To be aware of one’s ignorance is the best path towards knowledge.

Chinese proverb
For the Cancéropôle Lyon Auvergne Rhône-Alpes (CLARA), 2008 was the year of operational implementation of the ProCan program with its six Focus Areas, the launch of structural programs and the hosting of a number of forums and symposiums. CLARA also introduced a variety of new actions to strengthen industrial-academic partnerships.

CLARA has made a considerable effort to extend the Proof of Concept program to the entire region. Two top-priority themes - Nanomedicine & Cancer and Infections & Cancer (in collaboration with LyonBiopôle) - were promoted in 2008 calls for projects and five promising new initiatives have now been added to our portfolio thanks to the financial support of local authorities in the Rhône-Alpes Auvergne region.

The vitality of local research teams in the field of cancer was also observed in the number of proposals relayed by CLARA in the framework of the INCa calls for projects in February and November 2008.

In this thriving environment, CLARA intensified its collaboration with other organizations involved in research, such as LyonBiopôle and the Synergie Lyon Cancer and Finovi Foundations, in particular as part of ProCan Focus Area II on “Infections and Cancer.” CLARA will continue this approach and its promotion of scientific activities through a policy of outreach to other cancer clusters and through international development.

CLARA’s structure is now well in place, allowing the cluster to fully assume its role as a federating force. This is achieved by a scientific strategy aimed at optimizing resources and targeting skills. It takes strength from the effectiveness of industrial-academic partnerships, another key asset which will once again be a major focus in 2009.

Today, CLARA’s genuine contribution to cancer research has become increasingly visible, which enables the cluster to play a crucial role in coordinating the efforts of the Rhône-Alpes Auvergne region.
I - Mobilizing region’s players

In 2008, CLARA's new governance became operational, thus confirming that the organizational choices made in 2007 were sound.

1. Collegial governance

Cancéropôle relies on collegial governance that actively involves all of the network’s stakeholders. Funding providers, academic organizations and industrial partners all play a key role in the cluster’s governance through five committees:
- The Strategic Orientation Committee determines CLARA’s major orientations.
- The Executive Committee is in charge of implementing the decisions made by the Strategic Orientation Committee. It approves and allocates the funding.
- The Development Committee, created in 2008, guides CLARA’s scientific orientations.
- The Scientific Steering Committee manages CLARA’s scientific activities.
- The Industrial Steering Committee represents the interests of industrial partners.

CLARA: landmarks

- Role
  To coordinate the region’s skills and infrastructures to benefit cancer research in order to meet the aims of the French Cancer Plan.
- A dual aim
  To bring researchers, clinicians and industrial partners together in a single network and channel their joint efforts into operational research programs that promote:
  - rapid transfer of academic knowledge towards patient care
  - marketable applications for the research findings
- A broad network
  - 130 academic research teams
  - 80 clinical services
  - 60 industrial partners
- A privileged region: Lyon Rhône-Alpes Auvergne
  The Rhône-Alpes region has been a leading force in the fight against cancer for many years. Combined with the Auvergne region, it features:
  - Five universities, four university hospitals, the International Agency for Research on Cancer (IARC), two Cancer Centers (Léon Bérard in Lyon and Jean Perrin in Clermont-Ferrand), the Loire Cancer Institute (ICL in Saint-Etienne) and the Albert Bonniot Institute in Grenoble, as well as teams from the French National Institute for Health and Medical Research (INSERM), the French National Center for Scientific Research (CNRS), the Ecole Normale Supérieure Graduate School (ENS) and the French Nuclear Energy Commission (CEA).
  - High-level technological platforms
  - Network organizations, including the Lyonbiopôle competitiveness cluster and the Grenoble nanotechnology cluster, the “Synergie Lyon Cancer” RTRS Research Foundation and the Hadrontherapy project of the Centre Etoile.

A unique industrial-oriented research program

In order to develop partnerships between the academic and industrial spheres in Rhône-Alpes Auvergne, CLARA has set up a program to support high-potential innovative projects, leading to a Proof of Concept and to industrial transfer. Named “Proof of Concept,” this program has received €13 million funding from industrial partners to benefit 14 projects selected by CLARA.

A total budget of €110 million and diverse sources of funding

Since CLARA was founded, it has been granted subsidies from local authorities (€50 million), the French State and National Cancer Institute (€45 million), and industrial partners (€13 million). In addition, CLARA partners coordinate European projects accounting for an overall budget of €15 million.

CANCÉROPÔLE CLARA GOVERNANCE

- Development Committee
- Executive Committee
- Network Management
- Industrial Steering Committee
- Scientific Steering Committee
- Strategic Orientation Committee
- CLARA stakeholders
- Funding providers
- Academic stakeholders
- Network Management Team
- Outside Experts
- Networks
- Projects
- Platforms

CLARA stakeholders
- Strategic Orientation Committee
- Industrial Steering Committee
- Network Management Team
- Scientific Steering Committee
- Outside Experts

In 008, CLARA’s new governance became operational, thus confirming that the organizational choices made in 2007 were sound.
II - Organizing research around six key focus areas

The French National Cancer Institute (INCa) has renewed its trust in CLARA as part of the “ProCan 2007-2010” program. This trust has played a decisive role in its actions. In 2008, it led CLARA to organize the research efforts of the Auvergne Rhône-Alpes region’s 210 research teams around six focus areas. These strengths provide a true value for France’s national cancer research program.

2. An operational scientific steering committee

The Scientific Steering Committee specifically focuses on orienting and meeting the objectives of CLARA’s six focus areas. This multidisciplinary body is composed of 14 members.

Its missions:
• Facilitating progress in translational research.
• Optimizing the process for answering to calls for projects.
• Organizing CLARA’s Scientific Forum.
• Setting out effective strategies for collaborating with other research clusters.

• The organization of high-profile symposiums on specific topics.
• The setup of a regulatory unit combined with a training program, in order to facilitate the transition between research and product development.

These actions unite a number of the Rhône-Alpes Auvergne regional partners in the field of cancer research. We hope that this dynamic will continue to build and will benefit from the attractiveness of the network, which can bring in new members and further strengthen the working groups with their expertise.

3. A dynamic industrial steering committee

From its set up, CLARA initiated immediately an Industrial Steering Committee that represents its industrial partners in order to guide the cluster’s activities. Giving industrial partners an active role within CLARA illustrates the network’s strong willingness to transfer research findings towards clinical applications more quickly, to maximize the economic potential of these breakthroughs and to make the region more attractive.

In October 2008, this Committee organized an “Industrial - Academic Forum” – Based on a business convention concept, this event aims to encourage collaboration between academic, clinical and industrial partners and to prompt the development of concrete partnerships. The success of this “Industrial - Academic Forum” has revealed the industrial’s growing interest in CLARA.
FOCUS AREA I ADVANCES IN 2008

- High-impact scientific activities and events

Scientific activities and events are a cornerstone of Focus Area I. As nanotechnology originates from a non-medical technological field, its use requires complementary expertise. Thus, new participants are contributing to cancer research. CLARA sent out a call for letters of intent to identify research teams able to develop clinical applications for nanotechnology in the field of cancer. This process helped to highlight areas of expertise, as well as to build a targeted scientific activities and events program. Thus, topics such as nanoparticles, radiotracers, nanotracers, biomarkers, imaging and regulatory aspects of nanoparticles have mobilized the region’s researchers. Coordinated by a steering committee that represents research, clinical and industrial partners from Clermont-Ferrand, Grenoble, Lyon and Saint-Etienne, these scientific activities and events are playing their intended role. In addition to organizing meetings between the various parties, they have led to new collaborative ventures, including two new programs.

