-2006**	**Overall total paid 2003-2006**
	approved	**paid**	**approved**	**paid**			
Lyon Civil Hospitals		2 000,00			2 000,00	8 500,00	4 000,00
IARC				120,00	120,00	500,00	470,00
High-field NMR						2 350,00	2 350,00
Proof of Concept			550,00	440,00	440,00	900,00	790,00
Network Management Team						964,00	920,00
Total		**2 000,00**	**550,00**	**560,00**	**2 560,00**	**13 214,00**	**8 530,00**

Allocation of the funds approved by the main funding providers during the period 2003/2006
(not including high-field NMR)



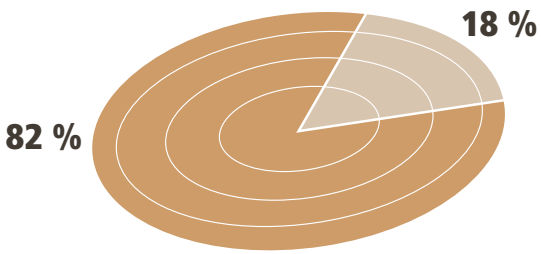
Emerging cancéropôles + INCa

Network Management Team
Scientific Projects



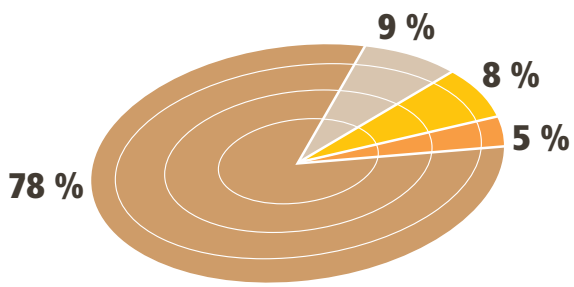
Rhône-Alpes Region

Saint-Étienne Platform
Proof of Concept
Network Management Team
Grenoble Platform



Rhône County

Centre Léon Bérard
Network Management Team



Greater Lyon

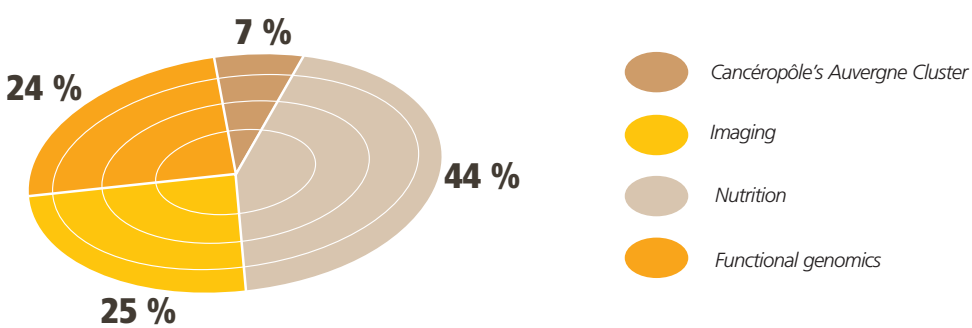
Lyon Civil Hospitals
Proof of Concept
Network Management Team
IARC

• **Status of the main sources of funding in the Auvergne area**

AMOUNT IN THOUSANDS OF €	2006				TOTAL	
Funding provider	**Investment approved**	**paid**	**Operation approved**	**paid**	**Total paid**	**Overall total approved 2003-2006**	**Overall total paid 2003-2006**
Massif Central ERDF*						945,00	
Region ERDF	600,00					600,00	
Massif Central FNADT						505,00	
Auvergne Region			600,00			800,00	
Clermont Community	100,00					200,00	
Puy-de-Dôme County						100,00	
Allier County						50,00	
Cantal County						40,00	
Haute-Loire County						40,00	
Total	**700,00**		**600,00**			**3 280,00**	

* Massif Central ERDF covers Auvergne and Loire County.

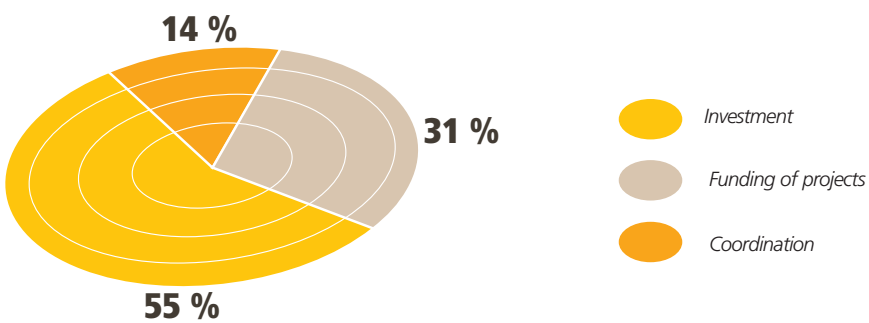
Allocation of the funds granted during the period 2003/2006



Overall orientation of funding by type of operation
(not including high-field NMR)

TYPE OF OPERATION	BREAKDOWN	AMOUNT 2006 IN THOUSANDS OF €	OVERALL 2003/2006 IN THOUSANDS OF €
Funding of projects	Biological Resource Center		1135
	Proof of Concept	810	1197
	International Agency for Research on Cancer		500
	Emerging cancéropôles + INCa projects	2669	10068
	Total	**2865**	**12900**
Investment	Léon Bérard Cancer Center		7500
	Lyon Civil Hospitals		8500
	Grenoble Platform	1476	3764
	Saint-Étienne Platform	410	410
	Clermont-Ferrand Platform	1300	3280
	Total	**3186**	**23454**
Coordination	Network Management Team	870	5675
	Total	**870**	**5675**

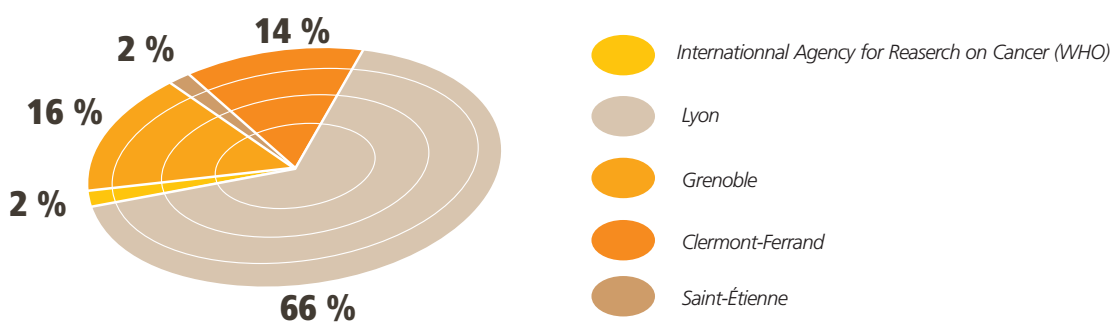
Orientation of funding during the period 2003/2006



Geographical breakdown of funding

SITE	AMOUNT 2006 IN THOUSANDS OF €	OVERALL 2003/2006 IN THOUSANDS OF €
Lyon		16 000
International Agency for Research on Cancer (WHO)		500
Grenoble	1 476	3 764
Saint-Étienne	410	410
Clermont-Ferrand	1 300	3 280
Total	**3 186**	**23 954**

Breakdown of funding during the period 2003/2006



Scientific coordination

Scientific coordination is one of the top priority missions that INCa has set for France's cancer research networks. CLARA's Network Management Team and Scientific Directors handle this mission through the activity of 2 clubs that bring together the major categories of members and organize scientific events of various scales.

