Editorial

2010, renewed momentum for CLARA

Peter PAUWELS
Executive Director

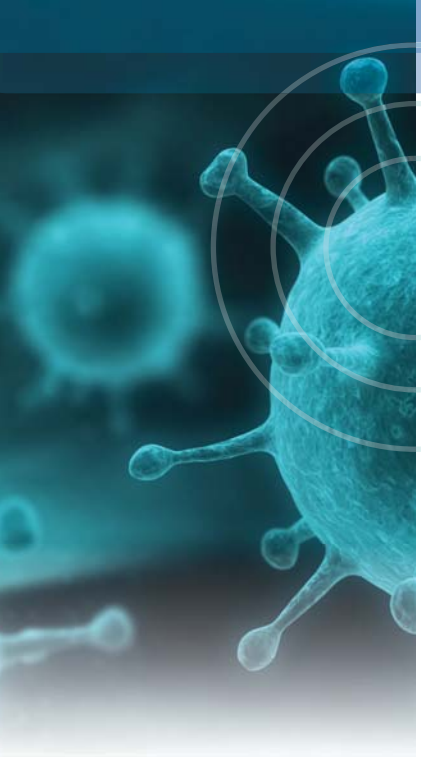
2010 has confirmed the efficacy of the Cancéropôle CLARA in responding to the major challenges of cancer research as outlined by the 2009-2013 Cancer Plan II which targets, in particular, support for fundamental research and sustained attention to translational research.
With 160 projects underway, the involvement of CLARA in this initiative has continued to grow at the inter-regional, national and international levels.

CLARA has distinguished itself this year in several respects:

- **The competitiveness of its research teams** in the context of calls for proposals from INCa (the French National Cancer Institute): 17% of the research projects accepted in 2010 originated from CLARA.
- **The quality of its network,** notably through the number and level of publications of its researchers. A study conducted by INSERM (the French National Institute of Health and Medical Research) in coordination with INCa shows that CLARA teams contribute 23% of high-level French scientific articles in oncology (IF> 20).
- **The efficacy of its approach to transfer of research results,** initiated in 2005 *via* its "Proof of Concept" program and intended to ensure technology transfer in oncology. At present, six successful proofs of concept on nine completed projects –including one product on the market– bear witness to the concrete results of CLARA's transfer activity. The "Proof of Concept" system exerts an influence beyond the territory of CLARA, both in its capacity to inspire emulation and its attractiveness to foreign companies, as in the French-speaking part of Switzerland, which is now integrated into the system, and with the Japanese company OncoTherapy Science, which has established a subsidiary in Lyon with the aim of conducting clinical trials supported by CLARA.
- **Improved visibility at the European and international levels:** 22 European projects are underway, 10 of them coordinated through CLARA teams. 2010 was also distinguished by international and high-visibility large-scale initiatives such as the launch of the European Lymphoma Institute and the World Sarcoma Network, the organization of an international forum for research in nanomedicine, participation in the International Cancer Genome Consortium (ICGC) and the development of new collaborations with China.
- **Its dynamic scientific leadership,** with the organization of 12 scientific events, five of them in collaboration with other Cancéropôles (Ile-de-France, Grand-Est, Grand Sud-Ouest or PACA). CLARA attaches great importance to bringing together research teams at high-quality events to promote the sharing of knowledge, creativity and the interdisciplinary approach which are at the foundation of all diagnostic and therapeutic progress.

Finally, the conclusion of the ProCan program also marked 2010, which was devoted in part to drawing up a detailed assessment of the 2007-2010 period and a new 2011-2014 Strategic Plan in accordance with the recommendations of the Cancer Plan II. It is currently under evaluation by AERES (the French Evaluation Agency for Research and Higher Education) and INCa.

Thanks to the involvement of its scientific and financial partners, the dynamic of the Cancéropôle CLARA has been productive: its influence has now reached further than national frontiers and the in-depth expertise of its network, unique in oncology, is able to provide a high-quality service to research and beyond to patients.



Key Figures for 2010

Characterized in 2009 by sustained success in calls for proposals, the increasing influence of its research transfer system and its efforts to open up to an international approach, the Cancéropôle CLARA successfully kept up this momentum through 2010.

Benchmarks: the figures for 2010

56 new projects for a total budget of €20M:

- 6 INCa projects (€10M)
- 4 "Proof of Concept" projects (€9M)
- 16 structuring projects (€500K)

The continuation of programs on an international scale for a total budget of €500K:

- the European Lymphoma Institute
- the World Sarcoma Network
- the Hygée Center, a regional platform for prevention, information and education on cancer

17% of INCa research projects allocated to CLARA

Concrete results: initiation of clinical trials in the treatment of hepatic metastases, nanoparticles for the follow-up of anticancer cellular therapy by medical imaging...

Economic dynamic: establishment of a first international subsidiary (OncoTherapy Science Inc., Japan), creation of two start-ups (Ecrin Therapeutics and Synthelis) and planned launch of a new start-up (EBV Biotech) in the framework of the "Proof of Concept" program

CLARA in key figures

2nd Cancéropôle on the national level

- **€150M of investment in cancer research (Overall Budget)**
- **160 projects underway (Overall Portfolio)**
- **25 projects with a total budget of €32M financed in relation to industrial transfer ("Proof of Concept" Program)**
- **250 research teams**

Diversified financing sources: State, local authorities (14), industrial partners, ERDF (European Regional Development Fund)

Procan 2007-2010
High points and advances

With a real inter-regional dynamic around its six guiding priorities, CLARA obtained excellent results from the INCa calls for proposals, initiated structuring projects and developed a public-private partnership model capable of stimulating research transfer (the "Proof of Concept" program) in the framework of the "2007-2010 ProCan strategic program".

Review of the high points and advances of the "2007-2010 CLARA ProCan Program"

AXIS I

The **Nanotechnologies, Imaging and Cancer** axis mobilized an inter-regional, multidisciplinary and dynamic critical mass. The resources for the axis are particularly invested in technological transfer of innovations, notably *via* the "Proof of Concept" program, which has allowed seven projects to be initiated. Two major activities have characterized the strong support of CLARA for this initiative:
- an ambitious program of identification and exploitation of tumor biomarkers relying on nanomedicine
- the creation of a regulatory unit to guide industrial and clinical transfer of diagnostic and therapeutic tools based on nanotechnologies, a foundation stone offering project support extended to all the other CLARA priorities.

AXIS II

Centered on a major program on hepatocellular carcinoma, the **Infections and Cancer** axis was devoted to the establishment of a number of research partnerships and shared tools with the aim of facilitating the launch of new projects. These resources and their organization were decisive with regard to CLARA's excellent results in the framework of the Hepatocellular Carcinoma program launched by INCa (PAIR 2009): of the 12 applications selected by the international jury, 1/3 originated from CLARA. Five "Proof of Concept" projects were also supported.

AXIS III

Originally particularly active in Clermont-Ferrand, the **Nutrition, Metabolism and Cancer** axis has been progressively supplemented by new teams from Lyon and Grenoble. It is the origin of a regional network, NuCaP (phytoNUtrients and Prostate Cancer) and a national network, OBACSE (OBésité, Adipocytes et Cancer du SEin: Obesity, Adipocytes and Breast Cancer). The Nutrition, Metabolism and Cancer axis will be integrated into a broader "Environment, Nutrition and Cancer" axis notably engaging the major involvement of the Lyon Cancer Research Center and the International Agency for Research on Cancer (IARC), the agency of WHO specialized in cancer research.

AXIS IV

The objective of the **Epidemiology, Human and Social Sciences, Patient Information and Organization of Care** axis consisted of promoting interactions between its four research disciplines with the aim of providing interdisciplinary results important for patients, health professionals and decision-makers. In addition to the development of a critical mass, the priority promoted connections between professionals in the organization of care and experts from the Human and Social Sciences. In three years, the number of teams has doubled, going from 19 to 39, with 14 of these originating from the Human and Social Sciences or organization of care.

AXIS V

Restructured to respond to the specific needs of clinicians, the **Therapeutic Targeting, Modelling and Clinical Research** axis concentrated its work on the Auvergne Rhône-Alpes Platform for Aid to Clinical Cancer Research (Plate-forme d'Aide à la Recherche Clinique en Cancérologie Auvergne Rhône-Alpes), PARCC-ARA. A fully operational branch of clinical research within CLARA, this platform provides clinicians in the inter-region with the methodological, statistical and logistical support necessary for conducting clinical trials.

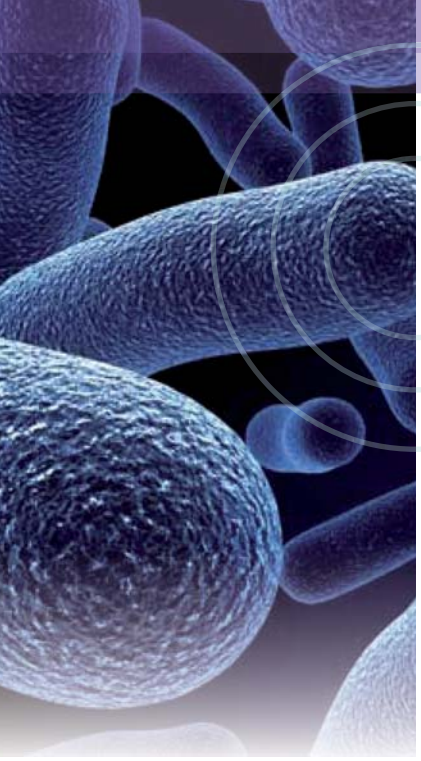
AXIS VI

Particularly prolific in high-level scientific publications, the **Tumor Escape** axis contributes significantly to progress in the biology of cancer. A major focus of CLARA, it is fundamental to large-scale achievements: a Laboratory for Tumor Modelling and a Bioinformatics Center (in the framework of a partnership with the Synergy Lyon Cancer Foundation and INCa) that constitutes the French participation in the International Cancer Genome Consortium (ICGC). In 2010 this priority showed significant progress in the calls for proposals on biomedical research, with a national score of 12 projects accepted out of 43. At the same time, four projects were selected within the "Proof of Concept" program.

Objectives

- To fulfil the priorities set by the National Cancer Institute (INCa) in a three-year strategic program
- To develop six guiding priorities as sources for progress and advances, relying on inter-regional strengths:
  (I) Nanotechnologies, Imaging and Cancer
  (II) Infections and Cancer
  (III) Nutrition, Metabolism and Cancer
  (IV) Epidemiology, Human and Social Sciences (HSS), Patient Information and Organization of Care
  (V) Therapeutic Targeting, Modelling and Clinical Research
  (VI) Tumor Escape
- To unite and support the academic, clinical and industrial strengths of the Auvergne Rhône-Alpes inter-region in an integrated research approach

See the summary chart of activities on the last pages



Competitive Research at both the National and European Levels

Objectives

- Unite inter-regional research teams within structuring projects
- Build innovative and competitive projects capable of responding to national priorities in cancer research
- Promote competitive positioning of the inter-regional teams at the European level

The continuation of a structuring initiative

In its drive to bring together research teams, CLARA has sustained its progress since 2009 with 16 new structuring projects in the framework of the ProCan axes.