Vital to the consistency of scientific activities in the region, theme-related events are the prelude to new collaborative projects. It helps:
• to promote the scientific aims
• to identify teams and bring them together in specific topic areas
• to encourage a cross-disciplinary approach.

- Outside collaborative projects: the PACA Cancer Research Cluster

The CLARA and PACA cancer research clusters have pooled their energies in the field of imaging. This collaborative venture is currently being set up.

TRAINING PROGRAM: “DEVELOPMENT OF A BIOLOGICAL AGENT FROM LAB BENCH TO HUMAN: REGULATORY ASPECTS”

This training program aims to specify the regulatory and practical framework for developing a biological product and transferring its use in humans. The principles of evaluation, processes and related issues are presented. The “Quality,” “Toxicology” and “Clinical evaluation” aspects are explored from a theoretical perspective as well as through actual case studies by specialists in the field.

- Two new programs

“Nanotracers”

This program aims to assist projects involving nanotechnology during the phase in which research findings are transferred to application for patients. Launched in partnership with Lyon Civil Hospitals (HCL), this initiative results from the observation that there is a lack of guidelines on study regulations and on the development of biological products derived from nanotechnology research. This program has enabled the setup of a regulatory unit. It is composed of a quality specialist with expertise in regulatory aspects, a specialist in pharmacotoxicology and an expert in charge of clinical evaluation. A training program on the regulatory aspects of nanotechnology completes this program (see box).

“Biomarkers”

This program involves implementing an integrated approach to nanomedicine for personalized prescription of antangiogenics. This cross-disciplinary program brings together oncologists, biologists and technology specialists in order to validate a process to predict response to targeted therapies.

- Outside collaborative projects: the PACA Cancer Research Cluster

The CLARA and PACA cancer research clusters have pooled their energies in the field of imaging. This collaborative venture is currently being set up.

III - Cancer research in Rhône-Alpes Auvergne

1. New nanotechnology-based diagnostics and treatment tools

Focus area I: Nanotechnology, Imaging and Cancer

Focus Area I aims to design new tools to detect and treat cancer, as well as to better understand the mechanisms of malignant tumors via imaging and nanotechnology. Combined with the analytical power of nanotechnology, the miniaturization of imaging tools enables earlier detection of cancers and less invasive treatment thanks to the development of more specific targeted therapies.

SPOTLIGHT

CLARA is France’s only cancer research cluster with a top priority focus area on nanotechnology research.

The scientific missions of Focus Area I
• Improving access to micro and nanotechnology: miniaturization, surface modification, microfluidics and nanoparticles.
• Developing imaging and contrast enhancement methodology.
• Integrating innovative biological analysis tools, from in vitro diagnostics (proteomics and genomics of circulating biomarkers) to molecular imaging.
• Contributing to the development of new molecular therapeutic strategies.
• Developing nanotoxicology research programs.
• Studying the social, economic and ethical impact of these new approaches.

PORTFOLIO

The main theme addressed in Focus Area I is the optimization of nanotechnology development in order to improve imaging, diagnostics and therapy.

This innovative and promising focus area has convinced a range of funding providers:
• INCa is supporting 10 projects related to breast, lung and brain cancers and to technological innovation studies.
• Six projects have been selected as part of the “Proof of Concept” program.
• Seven projects have received funding from the French National Research Agency (ANR) and European bodies.

In 2008, two patents were filed as a result of research conducted by CLARA teams. These results attest to the effectiveness of the cluster’s research transfer efforts.
Focus Area II: Infections and Cancer

Cancers either induced or associated to infections are a veritable public health scourge. This results from the action of specific infectious agents, mainly viruses:
- Liver cancer, with the hepatitis B and C viruses
- Cervical cancer, with human papillomavirus (HPV)
- Lymphoma, with Epstein-Barr virus
- Leukemia, with adult leukemia virus (HTLV)
- Kaposi’s sarcoma with the human herpes virus (HHV)
- Gastric cancer caused by the Helicobacter pylori bacterial strain.

The primary aim of the “Infections and Cancer” focus area is improving the prevention, diagnosis and treatment of viral-induced cancers. Prevention strategies, in particular, are a critical focus, as they provide an effective means of curtling incidence of these types of cancers.

SPOTLIGHT

15 to 20% of cancer cases worldwide (liver cancer, cervical cancer, leukemia, and others) are caused by or related to infections.

The scientific missions of Focus Area II
- Identifying mechanisms of immune responses and their regulation/deregulation in cancers, infections and more particularly viral-induced cancers.
- Describing the molecular mechanisms of malignant transformation, particularly in viral-induced cancer models.
- Developing new diagnostic and therapeutic strategies for improved treatment of cancers, particularly those related to infections.

Focus Area II ADVANCES IN 2008

- Structured scientific activities and events
  In 2008, the program of scientific activities and events for Focus Area II revolved around two key areas:
  - Immune response in cancers and infections.
  - Molecular mechanisms in malignant transformation.

- Three core programs
  **Dissection and targeting of telomere dysfunctions in telomerase during viral-induced carcinogenesis**
  This program aims to verify the gene regulation of telomere and of the hTERT promoter for diagnostic, prognostic and therapeutic purposes (development of potentially antineoplastic peptides).
  Project Leader: Eric Wattel (INSERM UMR 5537 – Claude Bernard University, Léon Bérard Cancer Center, Oncology and Biotechnology)“Federative program on Toll-Like Receptors (TLR) and innate immunity”
  This program aims to bring together the tools available in the Rhône-Alpes Auvergne region on Toll-Like Receptors (TLR) and innate immunity. It also meets the need to implement new tools and techniques.
  Coordination: Massimo Tommasino (International Agency for Research on Cancer – IARC, Infectious and Cancer Biology Group)“A platform to isolate primary human hepatocytes and progenegative hepatic cells”
  This program is devoted to setting up a platform to prepare and store human hepatocytes from resections and to analyze the early steps in carcinogenesis.
  Co-leaders: Philippe Merlio (INSERM U817 - Claude Bernard University, Hepatology and Gastroenterology Unit, Hôtel-Dieu Hospital, Molecular Pathophysiology and new treatments for viral hepatitis, Pathogenesis of Viral Hepatitis B and C, and Viral-Induced Hepatic Oncogenesis) and Bækary Sylla (International Agency for Research on Cancer – IARC, Infectious and Cancer Biology Group)

IN THE RHÔNE-ALPES AUVERGNE REGION, A NUMBER OF ORGANIZATIONS ARE INVOLVED IN THE INFECTIONS AND CANCER FOCUS AREA:
- Léon Bérard
- Synergie Lyon Cancer Foundation (RTRS network)
- The Finovi Foundation (RTRA network)
- The International Agency for Research on Cancer (IARC)
- The Léon Bérard Cancer Research Center
- Albert Benoit Institute
- École Normale Supérieure Graduate School (ENS)
- Lyon Civil Hospitals (HCL)
- French Blood Agency (EFS)
- INSERM, CNRS, Universities and CLARA, whose federating role is essential to structuring the research efforts.

