

The cover features a teal background with a large, stylized leaf graphic on the left. On the right, a DNA double helix is depicted with several target symbols (red dots in concentric circles) overlaid on it. In the top left, there are two white concentric circles. The title 'Progress Report 2009' is centered within a red rounded rectangle.

Progress Report 2009

The logo consists of a teal circle with a white dot in the center, followed by the word 'CLARA' in a bold, teal, sans-serif font.

CLARA

CANCÉROPOLE LYON AUVERGNE RHÔNE-ALPES

SPEEDING UP PROGRESS

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Peter PAUWELS
Executive Director

2009: CLARA's coming of age

CLARA has celebrated its sixth anniversary. A real turning point in its history, 2009 was a year of maturity and recognition for the Cancéropôle. It marked the solid development of the CLARA Cancer Research Cluster and its ability to respond to real expectations in the research landscape in the Rhône-Alpes Auvergne area. The network of partners is growing in size and confidence and CLARA has learned to adapt itself and its projects to local needs.

2009 was an especially productive year for CLARA. Several strategic approaches have produced remarkable results, which can be illustrated in four points:

- The scientific leadership project, initiated at the end of 2007, is well positioned, as evidenced by the share of CLARA projects selected by the French National Cancer Institute (INCa). For the first time, CLARA ranks as the second-leading Cancer Research Cluster in France, winning approximately 20% of the projects selected by INCa (across all subjects). Of particular note are the results in the hepatocellular carcinoma Integrated Research Action Program (PAIR), an ultra-competitive call for proposals (national success rate: 4/12) and the certification of reference centers for rare cancers in adults (national success rate: 4/11).
- CLARA's platform-based structure has gained considerable support, as four IBiSA (Biology, Health and Agronomy Infrastructures) certifications have been granted to CLARA platforms.
- The "Proof of Concept" program, set up in 2005, is growing fast: its portfolio now includes 21 projects (including seven initiated in 2009) with a total budget of €23M. The development of the program has resulted in its first success story: the VIKY mini-robot, which is revolutionizing laparoscopic surgery, is now in the commercialization phase. Other highly advanced projects testify to the vitality of "Proof of Concept". Its effectiveness is based on the crucial interaction between academic research, clinical R&D and industrial R&D: an effective triangle of skills organized by the Cancéropôle.
- Finally, CLARA's international relations have broadened through close collaborations with, for example, French-speaking Switzerland, Germany (DKFZ Heidelberg) and Spain (Institut de Bioenginyeria de Catalunya), as well as world-class projects such as the European Lymphoma Institute, the Global Sarcoma Network and the program "Fighting Infections Caused by the Hepatitis Viruses and their Consequence: Liver Cancer"...

In conclusion, the CLARA Cancer Research Cluster is leveraging its assets to meet a real need in Rhône-Alpes Auvergne: structuring oncology research and further support to the development of translational research and its contribution to concrete applications. In order to reach its goals, CLARA has not only succeeded in renewing the trust of its financial backers (local authorities), it has also gained the confidence of the European ERDF, and importantly, with a three-year perspective.

In 2010, it will persist in focusing all its energy and ambition into cancer research in the Rhône-Alpes Auvergne region.

CLARA: mission and key elements

CLARA's key numbers

- **2nd leading Cancer Research Cluster** in France
- **€130M** invested in cancer research (total budget)
- **153 projects** underway (total portfolio)
- **21 projects** with a total budget of **€23M** financed with industrial transfer
- **210** clinical and academic teams, **60** industrial partners
- **Diversified funding sources:** State, local authorities (14), industrial firms, ERDF...

2009: meaningful results...

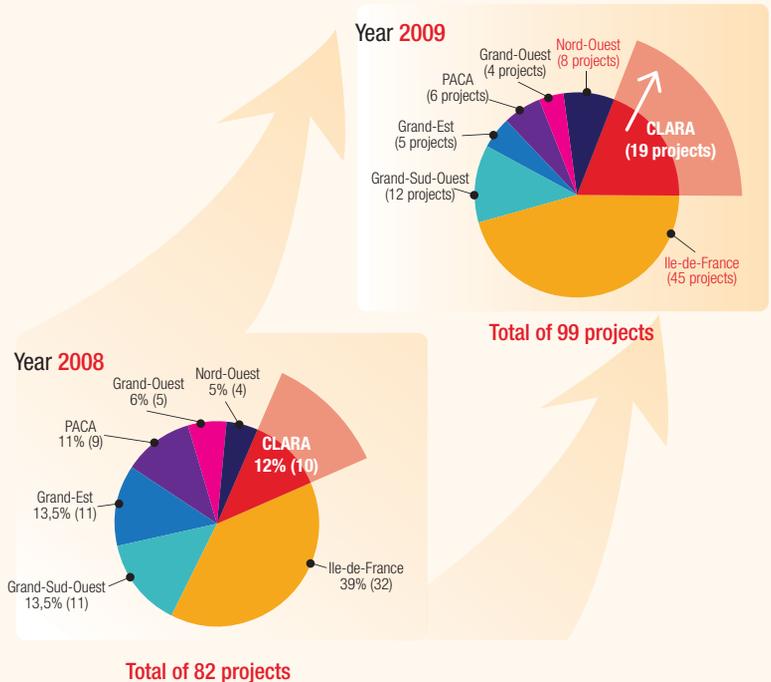
- **56** new projects with a total budget of **€15M**
- **19%** of INCa projects granted to the CLARA Cancer Research Cluster
- **1st cancer research cluster** to obtain funding from **ERDF***
- **Concrete results:** a surgical mini-robot, advances in the field of treating glioblastoma and therapeutic coverage of liver metastases...
- **Supporting new projects for launching start-ups**

* Three-year funding granted as part of the economic development of the CLARA Cancer Research Cluster

1 • Coordinating cancer research expertise and infrastructure of the inter-region

The CLARA Cancer Research Cluster strives to bringing together researchers, clinicians and industrial firms into a single network, and to pool their efforts on operational research programs with a two-fold objective of quickly transferring knowledge to patient care and developing marketable applications of research findings.

DISTRIBUTION OF SELECTED INCa PROJECTS BY CANCÉROPÔLE



2•Expert opinion: CLARA is an efficient structure

Set up in 2008, the Development Committee guides the scientific orientations of the CLARA Cancer Research Cluster. For the second year, the committee of independent, internationally renowned experts delivered its report evaluating CLARA's activity in 2009.

The Development Committee emphasized CLARA's vitality and clear **ability to mobilize diversified funding sources**, even beyond the funding allocated to Cancer Research Clusters. In terms of organization, in 2008, it had recommended increasing the involvement of the Scientific Steering Committee, whose role is to manage CLARA's scientific activities. According to the Development Committee, this distribution of roles has a positive effect on the **attractiveness, visibility and credibility** of the Cancéropôle. The committee encouraged CLARA to maintain this governance structure.

Evaluations and recommendations of the Development Committee - excerpt (24/11/2009)

Members of the committee: Christian Bréchet, Jean-Claude Martinou, Christine M'rini, Josep Samitier, Robert Souhami, Ian Tannock (Chair)

"CLARA is a solid, dynamic organization that has succeeded in diversifying its sources of funding. It receives support from INCa as a Cancer Research Cluster, but it has also succeeded in mobilizing the local authorities, the european ERDF and industrial partners. Its budget in 2009 was €8.4M, including €1.2M from INCa.

The members of the Development Committee were impressed by the quality of many of the projects and platforms, by the implementation of their 2008 recommendations and by the successes achieved in the past year.

The Development Committee recognizes that governance through the "Scientific Steering Committee" (including 14 members representing the focus areas and platforms) has been effective and that wise decisions have been made.

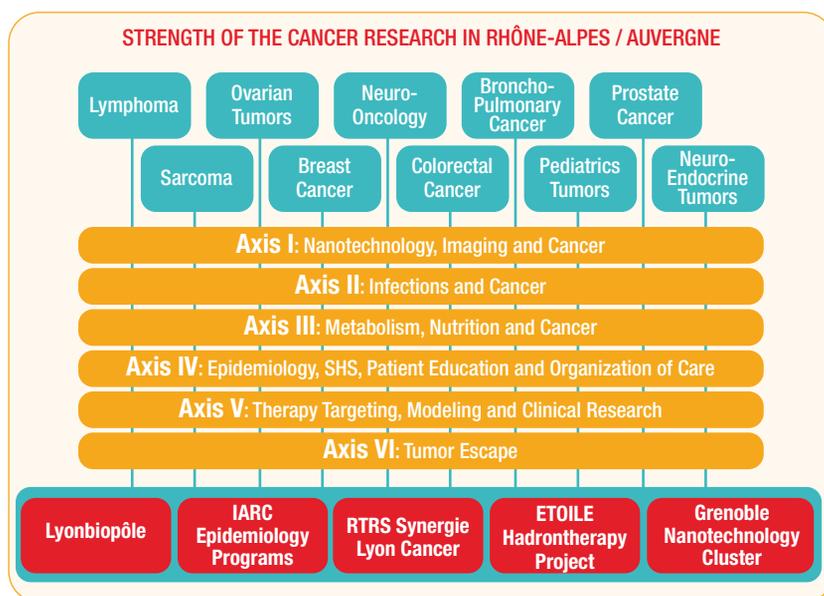
The Development Committee has stressed the relevance of the actions and programs set up in 2009, such as doubling the amounts granted for the promotion of translational research with the aim of attracting young researchers to this area and hiring post-doctorates.

The educational and networking roles of CLARA have also grown, thanks to the organization of several symposia and training programs on translational research."



Set up in 2007 for three years, the ProCan Program aims to design the roadmap of the Cancéropôle, consistent with the nationwide priorities for cancer research. It has led to the implementation of projects that unite and structure research teams around its various themes.

Supported by the National Cancer Institute (INCa), the ProCan Program of the CLARA Cancer Research Cluster is structured into six scientific focus areas, each pursuing the objective of structuring oncology research in Rhône-Alpes Auvergne, developing translational research, optimizing responses to calls for proposals, organizing scientific activities and events (scientific forums, symposia, meetings, etc.), developing partnership strategies...



In 2009, the ProCan Program made concrete progress in several different areas:

1 • In-depth structuring action

- **16 core programs:** here is proof of the federating force of the Cancéropôle, which greatly developed its portfolio in 2009, with three programs renewed in Focus Area II: *Infections & Cancer* and 13 new programs as part of Focus Area III: *Metabolism, Nutrition and Cancer* (3), Focus Area IV: *Epidemiology, Human and Social Sciences, Patient Information and Organization of Care* (6) and Focus Area VI: *Tumor Escape* in cooperation with the Synergie Lyon Cancer Foundation (4).