THE CLUBS

The Business Club

In 2006, the Executive Board of the Business Club continued to play an active role in running the Proof of Concept program, namely in the assessment of the projects *(see pages 12 and 13)*.
However, after 3 years of work, the Executive Board decided it was time to redefine its role and readjust its missions and priorities. With this in mind, a plenary meeting of the Business Club was held in Lyon on December 18th. This session brought together some thirty representatives of pharmaceutical laboratories, small biotech companies, service companies, and consulting and financial services firms.
After a review of its past accomplishments, its strengths and weaknesses, the needs and expectations of its members and of the Network Management Team, new focuses for action were laid out:

- The "club" philosophy was to be strengthened, with more meetings and discussions between corporate representatives;

- The need to develop an industrial lobbying activity, in order to demonstrate the progress accomplished to funding providers and widen the European horizons of the industrial interests beyond the scope of the Rhône-Alpes/Auvergne regions;
- The development of frequent contacts with the Academic Club in order to encourage synergy and foster, in the long term, the "hybridization", even the merging, of the two spheres;
- New elections for the President and the Executive Board *(see Web site, Structure section)*.

The Academic Club

The Academic Club, which entered into action in early 2006, took on the mission of promoting scientific forums and collaboration within the CLARA community. In this capacity, it invested much time and energy in organizing and providing support for scientific events.

The Club's Executive Board *(see Web site, Structure section)* is the forum that enables the sharing of projects that may be of interest to stakeholders in the network's geographic area. One priority it has set for 2007 is strengthening relations with the Business Club.

EVENTS

The First Scientific Forum

CLARA's first Scientific Forum was held March 16th-17th 2006 in Clermont-Ferrand, at the Vulcania facility. The Forum presented more than 175 scientific projects to some 300 cancer research experts from the Rhône-Alpes and Auvergne regions, and helped CLARA to start building network momentum for the long term.

Moreover, with the attendance of Gérard Escher, the Swiss Confederation's Vice Director of the State Secretariat on Education and Research, who gave a presentation on how research is organized in his country, CLARA demonstrated its desire to open up to cross-border collaborative projects, particularly with nearby Switzerland.

This Scientific Forum was a true rite of passage that everyone on hand deemed a success. It signaled the transition from CLARA's organization and setup phase, centered on the major research focuses to be explored at the platforms, towards a phase of project implementation and international cooperation.

CLARA Forums

The 3rd CLARA Forum was held at Grenoble's Institut Albert Bonniot on June 27th, 2006. It brought together some sixty participants, from both the academic and business spheres, for the presentation of 7 collaborative projects.

A special focus was placed on proteomics, the Grenoble platform's most prominent research topic, with presentations by Pierre-Antoine Defossez, a researcher in epigenetics at the Institut Curie, and by Peter Friedl of Würzburg University in Germany.

NETWORK DYNAMICS

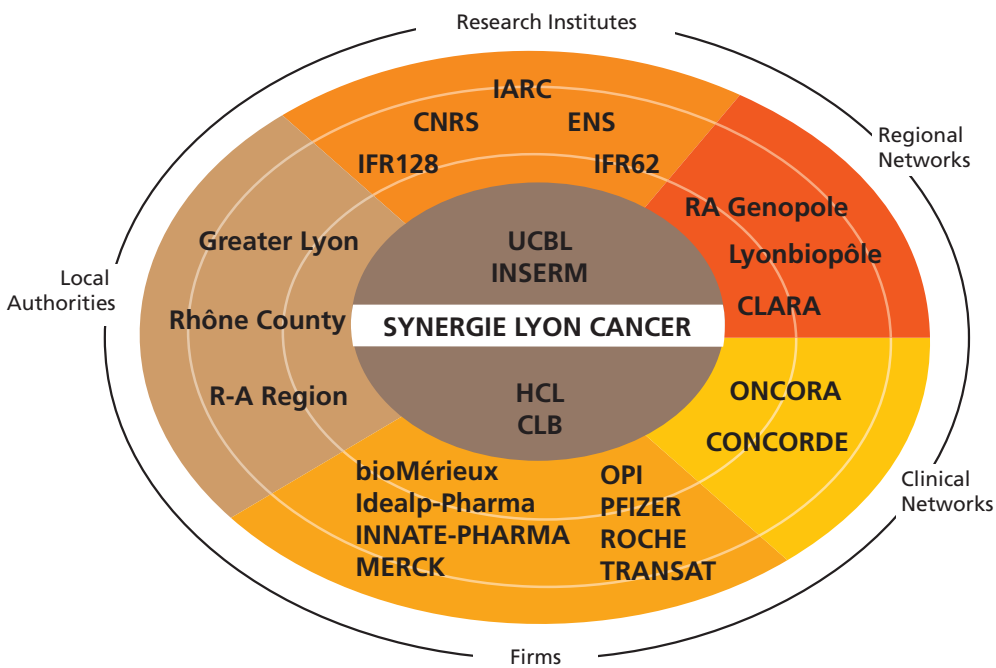
Candidacy of the "Synergie Lyon Cancer" RTRS-CTRS research and care network

The Research Program Law of April 18th, 2006 created three distinct new entities that aim to encourage research teams to combine their activities in order to boost their potential and become more visible on the international scene. These entities are the Higher Research and Education Clusters (PRES), the Advanced Research Theme Networks (RTRA) and the Research and Care Theme Centers or Networks (RTRS-CTRS).

To make cancer research a part of this new drive, CLARA provided support in preparing the application file initiated by Université Claude Bernard and Lyon-based cancer research teams in reply to the RTRS-CTRS call for proposals that closed on December 22nd, 2006. One aspect of this support involved funding a consulting firm to help design and prepare the project.