Focus Area III: Nutrition and Cancer

Combining nutrition, oncology, integrated physiology and genetics in order to prevent cancer is the aim of Focus Area III. Its ambition is to give a more solid scientific basis to nutritional recommendations made as part of national and international cancer prevention policies.

The research in this focus area falls under two main areas:
- Identifying food components able to curb the occurrence of hormone-dependent cancers (breast and prostate) and to describe their mechanisms of action using molecular approaches.
- Understanding the links between obesity and breast oncogenesis and developing nutrition-based prevention strategies.

The scientific missions of Focus Area III
- Developing cross-disciplinary research in order to foster complimentary skills.
- Specifying the nature and effects of active food substances and their metabolites in cancer prevention.
- Encouraging preventive and curative translational research.

FOCUS AREA III ADVANCES IN 2008

- Outside collaborative projects: Grand-Est Cancer Research Cluster - DFKZ (Germany) - International Agency for Research on Cancer (IARC) - Lyonbiopôle - Synergie Lyon Cancer Foundation (RTRS) – Finovi Foundation (RTRA)

The dynamism of the CLARA cancer research cluster’s partnership policy has led it to build relations with regional players active in various topics within the “Infections and Cancer” focus area. In 2008, several initiatives and accomplishments materialized:
- A brainstorm session (April 14, 2008) with the Lyonbiopôle competitiveness cluster, the Synergie Lyon Cancer Foundation (RTRS) and the Finovi Foundation (RTRA) in order to determine CLARA’s positioning in relation to these other organizations. This process led to stronger relations with Lyonbiopôle, namely the publication of a special “CLARA” issue of Lyonbiopôle’s newsletter, FO-CUS.
- Preparation of a joint symposium featuring the CLARA and Grand-Est cancer research clusters, DFKZ (Germany) and the International Agency for Research on Cancer (IARC).
- A workshop project on the theme of “virology and cancer”, in partnership with the Mérieux, FINOVI and Synergie Lyon Cancer Foundations and Lyonbiopôle.

PORTFOLIO

In anticipation of the INCa call for projects in the “Hepatocellular Carcinoma” category (November 2008), the network emphasized the consistency of its submissions by carrying out letters of intent to request funding. This was followed by a coordination meeting between potential project initiators.

- INCa is supporting seven projects related to breast and ovarian cancers, to hepatocellular carcinoma, to plasmacytoid dendritic cells and to leukemia.
- Four projects from the “Proof of Concept” program involve industrial members of the Lyonbiopôle competitiveness cluster.
- 17 national (IARN - ANR) and international projects are underway. They involve immunology, apoptosis, epigenetics and various types of viral-induced cancers.

The advances generated by research in the “Infections and Cancer” focus area led to two patent filings in 2008. The transfer of these findings to the industrial phase will thus enable them to be used in humans more quickly.

3. Nutrition-based cancer prevention strategies
FOCUS AREA III ADVANCES IN 2008

Structured scientific activities and events

The activities in the “Nutrition and Cancer” focus area target breast and prostate cancers and, more particularly, the identification of food components able to curb the occurrence of hormone-dependent cancers and understanding the links between obesity and breast oncogenesis.

In 2008, the scientific activities and events were geared towards:
- Finding research projects that are complementary from a scientific and clinical perspective.
- Broadening the expertise of the researchers in Focus Area III.

At an operational level, this was illustrated through networking at forums and meetings, actions to encourage mobility for young researchers and creation of three new core programs.

Three new core programs

“Ambivalent effects of soy phytoestrogens in breast cancer”

This program is dedicated to research on phytoestrogens’ epigenetic modifications of the BRCA1 and BRCA2 genes.

Leader: Dominique BERNARD-GALLON – Oncogenetics Department, Jean Perrin Center, Clermont-Ferrand.

“A study of the function of the LKB1 tumor suppressor and its interaction with HDAC6 during nutritional stress”

This study focuses on researching the effect of nutritional stress on the expression of the LKB1 and HDAC6 genes, suspected of playing a role in tumor development.

Leader: Jean-Louis Couderc – “Epithelial Differentiation and Morphogenesis” team, INSERM U83, CRN CNRS 6247, INSERM Unit 201, Clermont University Medical School.”

“Understanding and identifying lipid components in food capable of delaying or accelerating tumor development in the prostate or colon”

This program focuses on the role of lipids in tumor progression and on dialogue between the LXR and AR receptors.

Leader: Jean-Marie Loubauvies – “LXR, Oxytansin and Steroidogenic Tissues” team - CNRS, CRN CNRS 6247 INSERM Unit 931 Clermont University.

Strengthened expertise

In 2008, CLARA stepped up its drive to bring new multidisciplinary expertise into the “Nutrition and Cancer” focus area.

The launch of a “Young Researcher Mobility” call for projects enabled five researchers to gain the knowledge required to move forward in “Nutrition and Cancer” research projects. These scientists gained this valuable expertise at laboratories such as:
- Bayer CropScience in Sophia-Antipolis, France.
- The Marseille-Luminy Immunology Center.
- Institut für Toxikologie und Genetik, in Eggenstein-Leopoldshafen, Germany.

In addition to learning new techniques, these collaborative projects strengthened relationships between research teams and encouraged the design of new core programs.

Seven new teams were identified and contacted to participate in Focus Area III research projects. The events staged by CLARA, namely the Focus Area III Scientific Forum, held on June 3, 2008, brought to light prospects for joint projects. Clinical teams [urologists] showed their interest to take part, particularly in the field of prostate cancer.

New collaborative projects

In 2008, CLARA strengthened its relationships with regional institutions involved in research in the “Nutrition and Cancer” focus area, namely with:
- The European Ultra-High Field NMR Center (Lyon), which will bring its expertise in metabolomics.

The CLARA cluster has also been building links beyond the region. It initiated a national network, which involves academic and clinical research teams and encouraged the design of new core programs.

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- The European Ultra-High Field NMR Center (Lyon), which will bring its expertise in metabolomics.

The CLARA cluster has also been building links beyond the region. It initiated a national “Obesity, adipokines and cancer” network, which involves academic and clinical researchers beyond the Lyon – Rhône-Alpes Auvergne cluster framework.

PORTFOLIO

• 19 projects related to patient information, social and human sciences, epidemiology, quality of care and public health are funded by INCa.
• CLARA funded a project on validation of a breast cancer registry system and assessment of organized screening. The goal is to set up an exhaustive, high-quality histopathological registry of breast tumors in the Rhône-Alpes region. This registry can be used by public health laboratories, by the International Agency for Research on Cancer, and by the biological bank management center as a fundamental resource for overall assessment of screening.