New projects 2009

57 projects selected for a total

budget of nearly €15M,

115 research teams mobilized

• INCa : 25* projects - €6 528K

• CLARA Proof of Concept:
7 projects - €5 560K

• PHRC (Integrated Research
Action Program): 5 projects -
€1 395K

• STIC (Support for Innovative and
Costly Techniques): 1 project -
€510K

• New programs: 3 projects -
€500K

• ProCan core programs:
16 projects - €455K

TOTAL : 57 projects - €14 948K

* Including 4 Reference Center
Certification projects for Rare Cancer
in Adults, and 2 ANAPATHog projects.

- The **transfer of activities** from ProCan Focus Area V: *Therapy Targeting, Modeling and Clinical Research* to the Auvergne / Rhône- Alpes clinical cancer research assistance platform (PARCC-ARA), which provides methodological assistance or financial support for clinical research.
- The **opening** of the *Metabolism, Nutrition and Cancer* Focus Area to new stakeholders, with the aim of developing an *Environment, Nutrition and Cancer* Focus Area.
- **Visibility**: five high-visibility symposia were organized in order to enable the teams to highlight and share their results (see Special Moments section).

2 • Promoting translational research

- Organizing a major program on translational research on liver cancer, “*Viro-HCC*”, to boost this area and develop connections with multiple French, European and international partners.

3 • Supporting the development of nanomedicine

- **Project**: the development of an integrated nanomedicine approach, “*IMPACT*”, for the personalized prescription of anti-angiogenic drugs - NanobioTechno-Individualized Targeted Therapy project - on the response to treatment with Avastin®: clinical, biological, cognitive, ethical and economic aspects.
- **Training**: a cycle dedicated to the development of a nano-object, from the laboratory to humans.
- **Consulting**: the Regulatory Unit, set up in 2008 with the aim of bridging the gaps between research and product development, has supported five nanotracer projects. The consulting services offered were increased in 2009 with a second component, through the establishment of an Innovation Unit, which meets a strategic need and will help stakeholders to position the development of nanoparticles on the market and health applications level.

4 • Development of the ProCan program through the “Proof of Concept” program

The “Proof of Concept” program contributes to the focus areas of the ProCan program. 19 projects are concerned:

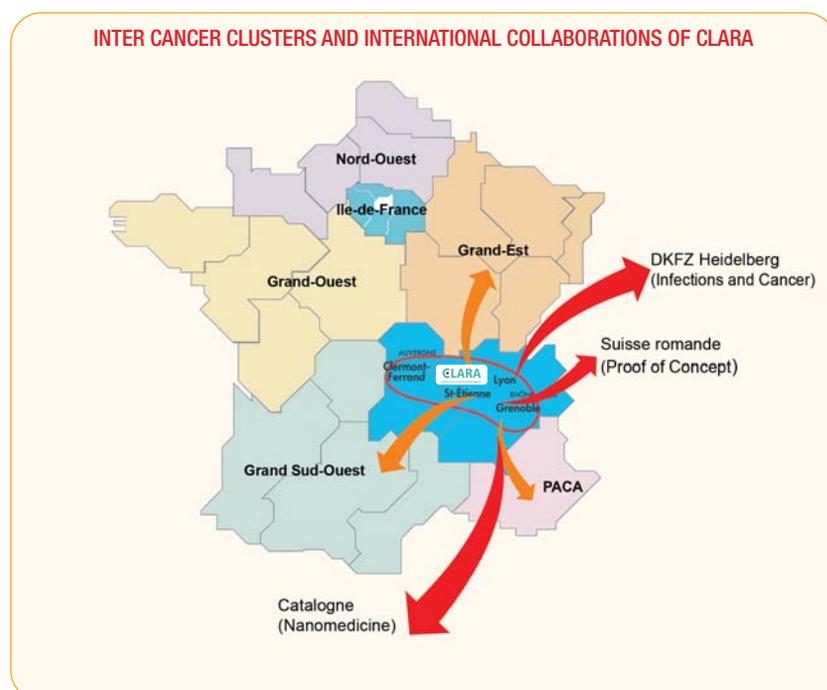
- Focus Area I: 8 projects with a total budget of €6.9M
- Focus Area II: 6 projects with a total budget of €12.2M
- Focus Area VI: 5 projects with a total budget of €3.5M

5 • A regional, national and international partnership-based approach

In 2009, special attention was paid to the development of strategic regional, national and international partnerships, leading to progress in the ProCan focus areas. 6 examples of key partnerships are detailed on page 14.

- CLARA was strongly involved in **partnerships between Cancer Research Clusters**, and in particular, with the Grand-Est, Grand Sud-Ouest and Provence Alpes Côte-d'Azur, so as to increase the number of collaborative projects on cancer topics in common, in connection with nanomedicine, imaging, infections and nutrition.
- The **internationalization** of the CLARA Cancer Research Cluster is being fostered through significant cooperative ventures with:
 - Germany and the European reference center DKFZ Heidelberg on the topic of Infections and Cancer
 - Spain and the Institute for Bioengineering of Catalonia (IBEC) in Barcelona, for the clinical development of nanomedicine
 - Switzerland and cross-border collaborative projects: a pilot program and the export of the "Proof of Concept" program model to the ISREC, formerly the Swiss Institute for Experimental Research (Lausanne)

And... Continuing the program for the mobility of young researchers, as part of the *Metabolism, Nutrition and Cancer Focus Area*.



III

Scientific excellence, marketable applications and visibility of research strengths

INCa 2009 Call for Proposals: CLARA at a glance

- 2nd leading Cancer Research cluster nationwide, after Ile-de-France
- €6.5M in funding granted by INCa
- 25* projects selected, including:
 - 4- i.e. one third of all proposals selected - as part of the Hepatocellular Carcinoma PAIR
 - 4 certifications of reference centers for rare cancers in adults
 - 9 applications selected in translational research

* Details in "INCa 2009 projects" in appendix 3

Plus...

- Projects supported by Associations that mobilize funding for research conducted by the Rhône-Alpes Auvergne teams:
 - Association pour la Recherche sur le Cancer : €1.9M
 - Ligue Nationale contre le Cancer : €1.7M (excluding funding by the County Committees)



Three forces driving CLARA projects

1 • Scientific excellence Recognized strengths and a heightened presence in nationwide calls for proposals

Validating the strategic choices of its governance, the Cancéropôle has seen significant progress in its share of INCa projects: 19% of all projects selected this year, up from 12% in 2008, with two of CLARA's strengths recognized in particular: liver cancer research and translational research.

RESULTS OF INCa'S CALLS FOR PROPOSALS

Integrated Research Action Program: Hepatocellular Carcinoma (PAIR CHC 2009) - National Aids Research Association (ANRS) - Association for Cancer Research (ARC) - INCa ▶ 4 projects selected (out of 12 nationwide)

Translational research in cancer research – DHOS INCa ▶ 3 projects selected

Support for training in translational research in cancerology for medical students and young physicians ▶ 6 projects selected

Research in Human and Social Sciences, Public Health and Epidemiology ▶ 3 projects selected

Open biomedical research projects 2009 ▶ 3 projects selected

Certifications of Reference Centers for Rare Cancer in Adults: ▶ 4 projects selected, equal to Ile-de-France

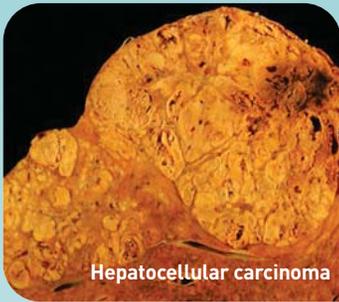
Out of 11 reference centers for rare cancer in adults certified by INCa, four come from CLARA for the following types of tumors: soft tissue and visceral sarcoma, rare peritoneal tumors, sporadic and hereditary malignant neuroendocrine tumors and the gestational trophoblastic diseases.

Reinforcement of the organization of anatomy and pathological cytology to promote a coordinated, multidisciplinary approach to the molecular analysis of cancer ▶ 2 projects selected in Lyon and Clermont-Ferrand

And... Clinical Research Hospitalization Program (PHRC) ▶ 5 projects selected in urothelial cancer, epidermoid carcinoma, colorectal polyposis, sarcoma and lymphoma

And... Support for Innovative and Costly Techniques (STIC) ▶ 1 project selected in prostate cancer, out of four nationwide

The program to support innovative and costly techniques (STIC) concerns innovative diagnostic and therapeutic technologies, validated by a preliminary clinical research stage and capable of having an important impact on the system of care.



Hepatocellular carcinoma

Integrated Research Action Program: Hepatocellular Carcinoma (PAIR CHC 2009)

- **L'influence de vie, du régime alimentaire, de l'obésité et de l'inflammation sur les risques de carcinome hépatocellulaire et de cholangiocarcinome : recherche prospective détaillée basée sur des cohortes françaises et européennes dans de cadre de l'étude EPIC**

Coordination: M. JENAB
€407 000

- **CTLR3, une nouvelle cible thérapeutique dans les hépatocarcinomes**

Coordination: S. LEBECQUE
€364 000

- **HCV-induced liver carcinogenesis: analysis of TGF- β pathway perturbations**

Coordination: V. LOTTEAU
€449 000

- **Early steps of NEoplastic transformation of Liver cells and interplays with Viral Infection**

Coordination: P. MERLE
€510 000

Strength

Liver cancer: recognized research potential

Ultra-competitive, the Hepatocellular Carcinoma Program (the most frequent type of liver cancer in the world) received numerous submissions. Out of the 12 applications selected by the international jury, **one third came from the CLARA Cancer Research Cluster**.

A growing pathology

Hepatocellular Carcinoma (HCC) is the most widespread liver cancer in the world. Highly malignant and often diagnosed at late stages, its prognosis is poor. HCC is a real public health problem, "due to the expected increase of its incidence because of the combination of hepatitis B and C infections and nutritional characteristics (alcohol and metabolic syndrome)". INCa has targeted this pathology as part of its 2009 cross-cutting research program (PAIR CHC) concerning pathologies for which prevention, detection and epidemiology aspects require further exploration.

* Source: INCa - Press release of Friday, April 10, 2009

...Ambitious research objectives

The objective of the four CLARA research programs consists in identifying early markers of malignant transformation of liver cirrhosis which, in over 90% of cases, cause primary liver cancer. The research will aim to identify signaling pathways and the most permissive cells in the process of malignant transformation.

Strength

Translational research: CLARA leads the way

A key priority for the CLARA Cancer Research Cluster, translational research consists in accelerating the transfer of results from basic research to the patient.

The last call for proposals by INCa validates the role of CLARA in this area: **six training applications in translational research out of seven submitted by CLARA***.

A priority action confirmed by the Cancer Plan II, translational research is an area in which INCa has reaffirmed its commitment. The programs entrusted to CLARA in 2009 will make it possible to train physicians in translational research in cancerology. They cover cutting-edge fields such as the role of tumor stem cells in the response of glioblastoma to hadrontherapy and the association of temozolomide with radiation.

Note: CLARA obtained 3 projects in translational research in cancer research - DHOS INCa.

*See Appendix 2

In 2009 the "Proof of Concept" program flourished

The number and quality of projects submitted are rising... Inauguration of the partnership with organizations for developing marketable applications of academic research and incubators... First-time support from ERDF

Numbers:

- Portfolio: **21** projects
- Outcome: **1** success story (LER – Endocontrol) and **2** underway (HIFU – EDAP and Lymphos1-Immun'ID).