Led by project managers Gilles Salles, Alain Puisieux and Patrick Mehlen, the project application entitled *"Synergie Lyon Cancer - Therapeutic targeting and tumor escape"* mobilized the members of 21 Lyon research units, teams of clinicians at Lyon Civil Hospitals (HCL) and Centre Léon Bérard (CLB) and senior management at the founding organizations and partners, in order to submit a high quality project to the Ministry of Higher Education and Research.

On February 6th, 2007, the national body responsible for examining candidate projects ranked the Lyon initiative among the projects to receive funding in 2007. As a result, a Scientific Cooperation Foundation (FCS) will soon be created and will have an ambitious budget, estimated at €9.6 million for the period 2007/2011.



The MIMACAN project

As part of the second call for applications sent out by the National Research Agency (ANR) for attribution of the Carnot Label, CLARA joined the MIMACAN project, headed by Jean-Yves Scoazec (Unit 865 "Digestive endocrine tumors: tumorigenesis and tumor progression mechanisms").

This project aims to provide the scientific and technological tools that are necessary for the industrial transfer of fundamental research findings on the mechanisms of metastatic invasion and spreading. This involves setting up an integrated organization focusing on Modeling, IMAging and targeting tumor progression in CANcer (MIMACAN). This project features a unique positioning thanks to:

- The multidisciplinary nature of the players involved;
- The complementary approaches to be used;
- Proven know-how in partnerships with industry and socio-economic stakeholders, illustrated by major successes;
- Support from a dense cancer research network and high-performance, professionally managed technological platforms, ensuring that the project will have the resources and capacities to successfully meet the scientific and technological challenges to be faced;
- Continuity with a hospital sector that is highly involved in clinical research in the field of cancer;
- The region-wide program of collaborative projects between academic and industrial partners, encouraged by CLARA and Lyonbiopôle.

MIMACAN brings together 20 laboratories and platforms, with a total of 380 research staff. Its governance is consistent with both the national policy on organizing research and with the local and regional specificities of the Institute. Indeed, the governance system actively involves the parent institutes and organizations, as well as the national and international players through Lyonbiopôle, CLARA and a high level of participation from the industrial sector, ensuring that supply is consistent with demand.

Coordination of INCa's "Mobile Clinical Research Teams" call for proposals

In November 2006, INCa launched a call for projects aiming to set up "Mobile Clinical Research Teams" (EMRC) to address the need to dynamize clinical research and thus encourage patients to participate in therapeutic trials.
This involves providing funding to recruit additional clinical research staff whose mission is to help investigators in tasks related to clinical trials, in order to reach a 10% inclusion rate in the studies.

This call for proposals targets healthcare centers that are neither University Hospitals (CHU) nor Regional Cancer Centers (CRLCC), but that have indeed undertaken clinical research activities in the field of oncology, which need support in terms of clinical research assistants or technicians, and that were not concerned by the last EMRC call for projects in 2004, which focused on reference centers. The targeted organizations participate in regional cancer networks, either working as part of, or on behalf of, a Cancéropôle.

After consulting with the Rhône-Alpes-Auvergne Interregional Clinical Research Division (DIRC) and the Regional Hospitalization Agency (ARH), CLARA offered to participate in consulting with the interested players in both regions, with a view to ensuring the consistency of the proposals, or even preparing a joint proposal, as suggested in the DHOS Circular dated November 7th, 2006.

CLARA contributed by bringing together representatives of the CHUs, CRLCCs, cancer networks and PARCC-ARA. The participants agreed to promote a joint project for the call for proposals, to be headed by CLARA. The parties agreed that this approach could boost the chances of success of each organization involved, as well as improve the efficiency, visibility and consistency of clinical research in the field of cancer throughout both regions.

More information

CRLCC: Regional Cancer Centers - DIRC: Interregional Clinical Research Division - ARH: Regional Hospitalization Agency - DHOS: Hospitalization and Healthcare Organization Division - PARCC-ARA: Auvergne Rhône-Alpes Assistance Platform for Clinical Research on Cancer

INTERNATIONAL AMBITIONS

Stronger links with Lausanne and Milan

In the first quarter of 2006, INCa offered the cancer research networks support for bilateral collaborative projects that encouraged twinning them with major research centers throughout Europe. This program will give several research teams from a given cancer research network the opportunity to develop joint research projects on cancer biology with teams from a research center or coordinating organization similar to a cancer research network in a neighboring European country.

Each project is funded by INCa based on the need to involve one or two post-doctoral students for a period of 2 to 3 years, with the understanding that the European partner is committed to investing in the project with an equivalent level of funding over the same period of time.

The call for projects launched by CLARA drew 9 applications, which were studied by members of CLARA's Scientific Advisory Board. In the end, two projects were selected.

The first, involving a collaborative project with the Milan Tumor Institute, was initiated and headed by Christian Brambilla, director of Inserm Unit 578, as part of a project entitled *Validation of apoptosis and cell cycle parameters as biomarkers for lung cancer early detection.* The second collaborative project, with the University of Lausanne, was initiated by Patrick Mehlen, director of the Centre Léon Bérard / Université Lyon 1 CNRS mixed research unit on "Apoptosis, Cancer and Development", as part of a project entitled *The dependence receptor signaling pathway and colorectal tumor progression.*

These two projects will receive €125,000 in INCa funding in 2007. This support can be renewed as part of a broader twinning program.

Preparing for the FP7

The European Union can be an important source of funding for research. In the race to obtain European funding, CLARA brings a number of clear assets into play.

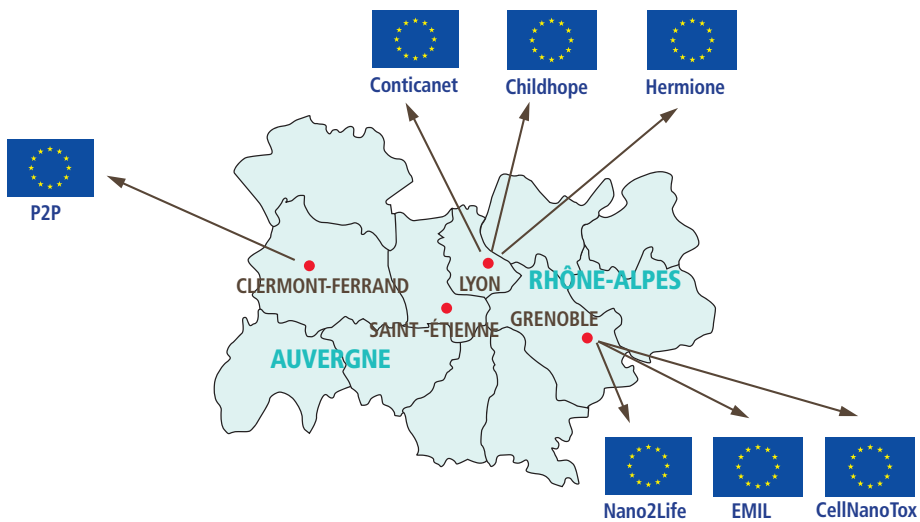
- **Community-wide renown: a driving force**
  The renown of the Rhône-Alpes/Auvergne region in three key topic areas, Nanotechnology, Oncology and Virology, is made even stronger thanks to the presence of European networks of excellence with local leadership: Nano2life, coordinated by the Grenoble office of the French Nuclear Energy Commission (CEA)(Patrick Boisseau), VIRGIL, coordinated by Inserm (Fabien Zoulim), and Conticanet, coordinated by Université Claude Bernard Lyon 1 (Jean-Yves Blay).