Axis I Nanotechnologies, Imaging and Cancer

- Impact Sociétal et Nouvelles Technologies
- Imagerie optique pré-clinique et clinique du Cancer

Axis II Infections and Cancer

- Interactions entre les virus des hépatites B et C et le dérèglement des voies intracellulaires au cours de la transformation cancéreuse des hépatocytes
- Programme fédérateur sur les récepteurs toll like (TLR) et l'immunité innée

Axis III Nutrition, Metabolism and Cancer

- Angiogenèse et stress oxydant : impact du microenvironnement tumoral sur les cellules mammaires saines ou néoplasiques
- Rôle des sphingolipides dans la perte musculaire associée au cancer
- Analyse des profils métaboliques liés au cancer du sein lors du diagnostic et au cours d'un programme nutritionnel concomitant au traitement initial
- Effet de l'excès et du manque de glucose sur la régulation (épissage et stabilité) des ARN impliqués dans l'apport de nutriments

Axis IV Epidemiology, Human and Social Sciences, Patient Information and Organization of Care

- Évaluation de prise en charge de la chimiothérapie en hôpital de jours vs. autres modalités au domicile
- Étude économique de la conformité aux recommandations pour la pratique dans le traitement des sarcomes
- Déterminants de la prise en charge des patients porteurs d'un cancer broncho-pulmonaire présentant au moins une défaillance d'organe. Cohorte bi-centrique
- Cancers du testicule : étude des expositions professionnelles et environnementales en Rhône-Alpes
- Éducation aux effets biologiques de la chimiothérapie : mise en place et évaluation préliminaire d'un programme d'éducation thérapeutique du patient appliqué à la prise en charge de la chimiothérapie anticancéreuse
- Décision médicale collective : le cas des réunions de concertation pluridisciplinaire en cancérologie

Axis VI Tumor Escape

- Role of the microenvironment in leukemic stem cell emergence and resistance in chronic myeloid leukemia
- An interactive network between ERRalpha and LSD1 (Lys-Specific Demethylase)/ Nucleophosmin (NPM) in prostate cancer

→ More information in Appendix 1

High profile in calls for national projects

The results achieved by Cancéropôles in calls for national projects demonstrate their ability to amalgamate relevant resources and expertise to meet national priorities for cancer research. In 2010, CLARA maintained an excellent level of representation in calls for INCa projects with **17% of research projects accepted**. 36 projects were selected with a total budget of **€10M**.
CLARA's results show several advantages:

- significant progress in the success rate of the Cancéropôle in the call for open-source biomedical research projects. With 12 projects accepted out of 43 at national level, CLARA is a Cancéropôle that **can provide new perspectives in oncology research**. The successful project applications are in the areas of lung cancer, osteosarcoma, breast cancer, pancreatic and thyroid cancer.
- a **significant role in the program supporting innovative and expensive techniques (STIC)** with two out of four projects accepted at national level, concerning aggressive prostate cancer and cancer of the oesophagus.
- a **"resource" territory for clinical research with the designation of three early-phase clinical trial centers for cancerology:** Léon Bérard Cancer Center, South-Lyon Civil Hospitals and Jean Perrin Center. The main mission of these centers is to design and conduct national and international early-phase clinical trials, meeting the requirements issued by INCa or industrial and academic players. These centers will strive to meet the growing requirements of international regulations concerning early clinical trials. They will also study innovative molecules after their marketing authorization.

And also...

Projects supported by Associations: €3M mobilized by ARC and €2M by the National League against Cancer (apart from departmental committee financing), for the benefit of Rhône-Alpes Auvergne research teams.

Establishment of a European dimension

In 2010, 22 projects showed European involvement of CLARA's academic, clinical and industrial teams. 10 of these are coordinated by CLARA teams:

- **6th Framework Program for Research and Technological Development (FP6):** **CONTICANET** (Réseau d'excellence sur les cancers des tissus conjonctifs tels que les sarcomes, coordinated by Jean-Yves BLAY – Centre de Recherche en Cancérologie de Lyon) et **CHILDHOPE** (Nouvelles approches thérapeutiques des cancers pédiatriques basées sur des cellules T chimériques, coordinated by Ève-Marie NEIDHARDT-BERARD – Centre de Recherche en Cancérologie de Lyon).
- **7th Framework Program for Research and Technological Development (FP7):** **DECanBio** (Nouvelles stratégies pour identifier et évaluer des biomarqueurs de cancer dans l'urine et leurs applications dans le diagnostic du cancer de la vessie, coordinated by Jérôme GARIN – CEA Grenoble), **oncoMiRNA-biogenesis** (Biogénèse des microARNs oncogéniques, coordinated by Eva PEBAY-PEYROULA – CEA-Leti, Grenoble), **p53Adhesion** (Rôle de p53 chez la Drosophile dans l'apoptose et l'adhésion – coordinated by Marie-Laure DICHTEL-DANJOY – ENS Lyon), **CD44 carcinogenosis** (Étude du rôle de CD44 dans la carcinogénèse – coordinated by Serge MANIÉ – Centre de Recherche en Cancérologie de Lyon), **NOTCH3DR** (Étude d'un nouveau rôle de Notch3 comme récepteur à dépendance et sa signification in vivo, coordinated by Patrick MEHLEN – Centre de Recherche en Cancérologie de Lyon).
- **EURONANOMED Program:** **TARGET-PDT** (Thérapie Photo Dynamique utilisant des nanoparticules organiques photo-sensibilisantes ciblées, coordinated by Patrick BOISSEAU – CEA-Leti, Grenoble), **BIBA** (Adressage des nanoparticules à travers les barrières biologiques, coordinated by Patrick BOISSEAU – CEA Grenoble), **iNanoDCs** (Design de nanoparticules multifonctionnelles ciblant les TLR ou les récepteurs à Nod pour la thérapie immunitaire des cellules dendritiques, Bernard VERRIER – Institut de Biologie et de Chimie des Protéines de Lyon).

For the future, the aim is to increase the participation of regional players in European programs by proposing new methods of assisting project leaders. Particular attention is already being given to information, to aiding the emergence of structuring initiatives in association with CLARA's strategic orientations and to means for supporting project creation.

And also...

The Chairs of Excellence "Cancer, environment and nutrition" in partnership with Léon Bérard Cancer Center, Merck-Serono and the City of Lyon (Coordination: B.FERVERS) and "Nutrition and Cancer" (coordination : S. BASU) financed by Auvergne University and Auvergne Regional Council.

Technology Transfer and Economic Development

After paving the way for five years, CLARA's "Proof of Concept" program in 2010 confirmed the quality of its results (new products, creation of companies...).
It supports CLARA in its role in the economic development and transfer of technology in oncology and permits an ambitious strategy for the future.

"Proof of Concept": results and know-how

Since 2005, the "Proof of Concept" program has shown substantial success: the marketing of a mini-robot dedicated to laparoscopic surgery, the clinical development of a treatment for liver metastases and the pre-clinical validation of three projects concerning glioblastoma, breast cancer and cell therapy.
25 innovative projects have been selected by CLARA. Each one brings together researchers, clinicians and young innovative companies in Rhône-Alpes Auvergne, in all fields of oncology.
With a total budget now reaching €32M, the system is continuing to develop. In 2010, four new high-potential projects were added to the portfolio of the Cancéropôle CLARA: a robot for treating tumors, antibodies with diagnostic and/or anti-tumor functions, and nano-encapsulated bimodal imaging agents.These projects present important clinical perspectives, one of which has an international dimension.
In 2010, to help follow up and support the maturation of emerging projects, the Cancéropôle CLARA created CATIC, the Committee for Aiding Industrial and Clinical Transfer.

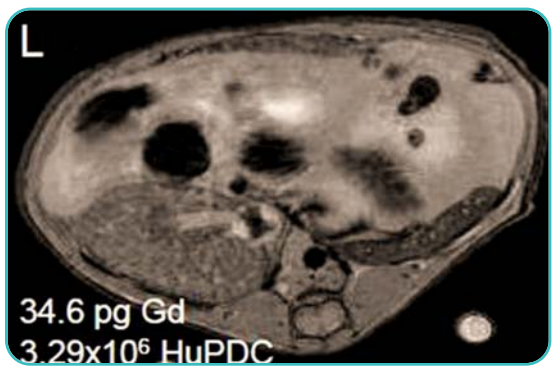
Objectives

- To enable patients to benefit as quickly as possible from cancer research results
- To support researchers and young and innovative biotechnology companies in their transfer process
- To provide oncology expertise in support of economic development of the Rhône-Alpes Auvergne regions

2010... "Proof of Concept": a program firmly established in the biotechnology sector

Figures

Portfolio:	• 25 projects • 9 completed projects • 6 successful proofs of concept
Results:	• New "success story" Nanoparticles for cell monitoring • 4 new projects (€9M)
Partners:	• 18 industrial partners including 6 creations of start-ups (€22M) • 36 academic teams and 4 clinical centers • 11 territorial communities + ERDF (€10M)
Budget:	**€32M**



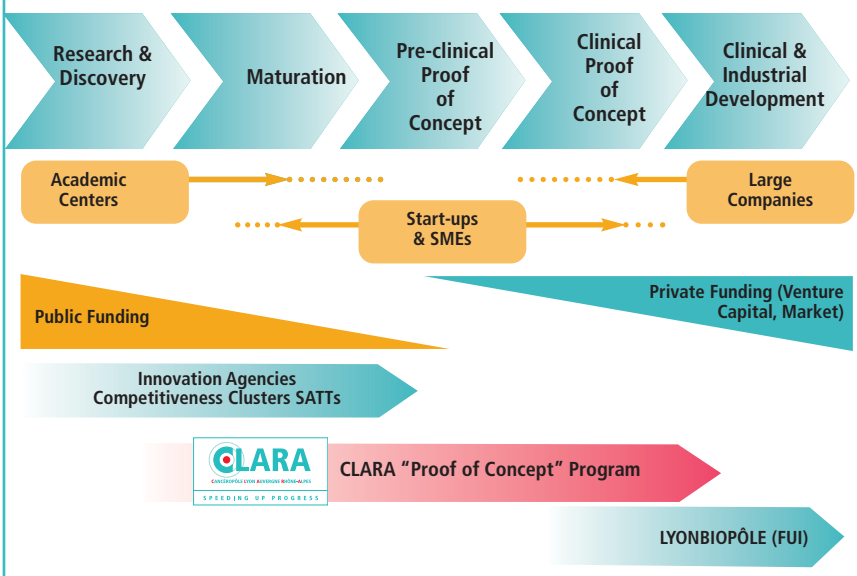
Visualisation by MRI of cellular marking

"Proof of Concept", a system that attracts followers

• In French-speaking Switzerland: to open up the "Proof of Concept" program to the potential synergies represented by this country –which is particularly dynamic in the life sciences field– this is CLARA's aim in joining forces, since 2009, with its neighbor across the border. With the help of its network of experts and its program, CLARA is actively establishing links with French-speaking Switzerland with a view to developing specific collaborative projects. One initiative has already been taken: the opening of CLARA's 2011 "Proof of Concept" projects to bids from across the border, thanks to a partnership with Éclosion.

• Throughout France with the MATWIN program – "Maturation and Accelerated Translation with Industry", created by the Cancéropôle Grand Sud-Ouest and its Industrial Committee (cf. Strategic Point: the future of the "Proof of Concept").

Proof of Concept: a key step in development



With the benefit of five years' standing, the CLARA Proof of Concept (PoC) program remains highly relevant and complements the various players in the development of innovation.

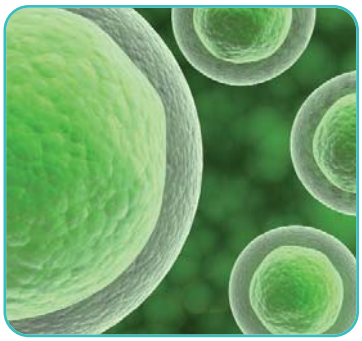
Relevant: Proof of Concept is still a poorly funded step and critical in attracting and involving private partners (companies and risk capital) necessary for industrial and clinical transfer.

Complementary: CLARA PoC is aimed at intermediate-sized projects, with an average budget of €1M, which combine a start-up or SME with academic and clinical teams. The system typically lies downstream of the intervention of academic transfer grants (including future SATTs) and upstream of collaborative research and industrial innovation programs (such as those of ANR, FUI or ISI).

FUI Single Inter-ministry Funds; **SATT** Technological Transfer Accelaration Companies

Economic development, more than a promise

The "Proof of Concept" program represents a total budget of €32M since 2005. It is funded by industrial partners, local authorities and the ERDF European fund. In this context, CLARA supports 18 innovative companies with direct repercussions on economic activity: six start-ups were created and 14 companies thus passed a significant milestone in their development. Among CLARA's industrial partners, three companies have joined the stock exchange or have been acquired and six of these have raised over €50M in funds. Particularly attractive for French industrial partners, the "Proof of Concept" program is also attractive beyond national boundaries. Thus the Japanese company OncoTherapy Science Inc. has set up its first subsidiary in Rhône-Alpes with a view to conducting clinical trials supported by CLARA (cf. p. 13). These results as a whole confirm the Cancéropôle's role as a major player in the inter-regional business environment of the oncology sector.