Partners:

- **14** industrial partners
- **33** academic teams
- **11** local authorities +ERDF

Budget: €23.3M

Proof of Concept in key words

The culture of collaboration between industrial firms, academics and clinical teams... A successful, spreading model... Optimization of the selection process in cooperation with experts of French-speaking Switzerland...

For the future, it is the top priority of the CLARA Cancer Research Cluster

2 • Economic development: CLARA's winning hand

From the laboratory to industrial production: CLARA constitutes the missing link by promoting the industrial transfer and commercial development of an idea. Leading a program to support innovative, high-potential projects in the area of health/oncology/biotechnology, called "Proof of Concept", the Cancéropôle is making a difference, confirming its role as an actor of economic development.

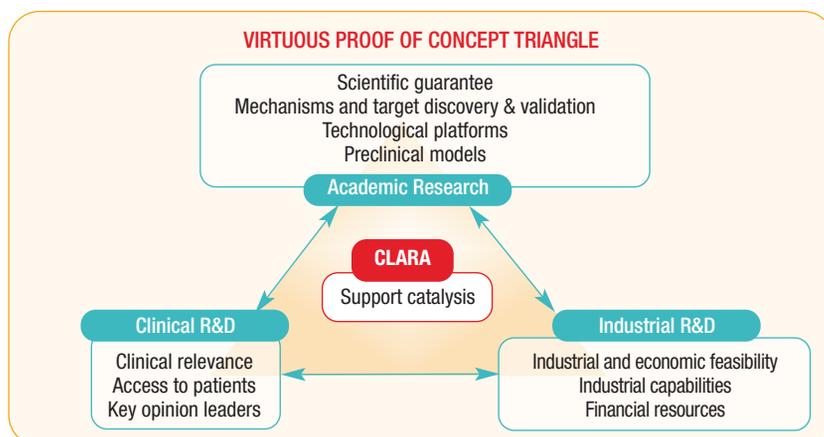
"Proof of Concept": from idea to reality

In order to conduct R&D and the transfer of technology in cancer research, CLARA opted in 2005 for the system of Private/Public Partnerships (PPP), which are perfectly adapted for bringing together academic and clinical teams from public institutions – INSERM, CNRS, CHU, CRLCC and others – with industrial firms: CLARA's "Proof of Concept" program now supports **21 projects corresponding to a total budget of over €23M**. In four years, it has confirmed its vitality and gone even further by getting involved earlier in the support of companies in the start-up phase.

Its success is based on two of CLARA's key missions:

- bringing complementary partners together (academic, clinical and industrial)
- access to financial support contributed by CLARA to academic and clinical partners and by other partners, such as OSEO, to the industrial partner involved in the project. The program thus presents the advantages of minimizing the risk factor for the industrial firm, creating lasting synergies between the academic, clinical and industrial partners and contributing to the vitality of the biotech sector.

In 2009, the Cancéropôle demonstrated its economic impact, through the diversification of funding sources and the growing attractiveness of the program with industrial firms (seven new projects in 2009 with a contribution of €2.9M from industrial partners and economic development organizations), the emergence of the first success stories and the first partnerships with economic development organizations and incubators (CANCERDRUG and LIPOBAK). These achievements are among the highlights of the year, for strengthening both research and economy in the Rhône-Alpes and Auvergne areas.





Success story: ViKY, the mini-robot that is revolutionizing laparoscopic surgery
Endocontrol

Over **300** surgical procedures have validated the mini-robot ViKY, developed by EndoControl. *“The CLARA Cancer Research Cluster has been a crucial player in the success of the mini-robot in the operating room”*, says Clément Vidal, the company’s CEO.

Dedicated to laparoscopic surgery – procedures performed via small incisions using miniature cameras - ViKY is a compact, mobile mini-robot that is safe and inexpensive. It is controlled directly and totally autonomously by the surgeon. It has the advantage of offering a highly stable image regardless of the operating time, giving the surgeon direct control of his vision and freeing up an operating hand for greater efficiency.

The innovation of ViKY lies in its extreme compactness, which gives more space in the operating field. Easy to use and maintain, it is totally sterilizable in an autoclave. ViKY is the first robotic architecture totally dedicated to surgery. Up until now, the most complete initiative was an anthropomorphic arm inspired by industrial robotics.

The first successes of “Proof of Concept”

Nanoparticles fighting glioblastoma

Nanobiotix

An innovative therapeutic alternative based on the nanotechnologies and non-medical modes of action (using physical principles): with the objective of targeting the tumor and limiting the side effects, the teams tested the applicability of nanoparticles to glioblastoma (one of the most common brain tumors in humans). Animal studies have shown that photosensitive nanoparticles (nanoPDT) are effective on human glioblastoma transplanted into immunodeficient mice, after activation with a laser.

Significant progress for the treatment of liver metastases

EDAP TMS

On September 23, 2009, the French Health Products Safety Agency (AFSSAPS) issued an authorization to continue with patients, the development of a treatment for liver metastases using a high-intensity focused ultrasound technique (HIFU). The decisive support of the Cancéropôle made it possible to bring the project to patients, having demonstrated the efficacy of this technique in animals, as part of the “Proof of Concept” program.

The HIFU technique makes it possible to destroy hepatic metastases with precision, while sparing the neighboring anatomic structures. This technique thus broadens the therapeutic scope for this pathology, providing considerable progress in this field.

3 • World-class projects for enhanced visibility and attractiveness of research forces in Rhône-Alpes Auvergne

In 2009, the ambition of the CLARA Cancer Research Cluster was, in parallel with its “Proof of Concept” portfolio, to select and develop major world-class research programs. The objective of the Cancéropôle is to develop the oncology research forces in the Rhône-Alpes Auvergne area, in order to enhance their visibility and improve the local area’s attractiveness.

European Lymphoma Institute

CLARA support: €150K/year for three years

Lymphoma is the sixth most common cancer in the world, causing tumors in the lymphatic system. In order to achieve progress in the diagnosis, characterization and treatment of lymphoma in adults, the ELI - The European Lymphoma Institute - project aims to create a European Lymphoma Institute at the Southern Lyon Hospital Center (HCL) by 2013. The project is based on an association between the *Study Group for Lymphoma in Adults (GELA)* and the *Study Group for Lymphoma in Adults – Clinical Research (GELARC)*, both comprising internationally renowned experts, and integrates a clinical research structure. The GELA and the GELARC are both dedicated to research into new therapies for lymphoma in adults. Together, they form a first-rate collaborative venture.

Global Sarcoma Network

CLARA support: €150K/year for three years

Sarcoma is a rare form of cancer (incidence of 6/100,000 per year) with more than 50 histological subtypes and 150 molecular subtypes, some of which are mutations. These characterized-mutation subtypes represent important potential models as Proof of Concept for innovative targeted therapies. Due to their rareness, no clinical trial evaluating therapies targeting these tumors can be conducted by a single center or group at national level.

The aim of the Global Sarcoma Network is to create and structure an environment that is favorable to the development and management of these clinical trials. It will group together at a global level 11 the networks of clinical and translational research on sarcoma, relying on a new methodology and collaborative tools to conduct these trials.

The Hyg e Center: a regional resource center for cancer information, prevention and education

CLARA support: €200K/year for three years

This new center, which relies on the region's mobilization for the prevention of cancer in high-risk population, is an integral component of the region's arsenal in the fight against cancer. This new organization is part of the development of prevention and the creation of regional healthcare agencies under the French law on hospitals, patients, healthcare and local areas (HPST), which places prevention squarely at the center of healthcare.

The Hyg e Center will allow the development a regional cancer prevention and research strategy in this area, based on an educational center: the Saint-Etienne platform. This project closely involves the Loire's local authorities and regional institutions in the efforts to structure the research and care promoted by the CLARA Cancer Research Cluster.



IV 2009: a year of partnerships

In 2009, the development of strategic partnerships has received special attention at regional, national and international levels. Significant advances have contributed to advancing the focus areas of the ProCan initiative. Thus CLARA has forged close ties with several partners: the Synergie Lyon Cancer Foundation, the LyonBiopôle cluster, the Grenoble nanotechnology cluster, the ETOILE Center and its Hadrontherapy research, the International Agency for Research on Cancer (IARC), together with patient associations.



1 • Synergie Lyon Cancer Foundation

Tumor escape and therapeutic targeting are fields of action shared by the Synergie Lyon Cancer Foundation and CLARA's ProCan Focus Area VI. Their research strives to understand the mechanisms of tumorigenesis (hereditary, environmental and random) and to explore ways of reestablishing physiological safekeeping mechanisms in order to prevent metastatic spread and resistance to drugs. They are pursuing the shared goal of obtaining, in the medium term, preclinical models so that tumor targets and therapeutic molecules can be screened. This partnership has seen two key stages and concrete advances:

- the **set up of a Tumor Model Laboratory** in Lyon
- the creation of a **Bioinformatics Center** designed to handle cancer genomics in Lyon



2 • Lyonbiopôle cluster

The Rhône-Alpes Auvergne area has many excellent teams in the field of molecular virology, the mechanisms of viral-induced oncogenesis, immune responses and clinical research: CLARA's ProCan Focus Area II, LyonBiopôle, the Synergie Lyon Cancer and Finovi Foundations, the International Agency for Research on Cancer (IARC), the Léon Bérard Cancer Center, the Albert Bonniot Institute...

The CLARA Cancer Research Cluster and the LyonBiopôle competitive cluster have developed synergies on the topic of Infections and Cancer, with three specific working areas:

- building collaborative R&D projects: six Lyonbiopôle members receive support, as part of the "Proof of Concept" program
- mobilizing the networks of scientific, clinical, technological and industrial players
- organizing events on the theme of *Infections and Cancer*, such as the *Joint Meeting of the CLARA and Greater East Cancer Research Clusters*, *DFKZ-Germany (Deutsches Krebsforschungszentrum)* and the *Christophe Mérieux Biennial Conference Cycle*.

“The CEA-Léti turned to the CLARA Cancer Research Cluster which represents an efficient interface with clinical research and oncologists. But CLARA’s support also came in another form, just as important as scientific and technical collaboration: advising us about the regulatory and economic aspects of our technologies,” says Patrick Boisseau, Head of the Nano-Medicine Program at CEA-Léti. “In the same way, the strategic analysis of the various markets for nanoparticles initiated by CLARA, performed jointly by EM Lyon, guides and orients our future development, so we can respond to the most relevant clinical needs.”

3 • CEA-Léti (Electronic and IT Laboratory)

The partnership set up between CLARA’s ProCan Focus Area I and the CEA-Léti is based on scientific and technical collaboration. It meets a three-fold objective: developing nanotechnology in cancer research, its clinical applications and industrial transfer. CLARA acts as a key interface between clinical and technical research and the oncologists. The Cancéropôle also provides support for regulatory, economic and strategic matters regarding these technologies, through its advisory **Regulatory Unit**, a *training cycle* and a partnership with EM Lyon to set up an innovation unit.