FOCUS AREA IV ADVANCES IN 2008

Multidisciplinary scientific activities and events

This CLARA cancer research cluster aims to encourage dynamic interactions between fields as diverse as epidemiology, the social and human sciences, patient information and care management and organization. This will provide patients, healthcare professionals and decision makers with a broad range of related knowledge.

With this in mind, CLARA implemented a program of multidisciplinary special events in 2008 that helped to:
- Specify top-priority research topics, namely cancer screening and at-home hospitalization.
- Perform a census of the Rhône-Alpes Auvergne region’s research teams related to the four aspects of Focus Area IV of the more than 31 teams identified in the region, two-thirds do not necessarily work in the field of cancer (in particular in the Human and Social Sciences). One of the aims for the coming year will be to convince them to take part in multidisciplinary research programs in the field of cancer.
- Initiate multidisciplinary projects: in October 2008, CLARA sent out a call for letters of intent in order to support core research programs. The ultimate aim is to build a portfolio of high-potential, high-quality projects with a view to answering INCa calls for projects. Seven projects have been selected, and they will be approved following an audit by a non-CLARA, third-party body. The results will be made public in February 2009.

Finally, the Focus Area IV team wrapped up 2008 with a major event, a symposium entitled “Epidemiological data on cancer: How can we interpret them? – What information do they provide for research and for public health action?”. Held in Lyon on December 17 and 18, 2008, this event drew more than 160 participants, primarily epidemiologists, clinicians and specialists in human and social sciences.

This symposium presented the major epidemiological results in terms of cancer incidence and survival. It aimed to highlight the vital links between the clinical and epidemiological spheres and to encourage new research teams to take part in focus area projects.

FOCUS AREA IV: Epidemiology, Human and Social Sciences, Patient Information and Organization of Care

The multidisciplinary “Epidemiology, Human and Social Sciences, Patient Information and Organization of Care” focus area aims to enhance research projects with the perspectives of various disciplines that traditionally are not so much involved in the study of cancer. Thus, this focus area combines Rhône-Alpes Auvergne research teams active in the fields of human and social sciences, epidemiology, patient support and care management. These research groups seek to assess the factors promoting cancer, to meet patient needs and to help medical staff and treatment teams to better understand the issues related to the disease.

SPOTLIGHT

Epidemiological studies include assessing the impact of mobile phone use, the risks of various types of pollution, the influence of ionizing radiation on the risk of cancer...

The missions of Focus Area IV

At the operational level, the work of Focus Area IV aims to provide new perspectives on:
- Cancer prevention (e.g. the risk of tobacco-related cancer, etc.).
- The development of therapeutic support for patients resulting from advances in patient care and longer patient lifespan.

FOCUS AREA IV ADVANCES IN 2008

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Focus Area V: Targeted Therapy, Modeling and Clinical Research

The “Targeted Therapy, Modeling and Clinical Research” focus area is setting up an information portal in the Rhône-Alpes Auvergne region for performance of early-phase drug trials. The aim is to avoid the dispersion of research efforts for the initial phases of development of candidate drugs. This portal will provide a true benefit to translational research and will provide industrial firms with a good view on the teams in the Rhône-Alpes Auvergne region with the expertise required to carry out clinical trials. It will also help to foster synergy between clinical, pharmacogenomic and clinical pharmacology teams.

The resulting increase in the volume of early-phase trials will lead to a greater number of therapeutic options for cancer patients. Thanks to their heightened visibility, research teams in Rhône-Alpes Auvergne will help to make the region more competitive.

SPOTLIGHT

Early-phase clinical trials help to assess the efficacy of new molecules in humans. The quality of the studies contributes to advances in translational research.

The missions of Focus Area V

• Incorporating the various approaches to targeted therapy (identification of cellular and molecular targets, pharmacogenetics, pharmacogenomics, pharmacokinetics and pharmacodynamics) via mathematical modeling, in order to predict the effects of therapeutics and personalized treatments.

FOCUS AREA V ADVANCES IN 2008

A research team census phase

In order to prepare the setup of a shared information portal, CLARA performed in 2008 a census of teams that are conducting early-phase trials in the field of cancer. To accomplish this, the cluster put together an inventory of teams involved in early-phase development of cancer medications. It was used information from a survey performed by the Clinical Research in Cancer in Auvergne, Rhône-Alpes Assistance Platform (PARCC-ARA). So far, about 30 early-phase clinical trials have been collected.

In order to better meet the needs of CLARA’s industrial partners, a working group dedicated to the early-phase trial information portal has been initiated within the Industrial Steering Committee.

FOCUS AREA VI ADVANCES IN 2008

Close collaboration with the synergie Lyon Cancer Foundation

In 2008, Michael Courtney came on board as Director of the Synergie Lyon Cancer Foundation. His mission is to provide support for research on tumor escape and therapeutic targeting, to facilitate the development of diagnostic and therapeutic applications, to promote the collaboration between clinical and fundamental research groups and to promote the Synergie Lyon Cancer network internationally.

PORTFOLIO

• 27 projects are being supported by INCa, including four new projects in 2008.

In 2009, Focus Area VI will channel its efforts into setting up projects on the following research topics:

• Epigenetic profiling of cancers.
• Signaling pathways in cancer.
• Cancer and Nuclear Magnetic Resonance.
• Tumor radiaresistance and genetic epidemiology of cancer.

FOCUS AREA VI: Tumor Escape

The “Tumor Escape” focus area explores the means of re-establishing the physiological mechanisms for cell protection and immune response in order to prevent metastatic dissemination and drug resistance. This focus area builds upon the expertise of the Synergie Lyon Cancer Scientific Cooperation Foundation. Today, the goal is to get laboratories of other cities of the CLARA region (Grenoble, Saint-Etienne and Clermont-Ferrand) connected to this topic. Focus Area VI concentrates primarily on studying cell survival, apoptosis and senescence, immunosurveillance and tumor escape. The research is performed using physiopathological models similar to human tumors. This involves speeding up development of these preclinical models in order to enable screening of tumor targets and therapeutic molecules.

Setup of a tumor model laboratory

The CLARA cancer research network contributed to the setup of a tumor modes laboratory in cooperation with Synergie Lyon Cancer and Claude Bernard University Lyon.

Four options for models are being considered:

• Xenograft studies with samples of human tumors.
• Predisposition models for specific tumors.
• Metastasis development and drug resistance models.
• Humanized mice to study immune surveillance and escape mechanisms.

This laboratory enables scientists to use tumor models, highly similar to human tumors and that are controlled by using anatomo-pathological analysis. The lab adds genuine value to the setup of large-scale research projects.
SUMMARY OF INCa CALLS FOR PROJECTS - SPRING 2008

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<td>UCB Lyon</td>
<td>Role of ribosomal alterations and translational specificity in tumorigenesis</td>
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<td>Assessment of the response of normal and tumour human brain cells to anti-glioma treatments</td>
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<td>B. BLAISE</td>
<td>RMN, Lyon</td>
<td>Métabonomique des tumeurs endocrines par RMN à Très Hauts Champs</td>
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*in thousands of €

IV - Visible results: a concrete project portfolio

1. The INCa project portfolio in 2008

In 2008, CLARA teams stepped up their efforts in response to calls for projects, in particular those from the INCa. As part of the INCa call for projects, sent out in spring 2008, 10 new projects were selected. They account for a budget of €3.6 million. Targeted tumors are lymphoma, sarcoma, glioma, endocrine and ovarian tumors, as well as breast and lung cancers. Thus, seven of CLARA’s 10 disease study networks are moving forward. The winning projects benefit from unique access to collections of tumors removed from patients, thus strengthening CLARA’s positioning in translational research.