  These networks generate a high level of visibility throughout Europe and the Commission relies heavily on them to organize research throughout the EU and the European Research Area (ERA).

  The involvement of the Nano2Life and Conticanet networks in European technological platforms Nanomedicine and Innovative Medicine Initiative (IMI) respectively brings the region's members added influence and stature in developing EU scientific strategies.

Finally, Conticanet is a serious contender (listed in the IMI platform's Strategic Research Agenda) for managing the development of a European Center for Rare Tumors.

The participation of CLARA members in European Union projects illustrates recognition of their scientific quality by the Commission as well as their motivation for European research.



CLARA members involved in the European sphere (6th FPRTD)

Building relations with the Weizmann Institute

The Weizmann Institute is an internationally renowned scientific institution with more than 1,000 researchers in a variety of disciplines (life sciences, mathematics, physics, the environment, etc.) including Cancer.

The idea of a collaborative project between the Rhône-Alpes region and the Weizmann Institute in the field of Cancer emerged during a visit to the Weizmann Science Institute on May 31st, 2006, as part of the Biomed exhibition in Jerusalem. This trip was organized for firms and representatives of Rhône-Alpes by the France-Israel Rhône-Alpes Chamber of Commerce and Industry. The subject of this collaboration was raised during interviews with Michaël Séla, former President of the Weizmann Institute.

In September 2006, a meeting was held under the joint authority of Alain Mérieux, President of the Rhône-Alpes delegation of Weizmann France Europe, François Gros, President of Weizmann France Europe and Bernard Winicki, Governor Emeritus of the Weizmann Institute, promoter of the project. It aimed to lay out a strategy that would enable the parties to build productive long-term scientific and industrial collaboration in the field of cancer research, associating the Weizmann Institute in Rehovot (Israel) and the Rhône-Alpes region.

The parties decided that the first step would be to identify Rhône-Alpes research teams interested in developing such a collaborative project. In March 2007, there will be a mission to discuss this collaboration in greater detail and find means of financial support.

CLARA BOOSTS ITS COMMUNICATION

In order to position itself as a reference in the fight against cancer, CLARA set a dual objective in 2006: to implement the tools enabling it to develop and support its strategy and to strengthen its image both inside and out.

Reorganization of the Website

In order to make the Website an effective tool to help the scientific strategy of CLARA and the research community:

1/ Two new sections were created:
- A "Research" section that clearly presents the main lines of CLARA's scientific strategy, its platforms and the programs underway. All site visitors can access this section.
- A "Calls for Projects" section listing all of the calls issued by major agencies and associations.

2/ The presentation of CLARA's organization and its bodies has been completely reworked (the "Structure" section).

3/ The "Current Issues" and "Events" sections have been enriched.

4/ A "Focus" column, included on every page, offers visitors the latest news at a glance.

Readers are encouraged to visit the site at www.canceropole-clara.com

A new visual identity

1/ The logo has been reworked to simplify the CLARA name and emphasize its mission:
- Targeting cancer, represented by the red dot encircled by the C in Cancéropôle;
- Becoming a reference in the fight against cancer, symbolized by the waves sent out around CLARA, originating from the research sphere and arriving at the patient.

The target also symbolizes advances in research: it brings to mind new "targeted" therapies, which attack only tumor cells, leaving the normal cells intact.

CANCÉROPÔLE
LYON AUVERGNE RHÔNE-ALPES
sous l'égide de la Fondation L&N Bullukian

→

CLARA
CANCÉROPÔLE LYON AUVERGNE RHÔNE-ALPES

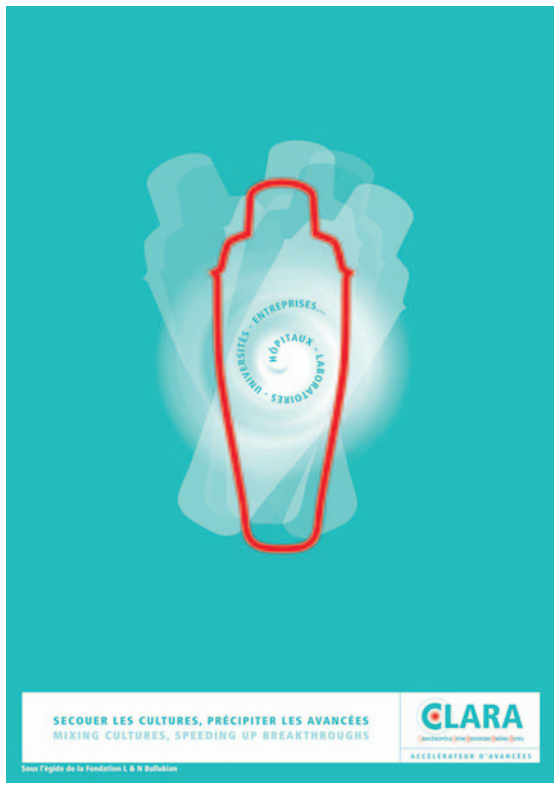
2/ CLARA developed a new baseline, "Speeding up progress", in order to better position itself in relation to other players in the fight against cancer.
This baseline perfectly illustrates the full scope and energy of CLARA's mission. Speeding up progress means acting as a research catalyst, encouraging new initiatives, supporting projects, bringing scientists and stakeholders together, opening gateways between the culture of science and that of industry, encouraging the sharing of knowledge, and much more.

3/ A graphic charter has been specified in order to ensure the consistency of the communication media that convey CLARA's messages and information.