A few notable examples of applications in nanomedicine:

- Fluoptics®, a start-up based on *in vivo* diagnostics. Its molecular imaging technology reveals tumor extensions through fluorescence, thereby providing improved detection of metastases using the naked eye. In order to enable the start-up to pursue its progress towards the 13 industrial productions of its technology, as part of the “Proof of Concept” program, CLARA granted Fluoptics® €450 000 in support for its project.
- Picprep, which is a system of miniaturized analysis for *in vitro* diagnostics in the blood. This project, which is supported by the CLARA Cancer Research Cluster and conducted in partnership with INSERM U836, is currently seeking a transition to the industrial transfer phase.



Picprep

4 • ETOILE Center and Hadrontherapy research

True to its goal of developing close ties with clinical research, CLARA has decided to collaborate with the ETOILE Hadrontherapy Center because this program shares common points with the ProCan Focus Areas IV, V and VI. Regional research on hadrontherapy, structured around the ETOILE Center since 1999, has thus incorporated the set of research themes promoted by the CLARA Cancer Research Cluster. Furthermore, it heralded the National Hadrontherapy Research program launched by INCa. The current development of the ProCan program, structured around six theme areas with CLARA, has enabled the integration of hadrontherapy research into the cancer research landscape in Rhône-Alpes Auvergne.

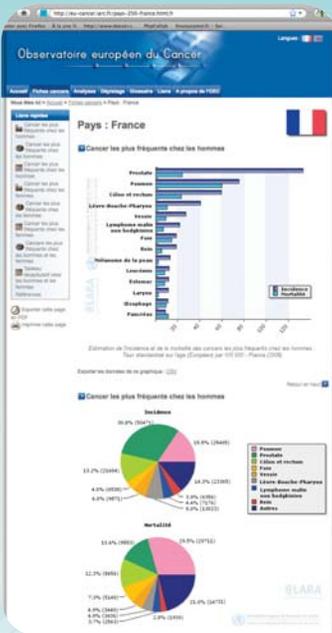


International Agency for Research on Cancer (IARC)

High visibility action: the launch of the European Cancer Observatory

The IARC and the CLARA Cancer Research Cluster have worked together towards establishing the European Cancer Observatory (ECO). This website presents the common base of knowledge regarding the prevalence and development of cancer in European countries. In particular, it provides epidemiological data for some 20 types of cancer in 27 European countries. The ECO provides easy access and use of data. It thereby contributes to enhanced visibility of the information supplied by cancer registries and greater use of publicly available data. The ECO constitutes an ideal tool for decision-making in the healthcare policy process. The involvement of cancer surveillance networks and registries, both European and national, should increase.

<http://eu-cancer.iarc.fr/>



6 • Inter-regional cancer patient Associations

Through the Associations that represent them, patients are an integral part of the CLARA network. In 2009, the Cancéropôle deployed several actions for patients, and in particular through ProCan Focus Area IV:

- their participation in the governance of the CLARA Cancer Research Cluster
- the development of themes concerning Epidemiology, Human and Social Sciences, Patient Information/Education and Organization of Care, through Focus Area IV of the ProCan program, which supports multidisciplinary projects such as home hospitalization in pediatric oncology or depression in patients
- their involvement in events organized under Focus Area IV
- the partner support of CLARA during events such as the Cancer Cell exhibition in Grenoble, the first National Cancer Info Kiosk Day, the first National Chronic Myeloid Leukemia Information Day (CML) and the public conference for the development of recommendations for access to early diagnosis of cancer after age 75.

V

Special highlights of 2009

The 4th Scientific Forum at a glance

A rich and cutting-edge program in keeping with the scientific excellence targeted by the event:

- Progress report on the ProCan and Translational Research Focus Areas
- Preview of the European Cancer Observatory website (<http://eu-cancer.iarc.fr>)
- Keynote lectures given by internationally renowned personalities in research
- Presentation time dedicated to young researchers
- 80 Poster presentations
- 3 "Poster Prizes" going to:
 1. *Viviana de Rosa (CEA Grenoble, INAC/SCIB/LAN) - "The anticancer effect of selenium : study of its role in DNA repair activity and resistance to oxidative stress"*
 2. *Sandrine de Seranno (INSERM U823 Équipe 2, La Tronche) - « Rôle des cellules progénitrices dans l'initiation et la progression du cancer du poumon à petites cellules »*
 3. *Sébastien Wieckowski (Centre Pluridisciplinaire d'Oncologie, CHU Vaudois, Suisse) - "Molecular characterization of CD8+T cell responses in melanoma patients following therapeutic peptide vaccination"*
- 14 Institutional and industrial partners

One of the missions of the CLARA Cancer Research Cluster is to unite the research actors and foster the sharing of latest advances in oncology. With this goal, the organization of seminars, symposia and conventions constitutes one of the most effective communication tool between researchers. These events, held throughout 2009, demonstrate the network's vitality. Out of some 50 meetings, 10 seminars/symposia, four calls for core proposals, one call for projects for Proof of concept and other activities organized in 2009, we will review some of the most representative CLARA's diversity and vitality.

1 • Leading the network in its various scientific focus areas

January 23-24

CLARA-DKFZ-CGE Joint Meeting (IARC, Lyon)

Cross-border collaboration and collaboration between cancer research clusters

The IARC, DFKZ-Germany (Deutsches Krebsforschungszentrum) and the French Cancer Research Clusters CLARA and Grand Est have reviewed strategies for treating viral-induced cancer, which concern 20% of all cancers in industrialized countries.

Detailed report available on www.canceropole-clara.com

March 24-25

4th CLARA Scientific Forum (Archamps, Haute-Savoie)

Organized in a location likely to foster **collaboration between Swiss Cancer Research actors and CLARA's research teams**, the 4th Scientific Forum had a positive outlook with 300 participants, including regional French and Swiss research actors and researchers of international standing: *Mina Bissell (Lawrence Berkeley Laboratory, Berkeley, U.S.A.)*, *Michael Clarke (Institute for Stem Cell Biology and Regenerative Medicine, Palo Alto, U.S.A.)*, *Oli Kallioniemi (Institute for Molecular Medicine, Helsinki, Finland)*, *Ivan Stamenkovic (University of Lausanne, Switzerland)*, *André-Pascal Sappino (University Hospitals of Geneva, Switzerland)*, *Christopher Wild (International Agency for Research on Cancer)*.



Papilloma Virus



4th CLARA Scientific Forum

October 1st

Nutrition and Hormone-Dependent Cancer Forum (Clermont-Ferrand)

The experts invited by the CLARA Cancer Research Cluster have characterized the **influence of diet on the prevention of hormone-dependent breast and prostate cancer**. This forum boosted collaborative projects at the national level. It made it possible to identify new teams capable of working on the research area of Nutrition, Metabolism and Cancer, through specific themes and know-how. Find out more on www.canceropole-clara.com

October 22-23

Human Sciences and Oncology Symposium (Lyon)

The symposium "*Human Sciences and Oncology: Tools, Stakes and Cooperation Serving the Patient*" resulted in **productive encounters, bringing about several projects and collaboration**.

2 • Fostering the emergence of new projects

October 20

2nd Industrial / Academic Encounters (Lyon)

Promoting synergies between academic, clinical and industrial players in the field of oncology. With an expanded system for detecting academic projects and increased mobilization of partner companies, the forum met the expectations of its 250 participants.

CLARA used the occasion to award two trophies to academic research projects with a high potential for the development of marketable applications and for finding an industrial partner:

- Joël Plumas for his work in the field of melanoma immunotherapy
- Jens Hasserodt for the development of a smart contrast agent for Magnetic Resonance Imaging

Key Information on the Industrial / Academic Encounters 2009

- **Priority objective:** detection and support of innovative R&D projects
- **250** participants
- **56** industrial/academic partnership projects
- **510** face-to-face meetings organized
- **2** CLARA trophies
- **16** institutional and industrial partners



2nd Industrial / Academic Encounters

3 • Supporting events in connection with its strategic themes

In 2009, CLARA contributed its expertise to the development of theme meetings, and supported several external events:

- For Development Biology to Anti Cancer Drugs – Wnts & Sonic Hedgehog - Nice, May 11 and 12
- ANOCEF Convention - Lyon, June 11 to 13
- 14th French Cytometry Convention - Saint-Etienne, September 8 to 12
- Highlights in Kinases and Cancer - Lyon, September 14
- 9th International Colloquium on Fundamental and Applied Radiobiology - Annecy, September 20 to 25
- Biological Research Day 2009 - Saint-Martin d'Hères, November 5
- Chronic Myeloid Leukemia (CML): 1st nationwide patient/family information day - Bordeaux, Lille, Lyon, Nice, Paris and Poitiers, November 14

4 • An active, renowned network ... and awarded in 2009*

- **Lucien Tartois 2009 Prize from the Foundation for Medical Research (FRM)**

Elected President of the European Organization for Research and Treatment of Cancer

Jean-Yves BLAY

- **Rosen Prize (Prize from the Foundation for Medical Research)**

Alain PUISIEUX

- **Ruban Rose Quality of Life Prize**

Elected Auvergnat of the Year by the Junior Economic Chamber of Auvergne and the Regional Council of Auvergne

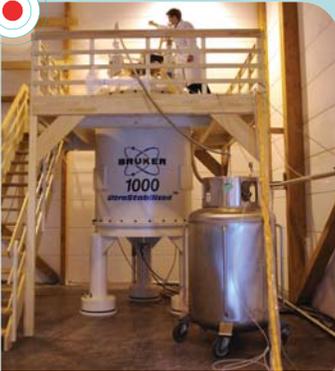
Yves-Jean BIGNON

*Non-exhaustive list



VI

CLARA's shared platforms and tools: recognition and development



The most powerful NMR in the world, in Lyon • The European Center for High Field NMR

The only machine with a power of 1GHz, this concentration of innovation is open to researchers from all over the world. It is a factor of attractiveness for international research projects, which require innovative spectroscopic methods and exceptional analysis capacity. Designed for numerous applications (medicine, structural biology, catalysis, the environment, etc.), the CNMR concerns cancer research with three priority research areas:

- Early diagnosis and predictive analysis of the response to a treatment
- The detailed study of the pathogenic character of mutations in connection with a tumor syndrome
- The exploration of the relationship between nutrition and cancer

Regarding metabolic profiling, very high NMR fields provide a key asset in terms of sensitivity and resolution, as compared with conventional fields.