This momentum is building, illustrating the commitment of local research teams to playing an active role: 44 projects were submitted in response to INCa’s autumn 2008 call for projects. Finally, moving beyond French borders, the CLARA project entitled "Candidate peptides of the molecular chaperones Bag-1L and NPM for molecular prostate cancer therapy" was selected as part of the "Joint Translational Research Program on Cancer" with the German Academic Exchange Service.

* Laurent Morel (Blaise Pascal University, Clermont-Ferrand) in collaboration with A. Cato (Institute of Toxicology and Genetics – Karlsruhe – Germany)
This year, four Hospital Clinical Research Program (PHRC) applications were selected, for a total of €1,000,000.

The four selected PHRC projects:
- A randomized phase II study of two associations of rituximab and chemotherapy, with a PET-driven strategy, in patients from 18 to 60 with DLBCL CD20 + lymphoma and 2 or 3 adverse prognostic factors of the age-adjusted IPI – €1,833 to CLARA research teams at the national level. Additional funding was provided by Local Committees.
- The French League Against Cancer (Ligue Contre le Cancer – CLARA) network management team conducted a review of its 2007-2008 projects in order to identify new opportunities for collaborative ventures with academic and, more importantly, industrial partners. The participation of project initiators in this process was truly remarkable and several opportunities were pinpointed:
  - The identification of H4K20me3 as a biomarker of intestinal and perihepatic adherences in colorectal cancer patients requiring surgical resection of hepatic metastases in two separate operations – €100,000.
  - Urinary Metabolomics, Pharmacogenetics and Enzyme Activity of Aldehyde Dehydrogenase as Predictive Markers of induced Fostamidine Nephrotoxicity in Pediatric Oncology (pilot study) – €115,000.
  - Determining the impact of radiotherapy on good prognosis of glial tumors in adults on neurocognitive functions: a prospective multicenter study – €186,000.
  - Developing high-level innovative translational research.
  - Speeding up the transfer of research findings to clinical applications.
  - Promoting economic development and making the region more attractive.

V - Promoting the transfer of research findings to industry

Building partnerships between industrial partners, clinical and academic teams as part of oncology research and innovation projects is one of CLARA’s top priorities, as seen in several key objectives:

- Developing high-level innovative translational research.
- Speeding up the transfer of research findings to clinical applications.
- Promoting economic development and making the region more attractive.

The speed at which patients have access to therapeutic innovations is based on interactions between the industrial and academic spheres. The effectiveness of these innovations requires clarity and a solid understanding of each stakeholder’s aims. CLARA plays a pivotal role in the development of this partnership strategy. With its operational vision, the Lyon Auvergne Rhône-Alpes cluster is a vital link between the academic and industrial spheres.

1. Transfer opportunities for INCa 2005-2006 projects

The CLARA network management team conducted a review of INCa 2005 and 2006 projects in order to identify new opportunities for collaborative ventures with academic and, more importantly, industrial partners. The participation of project initiators in this process was truly remarkable and several opportunities were pinpointed:

- The identification of H4K20me3 as a biomarker of intestinal and perihepatic adherences in colorectal cancer patients requiring surgical resection of hepatic metastases in two separate operations – €100,000.
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- Developing high-level innovative translational research.
- Speeding up the transfer of research findings to clinical applications.
- Promoting economic development and making the region more attractive.

The discovery of Apollo as a new telomeric protein that would enable a new anti-lysophospholipid therapeutic approach in the prevention of metastases.

The identification of a new cancer stem cell marker specific to glioblastoma, the protein IQGAP1.

The discovery of Netrin-1 as a prognostic marker of the development of metastases of breast cancer and the possibility of eliminating metastases or preventing their occurrence by causing the death of tumor cells by netrin-1 titration. Netrin could also be a valuable target for treatment of colon cancer.
A very good vintage in 2008: five new projects, including one «cancer nano transfer» project

In 2008, CLARA continued and extended its “Proof of Concept” program and a new «Cancer Nano Transfer» line specifically supports «Nanotechnologies & Cancer» liaison projects. The “Proof of Concept” call for projects, sent out in March 2008, featured an abundance of high-quality submissions and enabled the initiation of five new projects.

Launched in 2005 with a pilot project, CLARA’s «Proof of Concept» program took on a new importance in 2008, as one of the keys to develop applications for life sciences research in Rhône-Alpes Auvergne. 14 diverse innovative projects are currently underway. They account for an overall budget of nearly €18 million, including €13 million brought in by 11 industrial partners. Each project brings academic and clinical innovators in oncology together with industrial partners ready to take their breakthroughs to development.

2. CLARA’s Proof of Concept Program

Launched in 2005 with a pilot project, CLARA’s «Proof of Concept» program took on a new importance in 2008, as one of the keys to develop applications for life sciences research in Rhône-Alpes Auvergne. 14 diverse innovative projects are currently underway. They account for an overall budget of nearly €18 million, including €13 million brought in by 11 industrial partners. Each project brings academic and clinical innovators in oncology together with industrial partners ready to take their breakthroughs to development.

**SUMMARY OF PROOF OF CONCEPT PROJECTS**

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**PROJECTS SELECTED IN 2008 AS PART OF THE “PROOF OF CONCEPT” PROGRAM**

- Development of a new radiotracer that can be used for both Positron Emission Tomography (PET) imaging and vectorized internal radiotherapy of disseminated melanoma. With sharply rising incidences, melanoma is becoming a public health concern in industrialized countries. This project involves the various phases of preclinical development of a new compound for clinical applications as a radiopharmaceutical that can be used in vectorized internal radiotherapy of melanoma. The work will include design, chemical synthesis, radioactive labeling and preclinical evaluation (with two aspects, imaging and therapy) in order to lead to the selection of a candidate compound for transfer to clinical applications.

  - Coordination: Nicole Meina - EA 2321, University of Auvergne, in association with CYCLOPHARMAM (Auvergne).
  - Tracking distortions of the TCR (T-cell receptor) repertoire to predict lymphopenia and prevent death following chemotherapy-related infections in breast cancer patients. One woman in 10 will develop breast cancer in her lifetime. In 25% of cases, death occurring at the beginning of the relapse phase is due to infections. The team of Professors J.Y. Blay and C. Caux’s team (Léon Bérard Center – INSERM Unit 590) has demonstrated that this mortality is essentially related to an immune system dysfunction that leads to lymphopenia, which at the origin of opportunistic infections. The Lymphos1 project aims to validate the use of an immunopsychometric tool, (ImmunTracster-PB), developed by ImmunoB. By analyzing the immune repertoire, this tool enables identification of patients with a high risk of mortality following chemotherapy treatment. This tool will directly enable clinicians to adjust the dose and type of chemotherapy for immunodeficient patients, and to prescribe personalized alternative treatments.