The "Mixing Cultures" advertising campaign

The advertising campaign launched by CLARA is based on the concept of mixing cultures, symbolized by the cocktail shaker. Mixing and shaking up cultures means ensuring that the culture of knowledge - the realm of universities, hospitals and research centers - meets and combines with that of the industrial sphere. This helps to encourage cooperation between the academic and business worlds in order to speed up the transfer of research findings to routine treatment of patients.
Mixing cultures also means enriching fundamental and clinical research with a social and human science perspective.
CLARA is proud to position itself as a network that "breaks down borders". In this capacity, it aims to develop research focus areas at the crossroads between various disciplines *(see pages 8 to 11).*
Encouraging multidisciplinarity and mixing cultures, with a view to generating new advances based on existing knowledge and thus speed up breakthroughs: this is CLARA's ambition.

These messages are already being conveyed via the institutional brochure, launched at the December 4th, 2006 Steering Committee meeting, and the Flash animation that illustrates the shaker concept, which was sent out to the entire network by e-mail.



Action plan for 2007

The 2006 review of CLARA's progress and the strong local and regional mobilization of the main players in the field of cancer research open up important, promising perspectives.

In light of the new scientific cooperation foundation, *"Synergie Lyon Cancer - Therapeutic targeting and tumor escape"*, to be established in Lyon as a result of the RTRS project, and given the national reorientation of INCa towards translational research, CLARA's members will need to debate their shared vision for the future. This will serve as a springboard for the transformation of the Cancéropôle and a new contract with funding providers for the years 2007-2011.

Likewise, the powerful assets of the region's competitive clusters, Minalogic in Grenoble and Lyonbiopôle, will help to identify and develop truly innovative and attractive projects in the field of cancer research.

In these areas:

- Research and the establishment of a critical mass must always be encouraged and promoted - scientific excellence must be strongly boosted, including an active policy to attract the best talent, and constantly assessed in a spirit of healthy competition measured against the most relevant international standards;
- The resources for mobilizing, managing and supporting the powerful cancer research network that is being built before our very eyes must be brought together and greatly strengthened beyond institutional borders, which are ill-adapted to the challenges of globalization and the mixing and sharing of all knowledge. In addition, the governance must be overhauled and simplified; otherwise, the network risks suffocating from its own complexity.

CLARA, a humble organization, aims to be a part of this shared ambition and to work to meet these aims. In 2007, the network will strive to fully participate in the current development. The concrete actions in which it already participates, to various degrees, are as follows:

- Finalizing a panorama of the Rhône-Alpes/Auvergne region's assets in cancer research, to be completed in the first half of 2007;
- Supporting the creation of a network in the human and social sciences;
- Working more closely with the ETOILE project;
- Providing logistical support for the teams selected to build special project application files (calls for projects from the Ministry of Research, the European Commission and the Ministry of Health);
- Firming up the association with the "Synergie Lyon Cancer - Therapeutic targeting and tumor escape" RTRS project from an operational and scientific standpoint.

APPENDICES

APPENDIX 1: PROJECTS SELECTED BY INCa IN 2006

"European collaborative projects on various topics" / March 2006

- *The dependence receptor signaling pathway and tumor progression.*
  Patrick Mehlen - CNRS, Centre Léon Bérard, Université de Lyon
  €50,000 over 2 years
  Functional genomics - East Lyon

- *Validation of apoptosis and cell cycle parameters as biomarkers for lung cancer early detection.*
  Christian Brambilla - Inserm, Université Joseph Fournier
  € 75,000 over 2 years
  Clinical research - Grenoble

Post-doc / June 2006

- *A phase I/II multicenter study on the efficacy and safety of imatinib in adult patients with aggressive fibromatosis (AF) who cannot be treated by surgery or curative radiotherapy: definition of morphological response and identification of biological parameters to predict efficacy.*
  Jean-Yves Blay - Inserm/Centre Léon Bérard/Hospices Civils de Lyon
  € 40,000 over 1 year
  Clinical research - East Lyon

- *3ABrD: a new organization factor for the epigenome related to cancer.*
  Cécile Caron - Inserm
  Functional genomics - Grenoble

- *The role of dependence receptors in the cancerization process.*
  Charles Dumontet - Inserm
  Functional genomics - East Lyon, Grenoble

- *A study on the interest of combining cytology and molecular markers in the diagnosis of renal tumors in adults.*
  Christian Genin - Saint-Étienne University Hospital
  €80,000 over 2 years
  Clinical research - Saint-Etienne

- *The role of Apollo nuclease, a protein recently found to interact with TRF2, in the protection of human telomeres and tumorigenesis.*
  Éric Gilson - ENS
  Functional genomics - South Lyon

- *Translational research: incorporating pharmacokinetic and pharmacodynamic data in the design and follow-up of clinical trials.*
  François Gueyffier - Inserm
  €80,000 over 2 years
  Clinical research - East Lyon

"Projects on various topics" / June 2006

- *CirBioCancer Circulating Free DNA in plasma as a Biomarker for Cancer detection, progression and outcome.*
  Alain Puisieux - Centre Léon Bérard
  €240,000 over 2 years
  IARC, East Lyon

- *Analysis of secreted and targeted proteins from non-small cell lung cancers for the identification of new seric biomarkers.*
  Michel Seve - Université Joseph Fournier/Inserm
  €155,000 over 2 years
  Grenoble

- *Role of Autotaxin in breast cancer growth and metastasis.*
  Olivier Peyruchaud - Inserm
  €390,000 over 2 years
  East Lyon

- *Tumor targeting via genetically-modified cytotoxic t cells: A strategy for adoptive immunotherapy of leukemias.*
  Raphaël Rousseau - Centre Léon Bérard/Inserm
  €150,000 over 2 years
  East Lyon, Grenoble

"Detection of innovations in the field of Cancer" /June 2006

- *A microbiosensor for multi-parameter quantitative detection of tumor cells.*
  Claude Lambert - École nationale des Mines
  €100,000 over 1 year
  Saint-Étienne

- *A miniature scintillating endoscopic probe (endoscint).*
  Olivier Tillement - Université Claude Bernard Lyon 1
  €150,000 over 18 months
  East Lyon

- *A new anti-metastatic treatment for breast cancer by inhibiting netrin/receptor interaction.*
  Patrick Mehlen - CNRS
  €220,000 over 2 years
  Biotherapy - East Lyon

- *Optimization and validation of new chemical protein kinase CK2 inhibitors.*
  Claude Cochet - Inserm, CEA
  €150,000 over 2 years
  Biotherapy - Grenoble

Doctoral candidate projects / June 2006

- *Digital modeling of angiogenesis during cancer processes.*
  Jean-Yves Scoazec - Inserm
  Biotherapy - East Lyon, South Lyon

- *A comparative analysis of anti-cancer strategies in France and Great Britain.*
  Monika Steffen - IEP Grenoble
  €58,000 over 3 years
  Public health - Grenoble

- *The role of oxydant and antioxydant (csH) systems in tumor response to photo and light ion radiation therapy: digital simulations and measurements for an ENT squamous carcinoma cell model.*
  Claire Rodriguez-Lafrasse - Université Claude Bernard Lyon 1
  East Lyon, South Lyon

"Processes and perspectives for developments in cancer clinical research" / June 2006

- *A sociological analysis of physician participation in clinical research. A comparison of three randomized multicenter trials.*
  Patrick Castel - CNRS/Centre Léon Bérard
  €142,000 over 2 years
  Public health - East Lyon

Proteomics & Cancer "Innovations and development of new proteomics strategies in the search for tumor biomarkers"

- *Mining the hidden CSF proteome using a novel technique: equalization with ligand library beads: application to carcinomatous meningitis.*
  François Berger - Inserm
  €70,000 over 1 year
  Functional genomics - Grenoble

"Better understanding for better action: differential determining factors for occurrence, treatment and outcomes of cancers in France. For shared observation of cancers at the regional level."