Budget :

€9M paid by the State

€8.5M by the Region

€2.3M by Greater Lyon

2009 was a productive year for the platforms and tools of the CLARA Cancer Research Cluster. The year saw recognition and development through three inaugurations, the awarding of four IBiSA certifications and the creation of two new platforms. CLARA features high-performance, high-added-value tools. Distributed across seven sites in the local area, they correspond to the locations of the main cancer research actors and constitute a full offer of services, open to collaborations:

- IARC Epidemiology of cancer
- Clermont-Ferrand Nutrition and cancer
- Grenoble Clinical proteomics, functional imaging
- Eastern Lyon Functional genomics, pharmacogenomics
- Southern Lyon Epigenomics, targeted therapy
- Lyon Villeurbanne Metabolic and metabolomic profiling
- Saint-Etienne Patient education

In 2009, inaugurations set the pace for the platforms: the new research building of the Léon Bérard Cancer Center, the Grenoble platform, the cornerstone laying ceremony for the Hygiène Center and the European Center for High Field NMR in Lyon, the most powerful spectrometer in the world. Four IBiSA certifications were issued to the platforms in activity, and two new platforms are in the process of starting up.

1 • IBiSA certifications

The IBiSA certification (Infrastructure in Biology, Health and Agronomics) is dedicated to platforms that are defined as the grouping in a single location of equipment and human resources required to offer high-level technological resources to a community of users. The certification is issued following a national evaluation of the platform. Its degree of openness to outside teams is a major criterion. Getting IBiSA certification brings recognition to a platform and its specific resources (financing and personnel). It enables financial support to be granted to improve the equipment and hire more staff. In 2009, this certification was granted to the following sites:

- **ProfileXpert Platform (Lyon)** is a genomics platform specializing in DNA analysis (genotyping) and in gene expression (transcriptome) and in the analysis of protein/DNA interactions (ChIP or chip). It uses DNA chip technology. The result of a merger between two platforms, Transcriptome and Genotypage of the LCMT (Molecular Chemistry and Thio-Organic Laboratory) and ProfileXpert. It aims to establish microarray technology in Lyon, for the profitability and time-saving that it provides. The objective is also to provide an environment that favors the efficiency of data analysis. Certified IBiSA in July 2009, the platform received financial support of €353 000.



- **GENTYANE (Clermont-Ferrand)** is an acronym combining two platforms: GINA and INRA of Crouelle. Respectively dedicated to very high speed and high speed genotyping, the two sites host projects according to their typology, evaluated by the scientific and technical committee, which forwards the projects to either one; depending on the relevance of the sequencing program, the objectives and resources (10% of projects submitted are redirected to more traditional tools). Featuring the new generation of complete, robotized NGS (Next Generation Sequencing, Roche 18 Diagnostics 454 technology) sequencers, the Jean Perrin Center operates through the national IBISA network with 11 other sites.

- **Two *in vitro* and *in vivo* Life Science Imaging Platforms (Grenoble)** were IBISA certified in July 2009. Boasting cutting-edge technical centers associated with different laboratories, these platforms excel in the fields of clinical proteomics and imaging, alongside other areas of competence of the Grenoble area: nanotechnologies, lymphomas, bronchial and brain tumors.

The **Magnetic Resonance Imaging (MRI) platform** features human and animal clinical components through its six pooled facilities. Its three areas of focus: the methodological development of MRI techniques, preclinical studies of animal models and the transfer to clinical or cognitive-oriented research. The equipment and competencies of the platform are open to the scientific community. It also hosts industrial partners (Philips, Bruker, Guerbet, Oncodesign), representing 20% of its activity. It offers a continuum between preclinical and clinical methodological research in the field of neuroimaging.

2 • New platforms supported by CLARA

- **A tumor model laboratory:** this new tumor model laboratory, created on the initiative of the Synergie Lyon Cancer Foundation and the CLARA Cancer Research Cluster, aims to respond to the recognized, unmet need for access to relevant, well-adapted preclinical models. Services for research teams (public and private) will begin in 2010.

- **A Bioinformatics Center for the management of data from the International Cancer Genomics Consortium (ICGC):** the objective of the ICGC program is to produce high-quality data on the genomic study of 50 types of cancer. Each project will focus on tumor samples from around 500 patients and the information derived from them will have an important impact on preventive and treatment strategies. The creation of the Bioinformatics Center "Synergie Lyon Cancer Foundation", in collaboration with the CLARA Cancer Research Cluster, Claude Bernard Lyon 1 University, INSERM and the Lyon Civil Hospitals is based on a partnership with the National Cancer Institute (INCa). Already operational, the Bioinformatics Center is headed by Professor Gilles Thomas, Endowed Chair of the Synergie Lyon Cancer Foundation.

A tumor model laboratory

is a result of the collaboration between the Synergie Lyon Cancer Foundation, CLARA, Claude Bernard Lyon 1 University, INSERM, CNRS and the Léon Bérard Cancer Center.



VII Prospects for 2010

A few elements of CLARA's action plan for 2010

The certification of several platforms, the growing success of calls for proposals, the increasing development of marketable applications of research findings and the international outreach of the Cancéropôle are part of the progress made in 2009, which will serve the Cancéropôle in its future developments. These advances constitute fertile ground for the vitality of CLARA which, in 2010, will actively strive to:

- **Pursue its core business:** structuring oncology research and establishing a network amongst teams, building and stabilizing partnerships that are crucial to the sustainability of its actions, highlighting its assets.
- **Position the development of translational research and its contribution to tangible applications:** projects based on interactions between academic research, clinical R&D and industrial R&D are thus strongly encouraged and favored.
- **Support ambitious programs** on the advantages of translational research in oncology and its promotion at an international level: tumors such as lymphoma and sarcoma are already priorities of the Cancéropôle.
- **The development of marketable applications of research findings in oncology through the unique Proof of Concept program:** boosting its reaction capability within the framework of strategically important projects and opening up to French-speaking Switzerland.

VIII Finances

1st ERDF fund granted to CLARA

For the first time, the ERDF (European Regional Development Fund Rhône-Alpes) has granted funds to CLARA. The budget of **€1,8M** in 2009 went towards the industrial development of innovations from cancer research by companies in business incubators and start-ups. These first funds granted by ERDF to a Cancer Research Cluster signal a recognition of CLARA's economic dimension in the field of biotechnology applied to cancer research, in Rhône-Alpes. It also validates the successful Public/Private Partnership approach of CLARA in the past four years, through the "Proof of Concept" program.

2009 Report Assessment

The funding mobilized by CLARA since its start in 2003 comes to nearly €130M. The sources of this financing are diversified:

- 11 local governments of Rhône-Alpes Auvergne (€55M), in particular for the platforms (€40M) and Proof of Concept (€7M), for the Network Management and its major core programs
- The State (€54M), mainly as part of INCa support for research (€45M) and for the NMR platform (€9M)
- Industrial partners, as part of the Proof of Concept program (€16M)
- ERDF funds (€3.5M) dedicated to the platforms and to Proof of Concept

2009 was marked by the implementation of a three-year agreement through which 11 local governments of Rhône-Alpes Auvergne confirmed their support to CLARA for €2.5M a year, with priority going to the "Proof of Concept" program and core programs.

Summary of the multi-year scheduling of the CLARA program, 2003-2009

Status of the main sources of funding

Program		AMOUNT APPROVED in €K	
		2009	Overall total approved 2003-2009
Platforms	Hospices Civils de Lyon	2 500	8 500
	Léon Bérard Cancer Center		7 500
	Grenoble Platform		4 484
	Saint-Etienne Platform	1 100	5 207
	IARC Platform		1 100
	Auvergne Platform		4 040
	High Field NMR CNRS		19 850
	Total Plaforms	3 600	50 681
Funding of Projects	AAP INCa 2003 - 2009	9 896	38 781
	ProCan Scientific Axes (INCa)		2 550
	Proof of Concept Projects	3 685	8 213
	Biological Resource Center		1 135
	Total	13 581	50 679
Coordination	Network Management	2 370	11 734
	Total	2 370	11 734

Overall Orientation of approved funding during the period 2003-2009



Summary of the multi-year scheduling of the CLARA program, 2003-2009

Status of the main sources of funding on a national level



Recipient (funding)	2009				AMOUNT in €K	
	Investment		Operation		Overall total approved 2003-2009	Overall total paid 2003-2009
	Approved	Paid	Approved	Paid		
RMN Haut Champs - CNRS (MENRT)	-	-	-	-	9 000	9 000
Call for Projects (INCa) (a)			9 896	4 351	38 781	29 498
Biological Resource Center (CRB)	-	-	-	-	1 027	1 027
Network Management	-	-	-	-	2 138	1 744
PROCAN Scientific Axes (INCa)	-	-	-	-	2 550	1 530
Total	-	-	9 896	4 351	53 496	42 799

(a) Estimated amounts for Cancer Plan and INCa, STIC and PHRC included

Amounts approved by the State on a national level 2003-2009



Updated December 31, 2009

As per standard practice and in order to simplify the presentation, fundings are indicated in the year they were approved.

Summary of the multi-year scheduling of the CLARA program, 2003-2009

Status of the main sources of funding by the Rhône-Alpes Area



Recipient (funding)	2009				AMOUNT in €K	
	Investment		Operation		Overall total approved 2003-2009	Overall total paid 2003-2009
	Approved	Paid	Approved	Paid		
Proof of Concept	-	-	1 076	215	1 076	215
Network Management	-	-	700	140	700	140
Total	-	-	1 776	355	1 776	355

Amounts approved by ERDF Rhône-Alpes 2003-2009



Recipient (funding)	2009				AMOUNT in €K	
	Investment		Operation		Overall total approved 2003-2009	Overall total paid 2003-2009
	Approved	Paid	Approved	Paid		
Biological Resource Center (CRB)	-	-	-	-	108	108
Proof of Concept (DRRT RA)	-	-	-	-	37	37
Network Management	-	-	-	-	216	216
Total	-	-	-	-	361	361

Amounts approved by the State 2003-2009



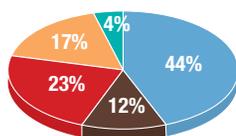
Summary of the multi-year scheduling of the CLARA program, 2003-2009

Status of the main sources of funding by the Rhône-Alpes Area

Rhône-Alpes Région

Recipient (funding)	2009				AMOUNT in €K	
	Investment		Operation		Overall total approved 2003-2009	Overall total paid 2003-2009
	Approved	Paid	Approved	Paid		
CHU Grenoble	-	-	-	-	1 708	1 368
UJF Grenoble	-	-	-	-	2 323	1 649
INSERM Grenoble	-	-	-	-	453	453
Grenoble Subtotal	-	-	-	-	4 484	3 470
CHU Saint-Etienne	-	-	-	-	410	225
Saint-Etienne Hygée Center	1 000	-	-	-	2 000	-
High Field NMR - CNRS	-	-	-	-	8 500	8 500
Proof of Concept	-	-	185	-	695	385
Network Management	-	-	315	-	3 239	2 504
Total	1 000	-	500	-	19 328	15 084

Amounts approved by the Rhône-Alpes Region 2003-2009



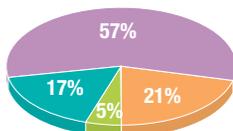
- Saint-Etienne Platform: €2 410K
- Grenoble Platform: €4 484K
- Network Management: €3 239K
- Proof of Concept: €695K
- High Field NMR - CNRS: €8 500K

RHÔNE

LE DÉPARTEMENT

Recipient (funding)	2009				AMOUNT in €K	
	Investment		Operation		Overall total approved 2003-2009	Overall total paid 2003-2009
	Approved	Paid	Approved	Paid		
CLB - East Lyon	-	-	-	-	7 500	7 500
CIRC	-	-	-	-	600	600
Proof of Concept	-	-	945	-	2 245	1 070
Network Management	-	-	555	-	2 706	2 151
Total	-	-	1 500	-	13 051	11 321

Amounts approved by the Rhône County 2003-2009



- East Lyon - Léon Bérard Cancer Center: €7 500K
- Network Management: €2 706K
- International Agency for Research on Cancer: €600K
- Proof of Concept: €2 245K

Updated December 31, 2009

As per standard practice and in order to simplify the presentation, fundings are indicated in the year they were approved.