  - Coordination: Christopher Casse of the «Cytokines and Cancers» team of INSERM Unit 590 (Léon Bérard Cancer Center, Lyon), in association with start-up firm ImmunID Technologies (Grenoble).
• Proof of Concept: Anetirine in lung cancer
This project aims to develop a first anticancer molecule based on the concept of dependence receptors discov-
ere d by CNRS laboratory UMR 5238 (Léon Bérard Center, Lyon). The creation of a start-up company from this project (NETRIS Pharma) aims to develop various mole-
cules produced by this innovative research. As part of the project, a proof of concept study in animals to assess the
efficacy of a molecule on lung cancer has been proposed. For this purpose, an optimized batch of this molecule
will be produced, and its pharmacokinetic and pharma-
codynamic (PK/PD) parameters will be determined, thus
enabling in vivo studies on murine models.

• Eight projects to be concluded soon
The eight projects started between 2005 and 2007 have been monitored by CLARA’s steering committees. In
general, 75% of the budgets planned for these projects have been paid out and most will finish by the end of
2009. Based on this, CLARA will conduct a posteriori
assessment of the selected projects. In addition to eva-
u luating whether or not proof of concept will be obtained,
the program will also examine the various types of direct
and indirect impact (in terms of jobs, patents, prospects
for collaborative ventures, regional attractiveness, etc.),
along with possible areas for improvement.

These eight projects were published in the Bulletin du
Cancer for the 3rd CLARA’s Scientific Forum held in Lyon
in March 2008.

• Prospects for 2009-2011
As part of the Framework Agreement with Local Autho-
rities, for the period 2009-2011, CLARA plans a yearly
“Proof of Concept” call for projects. The following orientations initiated in 2008 will be con-
tinued:
• Additional support for the most promising projects, particularly when they move into clinical phase
• Extending the program’s geographical coverage thanks to financial support from Isère and Auvergne local autho-
rities from 2009 onwards
• Promoting the involvement of start-ups by supporting academic partners who wish to use their services
• Emphasize CLARA’s key scientific areas, in particular Focus Area I on “Nanotechnology, Imaging & Cancer” and
Focus Area II on “Infections & Cancer” as part of a close partnership with the Grenoble Nanotechnology
platform that brings together local research leaders
and Focus Area II on “Infections & Cancer” as part of a close partnership with the Grenoble Nanotechnology
cluster and the lyo n biopol e competitiveness cluster,
respectively.

In addition, another initiative being studied is support for
“Proof of Concept” projects that have market potential
but do not yet have a well-established industrial partner. This support could be channeled via economic develop-
omizations and academic incubators, based on the meth-
ods as used by Cancer Nano Transfer.

Functional and structural genomics / Lyon Bé rard Cancer Research Center
In 2008, construction of the Chewey D Building was com-
pleted at the Léon Bérard Cancer Research Center site, where Unit 519, the Lyon Civil Hospitals / Léon Bérard
mixed unit, the Léon Bérard transfer laboratory and CNRS UMR 5201 are now located. Various investments
have been made, including creation of a Biosafety Level 3 laboratory, a Cytometrics platform, Experimental Sur-
gery Platform and the extension of a building for “small
animals” studies. An Attymètre platform was acquired for the Rockefeller University site as part of the pharma-
genomics platform run by Lyon Civil Hospitals.
The InaCancer, Mutacancer and CirBioCancer programs
are ongoing at these facilities.

A collaborative industrial venture is underway with bio-
Mérieux on the development of circulating nucleic mar-
kers for the treatment of breast and colorectal cancer
patients. Several CLARA «Proof of Concept» programs
- «tIL-6» with IDD Biotech, «v5-Fu» with Erytech Pharma,
- «HIFU» with EDAP TMS, «TWIST» with CavaAb and,
since late 2008, «Lymphos» with InmuneD and «Notrin
Lung» with Nitriss Pharma - are also involved.

Financial and structural genomics / Lyon Civil Hospitals

The Molecular Characterization of Tumors Laboratory
(LCMT) at the Rockefeller University (Lyon Civil Hospitals)
facility aims to develop tools to predict individual pa-
tients’ sensitivity to existing or new cancer drugs (phar-
macogenetics / pharmacogenomics) in order to persona-
lize cancer therapies.
The research programs on lung cancer (Pharmacogenos-
can), Myeloma (IFM), breast and colorectal cancers (with
bioMérieux), thyroid cancer and several collaborative
projects with pharmaceutical firms such as Roche and
Pierre Fabre are continuing.

LCMT will integrate a high-speed nucleic acid analysis
platform that brings together local research leaders
such as the University, INSERM and Lyon Civil Hospitals.
A second facet of the platform’s development involves
setting up a small-animal pharmacogenomics study that
will enable data on the anticancer activity of new molecu-
les from xenografts to be correlated with the expression
profiles of various tumors.
2. The South Lyon epigenomics and targeted therapy platform

Installation of the South Lyon platform continued, with the setup of new equipment at the South Lyon Hospital Center facility (CHLS – HCL) and at the Gerland campus (IFR 128). The main focus of the platform is targeted therapy. This involves developing tools to treat cancer based on a better knowledge of tumors and of how anticancer agents act on the disease.

In the fundamental research sphere, current projects include epigenetics in chronic lymphocyte leukemia, biotherapy in acute leukemia, the development of new vaccine strategies that take into account the role of lipids in immune response to hepatitis C, as well as a partnership with bioMérieux on screening markers in prostate cancer. Links with clinical research are being built, with the growth of pharmacological targeting and modeling platform of the effect of anticancer treatment, the collaboration program with the Etoile Hadrontherapy Center and studies on viral-induced cancers in association with Lyonbiopôle.

The regional Public Health platform run by the Loire Center facility (CHLS – HCL) and at the Gerland campus (IFR 128). The main focus of the platform is targeted therapy. This involves developing tools to treat cancer based on a better knowledge of tumors and of how anticancer agents act on the disease.

In the fundamental research sphere, current projects include epigenetics in chronic lymphocyte leukemia, biotherapy in acute leukemia, the development of new vaccine strategies that take into account the role of lipids in immune response to hepatitis C, as well as a partnership with bioMérieux on screening markers in prostate cancer. Links with clinical research are being built, with the growth of pharmacological targeting and modeling platform of the effect of anticancer treatment, the collaboration program with the Etoile Hadrontherapy Center and studies on viral-induced cancers in association with Lyonbiopôle.

Economic development potential is also enhanced thanks to industrial partnerships with firms such as EFS Electronics (development of a second device for chemotherapy-hyperthermia), Dénoplastic (a clinical trial on a cancer vaccine), bioMérieux (validation of an early diagnostic marker in breast cancer), Innate Pharma (immunotherapy), Roche/Genentech (biological factors that can predict the activity of Rituximab) and ImmunID (analysis of immune cell repertoires in leukemia and lymphoma).