Economic impact of the Proof of Concept program

- **Six successful proofs of concept** (see appendix 3 for more information)
  - One marketed in Europe and USA: the ViKY surgical mini-robot
  - One clinical development: focalized ultrasound technique (liver metastases)
  - One pre-clinical development: TLR3 agonists (lung cancer)
  - Two nanoparticles (pre-clinical): a photosensitive nanoparticle (glioblastoma) and a hybrid nanoprobe (imaging in cell therapy)
  - One miniature tool for ganglion sampling of proteins and cells (pre-clinical)

- **18 industrial partners**
  - €22M invested (with €10M added by local authorities and EDRF)
  - 14 companies have passed a significant stage in their development
  - Creation of five start-ups: IDD Biotech, Fluoptics, Ecrin Therapeutics, Netris Pharma, Synthelis
  - Establishment of one international company: OncoTherapy Science (Japan)
  - €50M of funds raised: EDAP, Endocontrol, ERYtech, Fluoptics, ImmunID, Nanobiotix
  - One IPO (Innate Pharma) and two purchases (Génome Express, OPi)

A new success story: nanoparticles for monitoring anti-cancer cell therapies by medical imaging

For the first time, the efficacy of monitoring human cells of the immune system by nanoparticles based on gadolinium, a widely used atom in MRI, has been demonstrated *in vivo* in humanized mice. Cell monitoring is based on a simple method applicable in routine clinical practice and counts as an anti-tumor vaccination project in the cancer field. By making it possible to monitor cells by imaging (MRI) until their destruction, this advance breathes new life into the progress of cell therapy –using human cells for therapeutic purposes so far has not resulted in the expected efficacy. This project, called "Nanosondes Hybrides pour une imagerie multimodale du suivi cellulaire en cancérologie" brings together CLARA researchers from several disciplines and an industrial partner, Nano-H, which has a foothold on the cell monitoring market. The next stage of the project is to continue developments in humans with the collaboration of INSERM U851 (F. BÉRARD). Project manager: C. BILLOTEY

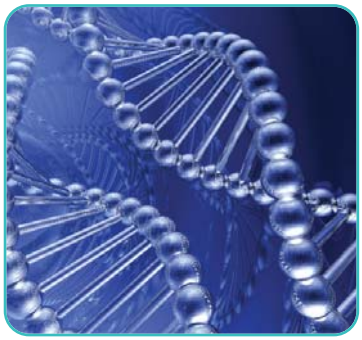
Strategy: the future of the "Proof of Concept" program

• **Developing synergies with the main regional partners** (scientific foundations, research support bodies, business incubators, clusters, development agencies...) is one of the main priorities of the Cancéropôle CLARA. It is complementary to the future Technology Transfer Acceleration Companies (SATTs) which will soon incorporate regional technology transfer and incubation resources of university establishments into the "Investments for the future Plan". There are two advantages to the complementary relationship between CLARA and the various SATTs:

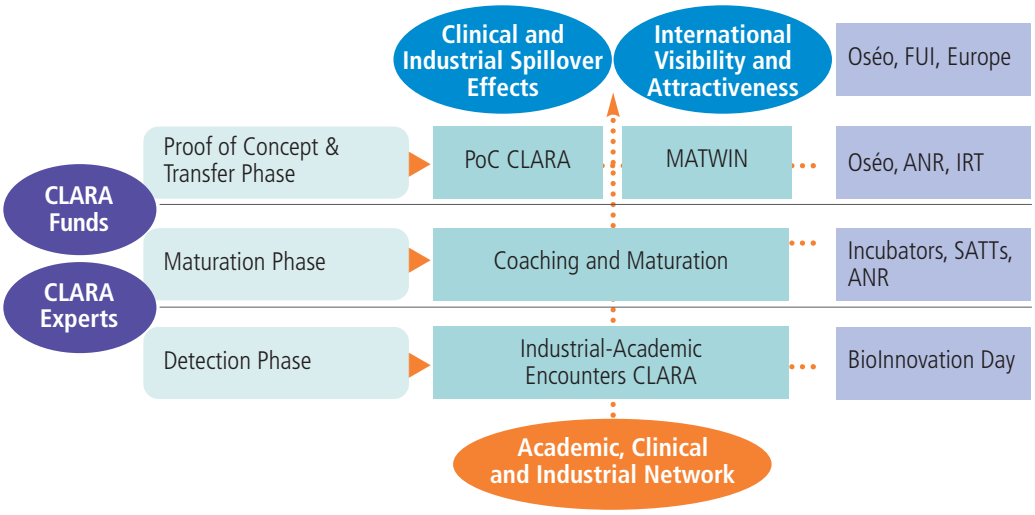
- dynamic boost to partnerships, especially by means of events such as Industrial/Academic Encounters
- global management of promising projects, with the support bodies dealing with the aspects concerning intellectual property and the first stages of scientific validation, and CLARA providing its expertise and network of partners in the oncology field, in particular for clinical and industrial matters. At the end of this maturation stage (for which a specific CLARA program is currently being created), the "Proof of Concept" program monitors the industrial-academic collaborations and the industrial and clinical transfer (Cf. diagram below).

• In 2009, the Cancéropôle Grand Sud-Ouest and its Industrial Committee, made up of the main pharmaceutical international players in oncology, created the MATWIN program "Maturation and Accelerated Translation with Industry". Its aim is to support academic projects at their proof of concept stage, by providing them with "preferential access" to the large industrial partners associated with the Cancéropôle Grand Sud-Ouest with funding of €3M to €5M for a period of three to four years.

CLARA will operate MATWIN in the Auvergne Rhône-Alpes inter-region starting in 2011.



Future Strategy of the " Proof of Concept " program (PoC)



ANR: French Agency for Research; **FUI:** Single Inter-Ministry Funds; **IRT:** Technological Research Institute; **Oséo:** French Innovation Agency
SATTs: Technological Transfer Accelaration Companies

International Influence

The achievements of 2010 reflect, in a threefold manner, the activities undertaken by the Cancéropôle CLARA since its foundation: firstly, the quest for credibility from recognized partners in cancer research; secondly, increasing visibility both on the European and international levels; and finally attractiveness, in particular *via* its program for the economic development of research (Proof of Concept).

Credibility

International Cancer Genome Consortium, (ICGC): participation in breast cancer research

Thanks to a solid partnership with the Synergy Lyon Cancer Foundation and the creation of the Center for BioInformatics, the CLARA Tumor Escape program is represented at the International Cancer Genome Consortium (ICGC), with Professor Gilles THOMAS leading the French contribution in relation to breast cancer. The goal of the ICGC program is to produce high quality data focused on the genomic study of 50 cancers. France is in charge of the studies related to breast cancer and to alcoholism-induced liver cancer.

Professor Zur HAUSEN, recipient of the Nobel Prize for Medicine in 2008, inaugurated the CLARA 2010 Scientific Forum

This year, the 5th Scientific Forum of the Cancéropôle CLARA had the great honor of welcoming Professor Zur HAUSEN, who received the Nobel Prize for Medicine in 2008 for his discovery of the link between human papilloma virus and cervical cancer. Professor Zur HAUSEN said that he was delighted to accept the CLARA invitation "on behalf of all his connections with French research teams, which are for the most part integrated in the CLARA Infections and Cancer program".

Development of collaboration with China

Following Health Week (June 2-6, 2010), organized at the Rhône-Alpes Pavilion during the 2010 World Expo, cooperation is developing between the Rhône-Alpes Region and Shanghai, and has already resulted in a project for a meeting of oncology experts. This symposium, organized in July 2011, will be coordinated by the Cancéropôle CLARA. The city of Shanghai, *via* its Science and Technology Committee, also plans to integrate cancer themes in a call for proposals specific to the "twinned cities".

Visibility

Emblematic projects: far-reaching accomplishments

The European Lymphoma Institute (ELI): thanks to the support of CLARA, which supplied critical funding amounting to €450,000, the European Lymphoma Institute was founded in June 2010. The institute is a part of the CLARA strategy for the creation of a critical mass of clinical and academic competences in view of promoting the efficient transfer of research and contributing to international visibility. ELI brings together the best European specialists in lymphoma, a heterogeneous and rapidly developing cancer for a better understanding which could significantly increase the life expectancy of patients. The creation of the European Lymphoma Institute was based on the efficacy of the clinical research transfer model, developed in Lyon by the partners involved in GELA (Working Group for Adult Lymphoma) and GELARC (GELA-clinical research) whose work has achieved worldwide recognition.

And... Creation of Lyon Cancer Research Center (CCRL) and the World Sarcoma Network (WSN)

Objectives

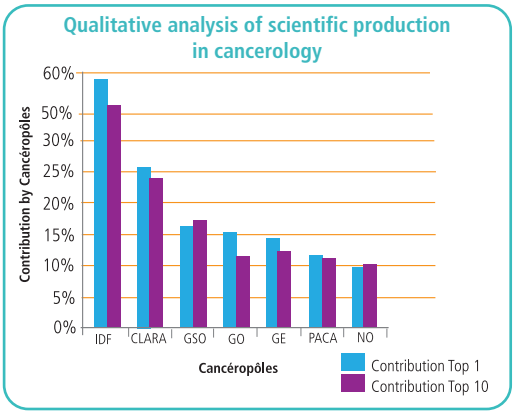
- To increase international visibility and to develop the appeal of the inter-regional research program.
- To subscribe to the Cancer Plan II objectives which encourage Cancéropôles to increase their visibility and extend their collaborations beyond national borders.

An international podium for Nanomedicine research

In January 2010, the Cancéropôles CLARA and GSO (Grand Sud-Ouest) organized an international colloquium on the clinical applications of nanotechnologies in cancer, in collaboration with the Institute for Bioengineering of Catalonia (IBEC-Spain), in Montpellier. The purpose of the colloquium was to increase the visibility of work conducted within the research groups of the three regions, and to strengthen synergies among researchers and physicians involved in highly innovative approaches in the Grenoble-Lyon/Toulouse-Montpellier-Bordeaux/Barcelona regions. Translation to clinical applications, proof of concept and ethical and regulatory aspects were the central themes.

Scientific Publications: volume and high impact

For the purpose of evaluating the visibility of research produced by the Cancéropôle teams, the INSERM department of program evaluation and monitoring, in coordination with INCa, analyzed their output of scientific literature from 2005 to 2009. This independent study served to supply bibliometric reference indicators in the domain of cancerology. It clearly demonstrated that over this period **both CLARA's international visibility and that of inter-regional research in general increased dramatically, both in quantitative and qualitative terms**. On a quantitative level, the number of published articles associating CLARA teams rose from 896 in 2005 to 1202 in 2009, thus recording the greatest increase. Close to one quarter of the Cancéropôle scientific production is generated by CLARA, which also presents the best citation index (12.4). On a qualitative level, CLARA teams contribute almost a quarter (23%) of high level national scientific production in oncology (IF>20).



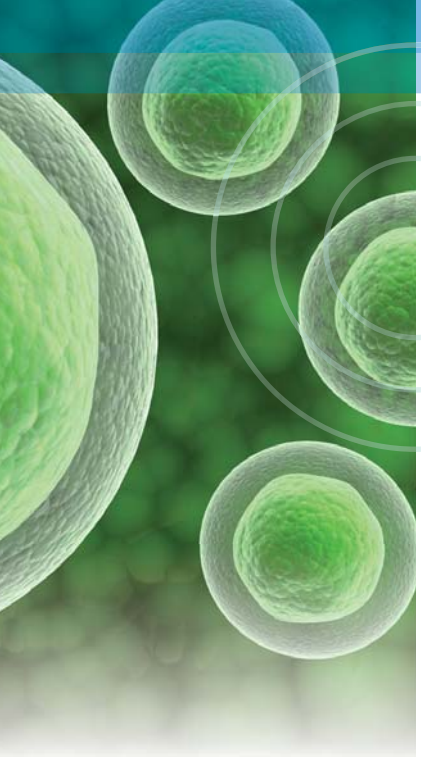
Attractiveness

"Proof of Concept", a strategy with appeal beyond France

The Japanese company OncoTherapy Science Inc. established its first branch in Rhône-Alpes in the view of performing a phase one clinical trial with patients diagnosed with synovialosarcoma resistant to doxorubicin. These clinical tests follow up on the discovery by Tokyo University researchers of the frizzled homolog 10 gene (FZD10), as a new target antigen specifically over-expressed in synovialosarcomas. With the perspective of developing a new immunotherapeutic approach, OncoTherapy Science Inc. successfully synthesized a chimeric antibody for the FZD10 gene. A pre-clinical study in which the team used an anti-FZD10 antibody associated with Yttrium-90 (90Y) resulted inefficient anti-tumor activity for this labeled antibody. Based on the these pre-clinical results, and within the context of the "Proof of Concept" program, CLARA is supporting the clinical phase of the Japanese OncoTherapy Science Inc. project, conducted in collaboration with the Léon Bérard Cancer Center.

Extension of the "Proof of concept" strategy in Switzerland

See page 9



Scientific Emulation

In 2010, CLARA organized 12 events, five of which were in collaboration with other Cancéropôles (Ile-de-France, Grand-Est, Grand Sud-Ouest or PACA). CLARA is striving to promote exchanges with national and international cancerology partners, for the purpose of scientific emulation. Thus, 27 events of increasing scale were organized during the "ProCan 2007-2010" period. *See the table below.*

Development of CLARA scientific leadership over time

	2007	2008	2009	2010
Scientific Forums	●	●	●	●
Industrial-Academic Encounters		●	●	●
Nanotechnologies, Imaging and Cancer				●●
Infections and Cancer			●	●●
Nutrition, Metabolism and Cancer		●	●	●
Epidemiology, Human and Social Sciences, Patient Information and Organization of Care		●	●●	●●
Therapeutic Targeting, Modelling and Clinical Research			●	
Tumor Escape	●		●●	●●●

● Event organized by CLARA ● Event co-organized with another Cancéropôle

Objectives

- To bring together research teams to promote shared knowledge, creativity and interdisciplinary activity, each a source of diagnostic and therapeutic progress.
- To reward and support innovative initiatives.