GRAND LYON

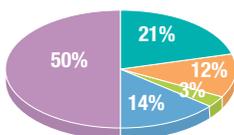
communauté urbaine

Recipient (funding)	2009				AMOUNT in €K	
	Investment		Operation		Overall total approved 2003-2009	Overall total paid 2003-2009
	Approved	Paid	Approved	Paid		
HCL*	2 500	1 750	-	-	8 500	7 750
IARC	-	-	-	-	500	500
High Field NMR - CNRS**	-	-	-	-	2 350	2 350
Proof of Concept	-	-	945	158	3 585	2 798
Network Management	-	-	555	93	2 165	1 659
Total	2 500	1 750	1 500	251	17 100	15 057

*HCL: The €2000K supplied in 2008 were reapproved in 2009

**High Field NMR: Program Authorization and Payment Appropriations of €2350K (in 2005) relate to the approval of Martin site (remove point)

Amounts approved by the Greater Lyon 2003-2009



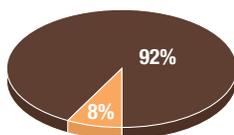
- East Lyon and South Lyon - Lyon Civil Hospitals: **€8 500K**
- International Agency for Research on Cancer: **€500K**
- Network Management: **€2 165K**
- Proof of Concept: **€3 585K**
- High Field NMR - CNRS: **€2 350K**



Recipient (funding)	2009				AMOUNT in €K	
	Investment		Operation		Overall total approved 2003-2009	Overall total paid 2003-2009
	Approved	Paid	Approved	Paid		
Saint-Etienne Hygée Center*	-	-	100	100	1 797	100
Network Management	-	-	25	25	150	150
Total	-	-	125	125	1 947	250

*Saint-Etienne Hygée Center 2009: Payment via the Network Management

Amounts approved by Saint-Etienne Métropole 2003-2009



- Saint-Etienne Platform: **€1 797K**
- Network Management: **€150K**

Summary of the multi-year scheduling of the CLARA program, 2003-2009

Status of the main sources of funding by the Rhône-Alpes Area



Recipient (funding)	2009				AMOUNT in €K	
	Investment		Operation		Overall total approved 2003-2009	Overall total paid 2003-2009
	Approved	Paid	Approved	Paid		
Saint-Etienne Hygée Center	-	-	-	-	1 000	-
Network Management	-	-	25	25	25	25
Total	-	-	25	25	1 025	25

Amounts approved by the Loire County 2003-2009



Recipient (funding)	2009				AMOUNT in €K	
	Investment		Operation		Overall total approved 2003-2009	Overall total paid 2003-2009
	Approved	Paid	Approved	Paid		
Network Management	-	-	10	10	10	10
Proof of Concept	-	-	100	30	100	30
Total	-	-	110	40	110	40

Amounts approved by the City of Grenoble 2003-2009



Updated December 31, 2009

As per standard practice and in order to simplify the presentation, fundings are indicated in the year they were approved.



Recipient (funding)	2009				AMOUNT in €K	
	Investment		Operation		Overall total approved 2003-2009	Overall total paid 2003-2009
	Approved	Paid	Approved	Paid		
Network Management	-	-	15	15	15	15
Proof of Concept	-	-	100	30	100	30
Total	-	-	115	45	115	45

Amounts approved by Grenoble Alpes Métropole 2003-2009



Recipient (funding)	2009				AMOUNT in €K	
	Investment		Operation		Overall total approved 2003-2009	Overall total paid 2003-2009
	Approved	Paid	Approved	Paid		
Network Management	-	-	15	15	15	15
Proof of Concept	-	-	150	-	150	-
Total	-	-	165	15	165	15

Amounts approved by the Isère County 2003-2009



Total Rhône-Alpes Region	3 500	1 750	5 816	856	54 978	42 553
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Summary of the multi-year scheduling of the CLARA program, 2003-2009

Status of the main sources of funding by the Auvergne Area



Recipient (funding)	2009				AMOUNT in €K	
	Investment		Operation		Overall total approved 2003-2009	Overall total paid 2003-2009
	Approved	Paid	Approved	Paid		
Auvergne Platform (a)	-	-	-	-	1 665	1 665
Proof of Concept	-	-	101	-	101	-
Total	-	-	101	-	1 776	1 665

(a) : Auvergne and ERDF Massif Central cover Auvergne and Loire County



Recipient (funding)	2009				AMOUNT in €K	
	Investment		Operation		Overall total approved 2003-2009	Overall total paid 2003-2009
	Approved	Paid	Approved	Paid		
Auvergne Platform	-	-	-	-	505	505
Total	-	-	0	0	505	505



Recipient (funding)	2009				AMOUNT in €K	
	Investment		Operation		Overall total approved 2003-2009	Overall total paid 2003-2009
	Approved	Paid	Approved	Paid		
Auvergne Platform (b)	-	-	-	-	1 355	1 146
Network Management	-	-	80	48	205	173
Proof of Concept	-	-	-	-	50	30
Total	-	-	80	48	1 610	1 349

(b) including €158 K expired in 2005

Updated December 31, 2009

As per standard practice and in order to simplify the presentation, fundings are indicated in the year they were approved.



Recipient (funding)	2009				AMOUNT in €K	
	Investment		Operation		Overall total approved 2003-2009	Overall total paid 2003-2009
	Approved	Paid	Approved	Paid		
Auvergne Platform	-	-	-	-	100	100
Network Management	-	-	45	15	70	40
Proof of Concept	-	-	30	10	30	10
Total	-	-	75	25	200	150



Recipient (funding)	2009				AMOUNT in €K	
	Investment		Operation		Overall total approved 2003-2009	Overall total paid 2003-2009
	Approved	Paid	Approved	Paid		
Auvergne Platform (c)	-	-	-	-	285	240
Network Management	-	-	30	30	80	80
Proof of Concept	-	-	44	-	44	-
Total	-	-	74	30	409	320

(c) including €45K expired in 2005



Recipient (funding)	2009				AMOUNT in €K	
	Investment		Operation		Overall total approved 2003-2009	Overall total paid 2003-2009
	Approved	Paid	Approved	Paid		
Auvergne Platform	-	-	-	-	50	50
Total	-	-	-	-	50	50

Summary of the multi-year scheduling of the CLARA program, 2003-2009

Status of the main sources of funding by the Auvergne Area



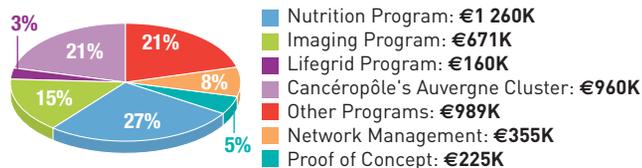
Recipient (funding)	2009				AMOUNT in €K	
	Investment		Operation		Overall total approved 2003-2009	Overall total paid 2003-2009
	Approved	Paid	Approved	Paid		
Auvergne Platform	-	-	-	-	40	40
Total	-	-	-	-	40	40



Recipient (funding)	2009				AMOUNT in €K	
	Investment		Operation		Overall total approved 2003-2009	Overall total paid 2003-2009
	Approved	Paid	Approved	Paid		
Auvergne Platform	-	-	-	-	40	40
Total	-	-	-	-	40	40

Total Auvergne Area	-	-	330	103	4 620	4 119
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Amounts approved in the Auvergne Area 2003-2009



IX Appendices

Appendix 1

Six focus areas to structure research at CLARA:

16 core programs within the focus areas of the ProCan program

Focus Area II “Infections and Cancer”

- Dissection et ciblage des dysfonctions télomériques et dans la télomérase pendant la carcinogénèse virale induite

Project Initiator: E.WATTEL (Oncovirologie et Biothérapies, Université Claude Bernard, Centre Léon Bérard)

Partners: P. JALINOT (Contrôle de l'Expression Génétique et Oncogénèse Virale, LBMC, UMR5239 CNRS/INSERM de Lyon, IFR 128 Biosciences Lyon Gerland), E. GILSON (UMR5239, Faculté de Médecine Lyon Sud, currently in Nice), J. GARIN (Laboratoire d'Étude de la Dynamique des Protéomes, CEA, DSV, IRTSV 3 Grenoble)

- Programme fédérateur sur les récepteurs toll like (TLR) et l'immunité innée

Project Initiator: M. TOMMASINO (Centre International de Recherche sur le Cancer, Lyon)

Partners: J. MARVEL (INSERM U851 Immunité, Infection et Vaccination, Équipe : Apoptose et mémoire CD8 memory, Lyon), C. CAUX (INSERM U590, Équipe Cytokines et Cancers, Centre Léon Bérard, Lyon), J. PLUMAS (INSERM U823/EFS Équipe Immunobiologie et Immunothérapie des cancers, Grenoble)

- Interactions entre les virus des hépatites B et C, et le dérèglement des voies intracellulaires au cours de la transformation cancéreuse des hépatocytes

Project Initiator: P.MERLE (INSERM U871 - Physiopathologie moléculaire et nouveaux traitements des hépatites virales, Lyon)

Partners: F. ZOULIM (INSERM U871 - Physiopathologie moléculaire et nouveaux traitements des hépatites virales – Équipe 1), M. OZTURK (INSERM-UJF U823 Institut Albert Bonniot, Équipe 12 : Génétique et Epigénétique de la Sénescence et du Cancer, Grenoble), C. CARON DE FROMENTEL (INSERM U590 - Cytokines et Cancer, Oncogenesis and Tumor Progression - Centre Léon Bérard,

Lyon), J.-Y. SCOAZEC (INSERM U865 – Tumeurs endocrines digestives : mécanismes de la tumorigénèse et de la progression tumorale, Hôpital Édouard Herriot, Lyon), M. RIVOIRE (INSERM U556 – Applications des ultrasons à la thérapie – Centre Léon Bérard, Lyon)

Focus Area III “Metabolism, Nutrition and Cancer”

- Microenvironnement tumoral et cancer du sein : implication des adipocytes et de leurs produits de sécrétion

Project Initiator: F. CALDEFIE-CHEZET (EA 4233, Laboratoire de Sciences Végétales et Fongiques Pharmaceutiques, Clermont-Ferrand)