- *Isère Cancer Registry. A descriptive study of the determining factors for treatment and breakdown by stage of diagnosis for lung cancers in France in 2004: a study of the general population using 2,000 cases from 10 French cancer registries.*
  Patricia Delafosse
  €72,000 over 2 years
  Public health - Grenoble

"An economic analysis of the use of expensive molecules in oncology"

- *An ex post and ex ante analysis of the use of expensive molecules in oncology. The case of Taxanes in the treatment of breast cancer.*
  Marie-Odile Carrere
  €47,000
  East Lyon

"Hospital platforms - Improving quality of care and access to innovations"

- **Jean-Paul Segade** - Clermont Ferrand University Hospital
  €100,000
  Clermont Ferrand

- **Bernard Rousset** - Hospices Civils de Lyon
  €300,000
  East Lyon

For more details on the projects listed above, please see the Research section of the CLARA website at www.canceropole-clara.com

APPENDIX 2: PHRC PROJECTS

- *The search for genetic factors creating predisposition to multiple myeloma.*
  C. Dumontet - Hospices Civils de Lyon (HCL)

- *A fag-3 multicenter trial: Treatment of patients over 70 years of age with advanced ovarian cancer by carboplatin: is assessment of vulnerability using a psycho-geriatric and epigenetic approach (telomeres) predictive of overall safety and survival?*
  G. Freyer - Hospices Civils de Lyon (HCL)

- *Applying medical imaging techniques to implant surgery in cancer in order to make the procedures less invasive.*
  R. Gourmet - Centre Léon Bérard, Lyon

- *Validation of a molecular screening test for differentiated thyroid cancer by analyzing transcriptome using fine-needle aspiration biopsy equipment: a prospective study.*
  B. Rousset - Hospices Civils de Lyon (HCL)

- *Superficial bladder tumors: Histological (validation phase) and prognostic (pilot phase) molecular signatures - Immunohistological application.*
  A. Ruffion - Hospices Civils de Lyon (HCL)

- *Setup and assessment of a patient education program, applied to treating fatigue in cancer.*
  F. Chauvin - Saint-Etienne University Hospital

APPENDIX 3: PROJECTS SELECTED AS PART OF THE STIC 2006 PROCEDURE IN ONCOLOGY

- *A medical/economic assessment of 3D image-guided radiotherapy in prostate cancers.*

  Medical coordinator: Dr Renaud de Crevoisier - Institut Gustave Roussy
  Economics coordinator: Professor Marie-Odile Carrere - GRESSAC Lyon

APPENDIX 4: EUROPEAN PROJECTS

- *CONTICANET*
  Jean-Yves Blay - Université Claude Bernard Lyon 1
  €9.5 million over 5 years
  launched in February 2006

- *ChildHope*
  Raphaël Rousseau - Centre Léon Bérard, Lyon
  €3.2 million over 4 years
  launched in November 2006

- *HERMIONE*
  Patrick Mehlen - Centre Léon Bérard, Lyon
  €2.4 million over 3 years
  launched in November 2006

- *P2P*
  Yves-Jean BIGNON - Centre Jean Perrin
  Clermont-Ferrand

APPENDIX 5: PROJECTS FUNDED BY THE CANCER RESEARCH ASSOCIATION (ARC)

YOUNG RESEARCHER AWARDS

- *The role of the Wnt/b-catenin signaling pathway in the development of cortical-adrenal tumors.*
  Beneficiary: Pierre Val - CNRS UMR 6547, Université Blaise Pascal, Clermont-Ferrand
  Amount awarded: €40, 800

- *The COSA (Breast and Ovarian Cancer in Auvergne) epidemiological study: a study on gene polymorphisms in sporadic breast cancers.*
  Beneficiary: Lætitia Delort - Inserm Unit 484, Clermont-Ferrand
  Amount awarded: €15,000

- *A study on the acquisition and expression of cell identity during myogenesis in fruit flies.*
  Beneficiary: Lætitia Bataille - Inserm Unit 384, Université Clermont-Ferrand 1
  Amount awarded: €36,000

- *Application of new nuclear magnetic resonance spectroscopy (NMRS), from proton to diagnosis, to characterization and therapeutic follow-up of brain tumors.*
  Beneficiary: Michaël Gottschalk - Inserm Unit 594, Université Grenoble 1, Grenoble University Hospital
  Amount awarded: €22,800

- *Magnetic resonance imaging of blood volume to describe neovascularization in experimental and human brain tumors.*
  Beneficiary: Adriana Teodora Barbacaru-Perles - Inserm Unit 594, Université Grenoble 1, Grenoble University Hospital
  Amount awarded: €16,800

- *Noxes (NADPH oxidases), new partners in tissue aging: the dynamics of assembly, structure and function.*
  Beneficiary: Minh Vu Chuong Nguyen - Université Grenoble 1, Grenoble University Hospital
  Amount awarded: €15,000

- *Detyrosinated microtubules: consequences on cells.*
  Beneficiary: Fabrice Caudron - Inserm Unit 366, CEA, Grenoble
  Amount awarded: €7,500

- *Research and development of pharmacological inhibitors of the sub-units of oncogenic protein kinase CK2.*
  Beneficiary: Béatrice Laudet - Inserm E 0104, CEA, Grenoble
  Amount awarded: €15,000

- *Development of an anti-angiogenic and anti-tumor therapy using the properties of TIS11b zinc finger protein.*
  Beneficiary: Séverine Planel - Inserm E0105, CEA, Grenoble
  Amount awarded: €16,800

- *Identification of the ligand of a receptor from the TGFbeta family involved in angiogenesis: ALK1 (Activin receptor-Like Kinase 1).*
  Beneficiary: Laurent David - CEA, Grenoble
  Amount awarded: €15,000