Scientific Forum and Industrial Academic Encounters: Two seminal events for CLARA

Scientific Forum - March 30 & 31, 2010

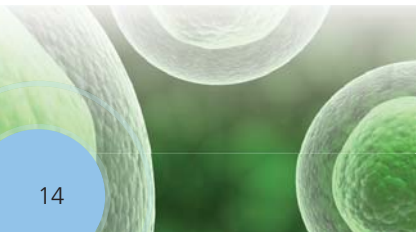
The CLARA 5th Scientific Forum brought together 475 academic researchers, clinicians and industry leaders to share the latest advances in cancerology. Highlights of the event included the attendance of Professor Zur HAUSEN, recipient of the Nobel Prize for Medicine in 2008, who presented an overview of and prospects for viro-induced cancer, a research topic in which CLARA is heavily committed. The Cancéropôle also welcomed international speakers and featured the work of young researchers as well as research transfer. An overview of the work carried out in 2009 was presented, highlighting the results of the national calls for proposals and the organization's know-how in the domain of the industrial promotion of research.

Industrial-Academic Encounters: November 29, 2010

Each year since 2008, with the aim of promoting synergies between academic, clinical and industrial partners in the domain of oncology, CLARA organizes the Industrial-Academic Encounters (RIA) in Lyon. The aim of this event is to promote identification and support for academic potential with a strategy of technology transfer, and also to strengthen the participation of industrial partners from the region. Prior to the event itself, an on-line platform facilitates the organization of strategic one-to-one meetings between participants.

For the first time, the 2010 meeting combined two events that had previously been held separately – CLARA's RIA and the BioInnovation Day organized by Lyon Science Transfer (LST), the transfer division of Lyon University. Called "November 29, 2010", the day was dedicated to cancer as a major pathology and more broadly to all biotechnology professionals working in the field of Life Sciences. The event was a great success, attracting 250 participants and offering the opportunity to present a selection of 20 projects as well as to identify potential collaborations.

Institutional partners: CREALYS, GRAVIT, GRAIN, Auvergne Valo, BUSI, Lyon Science Transfert (co-organizer).



CLARA 2010 symposia

January 17-19	Christophe Mérieux Conference: New Trends in Tumor Virology (Les Pensières, Annecy)
January 28-29	Cancéropôles CLARA and Grand Sud-Ouest/Institute for Bioengineering of Catalonia – IBEC (Montpellier) : Clinical Applications of Nanotechnologies in cancerology,
April 29-30	CLARA and Grand Est Inter-Cancéropôle Seminar: Cancer, metabolism and nutrition (Dijon)
June 2-6	Emerging Oncogenic Viruses (Puglia, Italy)
June 25-26	PACA and CLARA Inter-Cancéropôle Symposium LKB1-AMPK : Cancer Cell Signaling meeting (Marseille)
September 30 - October 1st	Inter-Cancéropôles Grand Sud-Ouest and CLARA workshop: First European Mouse Pathology meeting (Bordeaux)
October 7-8	Is it Possible to Actively Target Particles of 2 to 100 nm? (Grenoble)
November 17	CLARA Day on Operations Research in Cancer Treatment & Operation Management (Paris)
November 26-27	CLARA and Ile-de-France inter-Cancéropôles Symposium: Cancer and Access to Therapeutic Innovations (Paris)

More information on www.canceropole-clara.com

CLARA 2010 Awards

CLARA 2010 Young Researcher Awards

During the 5th CLARA Scientific Forum, the work of three researchers was rewarded within the context of the Poster Prize, with awards of €1 000 each:

- Sandra E. GHAYAD - Involvement of p53 in the IRES-dependent translational initiation and translational fidelity control *via* rRNA methylation - CNRS UMR 5534 – Centre Léon Bérard, Lyon
- Emilie VIENNOIS - Physiology and pathology of the prostate: Androgen receptor and liver-Xreceptor interactions - GReD CNRS UMR 6247 - INSERM U931, Université de Clermont-Ferrand
- Julie HAESEBAERT - Acceptability of HPV vaccination among women of Rhône-Alpes. HPV-FEM study – REMPAR project - Université Lyon 1, CNRS UMR 5558 - Centre Léon Bérard, Lyon

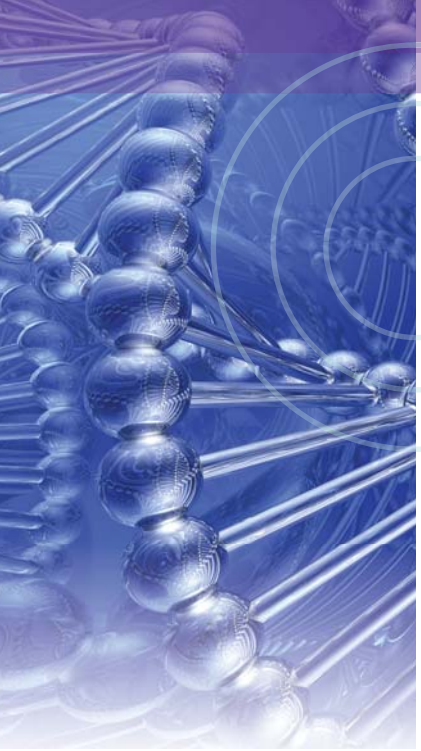
First Christiane Bernardin Award for cancer research: rewarding efforts made towards improving patient care

On June 18, 2010, the INSERM Research Unit 1032 was awarded the Christiane Bernardin Prize. It was awarded by the Rhône County, with the support of the Cancéropôle CLARA, consulted in the capacity of scientific expert. The prize is intended to encourage cancer research teams, and in particular their efforts to translate laboratory knowledge into patient care results. The prize is a grant of €45,000. The first award of this prize went to a new treatment for liver metastases using high intensity focused ultrasound (HIFU), for which the French health products safety agency has authorized the development in patients. This authorization paves the way for this groundbreaking application of focused ultrasound during surgery to destroy hepatic metastases, as a complementary treatment to the surgery itself.

CLARA 2010 Trophies: two researchers rewarded for their efforts

During "November 29 2010", the Cancéropôle awarded two prizes to projects with a high potential for applications beyond the laboratory:

- Marie Alexandra ALBARET's THERA8 project, with its approach of designing molecules capable of slowing the development of aggressive forms of colorectal cancer with the aim of increasing patient survival rates. Lyon Cancer Research Center (CRCL) - Nuclear and Pathology Domains Group (Jean-Jacques DIAZ).
- Philippe MERLE's project regarding the development of a synthesized peptide for the inhibition of the Frizzled-7 receptor in the treatment of primitive liver cancer - INSERM U871, Lyon Cancer Research Center (CRCL). Hepatocarcinogenesis and viral infections group (P. MERLE / I. CHEMIN)



The Future: 2011-2014 CLARA Strategies

Based on the objectives and priorities of Cancer Plan II, as well as local authority plans, CLARA has developed a strategy for 2011-2014 which aims to increase the performance of transfer research, which has formed a central pillar of the Cancéropôle since its inception, while simultaneously promoting economic development plans in the Auvergne Rhône-Alpes regions.

Three pillars of scientific axes

CLARA plans to focus efforts on three main scientific axes, for which an important critical mass has already been mobilized in order to promote international recognition. Distinguished by their specificity and their real added value in the national context, these axes pertain to the following disciplines:

- **Tumor Escape, Cell Plasticity and Targeted Therapy**
- **Infections and Cancer**
- **Nanotechnologies, Imaging and Cancer**

In these three domains, CLARA will continue to promote **scientific excellence** in addition to a particularly active partnership process. Within this perspective, and in **a service-oriented strategy, CLARA intends to facilitate access by its partners to all of the skills and know-how present within its vast network of experts**. The Cancéropôle strategy thus translates its objective to strengthen existing partnerships with local players and to develop new collaborations. This partnership process is also designed to promote synergies among the various priority fields, among the different Cancéropôles, and beyond national borders, to allow CLARA to develop a European dimension, in line with **Measure 5 of Cancer Plan II**. From this point of view, CLARA presents real advantages, in particular with the Lyon Cancer Research Center (CRCL), the European Lymphoma Institute and the World Sarcoma Network, recently created in Lyon and capable of promoting their international influence.

Cross-disciplinary actions to promote the transfer of research to the healthcare system

Since 2005, CLARA's **"Proof of Concept"** program has been designed to identify and to support projects with a potential for economic development. The Cancéropôle will accord particular attention to this program, to pursue research and innovation with the aim of swift transfer of research results to patients, and to fulfil the requirements of **Measure 1, action 1.5 of Cancer Plan II**.

Competition within the field of research transfer also depends on the relevance of the tools available to researchers. Thus, CLARA will also pursue **the development of biological resources and platforms** which play a major role in shortening critical phases of development.

Finally, CLARA will ensure **promotion and development of clinical research** in line with **Measure 4 of Cancer Plan II**. This support may, for example, take the form of the Auvergne Rhône-Alpes Platform for Assistance to Clinical Research in Cancerology (PARCC-ARA), a unique outcome and a real operational aid for clinical research in cancerology. This objective reflects CLARA's desire to revitalize the Program for Hospital Clinical Cancer Research (PHRC).

CANCER PLAN II 2009-2013 (Excerpt)

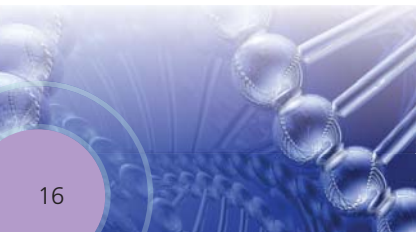
Measure 1.5
Strengthen the interaction between technology transfer offices and economic stakeholders to monitor and support projects with the potential for economic development

Measure 2
Understand through research and reduce inequalities in relation to cancer