In connection, Saint-Étienne University Hospital has set up a hematology and solid tumor genomics and proteomics platform. It is used for diagnosis and follow-up of hematology patients in national and international study protocols, as well as in applied and clinical research by the immunology team in order to identify new molecular tumor markers.

3. Saint-Étienne public health platform

The regional Public Health platform run by the Loire Oncology Institute (ICL) is designed to organize public health research in the oncology field and to develop research programs in various areas of primary prevention (HPV and obesity-related risks), secondary prevention (screening of breast and colon cancers, and of cancers in the elderly, shared decision making in breast cancer) and tertiary prevention (patient information on pain, motivation in quitting smoking, and prevention of breast cancer relapse through nutritional intervention).

A legal study was carried out on creation of the Hygée Center, for which Saint-Étienne Métropole will serve as contracting authority. An impact study, carried out beforehand in cooperation with key Rhône-Alpes Auvergne stakeholders in prevention and public health, will help fine-tune the project.

4. European Cancer Observatory / IARC

The European Cancer Observatory project led by IARC featured the construction of a bilingual (French/English) internet site. This site provides a homogeneous presentation of data and epidemiological trends for 20 tumor types and 27 European countries.

The site is scheduled to go online for public access in April 2009.

5. The European Ultra-High-Field NMR Center in Lyon-Villeurbanne

The European Ultra-High-Field NMR Center (CRMN) is operational since April 2008. It provides the environment for methodological and technological developments in NMR for cutting-edge liquid and solid phase spectroscopy applications in the fields of biology, medicine and materials. Key target applications include early diagnosis of cancer and chemical/biological analysis.

Three scientific projects involving CLARA researchers are currently underway in the field of breast cancer, neuroendocrine tumors and encoctymoma.

6. The Grenoble proteomics and imaging platform

The Grenoble platform aims to transfer advances in proteomics, nanotechnology and functional imaging to cancer patients.

The technological research emphasizes three main areas:

- Development of innovative protein analysis methods for clinical use.
- Development and validation of micro/nano-tools for the analysis of tumor mini-samples.
- Development of innovative functional imaging, optical, SPECT and NMR techniques in collaboration with industrial partners (in particular for the anti-angiogenics study).

In clinical research, the developments target:

- Identification of the proteins involved in cancer, followed by identification of biomarkers, thanks to the Biological Resource Centers associated with lung cancer, lymphoma and brain tumors.
- Description of the proteins involved in antitumor immune response and in its variations under immunotherapy.
- Application of functional imaging, MRI, SPECT or optics for in vivo characterization of therapeutic targets, analysis of biodistribution and drug efficacy.

7. The Auvergne Platform

The “Nutrition and Cancer” focus area, which includes both fundamental and clinical research, is coordinated by the Auvergne Platform. It relies on an INCa-accredited regional core network and on the Clermont-Ferrand Human Nutrition Research Center. This platform aims to study the impact of food components on the various steps in cancer, from carcinogenesis to nutrition for cancer patients, to the adjuvant action of food components in anticancer therapy.

The Auvergne research teams are also studying on functional imaging and therapeutics vectored by radiopharmaceuticals, functional genomics, tumor escape and clinical research.
VII - Action plan for 2009

CLARA’s roadmap involves pursuing the national ProCan program in order to strengthen the cluster’s focus areas, with top priority given to translational research. As well, the new Three-Year Plan for 2009-2011, finalized with local authorities in the Rhône-Alpes Auvergne region, aims to boost Cancéropôle’s capacity to identify and support academic-industrial partnerships.

The success of these two related approaches depends largely on the quality of scientific events and activities in the CLARA network and on its capacity to build several categories of research and development projects:

• Research Projects, which bring together several CLARA academic/clinical partners and are submitted to national competitive calls for projects.
• Core Programs, which bring together several CLARA partners. They do not aim to fund the work of individual teams, but rather to support a resource-pooling or coordination process for CLARA.
• Proof of Concept Projects, which involve at least one academic/clinical partner and, if possible, one of CLARA’s industrial partners. These projects aim to establish the pre-clinical or clinical Proof of Concept of a healthcare product in the field of cancer, with a view to industrial transfer and clinical use.

CLARA has the following objectives:

• To enhance its access to other Networks of Excellence in the region and build relationships with them;
• To strengthen its collaborative projects at the international level, namely with the International Agency for Research on Cancer and French-speaking Switzerland;
• To build relations with Patient Associations.

These aims will be adapted according to the Cancer Plan II.

VIII - Financial support

THE 2009-2011 FRAMEWORK AGREEMENT BETWEEN CLARA AND LOCAL AUTHORITIES

As early as 2001, even before the French National Cancer Plan was launched in 2003 and the birth of the Cancéropôle concept, several local authorities and personalities from the scientific, medical, and industrial spheres met in order to design an ambitious cancer research program uniting the region’s academic, clinical and business leaders. One of the main aims was to attract industrial partners and create, via innovative public-private partnerships, the conditions for greater economic development and creation of high-level jobs.

Since 2003, the Cancéropôle CLARA concept has become a reality, thanks to support from the French National Cancer Plan led by the National Cancer Institute (INCa), as well as from local authorities, in particular the Rhône-Alpes Regional Council, the Rhône County Council and Greater Lyon. Local authorities have granted CLARA nearly €50 million, primarily for the setup of seven cutting-edge platforms (€38 million).

In 2008, CLARA was on a twofold transition process, towards a partnership with the French State and a new partnership with local authorities. The State, through INCa, supports French cancer research clusters via the «ProCan 2008 – 2010» scientific activities program as well as through its national calls for research projects. Local authorities, after a period of large-scale investments, prefer to focus on the activities of CLARA’s Network Management in the areas of economic development and regional network activities. The 11 local authorities will thus allocate an annual budget of €3.5 million for the 2009 – 2011 period, with the majority of funding earmarked for the “Proof of Concept” program.

With this in mind, a Framework Agreement between CLARA and local authorities has been drafted for 2009-2011. It was presented to CLARA’s Executive Committee on October 27, 2008. The Agreement is subject to ratification by the following local authorities in early 2009: the Rhône-Alpes Regional Council, the Rhône County Council, the Lyon Urban Community, the Loire County Council, Saint-Etienne Métropole, the Isère County Council, Grenoble Alpes Métropole, the City of Grenoble, the Auvergne Regional Council, the Puy-de-Dôme Regional Council and the Clermont Urban Community.