- *Kinesins and cancer: the Eg5 and RabK6 human kinesin inhibitors, with antimitiotic and anticancer activities.*
  Beneficiary: Sergey Tcherniuk - CNRS UMR 5075, Institut de Biologie Structurale Jean-Pierre Ebel, Grenoble
  Amount awarded: €22,800

- *The role of the protein paxillin in the organization of podosomes, deterioration of the extracellular matrix and invasion of cells transformed by the v-src oncogene.*
  Beneficiary: Cédric Badowski - CNRS UMR 5538, Université Grenoble 1, Institut Albert Bonniot
  Amount awarded: €15,000

- *The histone macroH2A variant: epigenetic role and transcription control.*
  Beneficiary: Flore Mietton - Inserm Unit 309, Université Grenoble 1, Institut Albert Bonniot
  Amount awarded: €15,000

- *Functional description of 3A-Brd, a new testicular factor that remodels abnormally expressed chromatin in cancers.*
  Beneficiary: Cécile Lestrat - Inserm Unit 309, Université Grenoble 1, Institut Albert Bonniot
  Amount awarded: €7,500

- *Histone variants H2BFWT and macroH2A: from structure to epigenetic function.*
  Beneficiary: Mathieu Boulard - Inserm Unit 309, Université Grenoble 1, Institut Albert Bonniot
  Amount awarded: €15,000

- *The Aurora kinases and their partners: potential targets for anti-cancer therapy.*
  Beneficiary: Nhung Hoang Thi My - Inserm Unit 309, Université Grenoble 1, Institut Albert Bonniot
  Amount awarded: €15,000

- *Identification of the mechanisms behind induction of apoptosis via the Sp1 transcription factor.*
  Beneficiary: Emmanuelle Deniaud - Inserm Unit 503, Lyon
  Amount awarded: €15,000

- *The functional properties and pharmaceutical modulation of p53ser249, a p53 mutant specifically expressed in hepatocellular carcinoma.*
  Beneficiary: Hong Shi - IARC, Lyon
  Amount awarded: €9,800

- *The molecular mechanisms and biological role of DCC-induced apoptosis.*
  Beneficiary: Céline Furne - CNRS FRE 2870, Centre Léon Bérard, Lyon
  Amount awarded: €15,000

- *The role of the DCC and Unc5H1-4 dependence receptors in the development of breast cancer.*
  Beneficiary: Cécile Herbreteau - CNRS FRE 2870, Centre Léon Bérard, Lyon
  Amount awarded: €36,000

- *The dynamics and regulation of nucleoprotein assemblies of human telomeres: the functions of protein TRF2.*
  Beneficiary: Simon Amiard - CNRS UMR 5161, ENS, Lyon
  Amount awarded: €7,500

- *Does neurofibromin control bone formation and bone resorption via a central transcription factor, ATF4?*
  Beneficiary: Cyril Confavreux - Inserm Unit 403, Hôpital Edouard Herriot, Lyon
  Amount awarded: €27,600

- *The role of the protein CKIP-1 and of its isoform CKIP-1p28 in P-13K-regulated muscular differentiation.*
  Beneficiary: Sabine Caussanel-Boude - CNRS UMR 5161, ENS, Lyon
  Amount awarded: €7,500

- *The role of semaphorins in bone and their role in the establishment of bone metastases.*
  Beneficiary: Romain Dacquin - CNRS UMR 5161, ENS, Lyon
  Amount awarded: €22,800

- *Identification of direct transcriptional targets of retinoid/rexinoid receptors.*
  Beneficiary: Ingrid Masse - CNRS UMR 5161, ENS, Lyon
  Amount awarded: €36,000

- *A study on conditional invalidation of mTOR in mice in the skeletal muscle model.*
  Beneficiary: Lætitia Mazelin-Bowyer - CNRS UMR 5161, ENS, Lyon
  Amount awarded: €36,000

- *Molecular activation/proliferation mechanisms of quiescent B lymphocytes by EBV.*
  Beneficiary: Cahora Medina-Palaszon - Inserm Unit 758, ENS, Lyon
  Amount awarded: €22,800

- *Thyroid pathologies in the light of evolution: a study on the thyroid pathway in Ursidae.*
  Beneficiary: Marie Pages - CNRS UMR 5161, ENS, Lyon
  Amount awarded: €15,000

- *A study on the oncogenic activity of BARF-1 coded by Epstein-Barr virus associated with nasopharyngeal cancer: location of the protein and involvement in the cell cycle.*
  Beneficiary: Emma Sakka - CNRS UMR 5537, Université Lyon 1
  Amount awarded: €15,000

- *Identification of mechanisms involved in the progression in neuroendocrine tumors of the digestive tract (dNET).*
  Beneficiary: Jean-Claude Gevrey - Inserm Unit 45, Université Lyon 1
  Amount awarded: €45,600

- *Assessment of a targeted polytherapy on osteoclasts in the treatment of bone metastases in breast cancer.*
  Beneficiary: Céline Le Gall - Inserm Unit 664, Université Lyon 1
  Amount awarded: €15,000

- *The use of mouse knockout models for the gene causing predisposition to multiple endocrine neoplasia type 1: an in-depth study on the biological and oncosuppressive role of the gene in pancreatic endocrine cells.*
  Beneficiary: Jieli Lu - CNRS UMR 5201, Université Lyon 1
  Amount awarded: €16,800

- *The role of oncosuppressive protein LKB1 in epithelial-mesenchymal transitions.*
  Beneficiary: Karine Lefort-Leveques - CNRS UMR 5201, Université Lyon 1
  Amount awarded: €45,600

- *An analysis of the consequences of mutations on expression of breast cancer predisposition genes.*
  Beneficiary: Olga Anczukow-Camarda - CNRS UMR 5201, Université Lyon 1
  Amount awarded: €7,500

- *The role of tubulin conformation on tumorigenesis and chemoresistance mechanisms in breast cancer.*
  Beneficiary: Anne Beghin - Inserm Unit 590, Université Lyon 1
  Amount awarded: €10,000

- *A study on controlling the phosphorylation of ACCA residue S1263, a major site of BRCA1 interaction.*
  Beneficiary: Hind Ray-David - CNRS UMR 5201, Université Lyon 1
  Amount awarded: €22,800

- *The search for inhibitors and their action mechanism on ABC transporter ABCG2, involved in the chemoresistance of cancer cells.*
  Beneficiary: Alexandre Pozza - CNRS UMR 5086, IBCP, Lyon
  Amount awarded: €15,000

- *Perturbation of endoplasmic reticulum (ER) homeostasis provoked by RNA interference: a therapeutic approach to multiple myeloma.*
  Beneficiary: Anne-Sophie Michallet - Inserm Unit 404, Lyon
  Amount awarded: €16,800