Measure 3
Charaterize environmental and behavioural risks

Measure 4
Stimulate clinical research

Measure 5
Make France a reference country

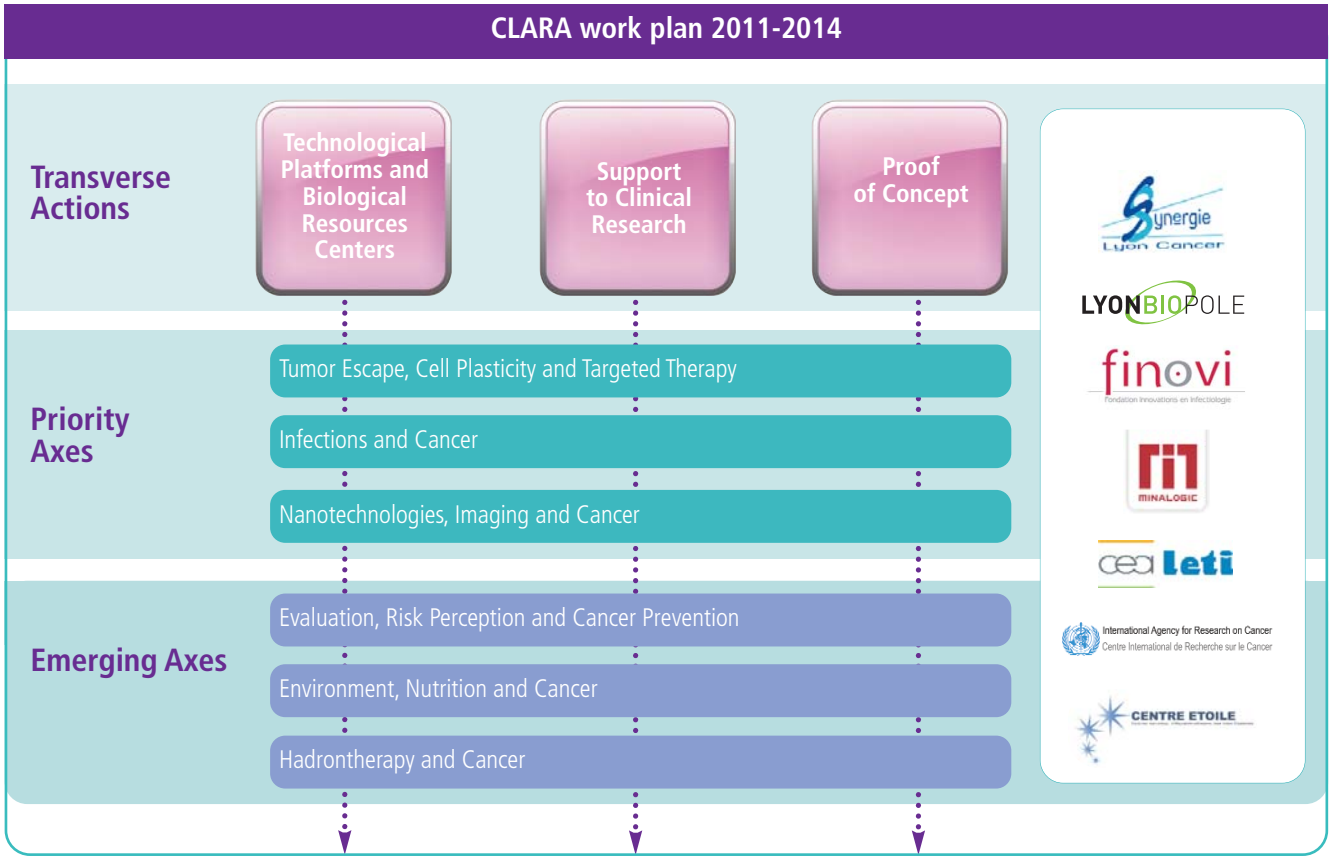


Three emerging scientific axes

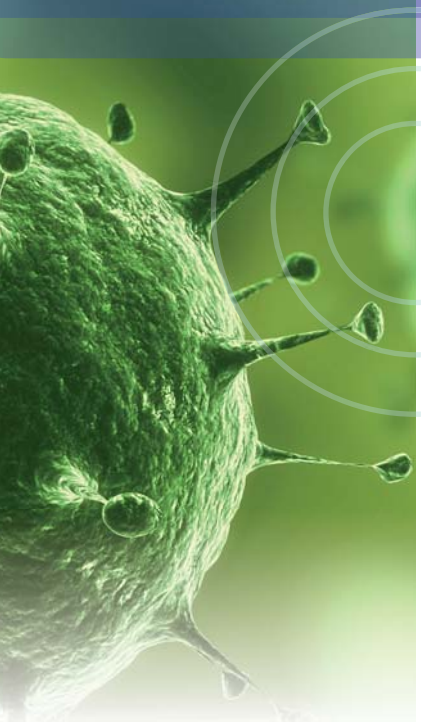
CLARA will also develop two emerging priorities designed to respond to **Measures 2 and 3 of Cancer Plan II** :

- The **Evaluation, Risk Perception and Cancer Prevention** axis, which will be dedicated to prevention and therapeutic care. It will rely on resources from the Hygee Center, a regional platform for prevention, information and cancer-related education.
- The **Environment, Nutrition and Cancer** axis, which will cover environmental and behavioral hazards with the critical support of the International Agency for Research on Cancer (AIRC), a WHO agency.

Finally, CLARA adopted the principle of emergence for a third emerging axis, **Hadrontherapy and Cancer**, for the purpose of promoting connections between hadrontherapy researchers and new research teams.



The CLARA 2011-2014 strategy will participate essentially in the financing of structuring projects, the development of young researchers' mobility and the creation of a Chair of Translational Research in Oncology. Thanks to the diversity of its funding sources, CLARA's strategy of economic development and international promotion of research will be able to rely on support from local authorities, European funds and its industrial partners.



Financial Overview 2010

CLARA thanks all of its partners for their loyalty, INCa, territorial authorities, the ERDF (European Regional Development Fund) and its industrial partners, who, despite a difficult budget context in 2010, were able to maintain and to undertake further financial commitments.
2011 will be a crucial year for CLARA, which will be discussing renewal of funding with local authorities and INCa.

€12.9M in new commitments for CLARA in 2010:

- €1.3M invested by local authorities within the context of the Saint-Étienne Hygée platform
- €10.2M allocated by INCa within the context of a call for research projects
- €1.4M contributed by local authorities for the benefit of the "Proof of Concept" program (€0.6M), CLARA scientific events (€0.4M) and projects with an international scope (€0.4M),

to which can be added €6.8M committed by industrial partners within the framework of "Proof of Concept" projects selected in 2010

€14.9M were mandated during 2010 (on all commitments made since CLARA's foundation):

- €2.3M disbursed by local authorities for the platforms, €1 M of which were for those of Lyon and Grenoble which are in the process of being finalized and €1.3M for the Hygée Center in Saint-Etienne (with a delivery scheduled for 2012)
- €9.2M disbursed by INCa for calls for research proposals (€8.2M) and for the ProCan CLARA 2008-2010 program (€1M)
- €3.4M disbursed by local authorities (Framework agreement 2009-2011) and the ERDF (Proof of Concept program 2009) for "Proof of Concept" projects (€1.5M), CLARA Scientific Events (€1.5M) and projects with an international scope (€400K)

In sum, **funding raised by CLARA, since 2003, amounts to €147.6M** (excluding European Projects):

- €58M from the 14 local authority partners of Rhône-Alpes Auvergne, within the framework of the seven CLARA platforms (close €41M), CLARA Proof of Concept projects (€7.6M), and from the Network and programs with an international scope (€9.3M), in particular the European Lymphoma Institute and the World Sarcoma Network
- Almost €64M from the French State, primarily within the context of support for INCa research projects (€49 M), platforms (€9.6M), as well as Scientific events and the ProCan program (€5.1M)
- €3.6M from the ERDF, spread between platforms (€1.7M) and Proof of Concept projects (€1.9M)
- €22M from the 18 industrial partners involved in the "Proof of Concept" projects

It should be noted that the three local authorities in Isère changed their mode of funding for the "Proof of Concept" program as of 2010 in view of benefiting from the leveraging effect of the ERDF.

Overview of CLARA's 2003-2010 multiyear plan

Breakdown of key funding by program and by source

Program		TOTAL (in €K)		
		Approved 2010	Paid 2010	Overall total approved 2003-2010
Platforms	Lyon Civil Hospitals (HCL)	0	750	8 500
	Léon Bérard Cancer Center (CLB)	0	0	7 500
	Grenoble platform	0	243	4 484
	Saint-Étienne Hygée Center*	1 250	1 307	6 476
	IARC platform	0	0	1 100
	Auvergne platform	0	37	4 040
	RMN Haut Champs CNRS	0	0	19 850
	Total platforms	**1 250**	**2 337**	**51 950**
Funding of projects	Calls for Proposals INCa 2003 - 2010	10 267	8 227	49 048
	ProCan scientific Axes (INCa)	0	1 020	2 550
	Proof of Concept projects	643	1 516	8 836
	Biological Resource Center (CRB)	0	0	1 135
	Total	**10 910**	**10 763**	**61 569**
Cordination	Network Management	770	1 859	12 504
	Total	**770**	**1 859**	**12 504**

* €200k still to be deliberated by the CG42

Overall orientation of approved funding during the period 2003-2010

Summary of the multi-year scheduling of the CLARA program, 2003-2010

Status of the main sources of funding on a national level

Liberté • Égalité • Fraternité
RÉPUBLIQUE FRANÇAISE

INSTITUT NATIONAL DU CANCER

Recipient (funding)	2010				TOTAL (in €K)		
	Investment		Operations		TOTAL PAID in 2010	Overall total approved 2003-2010	Overall total paid 2003-2010
	Approved	Paid	Approved	Paid			
RMN Haut Champs - CNRS (MENRT)	-	-	-	-	-	9 000	9 000
Saint-Etienne Hygée Center	150	5	-	-	5	150	5
Call for Projects (INCa) (a)			10 267	3 605	8 227	49 048	39 470
CRB	-	-	-	-	-	1 027	1 027
Network Management	-	-	175	175	569	2 313	2 313
ProCan Scientific Axes (INCa)	-	-	-	-	1 020	2 550	2 550
Total	**150**	**5**	**10 442**	**3 780**	**9 821**	**64 088**	**54 365**

(a) Figures for the Cancer Plan and INCa are estimates, including STIC and PHRC

Amounts approved by the State on a national level 2003-2010

Uptated December 31, 2010
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, 2003-2010

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

Recipient (funding)	2010				TOTAL (in €K)		
	Investment		Operations		TOTAL PAID IN 2010	Overall total approved 2003-2010	Overall total paid 2003-2010
	Approved	Paid	Approved	Paid			
Proof of Concept	-	-	-	-	-	1 076	215
Network Management	-	-	-	-	-	700	140
TOTAL	-	-	-	-	-	1 776	355

Amounts approved by ERDF Rhône-Alpes 2003-2010

Liberté • Égalité • Fraternité
RÉPUBLIQUE FRANÇAISE

Recipient (funding)	2010				TOTAL (in €K)		
	Investment		Operations		TOTAL PAID IN 2010	Overall total approved 2003-2010	Overall total paid 2003-2010
	Approved	Paid	Approved	Paid			
CRB	-	-	-	-	-	108	108
Proof of Concept (DRRT RA)	-	-	-	-	-	37	37
Network Management	-	-	-	-	-	216	216
TOTAL	-	-	-	-	-	361	361

Amounts deliberated by the Government 2003-2010

Uptated December 31, 2010
As per standard practice and in order to simplify the presentation, fundings are indicated in the year they were approved.

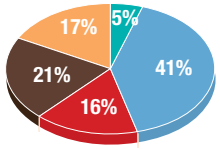
Summary of the multi-year scheduling of the CLARA program, 2003-2010

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

RhôneAlpes Région

Recipient (funding)	2010				TOTAL (in €K)		
	Investment		Operations		TOTAL PAID IN 2010	Overall total approved 2003-2010	Overall total paid 2003-2010
	Approved	Paid	Approved	Paid			
CHU Grenoble	-	-	-	-	97	1 708	1 466
UJF Grenoble	-	-	-	-	146	2 323	1 795
INSERM Grenoble	-	-	-	-	-	453	453
Subtotal Grenoble	-	-	-	-	243	4 484	3 714
CHU Saint-Étienne	-	-	-	-	0	410	225
Saint-Etienne Hygée Center	1 000	-	-	-	672	3 000	672
High Field NMR - CNRS	-	-	-	-	-	8 500	8 500
Proof of Concept	-	-	255	237	547	950	932
Network Management	-	-	315	284	599	3 554	3 103
TOTAL	1 000	-	570	521	2 061	20 898	17 145

Amounts approved by the Rhône-Alpes region 2003-2010

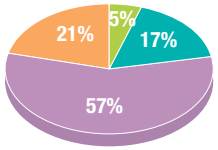


- Grenoble platform: **€4,484K**
- Saint-Etienne platform: **€3,410K**
- RMN Haut Champs: **€8,500K**
- Proof of Concept: **€950 K**
- Network Management: **€3,554K**

RHÔNE
LE DÉPARTEMENT

Recipient (funding)	2010				TOTAL (in €K)		
	Investissement		Operations		TOTAL PAID IN 2010	Overall total approved 2003-2010	Overall total paid 2003-2010
	Approved	Paid	Approved	Paid			
CLB - East Lyon	-	-	-	-	-	7 500	7 500
IARC	-	-	-	-	-	600	600
Proof of Concept	-	-	-	-	441	2 245	1 511
Network Management	-	-	-	-	259	2 706	2 410
TOTAL	-	-	-	-	700	13 051	12 021

Amounts approved by the Rhône County 2003-2010



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

Uptated December 31, 2010
As per standard practice and in order to simplify the presentation, fundings are indicated in the year they were approved.