Status of the main sources of funding on a national level

Summary of the multi-year scheduling of the CLARA program, 2003-2008

In thousands of €

<table>
<thead>
<tr>
<th>Recipient (Funding)</th>
<th>Investment</th>
<th>Operation</th>
<th>Overall total approved 2003-2008</th>
<th>Overall total paid 2003-2008</th>
</tr>
</thead>
<tbody>
<tr>
<td>INCa* Calls for Projects</td>
<td>-</td>
<td>-</td>
<td>9,000</td>
<td>9,000</td>
</tr>
<tr>
<td>Biological Resource Center (CRB)</td>
<td>-</td>
<td>-</td>
<td>28,885</td>
<td>23,452</td>
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<tr>
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<td>-</td>
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<td>1,027</td>
<td>1,027</td>
</tr>
<tr>
<td>PROCAN Scientific Axes (INCa)</td>
<td>-</td>
<td>-</td>
<td>1,346</td>
<td>1,346</td>
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<tr>
<td>Total</td>
<td>-</td>
<td>-</td>
<td>43,600</td>
<td>35,970</td>
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</tbody>
</table>

*Estimated amounts for Cancer Plan and INCa, STIC and PHRC included

As per standard practice and in order to simplify the presentation, payments are indicated in the year they were approved.
### Financial Support

#### In thousands of € 2008

<table>
<thead>
<tr>
<th>Recipient (funding)</th>
<th>Investment</th>
<th>Operation</th>
<th>Overall total approved 2003-2008</th>
<th>Overall total paid 2003-2008</th>
</tr>
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<tbody>
<tr>
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<td>Paid</td>
<td>Approved</td>
<td>Paid</td>
<td>Approved</td>
</tr>
<tr>
<td>Biological Resource Center (CRB)</td>
<td>-</td>
<td>-</td>
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<td>-</td>
</tr>
<tr>
<td>Proof of Concept (DRRT RA)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Network Management</td>
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<td><strong>Total</strong></td>
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#### In thousands of € 2008

<table>
<thead>
<tr>
<th>Recipient (funding)</th>
<th>Investment</th>
<th>Operation</th>
<th>Overall total approved 2003-2008</th>
<th>Overall total paid 2003-2008</th>
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<tr>
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<tr>
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<tr>
<td>UJF Grenoble</td>
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<tr>
<td>INSERM Grenoble</td>
<td>-</td>
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<tr>
<td>Grenoble Subtotal</td>
<td>-</td>
<td>-</td>
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<td>-</td>
</tr>
<tr>
<td>CHU Saint-Étienne</td>
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<td>-</td>
</tr>
<tr>
<td>Saint-Étienne Hygié Center</td>
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<td>-</td>
<td>-</td>
</tr>
<tr>
<td>High Field NMR - CNRS</td>
<td>-</td>
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</tr>
<tr>
<td>Proof of Concept</td>
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<td><strong>Total</strong></td>
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<td>520</td>
<td>260</td>
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#### In thousands of € 2008

<table>
<thead>
<tr>
<th>Recipient (funding)</th>
<th>Investment</th>
<th>Operation</th>
<th>Overall total approved 2003-2008</th>
<th>Overall total paid 2003-2008</th>
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<td>Approved</td>
<td>Paid</td>
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</tr>
<tr>
<td>CLB - East Lyon</td>
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<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>IARC</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Proof of Concept</td>
<td>-</td>
<td>-</td>
<td>1 300</td>
<td>640</td>
</tr>
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<td>Network Management</td>
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<tr>
<td><strong>Total</strong></td>
<td>-</td>
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<td>1 800</td>
<td>1 160</td>
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#### IN THOUSANDS OF € 2008

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<th>Overall total paid 2003-2008</th>
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<td>Paid</td>
<td>Approved</td>
</tr>
<tr>
<td>HCL</td>
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<tr>
<td>IARC</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>High Field NMR - CNRS</td>
<td>-</td>
<td>-</td>
</tr>
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<td>Proof of Concept</td>
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<tr>
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<tr>
<td><strong>Total</strong></td>
<td>-</td>
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</table>

#### In thousands of € 2008

<table>
<thead>
<tr>
<th>Recipient (funding)</th>
<th>Overall total approved 2003-2008</th>
<th>Overall total paid 2003-2008</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approved</td>
<td>Paid</td>
<td>Approved</td>
</tr>
<tr>
<td>Saint-Étienne Hygié Center</td>
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<tr>
<td><strong>Total</strong></td>
<td>1 000</td>
<td>-</td>
</tr>
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</table>

#### In thousands of € 2008

<table>
<thead>
<tr>
<th>Recipient (funding)</th>
<th>Overall total approved 2003-2008</th>
<th>Overall total paid 2003-2008</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approved</td>
<td>Paid</td>
<td>Approved</td>
</tr>
<tr>
<td>Saint-Étienne Hygié Center</td>
<td>1 000</td>
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</tr>
<tr>
<td><strong>Total</strong></td>
<td>1 000</td>
<td>-</td>
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</table>

#### Total Rhône-Alpes Region

<table>
<thead>
<tr>
<th>Recipient (funding)</th>
<th>Overall total approved 2003-2008</th>
<th>Overall total paid 2003-2008</th>
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</thead>
<tbody>
<tr>
<td>Approved</td>
<td>Paid</td>
<td>Approved</td>
</tr>
<tr>
<td>Total</td>
<td>3 191</td>
<td>2 017</td>
</tr>
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Updated December 31, 2008

As per standard practice and in order to simplify the presentation, payments are indicated in the year they were approved.
Summary of the multi-year scheduling of the CLARA program, 2003-2008

Status of the main sources of funding in the Auvergne area

<table>
<thead>
<tr>
<th>In thousands of €</th>
<th>2008</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recipient (funding)</strong></td>
<td><strong>Investment</strong></td>
<td><strong>Operation</strong></td>
</tr>
<tr>
<td>Massif Central ERDF*</td>
<td>Approved</td>
<td>Paid</td>
</tr>
<tr>
<td>Region ERDF</td>
<td>Approved</td>
<td>Paid</td>
</tr>
<tr>
<td>Massif Central FNADT</td>
<td>Approved</td>
<td>Paid</td>
</tr>
<tr>
<td>Auvergne Region</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Clermont Community</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Puy-de-Dôme County</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Allier County</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cantal County</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Haute-Loire County</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>-</td>
<td>-</td>
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</tbody>
</table>

*Massif Central ERDF covers Auvergne and Loire County.

Overall orientation of approved funding during the period 2003-2008

<table>
<thead>
<tr>
<th>Program</th>
<th>TOTAL</th>
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</thead>
<tbody>
<tr>
<td><strong>2008</strong></td>
<td><strong>Overall 2003-2008</strong></td>
</tr>
<tr>
<td>INCa 2003 - 2008 Calls for Projects</td>
<td>5,302</td>
</tr>
<tr>
<td>ProCan Scientific Axes (INCa)</td>
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</tr>
<tr>
<td>Proof of Concept Projects</td>
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</tr>
<tr>
<td>Biological Resources Center</td>
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</tr>
<tr>
<td>Total</td>
<td>7,202</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Coordination</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>Network Management</td>
<td>1,529</td>
</tr>
<tr>
<td>Total</td>
<td>1,529</td>
</tr>
</tbody>
</table>

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

Amended December 31, 2008

Overall Orientation of approved funding during the period 2003-2008

- Investment
- Funding of projects
- Coordination

Amounts approved in the Auvergne area, 2003-2008

- Nutrition Program
- Imaging Program
- Lifegrid Program
- Cancéropôle’s Auvergne cluster
- Other programs
- Network Management

Updated December 31, 2008

As per standard practice and in order to simplify the presentation, payments are indicated in the year they were approved.
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F69008 Lyon
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Fax +33 (04) 37 90 27 03
infos@canceropole-clara.com
www.canceropole-clara.com

OUR PARTNERS