Partners: M.-P. VASSON (EA 4233, Laboratoire de Biochimie, Biologie moléculaire et Nutrition, Clermont-Ferrand), H. Vidal (UMR INSERM 870 / INRA 1235, Lyon), O. DAMOUR (Banque de Tissus et Cellules, HCL, Lyon)

- Effets métaboliques, tissulaires et moléculaires d'un apport en tomates sur l'hyperplasie épithéliale de la prostate induite par un régime riche en lipides chez la souris invalidée pour les récepteurs aux oxystérols

Project Initiator: E. ROCK (Unité Nutrition Humaine, INRA, Clermont-Ferrand)

Partners: J.-M. LOBACCARO (UMR CNRS6247-Clermont Université-INSERM U931, Clermont-Ferrand), W. RACHIDI (CEA, Grenoble)

- Modélisation de l'évolution de réseaux de régulation transcriptionnelle au cours de la cancérogenèse, effet d'un apport nutritionnel

Project Initiator: G. STEPIEN (Unité de Nutrition Humaine, INRA U1019, Clermont-Ferrand)

Partners: J.-P. ISSARTEL (INSERM U836, Grenoble), J.-M. STEYAERT (Laboratoire d'Informatique, Ecole Polytechnique, Palaiseau)

Focus Area IV “Epidemiology, SHS, Patient Information and Organization of Care”

- **Analyse des déterminants socio-économiques de la participation au dépistage organisé des cancers colorectaux et évaluation de ce dépistage. Etude dans les départements de l'Isère, de la Savoie, de la Haute-Savoie et de l'Ain**

Project Initiator: P. DELAFOSSÉ (Registre du Cancer de l'Isère, Meylan)

Partners: Dr C. EXBRAYAT (Office de lutte contre le cancer 38), Dr A. PECOUD (Réseau pour le Dépistage des Cancers en Haute-Savoie, Annecy), Dr A. DELORAINÉ (Dépistage cancer en Savoie, Chambéry), Dr A. BATAILLARD (Office de lutte contre le cancer 01, Bourg-en-Bresse), Pr G. LAUNOY (Registre des cancers digestifs du Calvados, CHU Caen), Dr J. LABARÈRE (Unité d'évaluation du CHU de Grenoble)

- **L'expérience intime du cancer : représentation du corps et des traitements anti-cancéreux**

Project Initiator: C. DURIF-BRUCKERT (MCF, Université Lyon 2)

Partners: P. ROUX (GREPS, EA 4163, Lyon 2), J. GOFFETTE MCF et Dr R. GUILLoux (LEPS, EA 4148, Lyon 1), A. GUIOUX MCF et Dr E. LASSERRE (CREA, EA 3081, Lyon 2), Dr V. REGNIER (Département de Santé Publique, ICL, St-Priest-en-Jarez)

- **Registre des tumeurs trophoblastiques en Rhône Alpes-Auvergne : aspects épidémiologiques et socioéconomiques**

Project Initiator: Dr A. SCHOTT (Pôle IMER, HCL Lyon)

Partners: Dr F. GOMEZ (CLB), Dr F. OLIVE (CHU Grenoble), Dr B. TROMBERT (CHU St Etienne), Dr M. COLONNA (Registre du Cancer de l'Isère, Meylan), Dr N. BOSSARD et L. REMONTET (HCL, laboratoire de biostatistiques des Hospices Civils de Lyon), Pr D. RAUDRANT, Pr F. GOLFIER et Dr J. MASSARDIER (HCL, Hôtel Dieu), Dr L. FRAPPART (HCL, HEH)

- **ALTO 2 - assessing long term outcomes in anti cancer therapy part 2**

Project Initiator: Dr D. PEROL (CLB, Lyon, Unité de biostatistiques et d'évaluation des thérapeutiques du CLB, Lyon)

Partners: Dr C. DURIF-BRUCKERT (Institut de Psychologie GRePS EA4163, Lyon 2).

- **Étude prospective de la dépression chez les patients atteints de cancer et approche des critères modulant le processus décisionnel de la prise en charge**

Project Initiator: Dr P. SALTEL (Unité de Psycho-oncologie, CLB, Lyon)

Partners: W. RHONDALI (Département Interdisciplinaire de Soins de Support des Patients en Oncologie (DISSPO) – CLB)

- **Soins et hospitalisation à domicile en oncopédiatrie : analyse des comportements des soignants**

Project Initiator: Y. ZERBIB (Département de Médecine Générale de l'Université Claude Bernard Lyon 1)

Partners: N. MOUMJID, M. MORELLE et R. REMONAY (GATE, UMR 5824, CNRS), E. FOURNERET (Ecole Doctorante en Sciences Humaines et sociales ED n° 238)

Focus Area VI “Tumor Escape”

- **TCL1, chronic lymphocytic leukaemia, chemoresistance, tumoral escape, HDAC inhibitors**

Project Initiator: J.-O. BAY (EA 3846, Thérapie ciblée combinatoire en onco-hématologie, Université d'Auvergne, Clermont-Ferrand)

Partners: M. CALLANAN (INSERM U823, Institut Albert Bonniot, Grenoble), F.-LOÏC COSSET (INSERM U758, Ecole Normale Supérieure de Lyon/INSERM, Lyon), D. GUYOTAT (Service d'Hématologie Adulte, Université Jean Monnet, Saint Etienne), J.-Y. CAHN (Service d'Hématologie Adulte, Université de Grenoble, Grenoble)

- **Identification of the key targets of LKB1 tumor suppressor function using a Structure/function analysis approach**

Project Initiator: V. MIROUSE (UMR CNRS 6247, INSERM U931, Clermont Université, Clermont-Ferrand),

Partners: M. BILLAUD (UMR 5201, Lyon)

- **Phenotypic characterisation of human tumor cells using integrated microfluidic**

Project Initiator: J.-P. RIEU (Laboratoire de Physique de la Matière Condensée et Nanostructures, UMR 5586 CNRS Université Claude Bernard Lyon 1, Lyon)

Partners: R. FERRIGNO (Institut des Nanotechnologies de Lyon, Lyon), H. MERTANI (Centre Léon Bérard, UMR 5534 CNRS Université Claude Bernard, Lyon), F. BRUCKERT (Laboratoire des Matériaux et du Génie Physique, Grenoble), M. BLOCK (Institut Albert Bonniot, CR INSERM U823, Grenoble)

- **Regulation of the tumor angiogenic switch by a fragment derived from the extracellular matrix protein collagen V from molecular mechanisms to therapeutic perspectives**

Project Initiator: F. RUGGIERO (Institut de Biologie et Chimie des Protéines UMR CNRS 5086-Université Lyon 1, Lyon), *Partners:* J.-L. COLL (Institut Albert Bonniot, Grenoble), S. GUERRET (Novotec, Lyon)

And... The mobility of young researchers as part of ProCan Focus Area III “Metabolism, Nutrition and Cancer”

- Formation sur les logiciels d'analyse de biopuces obtenues après la technique de CHIP-on-Chip, plus particulièrement appliquée à la mesure des effets des phyto-oestrogènes du soja sur les marques épigénétiques dans les cancers du sein.
Support to: R. BOSVIEL (étudiant en thèse), Laboratory: EA 4233, Département d'Oncogénétique du Centre Jean Perrin
- Continuation de mise en place de co-cultures cellules tumorales mammaires / adipocytes en utilisant un modèle à trois dimensions de « peau adipeuse reconstruite », le but étant de mesurer l'impact de la sécrétion d'adipokines sur la tumeur.
Support to: L. DELORT (Maître de Conférences), Laboratory: EA 4233, Laboratoire de Sciences Végétales et Fongiques Pharmaceutiques.
- Acquisition de la technique « fat pad » pour la mise en place d'un modèle expérimental de cancer mammaire chez la souris afin d'étudier les relations entre le tissu adipeux mammaire (sécrétion d'adipokines), les cellules tumorales et les cellules NK.
Support to: B. LAMAS (étudiant en thèse), Laboratory: EA4233, Laboratoire de Biochimie, Biologie Moléculaire et Nutrition.
- Apprentissage d'une technique d'évaluation de l'apoptose par cytométrie en flux sur la lignée SW620 (colon) pour la mesure de l'effet pro-apoptotique des polyphénols de verveine par détection des récepteurs de mort Fas et TRAIL.
Support to: L. LENOIR (étudiant en thèse), Laboratory: EA4233, Laboratoire de Pharmacognosie et Phytothérapie.

And... Five projects supported by the Regulatory Unit of CLARA

The Regulatory Unit supported five nanotracer projects as part of ProCan Focus Area I “Nanotechnologies, Imaging and Cancer”. They use nanotechnologies for cancer diagnosis and therapy, in order to bridge the gaps between research and development of nano-objects:

- **Imagerie optique de fluorescence et nanotraceurs RAFT-RGD (détection per-opérateur / fluorescence) ;**
Project Initiator: O. ALLARD, Fluoptics.
- **Nano-émulsions pour imagerie optique de fluorescence**
Project Initiator: I. TEXIER-NOGUES, P. BOISSEAU - CEA, LETI, Dpt Microtechnologies pour la Biologie et la Santé, Grenoble.
- **Structures hétéroaromatiques halogénées pour l'imagerie par TEP et la radiothérapie interne vectorisée du mélanome.**
Project Initiator: N. MOINS - EA 4231 - UMR 484 INSERM, Université d'Auvergne, Clermont-Ferrand.
- **Particules hybrides comme agents de curiethérapie**
Project Initiator: C. BILLOTEY - Service de Médecine Nucléaire, Hôpital Edouard Herriot, Lyon.
- **Agents de contraste IRM à base de nanosondes hybrides**
Project Initiator: C. LOUIS - Nano-H.

The abstracts of CLARA core programs selected in 2009 by INCa are available on www.canceropole-clara.com

Appendix 2

CLARA projects selected by INCa in 2009

In 2009, INCa selected 25 CLARA projects through the various calls for proposals that it launched. This appendix presents the list of winning proposals. They are classified by the type of call for proposals.