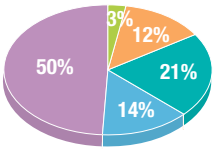
Summary of the multi-year scheduling of the CLARA program, 2003-2010

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

GRANDLYON communauté urbaine

Recipient (funding)	2010				TOTAL (in €K)		
	Investment		Operations		TOTAL PAID IN 2010	Overall total approved 2003-2010	Overall total paid 2003-2010
	Approved	Paid	Approved	Paid			
HCL	-	-	-	-	750	8 500	8 500
CIRC	-	-	-	-	-	500	500
High Field NMR-CNRS	-	-	-	-	-	2 350	2 350
Proof of Concept	-	-	-	-	315	3 585	3 113
Network Management	-	-	-	-	185	2 165	1 844
TOTAL	**-**	**-**	**-**	**-**	**1 250**	**17 100**	**16 307**

Amounts approved by the Greater Lyon 2003-2010

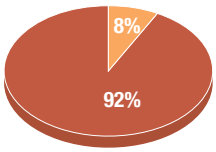


- East Lyon and South Lyon - Lyon Civil Hospitals: **€8,500K**
- International Agency for Research on Cancer: **€500K**
- High Field NMR-CNRS: **€2,350K**
- Proof of Concept: **€3,585K**
- Network Management: **€2,165K**

SAINT-ETIENNE métropole communauté d'agglomération

Recipient (funding)	2010				TOTAL (in €K)		
	Investment		Operations		TOTAL PAID IN 2010	Overall total approved 2003-2010	Overall total paid 2003-2010
	Approved	Paid	Approved	Paid			
Saint-Étienne Hygée Center	-	-	100	100	630	1 916	730
Network Management	-	-	25	25	25	175	175
TOTAL	**-**	**-**	**125**	**125**	**655**	**2 091**	**905**

Amounts approved by Saint-Etienne Métropole 2003-2010



- Saint-Etienne platform: **€1,916K**
- Network Management: **€175K**

Uptated December 31, 2010
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, 2003-2010

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

Recipient (funding)	2010				TOTAL (in €K)		
	Investment		Operations		TOTAL PAID IN 2010	Overall total approved 2003-2010	Overall total paid 2003-2010
	Approved	Paid	Approved	Paid			
Saint-Étienne Hygée Center	-	-	-	-	-	1 000	-
Network Management	-	-	25	25	25	50	50
TOTAL	**-**	**-**	**25**	**25**	**25**	**1 050**	**50**

Amounts approved by the Loire county 2003-2010

Recipient (funding)	2010				TOTAL (in €K)		
	Investment		Operations		TOTAL PAID IN 2010	Overall total approved 2003-2010	Overall total paid 2003-2010
	Approved	Paid	Approved	Paid			
Proof of Concept	-	-	94	28	49	194	79
Network Management	-	-	10	10	10	20	20
TOTAL	**-**	**-**	**104**	**38**	**59**	**214**	**99**

Amounts approved by the City of Grenoble 2003-2010

Uptated December 31, 2010
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, 2003-2010

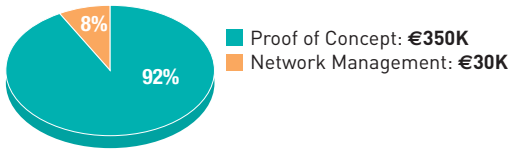
Status of the main sources of funding by the Rhône-Alpes Area

Recipient (funding)	2010				TOTAL (in €K)		
	Investment		Operations		TOTAL PAID IN 2010	Overall total approved 2003-2010	Overall total paid 2003-2010
	Approved	Paid	Approved	Paid			
Proof of Concept	-	-	94	28	49	194	79
Network Management	-	-	15	15	15	30	30
TOTAL	**-**	**-**	**109**	**43**	**64**	**224**	**109**

Amounts approved by Grenoble Alpes Métropole 2003-2010

Recipient (funding)	2010				TOTAL (in €K)		
	Investment		Operations		TOTAL PAID IN 2010	Overall total approved 2003-2010	Overall total paid 2003-2010
	Approved	Paid	Approved	Paid			
Network Management	-	-	15	15	15	30	30
Proof of Concept	-	-	200	-	30	350	30
TOTAL	**-**	**-**	**215**	**15**	**45**	**380**	**60**

Amounts approved by the Isère County 2003-2010



TOTAL RHÔNE-ALPES AREA	**1 000**	**-**	**1 148**	**767**	**5 082**	**57 145**	**47 413**

Uptated December 31, 2010
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, 2003-2010

Status of the main sources of funding by the Auvergne Area

UNION EUROPÉENNE en AUVERGNE

Recipient (funding)	2010				TOTAL (in €K)		
	Investment		Operations		TOTAL PAID IN 2010	Overall total approved 2005-2010	Overall total paid 2005-2010
	Approved	Paid	Approved	Paid			
Auvergne Platform (a)	-	-	-	-	0	1 665	1 665
Proof of Concept	-	-	-	-	41	101	41
TOTAL	**-**	**-**	**-**	**-**	**41**	**1 766**	**1 706**

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

Liberté • Égalité • Fraternité
RÉPUBLIQUE FRANÇAISE

Recipient (funding)	2010				TOTAL (in €K)		
	Investment		Operations		TOTAL PAID IN 2010	Overall total approved 2005-2010	Overall total paid 2005-2010
	Approved	Paid	Approved	Paid			
Auvergne Platform	-	-	-	-	-	505	505
TOTAL	**-**	**-**	**-**	**-**	**-**	**505**	**505**

AUVERGNE la région juste et grande

Recipient (funding)	2010				TOTAL (in €K)		
	Investment		Operations		TOTAL PAID IN 2010	Overall total approved 2005-2010	Overall total paid 2005-2010
	Approved	Paid	Approved	Paid			
Auvergne Platform (a)	-	-	-	-	37	1 355	1 183
Proof of Concept	-	-	-	-	20	50	50
Network Management	-	-	160	80	112	365	285
TOTAL	**-**	**-**	**160**	**80**	**169**	**1 770**	**1 518**

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

Uptated December 31, 2010
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, 2003-2010

Status of the main sources of funding by the Auvergne Area

CONSEIL GENERAL
DU PUY-DE-DOME

Recipient (funding)	2010				TOTAL (in €K)		
	Investment		Operations		TOTAL PAID IN 2010	Overall total approved 2005-2010	Overall total paid 2005-2010
	Approved	Paid	Approved	Paid			
Auvergne Platform	-	-	-	-	-	100	100
Proof of Concept	-	-	-	-	-	10	10
Network Management	-	-	-	-	15	70	55
TOTAL	**-**	**-**	**-**	**-**	**15**	**180**	**165**

CLERMONT
COMMUNAUTÉ

Recipient (funding)	2010				TOTAL (in €K)		
	Investment		Operations		TOTAL PAID IN 2010	Overall total approved 2005-2010	Overall total paid 2005-2010
	Approved	Paid	Approved	Paid			
Auvergne Platform	-	-	-	-	-	285	240
Proof of Concept	-	-	-	-	24	44	24
Network Management	-	-	30	30	30	110	110
TOTAL	**-**	**-**	**30**	**30**	**54**	**439**	**374**

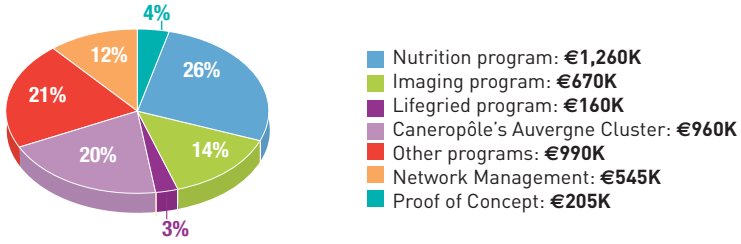
Uptated December 31, 2010
As per standard practice and in order to simplify the presentation, fundings are indicated in the year they were approved.

Summary of the multi-year scheduling of the CLARA program, 2003-2010

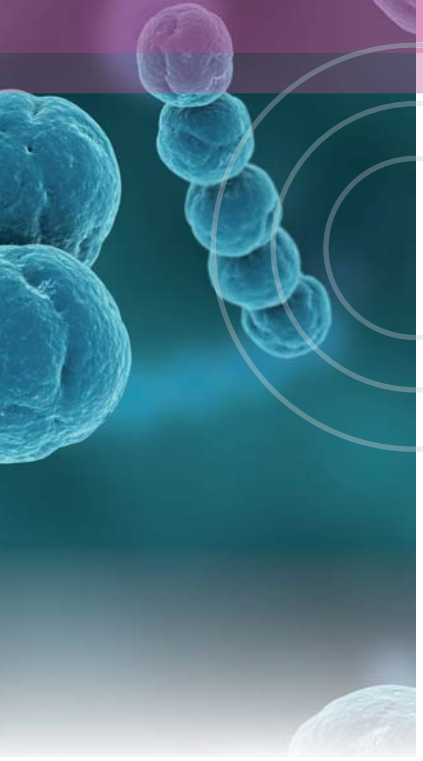
Status of the main sources of funding by the Auvergne Area

Recipient (funding)	2010				TOTAL (in €K)		
	Investment		Operations		TOTAL PAID IN 2010	Overall total approved 2005-2010	Overall total paid 2005-2010
	Approved	Paid	Approved	Paid			
Auvergne Platform	-	-	-	-	-	130	130
TOTAL	-	-	-	-	-	130	130
TOTAL AUVERGNE AREA	-	-	190	110	279	4 790	4 396

Amounts approved in the Auvergne Area 2003-2010



Uptated December 31, 2010
As per standard practice and in order to simplify the presentation, fundings are indicated in the year they were approved.



Appendix 1

CLARA projects launched in 2010 within the context of ProCan

Axis I Nanotechnologies, Imaging and Cancer

• Impact Sociétal et Nouvelles Technologies - Project initiators: M. CHARAVEL (LIPCSS, Université Pierre Mendès France, Grenoble 2) / F. BERGER (GIN, UJF, INSERM 836, CHU Grenoble) - Partners: M. MOUSSEAU (CHU Grenoble) ; D. ASSOULINE (Institut Privé de Cancérologie, Grenoble) ; M. GANDIT (LIPC2S, Université Pierre Mendès France, Grenoble 2) ; M. JANIER (Hôpital Édouard HERRIOT, Lyon) ; P. MATHEVET, P. CHABERT, C. RANNOU-HAVERLANT (Hôpital Femme Mère Enfant, CHU de Lyon) ; H. MIGNOTTE, S. CIMARELLI (Centre Léon Bérard, Lyon)

• Imagerie optique pré-clinique et clinique du Cancer - Project initiator: J-L COLL (INSERM U823, Ontogenèse et Oncogenèse Moléculaire, Institut Albert Bonniot, Grenoble) - Partners: J-M. DINTEN (CEA-LETI, Grenoble), J-C. VIAL (GIN/LSP, Grenoble), A. MOREAU GAUDRY (CIC-IT Grenoble)

Axis II Infections and Cancer

• 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, Lyon), M. OZTURK (INSERM-UJF U823 Institut Albert Bonniot, Équipe 12 : Génétique et Épigénétique 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 tumorigenèse et de la progression tumorale, Hôpital Édouard Herriot, Lyon), M. RIVOIRE (INSERM U556 – Applications des ultrasons à la thérapie – Centre Léon Bérard, Lyon).

• Programme fédérateur sur les récepteurs toll like (TLR) et l'immunité innée - Project initiator: M. TOMMASSINO (Centre International de Recherche sur le Cancer, Lyon) - Partners: J. MARVEL (INSERM U851 Immunité, Infection et Vaccination, Équipe : Apoptose et Mémoire Lymphocytaire T CD8, 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)

Axis III Nutrition, Metabolism and Cancer

• Angiogenèse et stress oxydant : impact du microenvironnement tumoral sur les cellules mammaires saines ou néoplasiques - Project initiator: F. CALDEFIE-CHEZET (SVFP, EA 4233 Nutrition, Cancérogenèse et Thérapie Anti-tumorale, Clermont-Ferrand) - Partners: A. ROSSARY (LB2MN, EA 4233, Clermont-Ferrand), F. PENAULT-LLORCA (Laboratoire d'Anatomopathologie, Clermont-Ferrand), O. DAMOUR (UMR 5086 IBCP Banques de Tissus et Cellules, HCL, Lyon), V. SCHINI-KERTH (Laboratoire de Biophotonique et Pharmacologie, CNRS 7213, Strasbourg)

• Rôle des sphingolipides dans la perte musculaire associée au cancer - Project initiator: G. NEMOZ (UMR INSERM 870/INRA 1235, Régulations Métaboliques, Nutrition, Diabètes, Lyon) - Partners: M. BILLAUD (UMR CNRS 5201, Centre Léon Bérard, Lyon), M. BONNEFOY (Service de Gériatrie Hôpital Lyon Sud, Lyon)

• Analyse des profils métaboliques liés au cancer du sein lors du diagnostic et au cours d'un programme nutritionnel concomitant au traitement initial - Project initiator: O. TREDAN (Unité Cancer et Environnement, Centre Léon Bérard, Lyon) - Partners: R. RIMOKH (INSERM U590, Oncogenèse et Progression Tumorale, Centre Léon Bérard, Lyon), S. ARANDA-BERTHOUZE (Centre de Recherche et d'Innovation du Sport, Université Lyon 1, Villeurbanne), I. ROMIEU (Section Nutrition et Métabolisme, NME, Centre International de Recherche sur le Cancer, Lyon), M-P. VASSON (LB2MN, Laboratoire de Biochimie, Biologie Moléculaire et Nutrition, Clermont-Ferrand), F. CLAVEL-CHAPELON (UMR1018, E3N, INSERM, Institut de Cancérologie Gustave Roussy, Villejuif)

• Effet de l'excès et du manque de glucose sur la régulation (épissage et stabilité) des ARN impliqués dans l'apport de nutriments - Project initiator: H. SIMONNET (UMR 5201 CNRS Génétique Moléculaire, Signalisation et Cancer, Centre Léon Bérard, Lyon) - Partners: B. EYMIN (INSERM U823 Bases Moléculaires de la Progression des Cancers du Poumon, Institut Albert Bonniot, Grenoble), C. FERRARO-PEYRET (INSERM U865 Tumeurs Endocrines Digestives, Lyon).