- *Interaction of the PARP gene and environmental hormone perturbing factors in testicular tumorigenesis.*
  Beneficiary: Bénazir Siddeek - Inserm Unit 407, Lyon
  Amount awarded: €7,500

- *A study on the effects of T-regulating lymphocytes CD4+CD25 on the activity of anti-CD20 antibodies in B-cell lymphoma.*
  Beneficiary: Roch Houot - South Lyon Hospital Center
  Amount awarded: €27,600

- *Oncogenes and regulation of alternative pre-messenger RNA splicing in erythroleukemic cells and during erythroid differentiation.*
  Beneficiary: Rand Blaybel - CNRS UMR 5534, Université Lyon 1
  Amount awarded: €16,800

- *The development of targeted oncolytic herpes viruses to treat primary liver cancers.*
  Beneficiary: Aldo Pourchet - CNRS UMR 5534, Université Lyon 1
  Amount awarded: €14,400

FIXED SUBSIDIES (€50,000)

- *Diversification and migration mechanisms of cardiac and muscular cells.*
  Beneficiary: Krzysztof Jagla - Inserm Unit 384, Université Clermont-Ferrand 1

- *Reversion of resistance to Tamoxifen and to Fulvestrant by modulation of the PI3K/Akt/mTOR pathway in hormone-dependent breast cancer.*
  Beneficiary: Pascale Cohen - Inserm Unit 590, Université Lyon 1

- *Description and function of proteins analogous to integrins in dictyostylium amoeba.*
  Beneficiary: François Letourneur - CNRS UMR 5086, IBCP, Lyon

- *CD46-induced Tr1 regulatory cells: identification of key molecules in the death, differentiation and identification of Tr1s.*
  Beneficiary: Mathias Faure - Inserm Unit 503, Hôpital Edouard Herriot, Lyon

- *The role of TGF-Beta in tumor escape from the immune system.*
  Beneficiary: Julien C. Marie - Inserm Unit 404, Lyon

- *The use of mouse knockout models for the gene causing predisposition to multiple endocrine neoplasia type 1: the biological and oncosuppressive role of the gene in pancreatic endocrine cells and hormone-dependent tissues.*
  Beneficiary: Chang-Xian Zhang - CNRS UMR 5201, Université Lyon 1

- *Molecular mechanisms of breast cancer resistance protein (BCRP), a transporter responsible for the chemoresistance of cancerous cells. The search for specific inhibitors.*
  Beneficiary: Attilio Di Pietro - CNRS UMR 5086, IBCP, Lyon

- *Breast cancer and protein metabolism: the molecular and cellular consequences of BRCA1 interaction with PAbP1, a key player in translation.*
  Beneficiary: Nicole Dalla-Venezia - CNRS UMR 5201, Université Lyon 1

- *Intra-cell signaling networks and their deregulations in myeloid progenitors: the regulation and role of the ERK1/2 MAP kinases.*
  Beneficiary: Guy Mouchiroud - CNRS UMR 5534, Université Lyon 1

- *A study on the functioning of the deterioration process of messenger RNA bearing a premature translation termination codon.*
  Beneficiary: Sylvie Mazoyer - CNRS UMR 5201, Université Lyon 1

- *The role of protein ABCC11 in mechanisms of breast cancer resistance to 5-Fluorouracil and Methotrexate.*
  Beneficiary: Léa Payen - Inserm Unit 590, Université Lyon 1

- *A functional genomic analysis of the melanoma region of the Xiphophorus fish.*
  Beneficiary: Jean-Nicolas Volff - ENS, Lyon

- *A functional in vivo study on histone variant macroH2A: gene invalidation in mice.*
  Beneficiary: Philippe Bouvet - CNRS UMR 5161, ENS, Lyon

- *Controlling the stability and size of telomeres in Saccharomyces cerevisiae yeast.*
  Beneficiary: Michel Charbonneau - CNRS UMR 5161, ENS, Lyon

- *Treatment of hepatic metastases by focused ultrasound.*
  Beneficiary: Michel Rivoire - Experimental Surgery Unit, Centre Léon Bérard, Lyon

- *Functional analysis of the target and partner genes of the protein Twist1.*
  Beneficiary: Stéphane Ansieau - Inserm Unit 590, Centre Léon Bérard, Lyon

- *Targeted apoptosis and immunity in breast cancer: development of therapeutic strategies.*
  Beneficiary: Christophe Caux - Inserm Unit 590, Centre Léon Bérard, Lyon

- *Functional duality of TGF-beta during tumor progression: the pancreatic adenocarcinoma model.*
  Beneficiary: Laurent Bartholin - Inserm Unit 590, Centre Léon Bérard, Lyon

- *Human molecular drivers and cancer II: validation of new targets and optimization of existing inhibitors.*
  Beneficiary: Frank Kozielski - CNRS UMR 5075, Institut de Biologie Structurale Jean-Pierre Ebel, Grenoble

- *Epigenetic control of the transcription and stability of the genome by the formation of heterochromatin-dependent RNAi.*
  Beneficiary: André Verdel - Inserm Unit 309, Université Grenoble 1, Institut Albert Bonniot

- *How protein acetylation regulation contributes to the tumor suppressing functions of p14ARF: its role in bronchial carcinogenesis.*
  Beneficiary: Sylvie Gazzeri - Inserm Unit 578, Université Grenoble 1, Institut Albert Bonniot

- *How genetic variations in the MHC region of the human genome contribute to predisposition to nasopharyngeal carcinoma.*
  Beneficiary: James D. Mac Kay - IARC, Lyon

FREE SUBSIDIES

- *A study on the structure and function of B4 leukotriene receptors as new therapeutic targets in cancer of the pancreas.*

Beneficiary: Laurence Serre - CNRS UMR 5075, Institut de Biologie Structurale Jean-Pierre Ebel, Grenoble
Amount awarded: €160,000

FUNDING FOR RESEARCH EQUIPMENT

- *Immunotherapy via living bacterial vectors. Application in glioblastoma and melanoma.*
Beneficiary: Bertrand Toussaint - Université Grenoble 1
Amount awarded: €40,000

- *Epigenetic control of a cell differentiation program using RNA interference (RNAi) and hematochromatin.*
Beneficiary: André Verdel - Inserm Unit 309, Université Grenoble 1, Institut Albert Bonniot
Amount awarded: €40,000

- *Tumor escape from the immune system and therapeutic targeting of tumor cells and of their immunological environment.*
Beneficiary: Christophe Caux - Inserm Unit 590, Centre Léon Bérard, Lyon
Amount awarded: €50,000

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