Integrated Research Action Program: Hepatocellular Carcinoma (PAIR CHC 2009) - National Aids Research Association (ANRS) - Association for Cancer Research (ARC) - INCa

- L'influence de vie, du régime alimentaire, de l'obésité et de l'inflammation sur les risques de carcinome hépatocellulaire et de cholangiocarcinome : recherche prospective détaillée basée sur des cohortes françaises et européennes dans de cadre de l'étude EPIC-*Coordination: M. JENAB (CIRC) - €407 000.*
- TLR3, une nouvelle cible thérapeutique dans les hépatocarcinomes - *Coordination: S. LEBECQUE - Université Claude Bernard - €364 000.*
- HCV-induced liver carcinogenesis: analysis of TGF-B pathway perturbations - *Coordination: V. LOTTEAU - INSERM - €449 000.*
- Early steps of NEoplastic transformation of Liver cells and interplays with Viral Infection - *Coordination: P. MERLE - INSERM - €510 000.*

Translational research in cancer research - DHOS INCa

- Tumeurs cérébrales : validation chez l'homme d'une stratégie innovante d'empreinte moléculaire et cellulaire destinée à la caractérisation de la région péri-tumorale des tumeurs cérébrales comme les gliomes - *Coordination: F. BERGER - €210 000.*
- Cancer du sein : validation de l'implication de la réponse immunitaire chez le patient dans l'efficacité thérapeutique de la chimiothérapie néo-adjuvante *Coordination: C. CAUX - €338 000.*
- Cancers hématologiques : développement d'une nouvelle approche pour leur détection précoce, leur diagnostic, leur pronostic et leur suivi - *Coordination: S. KHOCHBIN - €600 000.*

Support for training in translational research in cancerology for medical students and young physicians

- Modélisation de l'impact des signaux antigéniques et inflammatoires sur l'incidence et la nature des

néoplasies B chez la souris - Applicant: E. BACHY - Host laboratory: INSERM U851-Equipe « Apoptose et mémoire lymphocytaireB », LYON - €90 000.

- Rediriger les lymphocytes t cytotoxiques contre les antigènes leucémiques - Applicant: A. MARABELLE - Host laboratory: "Oncogenèse et Progression Tumorale" INSERM U590, Centre Léon Bérard, LYON - €190 000
- Développement et validation d'une signature métabonomique comme biomarqueur pronostique et/ou prédictif du cancer du sein - Applicant: O. TREDAN - Host laboratory: Centre Européen de RMN à Très Hauts Champs, FRE 3008 CNRS / ENS-Lyon / UCB, LYON 1 - €105 000.
- Dynamic analysis of tumor marker kinetics during treatment using modeling - Applicant: B. YOU - Host laboratory: EA 3738. Ciblage thérapeutique en oncologie, Faculté de médecine, LYON-SUD.
- Rôle des cellules souches tumorales dans la réponse des Glioblastomes à l'hadronthérapie et à l'association Témzolomide-irradiation. - Applicant: O. DIAZ - Host laboratory: Laboratoire de radiobiologie cellulaire et moléculaire EA 3738 - Faculté de médecine, LYON SUD - €35 000.
- Evaluation en clinique de l'angiogénèse tumorale cérébrale par imagerie par résonance magnétique : quantification du volume sanguin cérébral - Applicant: T.- A. PERLESBARBACARU - Host laboratory: Institut Neurosciences INSERM U 836, Team 5 : Neuroimagerie Fonctionnelle et Métabolique, Team 7 : Nano-médecine et cerveau, GRENOBLE - €100 000.

Research in Human and Social Sciences, Public Health and Epidemiology

- Quantification du sur diagnostic dans le programme de dépistage organisé du Cancer du sein - Coordination: A. SEIGNEURIN - Registre du Cancer de l'Isère, Université Joseph Fourier, UFR de médecine, CHU de Grenoble - €88 000.
- Variants de séquence du génome mitochondrial et risque de Cancer du sein - Coordination: O. SINILNIKOVA et D. COX - Centre Léon Bérard, Hospices Civils de Lyon €336 000.
- Modified lung cancer by multiple exposures at work and environmental risk factors combined - Coordination: P. BOFFETA - Centre International de Recherche contre le Cancer, Lyon - €344 000.

Open biomedical research projects 2009

- The dependence receptor TrkC and its ligand NT-3 in neuroblastoma, from basic research to drug therapy – Project Initiator: P. MEHLEN – €600 000.
- Functional basis of genetic susceptibility due to a common polymorphism in TP53 intron 3: effect on alternative splicing and on the synthesis of v Np53, an isoform which counteracts p53 function – Project Initiator: P. HAINAUT – €400 000.
- Reactivation of embryonic TWIST gene: a link between early phases of tumor progression and metastatic dissemination – Project Initiator: A. PUISIEUX – €207 000.

Certification of reference centers for rare cancer in adults

- Les sarcomes des tissus mous et des viscères – Coordination: clinique, J.-Y. BLAY – Centre Léon Bérard and anatomopathology, J.-M. Coindre – Institut Bergonié de Bordeaux – €400 000.
- Les tumeurs rares du péritoine, avec le Centre Hospitalier Lyon-Sud/HCL/Pierre Bénite – Coordination: F. GILLY – €150 000.
- Les tumeurs neuro-endocrines malignes sporadiques et héréditaires – Coordination: clinique, P. NICCOLI – Hôpital La Timone (AP-HM,) and anatomopathology J.-Y. SCOAZEC – Hôpital Édouard Herriot (HCL) – €150 000.
- Les maladies trophoblastiques gestationnelles – Coordination: D. Raudrant – Centre Hospitalier Lyon Sud/HCL/Pierre Bénite – €150 000.

Reinforcement of the organization of anatomy and pathological cytology for a coordinated, multidisciplinary approach to molecular analysis of cancer

- Organisation de la collecte, du conditionnement et du traitement des prélèvements en vue d'analyses biomoléculaires au CHU et au CRLCC de Clermont-Ferrand – Coordination: F. PENAULT-LLORCA – €150 000.
- Réseau lyonnais de pathologie moléculaire du cancer – Coordination: J.F. SCOAZEC – €300 000.

And... Five hospital-based Clinical Research Projects – Cancer – PHRC – DHOS INCa

- Evaluation prospective multicentrique d'une stratégie de préservation vésicale combinant chimiothérapie néo-adjuvante par mvac intensifié et résection tumorale endovésicale optimale chez des patients présentant un cancer urothélial infiltrant de stade localisé – Coordination: N. MOTTET – Clinique Mutualiste de Saint-Étienne – €250 000.
- Étude de phase III randomisée, multicentrique, estimant en situation post-opératoire l'efficacité d'une radiochimiothérapie versus une radiochimiothérapie suivie d'un traitement d'entretien par cetuximab chez des patients porteurs d'un carcinome épidermoïde des voies aéro-digestives supérieures – Coordination: S. RACADOT – Centre Léon Bérard – €395 000.
- Estimation du risque de polypose colorectale chez les porteurs monoalléliques d'une mutation du gène MYH – Coordination: J.-C. SAURIN – Centre Hospitalier Lyon Sud – €230 000.
- Étude prospective randomisée de phase III, ouverte et multicentrique, comparant l'allogreffe à l'autogreffe de cellules souches hématopoïétiques, suite à une chimiothérapie conventionnelle dans traitement de première ligne des lymphomes non hodgkiniens de phénotype T périphérique du sujet jeune (18-60 ans) – Coordination: O. TOURNILHAC – CHU Clermont-Ferrand – €215 000.
- Multicenter phase I/II study of continuous dosing of Sunitinib in non-GIST sarcomas with concomitant radiation therapy – Coordination: M.-P. SUNYACH – Centre Léon Bérard – €245 000.

And... One grant for Innovative and Costly Techniques (STIC)

- Evaluation médico-économique de la prostatectomie radicale coelioscopique assistée du robot chirurgical DA VINCI® ETUDE ROBOTCAP – Coordination: M. COLOMBEL – Hôpital Édouard Herriot – €510 000.

The abstracts of CLARA projects selected in 2009 by INCa are available on www.cancerpole-clara.com

Appendix 3

CLARA's 2009 "Proof of Concept" Projects

Seven new projects with a budget of €5.6M

CLARA is supporting seven new projects from its "Proof of Concept" call for proposals launched in March 2009. This appendix presents the list of winning proposals. They are

listed according to the program's three categories: "Industrial Proof of Concept", "Nano Transfer Cancer" and "Emergence".

- **"Industrial Proof of Concept"** supports innovative medical treatment and medical device projects in their proof of concept phase.
- **"Nano Transfer Cancer"** targets the field of nanomedicine in oncology, and in particular the development of biomarkers and biomedical devices for taking biological samples, including blood samples, the preparation of samples possibly including the use of lab-on-chip and high-speed molecular analysis.
- **"Emergence"** aims to provide additional resources to projects already supported by an economic development organization or an incubator of Rhône-Alpes Auvergne, in order to enable it to reach the Proof of Concept stage, so as to foster the development of marketable applications of research findings in the form of transfers or the creation / start-up of a company during the course of the project.

Four "Industrial Proof of Concept" Projects

- The CITCAP project with Innate Pharma seeks to establish proof of concept of combining different cancer treatments (chemotherapy, tyrosine kinase receptor inhibitors, monoclonal antibodies and radiation therapy) with a new candidate targeted agent, "TLR3" receptor ligand in non-small-cell lung cancer.
- The IPROMAH project with IDD Biotech seeks to develop new antibodies to confirm the efficacy in animals (preclinical) of monoclonal antibodies adapted to the treatment of malign lymphopathies, and to demonstrate the industrial application of the bioprocesses implemented.
- The CLARAFT project with Fluoptics aims to significantly improve the detection of tumor margins and metastases perioperatively in sarcomas overexpressing the $\alpha v \beta 3$ integrins, by fluorophores detectable by near infrared camera coupled with RAFT-c(RGD)₄ targeting the $\alpha v \beta 3$ receptors.
- The NT3-TARGET project with Netris-Pharma aims to establish the proof of concept in animals that inhibiting the NT-3/TrkC interaction with two types of candidate drugs as a promising therapeutic approach in metastatic breast cancer.

Budget of €3.7M for the four projects, including €1.6M granted by CLARA and €2.1M by innovative partner companies.

One "Cancer Nano Transfer" Project

- The LANTHARAD project targets the preclinical proof of concept of a new approach based on hybrid probes comprising rare earth elements (such as gadolinium) with a view to minimizing the dose delivered to the patient and to make radioresistant tumors, such as melanoma and chondrosarcoma, sensitive.

Budget: €660 000, including €410 000 granted by CLARA and €250 000 contributed by the partnering economic development organization (Lyon Ingénierie Projets) and by Nano-H.

Two "Emergence" Projects

- The CANCERDRUG project targets the preclinical development of new antiproliferative agents such as the D5 molecule, usable within the framework of chemotherapy treatments. The objective of the project is to exploit the patent and create an innovative new company, Ecrins Theurapeutics, to run the clinical trials.
- The LIPOBAK project is developing an innovative therapeutic approach based on the use of a proapoptotic membrane protein (Bak protein) inserted into a lipid vesicle (recombinant proapoptotic proteoliposomes) for the treatment of glioblastoma. The project will result in the creation of a start-up, Synthelis, for the next development phases.

Budget: €1.2M, including €0.7M granted by CLARA and €0.5M mobilized by Floralis, a subsidiary for the development of marketable applications of research findings of Joseph Fourier University, the GRAIN business incubator and Oseo-innovation.

The abstracts of CLARA "Proof of Concept" projects are available on www.cancerpole-clara.com

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Under the aegis of the Bullukian Foundation

CLARA

60, avenue Rockefeller

F69008 Lyon

Tel. +33 (0)4 37 90 17 10

Fax +33 (04) 37 90 27 03

infos@canceropole-clara.com

www.canceropole-clara.com

Our partners