Axis IV Epidemiology, Human and Social Sciences, Patient Information and Organization of Care

- Évaluation de prise en charge de la chimiothérapie en hôpital de jours vs. autres modalités au domicile - Project initiator: T. MONTEIRO (Laboratoire d'Analyse des Signaux et des Processus Industriels, LASPI EA 3059, Roanne) - Partners: E. MARCON (LASPI EA 3059, Roanne), X. XIE / V. AUGUSTO (Centre d'Ingénierie et Santé IFRESIS 143, École Supérieure des Mines, St-Étienne)
- Étude économique de la conformité aux recommandations pour la pratique dans le traitement des sarcomes - Project initiator: L. PERRIER (UMR CNRS 5824 Groupe d'Analyse et de Théorie Économique, GATE, Lyon) - Partners: I. RAY-COQUARD (Évaluation des Pratiques Médicales, Centre Léon Bérard, Lyon), F. CHAUVIN (Institut de Cancérologie de la Loire, St-Étienne), N. CAUTELA (Laboratoire d'Économie de la Firme et des Institutions LEFI, Lyon), A. BUJA (Dipartimento di Medicina Ambientale e Sanità Pubblica, Università di Padova, Italie)
- Déterminants de la prise en charge des patients porteurs d'un cancer broncho-pulmonaire présentant au moins une défaillance d'organe. Cohorte bi-centrique - Project initiator: J-F. TIMSIT (CHU Grenoble, Pôle Médecine Aigüe et Communautaire, Grenoble) - Partners: E. AZOULAY (Service Réanimation, Hôpital St-Louis, Paris)
- Cancers du testicule : Étude des expositions professionnelles et environnementales en Rhône-Alpes - Project initiator: B. FERVERS (Unité Cancer et Environnement, Centre Léon Bérard, Lyon) - Partner: A. FLECHON (Unité Cancer et Environnement, Centre Léon Bérard, Lyon)
- Éducation aux effets biologiques de la chimiothérapie : mise en place et évaluation préliminaire d'un programme d'éducation thérapeutique du patient appliqué à la prise en charge de la chimiothérapie anticancéreuse - Project initiator: D. PEROL (Unité de Biostatistique et d'Évaluation des Thérapeutiques UBET, Centre Léon Bérard, Lyon) - Partner: C. SEBBAN (UBET, Centre Léon Bérard, Lyon)
- Décision médicale collective : le cas des réunions de concertation pluridisciplinaire en cancérologie - Project initiator: J-L. RULLIERE (UMR 5824 Groupe d'Analyse et de Théorie Économique GATE, Lyon) - Partner: Groupe de recherche en Psychologie Sociale - GRePS EA4129- SIS

Axis VI Tumor Escape

- Role of microenvironment in leukemic stem cell emergence and resistance in chronic Myeloid Leukemia - Project initiator: V. MAGUER-SATTA (Oncogenèse et Progression Tumorale, Centre Léon Bérard, Lyon) - Partner: M. BERGER (Hématologie Biologique EA 3846, Université d'Auvergne, Clermont-Ferrand)
- An interactive network between ERRalpha and LSD1 (Lys-Specific-Demethylase)/Nucleophosmin (NPM) in prostate cancers - Project initiator: J-M. VANACKER (Institut de Génomique Fonctionnelle UMR 5242, Lyon) - Partners: J. SAMARUT (Institut de Génomique Fonctionnelle, Lyon), L. MOREL (Génétique Reproduction et Développement, UMR6247 Clermont-Ferrand)

And... Young researchers' mobility

Axis III Nutrition, Metabolism and Cancer

- Acquisition des techniques d'exploration de phénomènes d'angiogenèse en particulier des transcriptions dépendantes de HIF – Support for A. ROSSARY (EA 4233, Clermont-Ferrand)
- Analyse transcriptomique des cellules tumorales mammaires en co-culture 3D avec pré-adipocytes ou adipocytes – Support for V. DUBOIS (EA 4233, Clermont-Ferrand)
- Acquisition des compétences pour l'analyse post-génomique (sur PBMC, en lien avec l'essai clinique INEC) – Support for N. GONCALVES-MENDES (EA 4233, Clermont-Ferrand)

Axis VI Tumor Escape

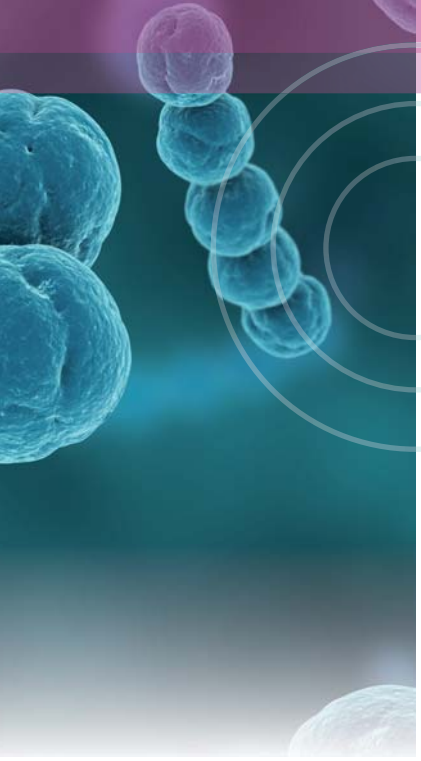
- Caractérisation par des outils microfluidiques, couplés à des analyses biophysiques et d'imagerie, la dynamique de la plasticité de cellules cancéreuses – Support for R. FERRIGNO (Institut des Nanotechnologies de Lyon)
- Acquisition de la technique de bourgeonnement de cellules endothéliales lymphatiques à partir d'anneaux du canal thoracique – Support for N. RICARD (INSERM U878 LAPV, Grenoble)
- Analyse des capacités de réparation mitochondriales au moyen de puces à ADN altéré (brevet CEA) – Support for P. VERNET (UMR CNRS 647 INSERM U931, Clermont-Ferrand)
- Étude du comportement des lymphocytes malins au sein des structures médullaires ou en présence de cellules mésenchymateuses sénescentes, en microscopie en temps réel – Support for M. BERGER (EA 3846, Hématologie Clinique, Clermont-Ferrand)

And... Four Projects supported by the Regulatory Unit of CLARA

The Regulatory Unit supported four projects in 2010, to faciliate pathways between research and development:

- Prediction BioSciences
- Synfrizz
- Nanobactérie
- Theranean

Abstracts of CLARA projects selected in 2010 are available on www.canceropole-clara.com



Appendix 2

CLARA projects selected by INCa in 2010

In 2010, INCa selected 36 CLARA projects through the various calls for proposals that it launched.
This appendix presents the list of winning proposals.

Integrated Research Program for Prostate Cancer ARC-INCa-AntiCancer League (French Ligue Contre le cancer)

- Évaluation de la position, du volume et de l'agressivité des foyers de cancer de prostate par imagerie multi-paramétrique – Coordination : O. ROUVIÈRE (HCL-UCBL – INSERM U556, Lyon) – €485,000

Open Biomedical Research Projects 2010

- Netrin-1 comme nouvelle cible thérapeutique dans le cancer du poumon – Coordination: A. BERNET (UMR 5238, Lyon) – €750,000
- Protéines des bouts + des microtubules, tétraploïdie et cancer – Coordination: A. ANDRIEUX (INSERM U836, Grenoble) – €395,200
- Chimio-résistance et adhérence cellulaire analysées dans un nouveau modèle murin ostéosarcome – Coordination: D. BOUVARD (INSERM U823, Institut Albert Bonniot, Grenoble) - €404,000
- Description et caractérisation de nouveaux gènes suppresseurs de tumeurs mammaires – Coordination: D. BERNARD (UMR 5238, Lyon) – €450,000
- Réponse biologique des tissus sains et tumoraux après radiothérapie par microfaisceau utilisant le rayonnement synchrotron : perspectives thérapeutiques – Coordination: G. LE DUC (Installation Européenne de Rayonnement Synchroton, Grenoble) – €473,000
- Poropeptides chasseurs-tueurs – Coordination: J.L. COLL (INSERM U823, Grenoble) – €500,000
- Interaction entre le TGFβ et la réponse au stress cellulaire dans l'adénocarcinome du pancréas et l'inflammation associée – Coordination: L. BARTHOLIN (INSERM U590, Lyon) – €600,000
- Mécanismes et approches thérapeutiques de la cachexie – Coordination: L. SCHAEFFER (UMR 5239, Lyon) – €550,000
- Ce que la protéine Tax de HTLV-1 peut nous apprendre sur la fonction biologique de NF-kB et son ciblage potentiel par des agents anti-cancéreux – Coordination: R. MAHIEUX (INSERM U758, Lyon) – €446,000
- Implication du gène Men1 dans le contrôle de la prolifération cellulaire normale et tumorale de la thyroïde – Coordination: S. SELMI-RUBY (UMR 664, Lyon) – €120,000
- 5'-Nucléotidase cN-II : une nouvelle cible en chimiothérapie ? – Coordination: C. DUMONTET (INSERM U590, HCL, UCBL1, Lyon) – €250,000
- Mériolines, de nouveaux agents dérivés d'organismes marins, contre les gliomes malins – Coordination: J. HONNORAT (UMR 842, Neurooncologie et neuroinflammation, Lyon) - €550,000

Support for Training in Translational Research in Cancerology for Medical Students and Young Doctors

- Destruction de tumeurs du rein par application extracorporelle d'ultrasons focalisés guidée en temps réel par IRM de thermographie (MRTIgFUS) - Coordination: F. COTTON (CREATIS-LRMN, INSA Lyon) – €34,000
- Potentialisation des chimiothérapies à base de sels de platine par inhibition de la réparation de l'ADN - Coordination: C. DUMONTET (Service Hématologie Biologique, HCL, Lyon) – €35,000
- Influence du bevacizumab sur la régénération hépatique après hépatectomie chez le lapin - Coordination: M. RIVOIRE (Institut de Chirurgie Expérimentale, Centre Léon Bérard, Lyon) – €35,000

Translational Research in Cancerology-DHOS INCa

- Familial dysglobulinemia - Coordination: C. DUMONTET (Hôpital Édouard Herriot HCL, Lyon) - €125,000

Research into Human and Social Sciences, Public Health and Epidemiology

- Étude de faisabilité en régions Rhône-Alpes et Auvergne d'une prise en charge à long terme des enfants survivants d'un cancer pédiatrique (à l'exclusion des leucémies) - Coordination : C. BERGER (Centre Hospitalier Universitaire de St-Etienne) – €440,000
- Pour une observation du cancer au niveau départemental en France : estimation de l'incidence et de la prévalence - Coordination : M. COLONNA (Registre des Cancers de l'Isère, Meylan) – €210,000
- Apport de la TEP/TDM au FDG et de l'IRM de diffusion dans l'évaluation de la réponse tumorale après traitement par radio-chimiothérapie et curiethérapie des cancers du col utérin opérables de stade IB2, IIA, IIB-Acronym: ERRICC - Coordination: F. GOLFIER (Centre Hospitalier Lyon-Sud, Pierre Bénite) – €293,000

• Évaluation, chez des patients nécessitant une chirurgie de résection de métastases hépatiques de cancers colorectaux, de l'utilisation per-opératoire d'ultrasons focalisés de haute intensité (HIFU) : faisabilité, innocuité et capacité de ciblage - Coordination: M. RIVOIRE (Centre Léon Bérard, Lyon) – €145,000

Support for Innovative and Costly Techniques (STIC)

• Ablation de la néoplasie épithéliale glandulaire de haut grade de l'œsophage par le système de radiofréquence halo : étude prospective multicentrique de l'efficacité et de la tolérance par rapport à la chirurgie oesophagienne avec évaluation des impacts médico-économiques – Coordination: T. PONCHON (Hôpital Édouard Herriot, Lyon) – €530,000

• Évaluation médico-économique de l'utilisation du test urinaire PCA3 dans la stratégie diagnostique (du PSA aux biopsies) des cancers de la prostate agressifs - Coordination: V. VLAEMINCK-GUILLEM (Hospices Civils de Lyon) – €490,000

Labeling of Early Phase Cancerology Clinical Trial Centers

• Institution: Centre Léon Bérard, Lyon - Coordination: J-Y. BLAY – €750,000

• Institution: Hospices Civils de Lyon, Lyon - Coordination : B. COIFFIER – €250,000

• Institution: Unité de Recherche du Centre Jean PERRIN, Clermont-Ferrand - Coordination: X. DURANDO – €500,000

Improvement in Quality and Safety at Radiotherapy Centers

• Institution: Centre Jean-Perrin, Clermont-Ferrand - Coordination: M. LAPEYRE – €23,000

• Institution: Groupe Hospitalier Mutualiste, Grenoble - Coordination : D. FRIC – €23,000

• Institution: SCP CHOLLET PASQUIE, Aurillac - Coordination : C. CHOLET – €23,000

Support for associations: Actions for combating inequalities and precariousness: launch of a tender for projects associations

• Réseau d'aide et d'information en faveur des populations défavorisées - Coordination: M-J. MAZA (Comité de la Loire, Ligue contre le Cancer, St-Étienne) - €9,720

• L'Escale LIGUE : un lieu d'accueil de proximité et une dynamique autour de la prise en charge corporelle et de la resocialisation des personnes fragilisées par le cancer en milieu rural et semi rural – Coordination: M. GROBERT (Comité de l'Ardèche, Ligue contre le Cancer, Privas) - €18,000

Support for Actions to improve Prevention, Screening and early Detection of Cancer

• Prise en charge du risque de surpoids ou d'obésité par un programme nutritionnel combinant une activité physique adaptée et une alimentation saine, chez des patientes atteintes d'un premier cancer et traitée par chimiothérapie adjuvante - Coordination: P. BACHMANN (Centre Léon Bérard, Lyon) – €109,000

Study of the Impact of Personalized Methods of Care during and after Cancer

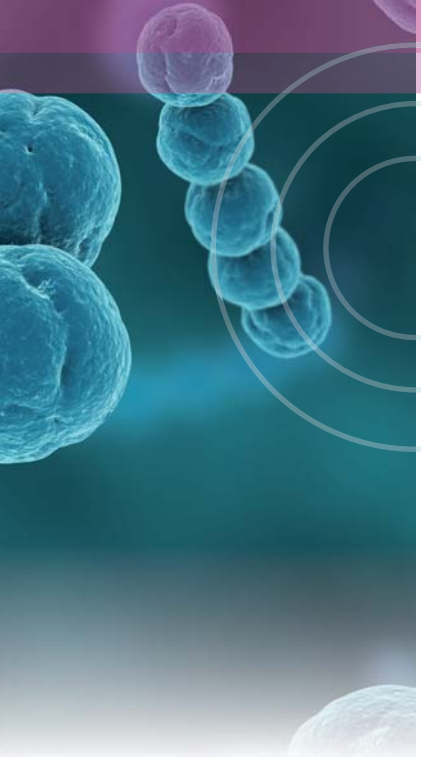
• Projet personnalisé de soins après la première prise en charge - Coordination: Y. DEVAUX (Centre Léon Bérard, Lyon) – €100,000

• Coordination personnalisée médico-sociale ville / hôpital pendant et après le cancer - Coordination: X. DURANDO (Centre Hospitalier Universitaire, Clermont-Ferrand) – €100,000

• Parcours de soins personnalisé à l'Institut Daniel HOLLARD - Coordination: C. GARNIER (Groupe Hospitalier Mutualiste, Grenoble) – €100,000

• Mise en œuvre du parcours personnalisé du patient pendant et après le cancer à la clinique mutualiste de Lyon - Coordination : Y. MATAIX (Clinique Mutualiste Eugène André, Lyon) – €99,750

Summaries of CLARA projects selected in 2010 are available on www.canceropole-clara.com



Appendix 3

Current CLARA "Proof of Concept" projects

2010: 4 new projects for a total budget of €9M

Doc-Calipso: Geo-localisation and robotic focal treatments for tumors

The objective of the Doc-Calipso project is to establish proof of the pre-clinical concept for a new generation of polyvalent surgical robot from a pre-existing robot. This new robot integrates a system of navigation to move automatically on a tumor using a three-dimensional geo-localisation system implanted into the organ to be treated. Particularly suited to treating solid tumors, this new generation of robot has great perspectives both for therapeutics and economics: removal of radiological exposure for treating small tumors and use of highly effective focused treatments.

This project leans on the competencies of partners in the areas of focused treatment of urogenital tumors, surgical engineering (Ablaterm Project), experimental surgery and robotics. The indications targeted by this project are solid parenchymatous tumors: liver, kidney, prostate, pancreas, lung.

Partners: Experimental Surgery Laboratory, UFR, East-Lyon/Lyon Civil Hospitals ADEPT (Haute-Savoie).

Synfrizz: radio-immunotherapy for synovial sarcoma targeting antigen FZD10

Synovialsarcomas (SS) are rare tumors that represent 5-10% of all tissue sarcomas, which represent 2% of all malignant tumors. There is no effective curative treatment and the median survival rate for these tumors is around 12 months from the diagnosis of metastases. Scientists at the University of Tokyo have identified homologue 10 of the Frizzled gene (FZD10) as a new antigen target specifically over-expressed in SS. To provide a new approach for immunotherapy, OncoTherapy Science Inc. (Japan) has successfully synthesized a chimeric antibody for FZD10. A pre-clinical study in which the team has used an anti-FZD10 antibody combined with yttrium-90 (90Y) showed this antibody to have an antitumor effect. On the basis of these preclinical results, the project aims to develop a Phase I clinical study in patients with an SS who are resistant to doxorubicin.

Partners: Léon Bérard Cancer Center; OncoTherapy Science (Japan).

EBV Biotech: diagnosis and immunotherapy for cancers associated with the Epstein-Barr virus (EBV)

Epstein-Barr virus (EBV) is involved in various cancers, such as nasopharyngeal carcinoma (NPC), gastric carcinoma (GC), Burkitt's lymphoma B (BL), Hodgkin's lymphoma (HD), non-Hodgkin's lymphoma (NHD, observed particularly in patients with AIDS), T lymphomas, and primary effusion lymphomas (PEL). Most of these pathologies are a major public health challenge worldwide. Current strategies for diagnosing and treating these cancers are not satisfactory.

The "theranostic" approach for the EBV Biotech project consists in developing a diagnostic tool coupled with effective preventive and curative immunotherapy.

This will specifically destroy tumor cells that are positive for the Epstein-Barr virus. The project first aims to develop an ELISA diagnostic kit predictive for tumor development. It will lead to the creation of EBV Biotech.

Partners: Crealys project incubator, Human Virology and Pathologies Unit CNRS 3011 in association with Lyon 1 University, CH Lyon-Sud (HCL) and Léon Bérard Cancer Center.

Nano-ENO: Agent for nuclear imaging / nanovectorized optics

NanoENO aims to develop a contrast agent applicable to two modalities of molecular imaging: nuclear (with PET or SPECT tracers) and optical. This imaging agent will be based on encapsulation of a fluorophore in patented lipid nanovectors (Lipidots™), whose surface will be functionalized by the presence of a radioisotope emitting positrons or gamma rays. The product developed will be tested on animal models, both healthy and with tumors, to prove the validity of the concept by quantifying the contrast for images of healthy tissue and pathological tissue. The tumors will be targeted using a peptide agent that recognizes receptors (for tumors over-expressing these specific receptors) or passively via "EPR" (enhanced tumor permeability and retention). The clinical justification for this project lies on the combined exploitation of the respective advantages of two types of imaging.

Firstly, nuclear markers deliver images with high resolution; secondly, the optical contrast agent means tumour tissue can be identified in real time by the surgeon. This product will be used for preoperative nuclear imaging to identify and quantify tumours, then for perioperative optical imaging to guide tumour ablation or to analyse biopsies.

Partners: CEA-Leti Grenoble and nuclear medicine department at the Hopital d'Orsay, AAA (Ain), specialised in the use of radiopharmaceuticals and Fluoptics (Isère), a start-up that develops real-time fluorescence imaging systems for cancer surgery.

Six successful proofs of concept thanks to CLARA support

LER, CLARA's first success with a clinical proof of concept
A miniature robot for assisting mini-invasive surgical operations in cancerology was developed by Endocontrol Medical (Grenoble) in collaboration with the CNRS 5525 Research Unit (Joseph Fourier University). It is now marketed in Europe and the USA.

HIFU, the first pre-clinical proof of concept approved by AFFSSAPS pending clinical development
A high-intensity focalized ultrasound (HIFU) technique was developed to treat metastases of the liver derived from colorectal cancer by EDAP TMS (Lyon) in collaboration with INSERM Unit 1032 and Léon Bérard Cancer Center (Lyon).

A pre-clinical proof of concept (TLR-3) is evolving towards a new pre-clinical target indication (CITCAP)
TLR-3 agonists have been developed by Innate Pharma in collaboration with the CNRS 5201 research unit (Centre Léon Bérard). They were first tested for breast cancer (TLR-3 project) and currently as a combined therapy agent for lung cancer.

Three pre-clinical proofs of concept in course of transfer
A photosensitive nanoparticle has been developed and validated in a mouse model of glioblastoma in collaboration between Nanobiotix and INSERM U 842 in Lyon (GLIO pilot project).
Lanthanide-based hybrid nanoprobes have been developed as a contrast agent for non-invasive monitoring of cell therapies (anti-tumor vaccination) using dendritic cells (NSH project) with Nano-H and the nuclear medicine department of Lyon Civil Hospitals.
A miniature tool, ProTool™, for ganglion sampling of proteins and cells (GANGLIOTOOL project). The project was conducted by CEA-Leti in collaboration with several CLARA academic and clinical teams. It is currently continuing with regional and national partners.

Current CLARA "Proof of Concept" projects

Project name	Project title	Academic Coordinator	Industrial Partner
CANCERDRUG	Preclinical validation of a novel Vascular-Disrupting Agent	A. POPOV, GIN, Institut des Neurosciences de Grenoble, CRI INSERM 836, CEA, CHU Grenoble, UJF	Ecrins Therapeutics
CITCAP	Combined therapy including TLR3 targeting in lung squamous cell cancer	S. LEBECQUE, UMR CNRS 5201, Université Claude Bernard Lyon 1, Centre Léon Bérard, Hospices Civils de Lyon	Innate Pharma
CLARAFT	Association of $\alpha\beta 3$ integrins targeting raft-crgd and IR probe for intraoperative detection of tumour margins and metastases in sarcoma	A. Dutour, Unité INSERM 590 Université Claude Bernard Lyon 1, Centre Léon Bérard, Hospices Civils de Lyon	Fluoptics
DOC-CALIPSO	Robot navigation for tumour focal therapy	M. COLOMBEL, HCL, Université Claude-Bernard, Lyon I	ADEPT
EBV Biotech	Diagnosis and Immunotherapy of Epstein-Barr Virus-associated cancers	B. LINA, FRE3011, CNRS, Université Claude Bernard Lyon 1	EBV-Biotech
GR-SIL01	Use of red blood cells to deliver siRNA for treating an inflammatory condition	T. RENNO, UMR CNRS 5201, Université Claude Bernard Lyon 1, Centre Léon Bérard, Hospices Civils de Lyon	ERYtech Pharma
IPROMAH	Industrial proof of concept for new monoclonal antibodies for haematological malignancies	C. DUMONTET, Unité INSERM 590, Université Claude Bernard Lyon 1, Centre Léon Bérard, Hospices Civils de Lyon	iDD-Biotech
LANTHARAD	Hybrid radiosensitizer nanoparticles allowing treatment of radio-resistant tumours	M. JANIER, CREATIS UMR CNRS 5220, INSERM U630, Université Claude Bernard Lyon 1	Nano-H
LIPOBAK	Therapeutic proteoliposomes for glioblastoma treatment	J.-L. LENORMAND, UMR CNRS 5525 " TIMC-IMAG ", Université JF Grenoble	Synthelis
LYMPHOS1	Tracking TCR repertoire distortions to predict lymphopenia and prevent deaths due to infections associated with chemotherapy in patients with breast cancer	C. CAUX, Unité INSERM 590 Université Claude Bernard Lyon 1, Centre Léon Bérard, Hospices Civils de Lyon	ImmunID Technologie
Nanobiop	An innovative strategy for molecular nanobiopsy using magnetic nanoparticles	F. BERGER, GIN, CRI INSERM 836, CHU Grenoble, Université Joseph Fourier	CEA Leti
Nano-ENO	Nano Encapsulated Nuclear / Optical imaging probe	I. TEXIER-NOGUES, CEA-Leti, Grenoble	AAA
Netris-lung	Proof of concept of the efficiency of a candidate drug in the treatment of lung cancer	J.-G. DELCROS, UMR CNRS 5238, Université Claude Bernard, Centre Léon Bérard, Lyon	Netris Pharma
NT3-Target	Inhibition of the NT-3/TrkC interaction and its application to the treatment of metastatic breast cancer	S. TAUSZIG-DELAMASURE, UMR CNRS 5238, Université Claude Bernard, Centre Léon Bérard, Lyon	Netris-Pharma
SYNFRIZZ	Novel antibody therapy against Synovial sarcoma targeting	J.-Y. BLAY, Centre Léon Bérard, UCBL, Lyon	OncoTherapy Science
TRT/PETMEL	Development of new heteroaromatic halogenated radiotracers for PET imaging and targeted radionuclide therapy of melanoma	N. MOINS, INSERM UMR 484 Université d'Auvergne	Laboratoires Cyclopharma

In red: projects initiated in 2010